American Urological Association

AUA NEWS

SEPTEMBER 2020 | THE OFFICIAL NEWSMAGAZINE OF THE AMERICAN UROLOGICAL ASSOCIATION | VOLUME 25 | ISSUE 9

INSIDE THIS ISSUE

Decision Fatigue May Help Explain Low Value Prostate Specific Antigen Testing

Trevor C. Hunt, BA **Brock B. O'Neil, MD**

Salt Lake City, Utah

Decision fatigue refers to a unique aspect of human decision making in which the quality and consistency of choices made decreases as the decision process is repeated.[1] The concept is borrowed from behavioral economics, a field that attempts to adapt rational economic theories to better explain nonrational human behaviors. The first and perhaps best known case of decision fatigue capturing the public eye was in 2011 when a study of courtroom parole cases found a stark decline in decisions in favor of the parolee as time progressed.[2]

Recently, evidence for decision fatigue in common health care behaviors has begun to appear. One such example is a 2019 study that evaluated the relationship of clinic appointment time and physician ordering of indicated breast and colorectal cancer screening.[3] The authors found a significant decline in completion of screening as the day progressed, supporting the notion that decision fatigue plays a role in physician choices in outpatient settings. Studies including other clinical scenarios have reached similar conclusions, and evidence of decision fatigue's influence on health care delivery continues to accrue.

Our team is currently investigating the provision of low value urological care and the wasteful spending and downstream patient harms that ensue. A recent study of our large academic health system found that up to 56% of all prostate specific antigen (PSA) tests ordered in men without prostate cancer could be considered low value based on current guidelines.[4] Given how often PSA tests are ordered by urologists and nonurology clinicians alike, we believe PSA testing represents an actionable target for efforts to reduce the over $200 billion in wasteful health care spending that occurs each year.

Therefore, we hypothesized that decision fatigue plays a role in the current abundance of low value PSA testing performed by outpatient clinicians. In this study we aimed to test this hypothesis by identifying outpatient appointments for men without prostate cancer over a 7-year period and classifying them based on clinical guidelines as whether a PSA test order would have been appropriate or low value.[4] For example, tests ordered for men younger than 40 years old or older than 75 years old, men younger than 45 years old without additional risk factors, or men with a life expectancy of less than 10 years were all considered low value. We then conducted a regression analysis to determine the adjusted odds of appropriate and low value PSA test orders as the clinic day progressed.

▼ Continued on page 2

TAKE HOME *Message*

The following is a summary overview of the Annual Meeting abstracts. Abstract numbers are in parentheses (J Urol, suppl., 2020; **203**: e1-e1310).

Psychosocial Considerations for Patients with Localized Prostate Cancer

Zachary Klaassen, MD, MSc
Augusta, Georgia

Christopher J. D. Wallis, MD, PhD, FRCSC
Nashville, Tennessee

During the last several years there has been increasing attention paid to the importance of the psychosocial health and outcomes of patients with localized prostate cancer. Patient reported outcomes as a metric for localized prostate cancer treatment has been spearheaded by initiatives such as the prospective

▼ Continued on page 3

NON-PROFIT ORG.
U.S. POSTAGE
PAID
PERMIT NO. 797
RICHMOND, VA

American Urological Association
1000 Corporate Boulevard
Linthicum, Maryland 21090

Decision Fatigue in Low Value PSA Testing

▼ Continued from page 1

Of nearly 1.6 million outpatient appointments identified in the analysis sample a PSA test order would have been appropriate in just 36.8% based on the clinical guidelines we applied (fig. 1). Next, we examined the unadjusted rates of actual PSA test orders by date and time, and stratified these by testing appropriateness (fig. 2). We observed stark differences in the percentage of appointments that resulted in a PSA test order, such as generally higher rates of testing in the morning hours. Appropriate testing also appeared to be more common than low value testing at most times.

Further investigation with carefully designed regression analyses adjusted for relevant patient, appointment and clinician covariates found what we interpret as strong evidence for the role of decision fatigue in low value PSA testing. These results are summarized in figure 3, which depicts the adjusted odds of a PSA test order for all clinicians by hour of day and testing appropriateness. Two major conclusions can be drawn from this graph. First, the likelihood of appropriate and low value testing declines throughout the day as clinicians increasingly opt to not order PSA testing. Second, the magnitude of this decline is significantly greater for appropriate testing.

We posit that these conclusions when considered together present strong evidence for the influence of decision fatigue on outpatient PSA testing practices. Decision fatigue is thought to entail the gradual depletion of a finite cognitive resource as each subsequent decision is made.[1] With less fuel remaining in this cognitive tank complex decisions are harder to make and individuals tend to fall back on a default action that represents the status quo.[5] In the courtroom example cited previously the default was against approving inmate parole. In assessing whether a patient needs a PSA test the default is likely against routine PSA testing.

As the day proceeds and clinicians continue to assess each male patient's need for a PSA test, decision fatigue appears to set in as they increasingly fall back on the default option of not testing. This seems to be the case regardless of whether the testing would be appropriate or low value for a given patient. Furthermore, the effect observed was proportionately greater in appointments where a PSA test would be deemed appropriate. We suspect this is because deliberately overriding the default position of

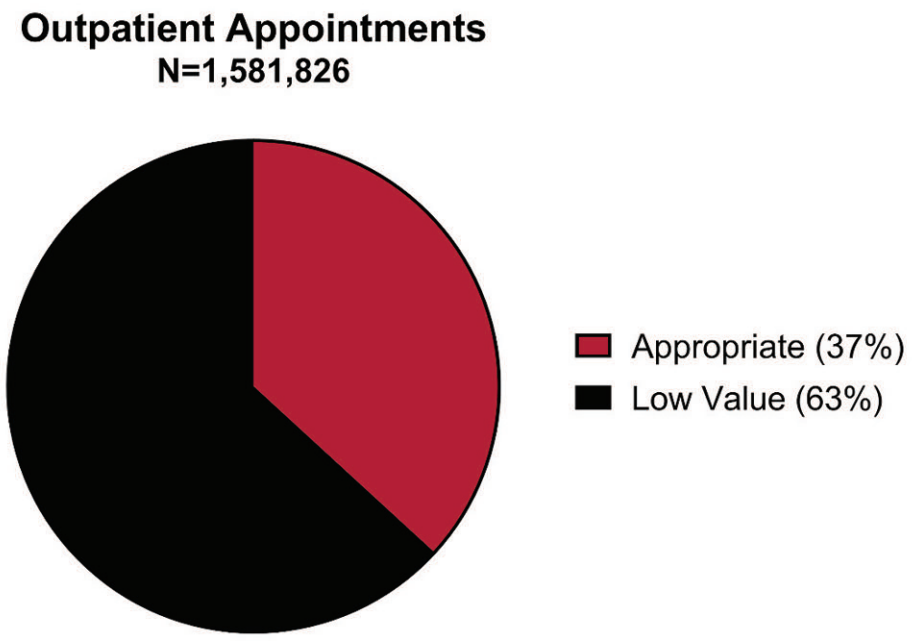


Figure 1. Appropriateness of PSA testing in outpatient appointments identified.

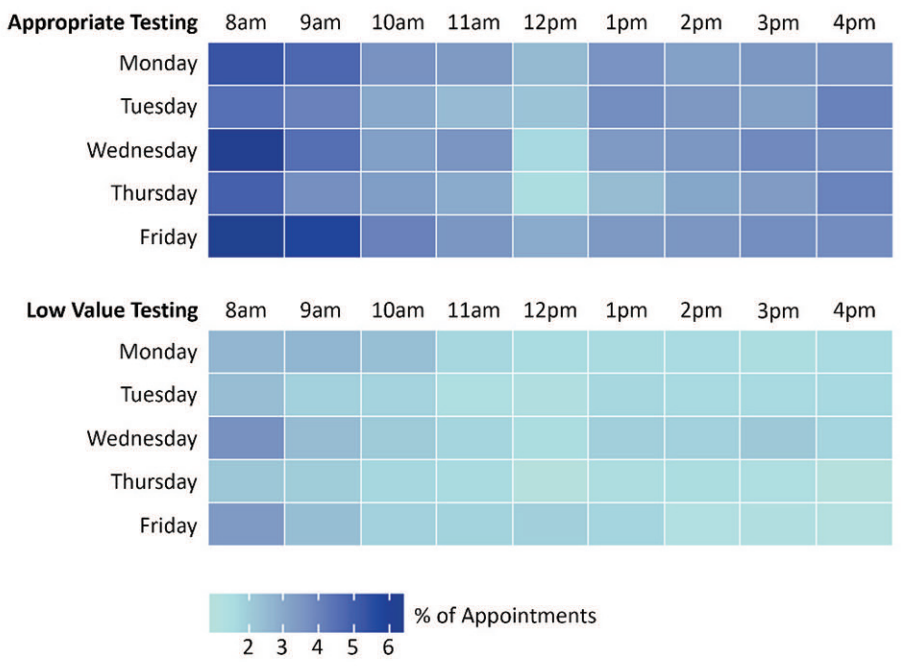


Figure 2. Rate of PSA testing in outpatient appointments by appropriateness.

▼ Continued on page 3

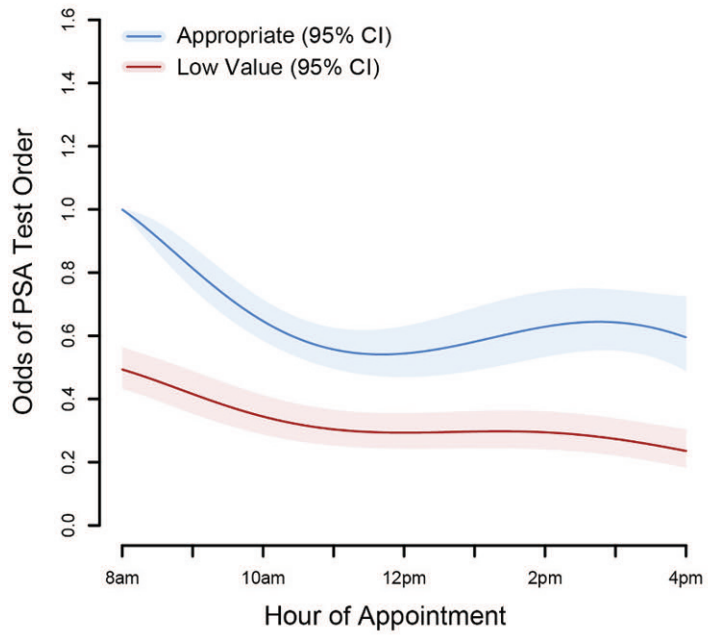


Figure 3. Likelihood of outpatient PSA testing performed by all clinicians.

AUA NEWS
September 2020 Volume 25 | Issue 9

AUA*News* is the official newsmagazine of the American Urological Association, located at 1000 Corporate Blvd., Linthicum, MD 21090, and is a function of the AUA Education and Research, Inc. **AUA*News*** is published 12 times a year by the American Urological Association. Published free of charge for AUA membership. Annual non-member subscription rates: individual $110 ($155 foreign); institution $135 ($180 foreign); industry $65 ($135 foreign). U.S. POSTMASTER: Send address changes to **AUA*News***, American Urological Association, 1000 Corporate Blvd., Linthicum, MD 21090. Library of Congress ISSN: 1088-7350. All correspondence on editorial matters should be addressed to: Executive Editor, American Urological Association, 1000 Corporate Boulevard, Linthicum, MD 21090.

Take Home Message—Prostate Cancer

▼ Continued from page 1

population based Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study, which recently published 5-year outcomes.[1] Several abstracts presented at the 2020 AUA virtual annual meeting highlighted important psychosocial considerations for patients with localized prostate cancer.

Luckenbaugh et al presented their study "Association between Treatment for Localized Prostate Cancer and Mental Health Outcomes" (MP67-17), which utilized the CEASAR cohort of patients. Among 1,509 (52.4%) patients undergoing radical prostatectomy, 961 (33.4%) undergoing radiation therapy and 409 (14.2%) undergoing active surveillance there were no significant differences in depression (using the Center for Epidemiological Depression [CES-D] score) or SF-36 scores between treated patients and those undergoing active surveillance. Significant predictors of depression included older age, poor overall health and being unmarried. Matta et al previously showed in a Canadian cohort of patients undergoing treatment for nonmetastatic prostate cancer that men had increased odds of antidepressant use up to 5 years after surgery (OR 1.49, 95% CI 1.34–1.64) or radiotherapy (OR 1.33, 95% CI 1.21–1.47), whereas active surveillance did not (OR 1.15, 95% CI 0.94–1.41).[2] These results from CEASAR are encouraging in that no specific treatment modality for localized prostate cancer resulted in an uptick in depressive symptoms.

Naha et al presented "The Association of Cancer Specific Anxiety with Disease Aggressiveness in Men on Active Surveillance of Prostate Cancer" (MP23-09), which used the Reduction by Dutasteride of Clinical Progression Events in Expectant Management (REDEEM) cohort of patients. There were 302 patients included in this study with biopsies obtained at 18 and 36 months. Anxiety was measured at baseline and 3, 6, 12, 18 and 36 months using the Memorial General Anxiety Scale for Prostate Cancer (MAX-PC). Among these men on active surveillance the MAX-PC scores

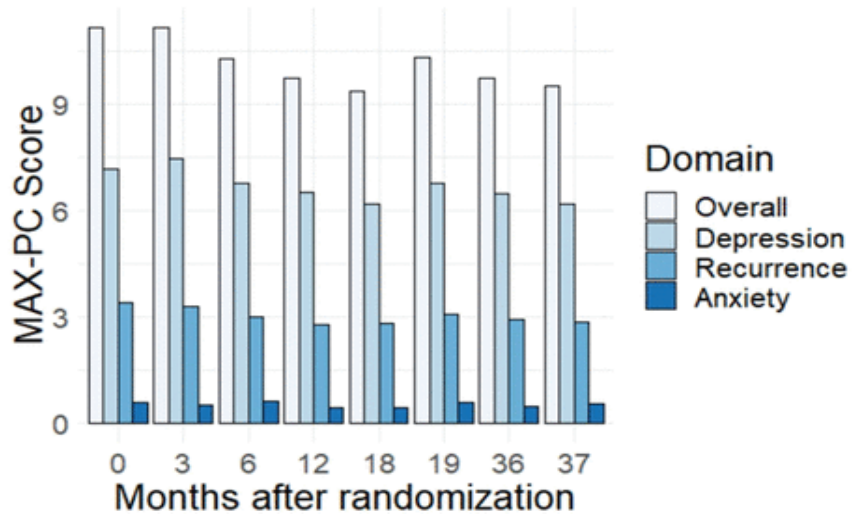


Figure. Natural history of MAX-PC scores in men undergoing active surveillance for prostate cancer.

decreased from baseline to 18 months with a slight increase in anxiety after receiving prostate specific antigen results at 18 months before subsequently declining (see figure). On multivariable analysis the percentage of positive cores was associated with baseline anxiety (p=0.003). Previous work from Memorial Sloan Kettering Cancer Center failed to demonstrate a significant association between pathological or demographic characteristics and patient anxiety but as with the abstract presented by Naha et al did report reduced cancer specific anxiety after 1 year on active surveillance.[3] Data on active surveillance related anxiety are important for urologists to recognize and address with patients not only to improve patient quality of life, but also to maintain patient adherence to active surveillance protocols.

Berry et al presented results from their study "Decision Regret, Adverse Outcomes and Treatment Choice in Men with Localized Prostate Cancer: Results from a Multi-Site Randomized Trial" (MP23-19). This study included 392 men with localized prostate cancer from 10 urology institutions who were randomized to receive personalized decision support via the Personal Patient Profile-Prostate vs standard of care for treatment decision planning. At 6 months 287 (73%) men had returned questionnaires of whom 257 (89%) had made a treatment choice. Among these patients 201 (78%) men completely answered the regret scale, which showed no significant difference between those receiving Personal Patient Profile-Prostate compared to standard of care (p=0.360). However, univariate analyses showed that Black men (p=0.019), men with any hormonal symptoms (p=0.009) and men with any bowel symptoms (p=0.032) reported higher treatment decision regret. There were significant interactions found between race and study group (Personal Patient Profile-Prostate vs standard of care) in that Black men who used the Personal Patient Profile-Prostate platform had significantly less decisional regret (p=0.037). In a Dutch study of 434 men treated with localized prostate cancer 23% of men had treatment regret irrespective of treatment modality.[4] Given the excellent survival outcomes for any treatment modality for localized prostate cancer knowledge of short-term and long-term side effects of each modality is paramount for appropriate shared decision making and hopefully decreasing treatment regret.

In an effort to provide a holistic approach to the treatment of localized prostate cancer, urologists need to be aware of associated depression, anxiety and regret throughout the treatment decision making process, during the period of treatment and immediate post-treatment, and during surveillance followup. Providing adequate psychosocial and mental health support for patients with localized prostate cancer are key components to a survivorship care plan, and should be individualized and revisited throughout the treatment/surveillance process. ◆

1. Hoffman KE, Penson DF, Zhao Z et al: Patient-reported outcomes through 5 years for active surveillance, surgery, brachytherapy, or external beam radiation with or without androgen deprivation therapy for localized prostate cancer. JAMA 2020; **323**: 149.
2. Matta R, Wallis CJD, Goldenberg MG et al: Variation and trends in antidepressant prescribing for men undergoing treatment for nonmetastatic prostate cancer: a population-based cohort study. Eur Urol 2019; **75**: 3.
3. Marzouk K, Assel M, Ehdaie B et al: Long-term cancer specific anxiety in men undergoing active surveillance of prostate cancer: findings from a large prospective cohort. J Urol 2018; **200**: 1250.
4. van Stam MA, Aaronson NK, Ruud Bosch JLH et al: Patient-reported outcomes following treatment of localised prostate cancer and their association with regret about treatment choices. Eur Urol Oncol 2020; **3**: 21.

Decision Fatigue in Low Value PSA Testing

▼ Continued from page 2

not testing is easier to do early in the day when cognitive resources are still intact and decision fatigue has not yet accumulated.

These findings are the first to our knowledge of decision fatigue in urological care and establish it as a new target for interventions aimed at reducing low value practices and wasteful spending in PSA testing. For example, efforts to increase guideline concordance in PSA testing might center around clinical decision support tools that intentionally manipulate the clinician's default action to fend off the effects of decision fatigue.[5] Our future work will more closely examine decision fatigue in urologists, whose PSA testing patterns were quite different than those of other clinicians, to determine if factors other than decision fatigue are predominantly driving low value PSA testing practices among specialists.

AUA 2020 Virtual Science Best Poster winner. ◆

1. Pignatiello GA, Martin RJ and Hickman RL Jr: Decision fatigue: a conceptual analysis. J Health Psychol 2020; **25**: 123.
2. Danziger S, Levav J, Avnaim-Pesso L: Extraneous factors in judicial decisions. Proc Natl Acad Sci U S A 2011; **108**: 6889.
3. Hsiang EY, Mehta SJ, Small DS et al: Association of primary care clinic appointment time with clinician ordering and patient completion of breast and colorectal cancer screening. JAMA Netw Open 2019; **2**: e193403.
4. O'Neil B, Martin C, Kapron A et al: Defining low-value PSA testing in a large retrospective cohort: finding common ground between discordant guidelines. Cancer Epidemiol 2018; **56**: 112.
5. Cho I and Bates DW: Behavioral economics interventions in clinical decision support systems. Yearb Med Inform 2018; **27**: 114.

Nocturia in the Elderly

Alan J. Wein MD, PhD (hon), FACS
Philadelphia, Pennsylvania

Aging is a normal process. A spectrum of changes exists, but some deleterious changes occur in everyone if they live long enough. Examining age-sex population pyramids based on U.S. census data leads to the inevitable conclusion that by the year 2030 a substantial portion of the population will be over the age of 65 years old.

The lower urinary tract changes that are common with aging include a decrease in bladder sensation, the ability to postpone urination, bladder capacity, bladder contractility (not at the myocyte level), maximum urethra closure pressure in women and an overall decrease in body mobility. Other changes include an increase in detrusor overactivity, postvoid residual, prostate size and outlet obstruction, pelvic organ prolapse, atrophic vaginitis and nocturia.[1–3] Nocturia 2 or more times a night occurs in approximately 35% of all individuals 60 years old or older. The prevalence rises proportionally with age so that the prevalence of nocturia 3 or more times a night in men and women over the age of 80 years old approaches 60%.

Having to wake or not because of the need to pass urine is a product of the relationship between the amount of urine produced at night and the ability of the bladder to store urine. The ability of the bladder to store urine normally at night depends upon maintaining a low intravesical pressure, having normal sensation, absence of involuntary bladder contractions, adequate sphincter function, minimal residual urine and no excess urine production at night.

In addition, there are many factors outside of the lower urinary tract and pelvic floor that can affect the frequency of nocturia. As we age there is a gradual decrease in maximum urine concentrating ability thought most likely to be caused by a decrease in renal sensitivity to arginine vasopressin (AVP) possibly due to a decrease in V-2 receptor expression or decreased AVP binding to this receptor.[4] For young individuals the peak AVP concentration occurs around midnight and there is a decrease during the daytime with the lowest levels in the afternoon. For the elderly this circadian rhythm is frequently lost and there are relatively low levels at night.

Broadly, the etiology of nocturia can be divided into sleep disturbances, psychological factors, bladder storage problems, polyuria (24-hour or nocturnal) or a combination of more than 1 of these factors. Nocturia generally becomes bothersome at a level of 2 or more times per night. Virtually everyone agrees that nocturia 3 or more times at night constitutes a moderate or serious bother.

Classically, nocturia is associated with significant decreases in many of the dimensions of health related quality of life.[5] Short-term consequences are said to include increased daytime sleepiness, reduced daytime alertness, longer reaction time, decreased daytime energy, reduced psychomotor performance, decreased memory/cognitive function and poor mood. Longer-term consequences are said to include depression, increased susceptibility to somatic disease and increased risk of cardiovascular disease, car accidents, fall/fractures and mortality.[6,7]

In the evaluation of an elderly patient with significant nocturia there must be recognition of nocturia as a possible manifestation of or association with systemic disease such as congestive heart failure, other causes of peripheral edema, hypertension, diabetes, sleep apnea, chronic obstructive pulmonary disease, neurologic disease, arthritis, depression/anxiety, alcohol or drug abuse, metabolic syndrome, and the use of certain therapeutic drugs such as diuretics, calcium channel blockers, lithium, central nervous system stimulants, and many others. The evaluation of such a patient should identify clearly relevant contributors to nocturia that can be treated by mechanism specific approaches. The nonurological issues I call "the big six" are excess intake, diabetes, congestive heart failure, peripheral edema, hypertension that does not decrease in the evening or night time and sleep apnea.

Along with initial attempted correction of these issues, behavioral and lifestyle modifications are an important part of the management strategy, especially for the elderly. These include preemptive voiding, a decrease in nocturnal and late afternoon fluids, dietary advice regarding caffeine, alcohol, salt and protein, exercise and weight loss, timing of medication (such as taking a diuretic in the late afternoon rather than the early morning, with the permission of patient internist), and compression stockings with late afternoon/evening leg elevation if there is peripheral edema.

If a patient has overactive bladder and/or prostatic enlargement/obstruction, then by all means treat them pharmacologically in the usual fashion, but don't expect much of a result on nocturia frequency. In actual fact, little response has been seen from antimuscarinic agents and alpha blockers. Unless a man has significant residual urine, do not expect much of a decrease following outlet reduction unless associated with a long-term decrease of detrusor overactivity secondary to the relief of outlet obstruction.

There is substantial evidence for significant relief in many older patients with obstructive sleep apnea (OSA) when this is properly corrected. Ultimately, the pathology in OSA with respect to nocturia is thought to be nocturnal polyuria due to increased atrial natriuretic peptide and decreased arginine vasopressin. Afternoon administration of diuretics with appropriate precautions has been used with reported success. For patients with nocturnal polyuria the early nocturnal diuresis rate during the first uninterrupted sleep is generally the greatest in terms of urine production. There exists a substantial drop off in the nocturnal diuresis after the time of first awakening that is significant and unique to patients with nocturnal polyuria syndrome. Therefore, it would be rational to use short acting antidiuretics in the treatment of such patients.

Desmopressin is a synthetic analog of arginine vasopressin, a relatively selective V-2 receptor agonist, and it increases reabsorption of water in the distal and collecting tubules concentrating the urine and decreasing urine production. It has a grade-A, level 1 recommendation by the International Consultation on Incontinence and the European

▼ Continued on page 5

	Desmopressin 0.2 mg Tablets	Nasal Spray 0.83–1.66 µg/0.1 ml (Noctiva)	Sublingual Wafers 25–50 µg, (Nocdurna)
Baseline sodium checks + followup age	65	65	65
Fluid restriction	Restrict	Moderation advised (do not drink large amounts close to bedtime)	Restrict 1 hr before to 8 hrs after administration
GFR (lower limit for prescribing)	50 or 60*	50	50–60*
Sodium checks after baseline (65 yrs or older)	3 days + after uptitration	Within 7 days + after uptitration	4–8 Days + 1 mo or 4–8 days, 1 mo, every 3–6 mos, depending on clinical need
Cardiovascular contraindication	Cardiac insufficiency or conditions requiring diuretics	New York Heart Association class II or higher congestive heart failure	Heart failure, edema
		Diuretic use	
Frail elderly	Not mentioned	Not mentioned	Contraindicated

* Moderate to severe renal failure or less than 50–60 ml/min depending on formula and cutoff used.

Nocturia in Elderly

▼ Continued from page 4

Association of Urology for treatment of nocturia with nocturnal polyuria. The potential problem in the use of vasopressin especially in the elderly is hyponatremia. A meta-analysis quoted the overall incidence of this with desmopressin use as 7.6%. Risk factors for hyponatremia include age older than 65 years old, female sex, decreased renal function and low sodium at baseline. There are currently 2 desmopressin products approved by the U.S. Food and Drug Administration for patients with nocturnal polyuria. The table details characteristics of the 2 preparations.[8]

For those using a desmopressin derivative it is imperative to follow the serum sodium on a fixed schedule, the first determination within 7 days of starting the drug, 1 at a month and at later intervals at the discretion of the treating physician. There does not seem to be any reason why desmopressin cannot be used as an add-on therapy to the drug treatments of benign prostatic hyperplasia or overactive bladder.

Other contraindications to the use of a desmopressin derivative listed for both drugs include polydipsia, illnesses that can cause fluid or electrolyte imbalance, loop diuretics, systemic or inhaled glucocorticoids (not preparations for nasal use only), hyponatremia, polydipsia, glomerular filtration rate (GFR) less than 50 ml/min/1.73 m^2, syndrome of inappropriate diuretic hormone secretion and uncontrolled hypertension.

As all of these are more common in the elderly population it seems reasonable to encourage the inclusion of a debate for the next AUA meeting regarding whether desmopressin is in any form a safe drug after more conservative measures have failed for the treatment of nocturia in the elderly. If so, what precautions need to be observed? ◆

1. Gibson W and Wagg A: New horizons, urinary incontinence in older adults. Age Ageing 2014; **43**: 157.
2. Resnick N and Yalla S: Geriatric incontinence and voiding dysfunction. In: Campbell-Walsh Urology, 10th ed. Edited by AJ Wein, LR Kavoussi, AC Novick et al. Philadelphia: Elsevier Saunders 2012; chapt 76.
3. Griebling TL: Aging and geriatric urology. In: Campbell-Walsh-Wein Urology, 12th ed. Edited by AW Partin, CA Peters, LR Kavoussi et al. New York, New York: Elsevier 2020; chapt 88, p 2905.
4. Tamma G, Goswami N, Reichmuth J et al: Aquaporins, vasopressin, and aging: current perspectives. Endocrinol 2015; **156**: 777.
5. Tikkinen KAO, Johnson TM, Tammela TLJ et al: Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. Eur Urol 2010; **57**: 488.
6. Abrams P: Nocturia: the effect on sleep and related health consequences. Eur Urol Suppl 2005; **3**: 1.
. Weiss J, Blaivas J, Van Kerrebroeck P et al: Nocturia: Causes, Consequences and Clinical Approaches. New York, New York: Springer 2012.
8. Everaert K, Hervé F, Bosch R et al: International Continence Society consensus on the diagnosis and treatment of nocturia. Neurourol Urodyn 2019; **38**: 478.

Individualized Approaches to Partial Nephrectomy: Correlation between Ischemia Time and Patient Health Status (RECORD2 Project)

Carlo Andrea Bravi, MD
Alessandro Larcher, MD
Roberto Bertini, MD
Andrea Gallioli, MD
Francesco Montorsi, MD
Umberto Capitanio, MD
Milan, Italy

Andrea Mari, MD
Fabrizio di Maida, MD
Vincenzo Li Marzi, MD
Riccardo Tellini, MD
Marco Carini, MD
Andrea Minervini, MD, PhD
Florence, Italy

Daniele Amparore, MD
Cristian Fiori, MD
Paolo Gontero, MD
Francesco Porpiglia, MD
Turin, Italy

Alessandro Antonelli, MD
Claudio Simeone, MD
Brescia, Italy

Walter Artibani, MD
Salvatore Siracusano, MD
Verona, Italy

Pierluigi Bove, MD
Rome, Italy

Eugenio Brunocilla, MD
Riccardo Schiavina, MD
Bologna, Italy

Luigi Da Pozzo, MD
Bergamo, Italy

Nicola Longo, MD
Vincenzo Mirone, MD
Naples, Italy

Bernardo Rocco, MD
Modena, Italy

Luigi Schips, MD
Chieti, Italy

Carlo Terrone, MD
Genoa, Italy

Carlo Trombetta, MD
Trieste, Italy

Vincenzo Ficarra, MD, FEBU
Messina, Italy

Acute kidney injury (AKI) occurs in approximately 20% of partial nephrectomies.[1] It has been established that AKI negatively affects long-term renal function,[2] and it consequently has relevant implications on survival and quality of life after surgery. Ischemia time is among the greatest determinants of AKI, and it is widely accepted that a warm ischemia shorter than 20 to 25 minutes might avoid functional consequences.[3] However, evidence of AKI after clampless procedures makes a strong argument toward a multifactorial etiology of AKI, suggesting that duration of ischemia and the individual risk contribute to functional damage. In this regard it seems reasonable that ischemia might have different implications according to the individual health profile. That is, the same clamp time might be more harmful for an 80-year-old patient with several comorbidities than for a healthy 50-year-old.

To test this hypothesis we analyzed data of 944 patients diagnosed with a cT1, PADUA (preoperative aspects and dimensions used for an anatomical) less than 10 renal mass at conventional imaging and treated with on-clamp partial nephrectomy from 2013 to 2016.[4] Data were collected as part of the Italian Registry of Conservative and Radical Surgery for Cortical Renal Tumor Disease (RECORD 2 Project), a prospective, observational project promoted by the Italian Society of Urology. AKI was defined according to the RIFLE (risk, injury, failure, loss of kidney function and end stage kidney disease) criteria. A multivariable logistic regression was used to calculate the individual preoperative risk of AKI. Covariates consisted of age, clinical T stage, preoperative estimated glomerular function rate (eGFR), total PADUA score and surgical approach. The individual probability of AKI derived was used as the independent variable for classification and regression tree (CART) analysis. According to the first split at CART analysis, we then stratified patients as at "high" and "low" risk for AKI. Finally, we plotted the preoperative probability of AKI through the duration of ischemia stratified by preoperative risk using a nonparametric curve fitting method.

Overall, 235 (25%) patients had postoperative AKI. Acute injury was more frequent for older patients, those treated with open surgery and those who had more complex tumors. Ischemia during surgery was longer among patients who experienced postoperative AKI. On multivariable analysis, age (OR 1.03, 95% CI 1.02–1.05, p <0.0001), preoperative eGFR (OR 1.02, 95% CI 1.01–1.03, p=0.003), clinical T1b stage (OR 1.88, 95% CI 1.35–2.62, p=0.0002) and higher PADUA score (OR 1.20, 95% CI 1.05–1.37, p=0.007) were associated with increased risk of AKI. Conversely, laparoscopic (OR 0.47, 95% CI 0.26–0.84, p=0.011) and robotic (OR 0.39, 95% CI 0.25–0.60, p <0.0001) surgery had lower probability of AKI compared to open surgery. According to the first split at CART analysis, patients were considered at high risk of AKI if their preoperative probability was greater than 40%. Patients who had a baseline probability smaller than 40% were considered at low risk.

As shown in the figure the relationship between duration of ischemia and probability of AKI was different according to preoperative risk of AKI. As an example, in the case of less than 10 vs more than 20 minutes of ischemia low risk patients had a risk of AKI of 13% (95% CI 10–17) and 28% (95% CI 22–34), respectively (absolute risk increase 15%, 95% CI 7–22). By contrast, the risk of AKI for high risk patients who had less than 10 vs more than 20 minutes of ischemia was 31% (95% CI 17–51) and 77% (95% CI 63–89), respectively. This corresponds to an absolute risk increase of 45% (95% CI 19–68).

The same duration of ischemia might have different implications according to the individual risk of functional harm. As such, stating that an ischemia shorter than 20 minutes will be without consequences might not be correct for all the patients. Surgical planning cannot rely on a one size fits all approach but should take into account individual characteristics. Our findings suggest that ischemia time cannot be considered an absolute value but rather that the right surgery

▼ Continued on page 9

RECOMMENDED

Olaparib (LYNPARZA) is the only PARPi included in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a Category 1† recommended option for men with HRRm mCRPC adenocarcinoma who have progressed on prior treatment with enzalutamide and/or abiraterone, regardless of prior docetaxel therapy.[6]

†Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

INDICATION

LYNPARZA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in <1.5% of patients exposed to LYNPARZA monotherapy, and the majority of events had a fatal outcome. The duration of therapy in patients who developed secondary MDS/AML varied from <6 months to >2 years. All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy, and some also had a history of more than one primary malignancy or of bone marrow dysplasia.

Do not start LYNPARZA until patients have recovered from hematological toxicity caused by previous chemotherapy (≤Grade 1). Monitor complete blood count for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities, interrupt LYNPARZA and monitor blood count weekly until recovery.

If the levels have not recovered to Grade 1 or less after 4 weeks, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. Discontinue LYNPARZA if MDS/AML is confirmed.

Pneumonitis: Occurred in <1% of patients exposed to LYNPARZA, and some cases were fatal. If patients present with new or worsening respiratory symptoms such as dyspnea, cough, and fever, or a radiological abnormality occurs, interrupt LYNPARZA treatment and initiate prompt investigation. Discontinue LYNPARZA if pneumonitis is confirmed and treat patient appropriately.

Embryo-Fetal Toxicity: Based on its mechanism of action and findings in animals, LYNPARZA can cause fetal harm. A pregnancy test is recommended for females of reproductive potential prior to initiating treatment.

Females

Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months following the last dose.

Males

Advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 3 months following the last dose of LYNPARZA and to not donate sperm during this time.

Venous Thromboembolic Events: Including pulmonary embolism, occurred in 7% of patients with metastatic castration-resistant prostate cancer who received LYNPARZA plus androgen deprivation therapy (ADT) compared to 3.1% of patients receiving enzalutamide or abiraterone plus ADT in the PROfound study. Patients receiving LYNPARZA and ADT had a 6% incidence of pulmonary embolism compared to 0.8% of patients treated with ADT plus either enzalutamide or abiraterone. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism, and treat as medically appropriate, which may include long-term anticoagulation as clinically indicated.

ADVERSE REACTIONS—HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of patients in clinical trials of LYNPARZA for **PROfound** were: anemia (46%), fatigue (including asthenia) (41%), nausea (41%), decreased appetite (30%), diarrhea (21%), vomiting (18%), thrombocytopenia (12%), cough (11%), and dyspnea (10%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients in clinical trials of LYNPARZA for **PROfound** were: decrease in hemoglobin (98%), decrease in lymphocytes (62%), decrease in leukocytes (53%), and decrease in absolute neutrophil count (34%).

DRUG INTERACTIONS

Anticancer Agents: Clinical studies of LYNPARZA with other myelosuppressive anticancer agents, including DNA-damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.

CYP3A Inhibitors: Avoid coadministration of strong or moderate CYP3A inhibitors when using LYNPARZA. If a strong or moderate CYP3A inhibitor must be coadministered, reduce the dose of LYNPARZA. Advise patients to avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice during LYNPARZA treatment.

CYP3A Inducers: Avoid coadministration of strong or moderate CYP3A inducers when using LYNPARZA.

USE IN SPECIFIC POPULATIONS

Lactation: No data are available regarding the presence of olaparib in human milk, its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in the breastfed infant, advise a lactating woman not to breastfeed during treatment with LYNPARZA and for 1 month after receiving the final dose.

Pediatric Use: The safety and efficacy of LYNPARZA have not been established in pediatric patients.

Among men with **BRCA1/2- or ATM-mutated mCRPC following progression on enzalutamide or abiraterone**

LYNPARZA more than doubled median rPFS vs retreatment with enzalutamide or abiraterone[1,7]

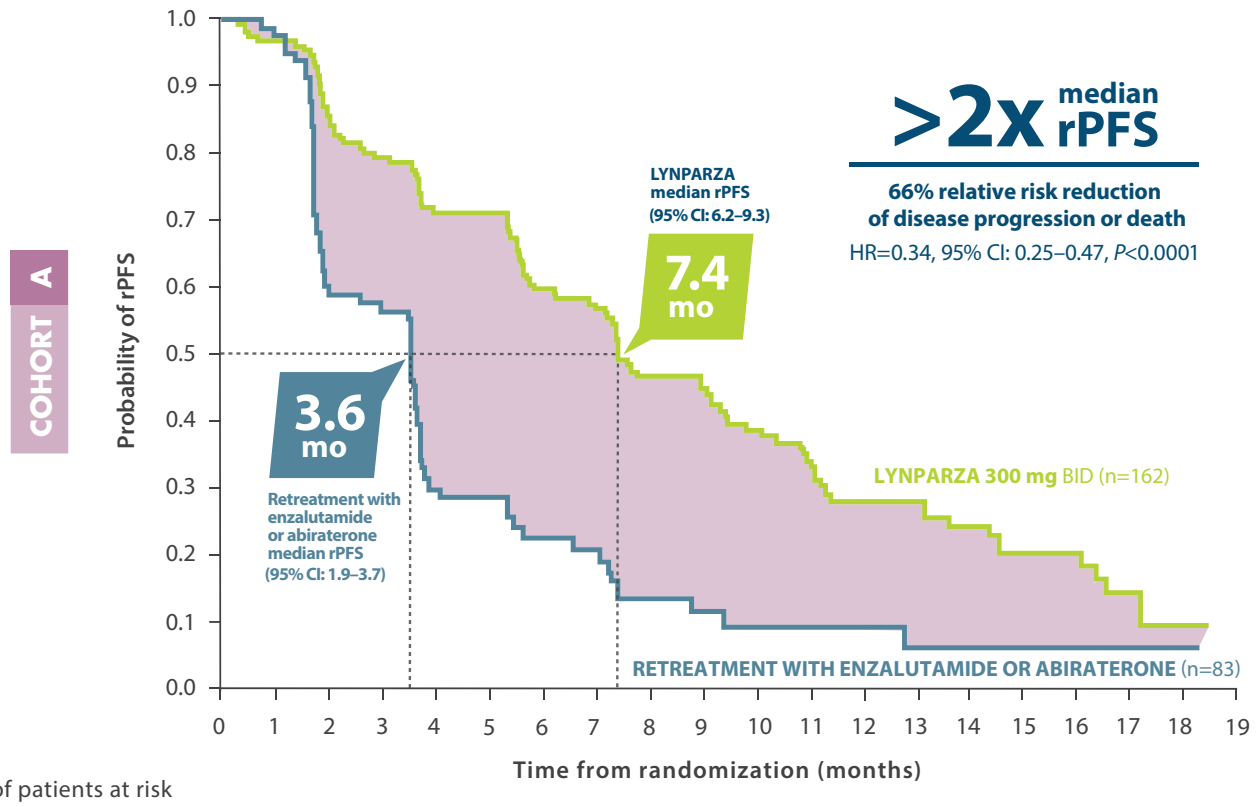
PROfound: A PHASE 3 trial of a PARPi in mCRPC[1,7]

TRIAL DESIGN[1,7]

- The PROfound trial was a prospective, multicenter, randomized, open-label, phase 3 trial of LYNPARZA in patients with HRRm mCRPC
- Key eligibility criteria: Metastatic castration-resistant prostate cancer; progression on prior enzalutamide or abiraterone treatment for metastatic prostate cancer and/or CRPC; a tumor mutation in at least 1 of 15 genes* involved in the HRR pathway
- Patients were divided by mutation: ***BRCA1/2* or *ATM* gene mutation (Cohort A [n=245]†‡) and other HRR gene mutations (Cohort B [n=142]‡§)**, and randomization was stratified by prior receipt of taxane chemotherapy and presence of measurable disease by RECIST 1.1
- Each cohort was randomized 2:1 to receive LYNPARZA (tablets, 300 mg per dose, twice daily) or an active comparator (retreatment with investigator's choice of enzalutamide or abiraterone)

*HRR gene mutations (*BRCA1*, *BRCA2*, *ATM*, *BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D*, and/or *RAD54L*) were identified by tissue-based testing using the Foundation Medicine FoundationOne® clinical trial HRR assay performed at a central laboratory. No patients were enrolled who had mutations in 2 of the 15 prespecified HRR genes: *FANCL* and *RAD51C*.
†Patients with co-mutations (*BRCA1*, *BRCA2*, or *ATM* plus a Cohort B gene) were assigned to Cohort A.
‡All patients received a GnRH analog or had prior bilateral orchiectomy.
§*BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D*, or *RAD54L*.
Although patients with *PPP2R2A* gene mutations were enrolled in the trial, LYNPARZA is not indicated for the treatment of patients with this gene mutation due to unfavorable risk-benefit ratio.

PRIMARY ENDPOINT: RADIOLOGICAL PROGRESSION-FREE SURVIVAL (rPFS)[1,7]



Number of patients at risk

LYNPARZA	**162**	**149**	**126**	**116**	**102**	**101**	**82**	**77**	**56**	**53**	**42**	**37**	**26**	**24**	**18**	**11**	**11**	**3**	**2**	**0**
Retreatment with enzalutamide or abiraterone	83	79	47	44	22	20	13	12	7	6	3	3	3	2	2	1	1	1	1	0

>2x median rPFS

66% relative risk reduction of disease progression or death

HR=0.34, 95% CI: 0.25–0.47, *P*<0.0001

- rPFS in Cohort A was determined by BICR using RECIST version 1.1 and PCWG3 (bone) criteria
- Consistent results were observed in exploratory analyses of rPFS:
  - For patients who received or did not receive prior taxane therapy
  - For those with germline *BRCA* mutations identified using the Myriad BRACAnalysis CDx assay compared with those with *BRCA* mutations identified using the Foundation Medicine F1CDx assay

The PROfound study included additional secondary endpoints not present here.

From *The New England Journal of Medicine*, de Bono J, Mateo J, Fizazi K, et al. Olaparib for metastatic castration-resistant prostate cancer. *N Engl J Med*. 2020;382(22): 2091-2102. Copyright © 2020 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

EXPLORE THE DATA, including secondary endpoints, and testing recommendations at LYNPARZAprchcp.com

IMPORTANT SAFETY INFORMATION (CONT'D)

USE IN SPECIFIC POPULATIONS (CONT'D)

Hepatic Impairment: No adjustment to the starting dose is required in patients with mild or moderate hepatic impairment (Child-Pugh classification A and B). There are no data in patients with severe hepatic impairment (Child-Pugh classification C).

Renal Impairment: No dosage modification is recommended in patients with mild renal impairment (CLcr 51-80 mL/min estimated by Cockcroft-Gault). In patients with moderate renal impairment (CLcr 31-50 mL/min), reduce the dose of LYNPARZA to 200 mg twice daily. There are no data in patients with severe renal impairment or end-stage renal disease (CLcr ≤30 mL/min).

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see accompanying Brief Summary of Prescribing Information on the following pages.

BICR=blinded independent central review; BID=twice a day; CI=confidence interval; CRPC=castration-resistant prostate cancer; GnRH=gonadotropin-releasing hormone; HR=hazard ratio; HRR=homologous recombination repair; HRRm=homologous recombination repair gene–mutated; mCRPC=metastatic castration-resistant prostate cancer; NCCN=National Comprehensive Cancer Network; PARPi=poly (ADP-ribose) polymerase inhibitor; PCWG3=Prostate Cancer Working Group 3; RECIST=Response Evaluation Criteria in Solid Tumors; rPFS=radiological progression-free survival.

References: 1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2020. **2.** Zejula® (niraparib) [prescribing information]. Waltham, MA: TESARO, Inc.; 2020. **3.** Rubraca® (rucaparib) [prescribing information]. Boulder, CO: Clovis Oncology, Inc.; 2020. **4.** Talzenna® (talazoparib) [prescribing information]. New York, NY: Pfizer Inc.; 2020. **5.** Teo MY, Rathkopf DE, Kantoff P. Treatment of advanced prostate cancer. *Annu Rev Med.* 2019;70:479-499. **6.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.2.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed May 21, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **7.** de Bono J, Mateo J, Fizazi K, et al. Olaparib for metastatic castration-resistant prostate cancer. *N Engl J Med.* 2020;382(22):2091-2102.

MERCK AstraZeneca

LYNPARZA® (olaparib) tablets, for oral use

Initial U.S. Approval: 2014

Brief Summary of Prescribing Information. For complete prescribing information consult official package insert.

INDICATIONS AND USAGE

HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

Lynparza is indicated for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza *[see Dosage and Administration (2.1) in the full Prescribing Information]*.

DOSAGE AND ADMINISTRATION

Patient Selection

Information on FDA-approved tests for the detection of genetic mutations is available at http://www.fda.gov/companiondiagnostics.

Select patients for treatment with Lynparza based on the presence of deleterious or suspected deleterious HRR gene mutations, including *BRCA* mutations, or genomic instability based on the indication, biomarker, and sample type (Table 1).

Table 1 Biomarker Testing for Patient Selection

Indication	Biomarker	Sample type	
		Tumor	Blood
Germline or somatic HRR gene-mutated metastatic castration-resistant prostate cancer*	*ATM*m, *BRCA1*m, *BRCA2*m, *BARD1*m, *BRIP1*m, *CDK12*m, *CHEK1*m, *CHEK2*m, *FANCL*m, *PALB2*m, *RAD51B*m, *RAD51C*m, *RAD51D*m, *RAD54L*m	X	
	g*BRCA1*m, g*BRCA2*m		X

* Where testing fails or tissue sample is unavailable/insufficient, or when germline testing is negative, consider using an alternative test.

Recommended Dosage

The recommended dosage of Lynparza is 300 mg taken orally twice daily, with or without food.

If a patient misses a dose of Lynparza, instruct patient to take their next dose at its scheduled time. Instruct patients to swallow tablets whole. Do not chew, crush, dissolve, or divide tablet.

HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

Continue treatment until disease progression or unacceptable toxicity for:

- HRR gene-mutated metastatic castration-resistant prostate cancer

Patients receiving Lynparza for mCRPC should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

Dosage Modifications for Adverse Reactions

To manage adverse reactions, consider interruption of treatment or dose reduction. The recommended dose reduction is 250 mg taken twice daily.

If a further dose reduction is required, then reduce to 200 mg taken twice daily.

Dosage Modifications for Concomitant Use with Strong or Moderate CYP3A Inhibitors

Avoid concomitant use of strong or moderate CYP3A inhibitors with Lynparza.

If concomitant use cannot be avoided, reduce Lynparza dosage to:

- 100 mg twice daily when used concomitantly with a strong CYP3A inhibitor.
- 150 mg twice daily when used concomitantly with a moderate CYP3A inhibitor.

After the inhibitor has been discontinued for 3 to 5 elimination half-lives, resume the Lynparza dose taken prior to initiating the CYP3A inhibitor *[see Drug Interactions (7.2) and Clinical Pharmacology (12.3) in the full Prescribing Information]*.

Dosage Modifications for Renal Impairment

Moderate Renal Impairment

In patients with moderate renal impairment (CLcr 31-50 mL/min), reduce the Lynparza dosage to 200 mg orally twice daily *[see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3) in the full Prescribing Information]*.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia

In clinical studies enrolling 2351 patients with various cancers who received Lynparza as a single agent *[see Adverse Reactions (6.1) in the full Prescribing Information]*, the incidence of Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) was <1.5% (28/2351) and the majority of events had a fatal outcome. Of these, 25/28 patients had a documented *BRCA* mutation, 2 patients had g*BRCA* wildtype and in 1 patient the *BRCA* mutation status was unknown. Additional cases of MDS/AML have been documented in patients treated with Lynparza in combination studies and in postmarketing reports. The duration of therapy with Lynparza in patients who developed secondary MDS/cancer-therapy related AML varied from <6 months to >2 years. All of these patients had received previous chemotherapy with platinum agents and/or other DNA damaging agents including radiotherapy. Some of these patients also had a history of more than one primary malignancy or of bone marrow dysplasia.

Do not start Lynparza until patients have recovered from hematological toxicity caused by previous chemotherapy (≤Grade 1). Monitor complete blood count for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities, interrupt Lynparza and monitor blood counts weekly until recovery. If the levels have not recovered to Grade 1 or less after 4 weeks, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. If MDS/AML is confirmed, discontinue Lynparza.

Pneumonitis

In clinical studies enrolling 2351 patients with various cancers who received Lynparza as a single agent *[see Adverse Reactions (6.1) in the full Prescribing Information]*, the incidence of pneumonitis, including fatal cases, was <1% (20/2351). If patients present with new or worsening respiratory symptoms such as dyspnea, cough and fever, or a radiological abnormality occurs, interrupt Lynparza treatment and promptly assess the source of the symptoms. If pneumonitis is confirmed, discontinue Lynparza treatment and treat the patient appropriately.

Embryo-Fetal Toxicity

Lynparza can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. In an animal reproduction study, administration of olaparib to pregnant rats during the period of organogenesis caused teratogenicity and embryo-fetal toxicity at exposures below those in patients receiving the recommended human dose of 300 mg twice daily. Apprise pregnant women of the potential hazard to a fetus and the potential risk for loss of the pregnancy. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of Lynparza. Based on findings from genetic toxicity and animal reproduction studies, advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 3 months following the last dose of Lynparza *[see Use in Specific Populations (8.1, 8.3) in the full Prescribing Information]*.

Venous Thromboembolic Events

Venous thromboembolic events, including pulmonary embolism, occurred in 7% of patients with metastatic castration resistant prostate cancer who received Lynparza plus androgen deprivation therapy (ADT) compared to 3.1% of patients receiving enzalutamide or abiraterone plus ADT in the PROfound study. Patients receiving Lynparza and ADT had a 6% incidence of pulmonary embolism compared to 0.8% of patients treated with ADT plus either enzalutamide or abiraterone. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate, which may include long-term anticoagulation as clinically indicated.

ADVERSE REACTIONS

The following adverse reactions are discussed elsewhere in the labeling:

- Myelodysplastic Syndrome/Acute Myeloid Leukemia *[see Warnings and Precautions (5.1) in the full Prescribing Information]*
- Pneumonitis *[see Warnings and Precautions (5.2) in the full Prescribing Information]*
- Venous Thromboembolic Events *[see Warnings and Precautions (5.4) in the full Prescribing Information]*

Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described in the WARNINGS AND PRECAUTIONS reflect exposure to Lynparza as a single agent in 2351 patients; 1585 patients with exposure to 300 mg twice daily tablet dose including five controlled, randomized, trials (SOLO-1, SOLO-2, OlympiAD, POLO, and PROfound) and to 400 mg twice daily capsule dose in 766 patients in other trials that were pooled to conduct safety analyses. In these trials, 55% of patients were exposed for 6 months or longer and 31% were exposed for greater than one year in the Lynparza group.

In this pooled safety population, the most common adverse reactions in ≥10% of patients were nausea (60%), fatigue (55%), anemia (37%), vomiting (34%), diarrhea (25%), decreased appetite (23%), headache (16%), neutropenia (15%), dysgeusia (15%), cough (15%), dyspnea (14%), dizziness (12%), dyspepsia (12%), leukopenia (11%), thrombocytopenia (11%), and abdominal pain upper (10%).

HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

PROfound

The safety of Lynparza as monotherapy was evaluated in patients with mCRPC and HRR gene mutations who have progressed following prior treatment with enzalutamide or abiraterone in PROfound *[see Clinical Studies (14.7) in the full Prescribing Information]*. This study was a randomized, open-label, multi-center study in which 386 patients received either Lynparza tablets 300 mg orally twice daily (n=256) or investigator's choice of enzalutamide or abiraterone acetate (n=130) until disease progression or unacceptable toxicity. Among patients receiving Lynparza, 62% were exposed for 6 months or longer and 20% were exposed for greater than one year.

Fatal adverse reactions occurred in 4% of patients treated with Lynparza. These included pneumonia (1.2%), cardiopulmonary failure (0.4%), aspiration pneumonia (0.4%), intestinal diverticulum (0.4%), septic shock (0.4%), Budd-Chiari Syndrome (0.4%), sudden death (0.4%), and acute cardiac failure (0.4%).

Serious adverse reactions occurred in 36% of patients receiving Lynparza. The most frequent serious adverse reactions (≥2%) were anemia (9%), pneumonia (4%), pulmonary embolism (2%), fatigue/asthenia (2%), and urinary tract infection (2%).

Dose interruptions due to an adverse reaction of any grade occurred in 45% of patients receiving Lynparza; dose reductions due to an adverse reaction occurred in 22% of Lynparza patients. The most frequent adverse reactions leading to dose interruption of Lynparza were anemia (25%) and thrombocytopenia (6%) and the most frequent adverse reaction leading to reduction of Lynparza was anemia (16%). Discontinuation due to adverse reactions occurred in 18% of Lynparza. The adverse reaction that most frequently led to discontinuation of Lynparza was anemia (7%).

Tables 16 and 17 summarize the adverse reactions and laboratory abnormalities, respectively, in patients in PROfound.

Table 16 Adverse Reactions* Reported in ≥10% of Patients in PROfound

Adverse Reactions	Lynparza tablets n=256		Enzalutamide or abiraterone n=130	
	Grades 1-4 (%)	Grades 3-4 (%)	Grades 1-4 (%)	Grades 3-4 (%)
Blood and lymphatic disorders				
Anemia†	46	21	15	5
Thrombocytopenia‡	12	4	3	0
Gastrointestinal disorders				
Nausea	41	1	19	0
Diarrhea	21	1	7	0
Vomiting	18	2	12	1
General disorders and administration site conditions				
Fatigue (including asthenia)	41	3	32	5
Metabolism and nutrition disorders				
Decreased appetite	30	1	18	1
Respiratory, thoracic, and mediastinal disorders				
Cough	11	0	2	0
Dyspnea	10	2	3	0

* Graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03

† Includes anemia and hemoglobin decreased

‡ Includes platelet count decreased and thrombocytopenia

In addition, adverse reactions of clinical relevance in PROfound that occurred in <10% of patients receiving Lynparza were neutropenia (9%), venous thromboembolic events (7%), dizziness (7%), dysgeusia (7%), dyspepsia (7%), headache (6%), pneumonia (5%), stomatitis (5%), rash (4%), blood creatinine increase (4%), pneumonitis (2%), upper abdominal pain (2%), and hypersensitivity (1%).

Table 17 Laboratory Abnormalities Reported in ≥25% of Patients in PROfound

Laboratory Parameter*	Lynparza tablets n†= 256		Enzalutamide or abiraterone n†=130	
	Grades 1-4 n= 247 (%)	Grades 3-4 n=247 (%)	Grades 1-4 n=124 (%)	Grades 3-4 n=124 (%)
Decrease in hemoglobin	242 (98)	33 (13)	91 (73)	5 (4)
Decrease in lymphocytes	154 (62)	57 (23)	42 (34)	16 (13)
Decrease in leukocytes	130 (53)	9 (4)	26 (21)	0
Decrease in absolute neutrophil count	83 (34)	8 (3)	11 (9)	0

* Patients were allowed to enter clinical studies with laboratory values of CTCAE Grade 1.

† This number represents the safety population. The derived values in the table are based on the total number of evaluable patients for each laboratory parameter.

Postmarketing Experience

The following adverse reactions have been identified during post approval use of Lynparza. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: Hypersensitivity (rash/dermatitis).

DRUG INTERACTIONS

Use with Anticancer Agents

Clinical studies of Lynparza with other myelosuppressive anticancer agents, including DNA damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.

Effect of Other Drugs on Lynparza

Strong and Moderate CYP3A Inhibitors

Coadministration of CYP3A inhibitors can increase olaparib concentrations, which may increase the risk for adverse reactions *[see Clinical Pharmacology (12.3) in the full Prescribing Information]*. Avoid coadministration of strong or moderate CYP3A inhibitors. If the strong or moderate inhibitor must be coadministered, reduce the dose of Lynparza *[see Dosage and Administration (2.4) in the full Prescribing Information]*.

Strong and Moderate CYP3A Inducers

Concomitant use with a strong or moderate CYP3A inducer decreased olaparib exposure, which may reduce Lynparza efficacy *[see Clinical Pharmacology (12.3) in the full Prescribing Information]*. Avoid coadministration of strong or moderate CYP3A inducers.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on findings in animals and its mechanism of action *[see Clinical Pharmacology (12.1) in the full Prescribing Information]*, Lynparza can cause fetal harm when administered to a pregnant woman. There are no available data on Lynparza use in pregnant women to inform the drug-associated risk. In an animal reproduction study, the administration of olaparib to pregnant rats during the period of organogenesis caused teratogenicity and embryo-fetal toxicity at exposures below those in patients receiving the recommended human dose of 300 mg twice daily *(see Data)*. Apprise pregnant women of the potential hazard to the fetus and the potential risk for loss of the pregnancy.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. The estimated background risk in the U.S. general population of major birth defects is 2-4%; and the risk for spontaneous abortion is approximately 15-20% in clinically recognized pregnancies.

Data

Animal Data

In a fertility and early embryonic development study in female rats, olaparib was administered orally for 14 days before mating through to Day 6 of pregnancy, which resulted in increased post-implantation loss at a dose level of 15 mg/kg/day (with maternal systemic exposures approximately 7% of the human exposure ($AUC_{0\text{-}24h}$) at the recommended dose).

In an embryo-fetal development study, pregnant rats received oral doses of 0.05 and 0.5 mg/kg/day olaparib during the period of organogenesis. A dose of 0.5 mg/kg/day (with maternal systemic exposures approximately 0.18% of human exposure ($AUC_{0\text{-}24h}$) at the recommended dose) caused embryo-fetal toxicities including increased post-implantation loss and major malformations of the eyes (anophthalmia, microphthalmia), vertebrae/ribs (extra rib or ossification center; fused or absent neural arches, ribs, and sternebrae), skull (fused exoccipital), and diaphragm (hernia). Additional abnormalities or variants included incomplete or absent ossification (vertebrae/sternebrae, ribs, limbs) and other findings in the vertebrae/sternebrae, pelvic girdle, lung, thymus, liver, ureter, and umbilical artery. Some findings noted above in the eyes, ribs, and ureter were observed at a dose of 0.05 mg/kg/day olaparib at lower incidence.

Lactation

Risk Summary

No data are available regarding the presence of olaparib in human milk, or on its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in the breastfed infants from Lynparza, advise a lactating woman not to breastfeed during treatment with Lynparza and for one month after receiving the last dose.

Females and Males of Reproductive Potential

Pregnancy Testing

Recommend pregnancy testing for females of reproductive potential prior to initiating treatment with Lynparza.

Contraception

Females

Lynparza can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1) in the full Prescribing Information]*. Advise females of reproductive potential to use effective contraception during treatment with Lynparza and for at least 6 months following the last dose.

Males

Based on findings in genetic toxicity and animal reproduction studies, advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 3 months following the last dose of Lynparza. Advise male patients not to donate sperm during therapy and for 3 months following the last dose of Lynparza *[see Use in Specific Populations (8.1) and Nonclinical Toxicology (13.1) in the full Prescribing Information]*.

Pediatric Use

Safety and effectiveness of Lynparza have not been established in pediatric patients.

Geriatric Use

Of the 2351 patients with advanced solid tumors who received Lynparza tablets 300 mg orally twice daily as monotherapy, 596 (25%) patients were aged ≥65 years, and this included 137 (6%) patients who were aged ≥75 years. Seven (0.3%) patients were aged ≥85 years. *[see Adverse Reactions (6.1) in the full Prescribing Information]*.

Of the 535 patients with advanced solid tumors who received Lynparza tablets 300 mg orally twice daily in combination with bevacizumab, 204 (38%) patients were aged ≥65 years, and this included 31 (6%) patients who were aged ≥75 years.

No overall differences in the safety or effectiveness of Lynparza were observed between these patients and younger patients.

Renal Impairment

No dosage modification is recommended in patients with mild renal impairment (CLcr 51 to 80 mL/min estimated by Cockcroft-Gault). Reduce Lynparza dosage to 200 mg twice daily in patients with moderate renal impairment (CLcr 31 to 50 mL/min) *[see Dosage and Administration (2.5) in the full Prescribing Information]*. There are no data in patients with severe renal impairment or end-stage disease (CLcr ≤30 mL/min) *[see Clinical Pharmacology (12.3) in the full Prescribing Information]*.

Hepatic Impairment

No adjustment to the starting dose is required in patients with mild or moderate hepatic impairment (Child-Pugh classification A and B). There are no data in patients with severe hepatic impairment (Child-Pugh classification C) *[see Clinical Pharmacology (12.3) in the full Prescribing Information]*.

Distributed by:
AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850

5/2020 US-34783 6/20

Individualized Approaches to Partial Nephrectomy

▼ Continued from page 5

should be given to the right patient according to the risk of functional harm. This entails a second critical point, which is a clear need for standardization of functional profile before, during and after renal surgery. While tumor complexity guides indication for surgery (eg radical vs partial nephrectomy) we have to bear in mind that the final goal of partial nephrectomy is to preserve renal function and as such an appropriate estimation of functional risk is necessary to optimize ischemia time. Although the general recommendation towards shortening ischemia time still holds true,[3] surgeons should consider a more granular approach based on the assessment of functional profile.

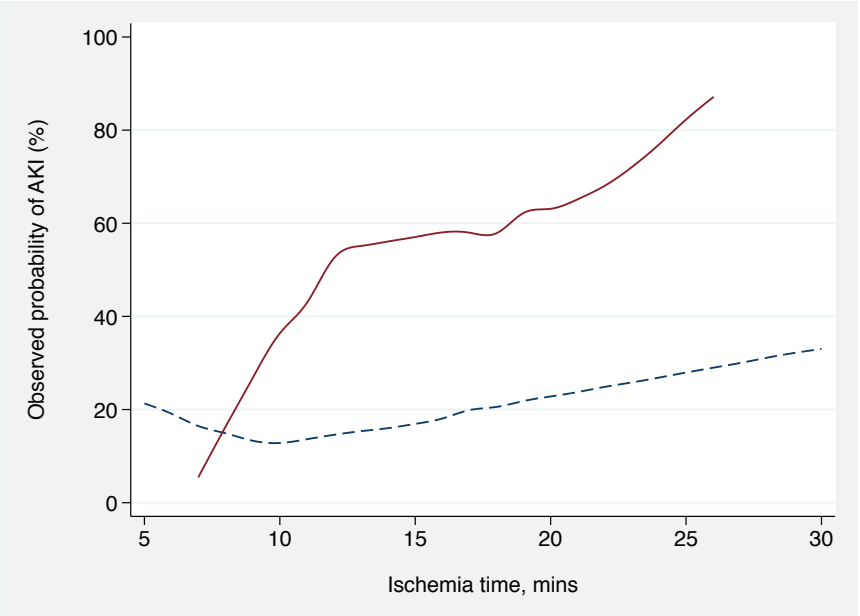


Figure. Relationship between observed AKI and ischemia time stratified by preoperative risk of AKI, with preoperative risk greater than 40% (red line) and 40% or less (dashed line).

Our results suggest that more serious attention should be paid to functional profile before partial nephrectomy. It seems established that AKI should be prevented as it is associated with long-term function.[2,5] A generic recommendation is for preoperative correction of medical conditions. Moreover, there is evidence that acute damage is often related with intraoperative factors such as operative time, blood loss and ischemia time. For this reason systematic research is required to identify critical aspects of partial nephrectomy that are associated with AKI.

Other implementations should also be investigated. For instance, serum creatinine may be inadequate for gauging side specific renal function. This is extremely relevant as the affected kidney might be the one contributing less to global function, resulting in a risk/benefit ratio in favor of radical rather than partial nephrectomy. Conversely, more efforts for partial nephrectomy might be considered if surgery was needed in the kidney with the highest contribution to global function. In this regard, imaging modalities such as renal scintigraphy might be of added value for preoperative planning. It is reasonable that the implementation of renal scintigraphy in preoperative counseling might result in a more accurate risk stratification, thereby improving surgical planning and likely translating to better surgery.

In conclusion, clamp time seems less clinically relevant for patients in good condition who may endure prolonged ischemia with a mild increase of AKI risk, whereas frail patients seem more vulnerable to ischemia damage and may require additional interventions in the postoperative period. This should be taken into account toward individualized management before and after partial nephrectomy.

AUA 2020 Virtual Science Best Poster winner. ◆

1. Capitanio U and Montorsi F: Renal cancer. Lancet 2016; **387**: 894.
2. Bravi CA, Vertosick E, Benfante N et al: Impact of acute kidney injury and its duration on long-term renal function after partial nephrectomy. Eur Urol 2019; **76**: 398.
3. Volpe A, Blute ML, Ficarra V et al: Renal ischemia and function after partial nephrectomy: a collaborative review of the literature. Eur Urol 2015; **68**: 61.
4. Bravi CA, Mari A, Larcher A et al: Toward individualized approaches to partial nephrectomy: assessing the correlation between ischemia time and patient health status (RECORD2 project). Eur Urol Oncol 2020; doi:10.1016/j.euo.2020.05.009.
5. Bravi CA and Vickers A: Why acute kidney injury during partial nephrectomy matters. Ann Transl Med, suppl., 2019; **7**: S317.

Indocyanine Green Guidance during Radical Prostatectomy

Francesco Claps, MD
Valencia, Spain

Miguel Ramirez-Backhaus, MD, PhD, FEBU
Trieste, Italy

Prostate cancer (PCa) is the most frequent urological malignancy in men worldwide. For this reason there is great interest in maintaining the highest cancer care quality and identifying an optimal management avoiding side effects of overtreatment or undertreatment considering factors such as disease stage, age, performance status and quality of life.

Information regarding the presence of lymph node metastasis (LNMs) is important for the staging, management and pretreatment workup of PCa. Computational prediction of a positive lymph node (LN) can be estimated using several nomograms based on parameters including prostate specific antigen (PSA), Gleason score, positive biopsy cores or multiparametric magnetic resonance imaging (mpMRI) features of the prostate index lesion and the decision to perform an extended lymph node dissection (ePLND) is currently recommended for intermediate or high risk patients.

However, meticulous ePLND is time consuming, surgeon dependent and associated with an increased risk of morbidity.[1] In order to improve these aspects sentinel LN mapping with different guided techniques has been proposed through the years. Indocyanine green (ICG) is a nontoxic, nonradioactive compound that exhibits fluorescence when stimulated by near infrared light allowing deeper tissue penetration that can be visualized even in a bloody operative field. ICG may be useful during prostatectomy (RP) based on its ability to mark target prostate tissue with limited diffusion while acting as a lymphangiography agent to visualize sentinel prostatic drainage.[2]

The primary aim of this study was to evaluate the diagnostic performance of an ICG guided ePLND. For this purpose we evaluated the pathological outcomes of a selective ICG guided ePLND with removal of fluorescent nodes and compared these with the confirmatory extended template. The secondary objective was to evaluate the potential role of a selective ICG guided ePLND for patients with 2 or fewer LNMs who according to the literature may benefit more from ePLND.[3]

Data for about 226 consecutive patients who underwent laparoscopic RP for clinically localized PCa with ICG guided ePLND at our department were prospectively evaluated. A solution of 25 mg ICG in 5 ml sterile water was transperineally injected, and ePLND started with the ICG stained nodes followed by extended template. All available tissue from ICG stained LNs was sliced at 250 µm, and each level was assessed by hematoxylin-eosin and immunohistochemistry staining. The other LNs coming from ePLND were processed in the standard manner. Primary outcome measures were accuracy (Acc), sensitivity (Se), specificity (Sp), negative predictive value (NPV) and likelihood ratio of a negative test (LRn) of ICG guided procedure. To our knowledge this study shows data about the largest cohort of patients who underwent ICG guided ePLND.

Overall, the median age of patients was 64.8 years with a median PSA of 6.6 ng/ml. Extracapsular disease occurred in 50.9% of patients, Gleason score 8 or greater was reported in 11.9% of cases and the positive surgical margin rate was 24.3%. Median number of nodes retrieved was 22 (IQR 16–27) and median number of ICG stained nodes per patient was 6 (IQR 4–9).

In total, 4,939 nodes were removed and 1,599 (32.4%) were fluorescent in vivo. Node positive disease was found in 58 (25.7%) cases, of which 53 (91.4%) had some of the metastatic LNs stained by ICG while 5 (8.6%) were false-negative. Therefore, 97.8% of the sample was properly classified by ICG guided ePLND (Se 91.4%, NPV 97.1% and LRn 8.6%). In all, 172 (3.5%) LNs retrieved were positive for disease. Considering 209 (92.5%) patients with 0, 1 or 2 LNMs, 39 (18.7%) had a node positive disease of which 34 (87.2%) had metastatic ICG stained LNs. Therefore, false-negative nodes were found in 5 patients. Again, 97.6% were properly classified by ICG approach (Se 87.2%, NPV 97.1% and LRn 12.8%). These 39 node positive patients had a total of 48 metastatic LNs with only 9 false-negative LNs that were not fluorescent in vivo (Se 81.2%, NPV 99.7%, see table).

In this prospective study we reported that ICG guided ePLND during laparoscopic RP for clinically localized PCa is a safe, reliable, cost-effective and radiation-free procedure to evaluate nodal status with a high rate of correctly staged patients. To our knowledge only 1 randomized clinical trial evaluated the role of ICG guided procedure in PCa showing a 78% Se in 59 patients with a total of 2.5 mg ICG transrectally applied.[4] A possible explanation of these results could be the low sample of ICG procedure and low rate of overall pN positive cases (12.7%). Furthermore, information about pathological evaluation was not available. With a thickness of 250 µm we tried to manage the same setting used in other malignancies where the concepts of micrometastases and macrometastases are well established as the role of the sentinel lymph node.

Only 3.5% of the evaluated LNs harbored metastasis of PCa and for 168 (74.3%) patients ePLND could have been avoided. These findings may suggest that a more conservative approach can be performed in selected patients especially to minimize the perioperative morbidity. Furthermore, with such a high NPV we could have potentially avoided ePLND once we knew that the ICG stained LNs did not harbor metastasis. The possibility to achieve a reliable intraoperative histopathological technique to assess the status among ICG stained LNs will be the perfect integration during an imaging guided procedure.

Recently, Winter et al reported the first results from 1 step nucleic acid amplification (OSNA) in PCa quantifying the ckytokeratin 19 (CK19) mRNA copies.[5] OSNA was performed on frozen samples using a ready-to-use amplification kit in an automated real-time detection system and compared with standard histopathological and immunohistochemical examinations.

Table. Diagnostic efficacies of ICG guided procedure

	% (95% CI)
At pt level in overall cohort (226):	
Mets. prevalence	26.5 (20.8–32.9)
Accuracy	97.8 (94.8–99.3)
Sensitivity	91.4 (81.0–97.1)
NPV	97.1 (93.1–99.1)
LRn	8.6 (3.7–19.9)
At node level in overall cohort (4,939):	
Mets. prevalence	3.6 (3.1–4.2)
Accuracy	68.9 (67.5–70.2)
Sensitivity	63.4 (55.7–70.6)
Specificity	69.1 (67.7–70.4)
NPV	97.1 (97.5–98.5)
LRn	53.0 (43.5–64.6)
At pt level in 2 or fewer LNMs cohort (209):	
Mets. prevalence	18.8 (13.8–24.8)
Accuracy	97.6 (94.5–99.2)
Sensitivity	87.2 (72.6–95.7)
Specificity	100.0 (97.8–100.0)
NPV	97.1 (93.4–99.1)
LRn	12.8 (5.7–29.1)
At node level in 2 or fewer LNMs cohort (4,470):	
Mets. prevalence	1.1 (0.8–1.4)
Accuracy	68.2 (66.8–69.6)
Sensitivity	81.2 (67.4–91.1)
Specificity	68.1 (66.7– 69.4)
NPV	99.7 (99.4–99.9)
LRn	27.6 (15.3–49.7)

Mets., metastasis.

▼ Continued on page 13

FROM THE *AUA Secretary*

Dr. Anthony Fauci Presents Compelling Information on COVID-19 during AUA Live

John D. Denstedt, MD, FRCSC, FACS, FCAHS
London, Ontario, Canada

As part of the new AUA Virtual Experience, AUA Live included 36 hours of education, 65 presentations and nearly 170 different speakers, including Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, who provided an informative and inspiring keynote presentation titled "Coronavirus Infections: More Than Just the Common Cold."

Dr. Fauci's presentation included background information on the novel coronavirus, as well as current statistics, containment measures and the progress in research toward therapies and a vaccine for this disease. He explained that among the coronaviruses that affect humans there is a group of viruses we have known about for a considerable period of time, ones that account for 15% to 30% of common colds. He also reminded us of disease outbreaks similar to COVID-19 including severe acute respiratory syndrome (SARS) in 2002 and Middle East respiratory syndrome (MERS) in 2012. Similar to COVID-19, SARS and MERS containment strategies included quarantine, isolation of cases, travel advisories and more, which helped bring an end to the spread of the diseases. However, unlike COVID-19, both SARS and MERS were poorly transmittable from human to human.

He outlined details for how human-to-human COVID-19 transmission happens as the result of close contact, less than 6 feet in distance. He discussed the transmission of COVID-19 via infected surfaces, as well as particles that remain in the air over time and distance, and highlighted how coronavirus has been detected in blood, stool, ocular secretions and semen, but it was still unclear if it is transmitted this way.

Public health measures, including social distancing orders, stay-at-home orders, travel restrictions and closure of nonessential businesses, as well as implementation of personal preventive measures, such as diligent hand washing, avoiding close contact, covering mouth and nose with a face covering, avoiding face touching and regularly cleaning frequently touched objects, have averted 60 million COVID-19 infections in the United States and prevented more than 3.1 million deaths in 11 countries in Europe.

He showcased the research community as making important strides in developing therapies to treat COVID-19, and ultimately developing a vaccine to prevent it. He shared his cautious optimism that if trials go well, there could be

▼ Continued on page 13

"We are experiencing a historic outbreak right now, and it isn't over yet. Emerging infections are a perpetual challenge and we need to be perpetually prepared. When we get through this, which we will, we should not lose our corporate memory that this has the potential, and the reality, of happening again."

—Dr. Anthony Fauci

CASE *Report*

Broken Infant Feeding Tube Inside the Ureter: An Unusual Complication and Lessons Learned



Madhusudan Patodia, MD
Jaipur, Rajasthan, India

Manoj Kumar, MD
Apul Goel, MBBS, MS, MCh
Lucknow, Uttar Pradesh, India

Introduction

Ureteral splints are an integral part of urology practice. These are placed after ureteral anastomosis, ureteral repair or endourological procedure. Splinting is done by Double-J® stent (DJS) or infant feeding tube (IFT). Stent and IFT have their merits and demerits. IFT as a splint is safe and effective with only the occasional problem of slippage. We encountered a rare situation where the IFT broke inside the ureter at time of removal.

Case Report

A 3-year-old girl underwent left nephroureterectomy for left nonfunctioning kidney due to vesicoureteral reflux and right Cohen's cross trigonal ureteric reimplantation for right ectopic ureter. A 5Fr IFT was placed as a splint through right ureterovesical anastomosis and exteriorized through suprapubic route. Catgut 3-zero suture was passed through-and-through the IFT to stabilize it with the bladder, which is common in our practice (fig. 1).

While removing the IFT on the fourteenth postoperative day it broke with a part of it remaining inside the ureter. Intravenous pyelogram confirmed the presence of tube inside the renal pelvis and ureter (fig. 2). Removal of the broken tube was not possible by ureteroscopy as the guide wire could not be negotiated through the ureteral orifice because of Cohen's cross trigonal ureteral reimplantation.

A percutaneous approach was used for the removal of the IFT. The pelvicalyceal system (PCS) was punctured under ultrasound guidance and contrast was instilled to delineate the PCS under fluoroscopy (fig. 3). Using the superior calyx for access the tract was dilated up to 18Fr using telescopic metallic dilators and the IFT was removed intact by mininephroscope.

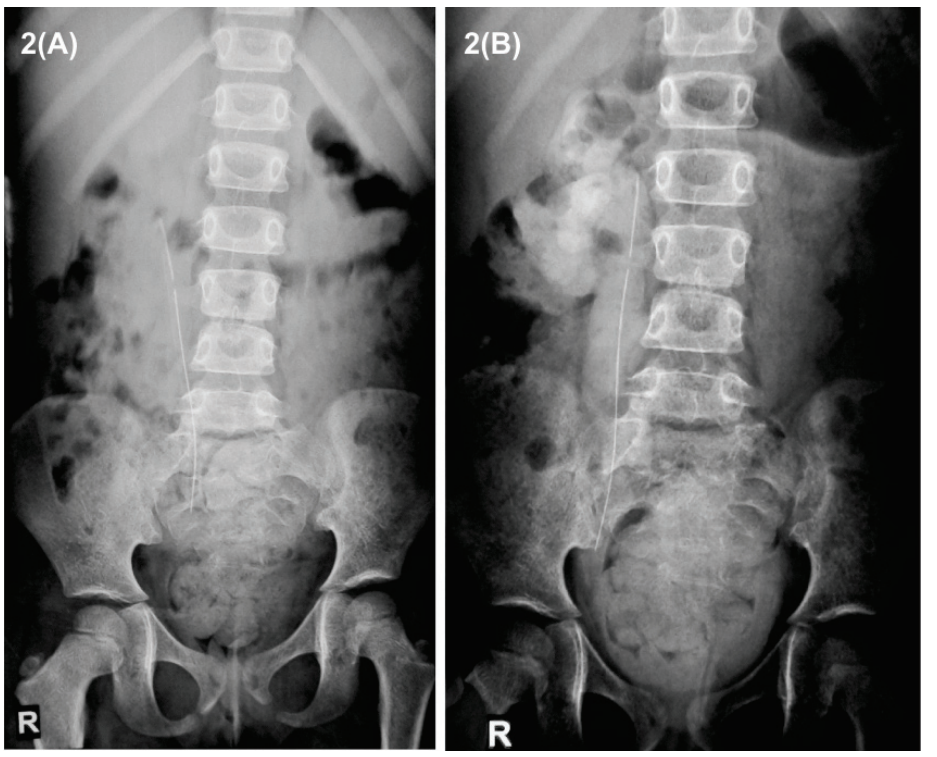


Figure 2. X-ray and intravenous pyelogram showing (*A*) upper end of feeding tube in pelvis and (*B*) lower end in ureter.

Discussion

Ureteral stent placement is performed in a variety of open surgical procedures. An ideal splint is soft and flexible, resistant to encrustation, has uniform diameter, is radiopaque, easy to place and does not migrate.[1] Despite benefits DJS can cause complications including pain, urinary tract infection, encrustation, stone formation, migration,

▼ Continued on page 13

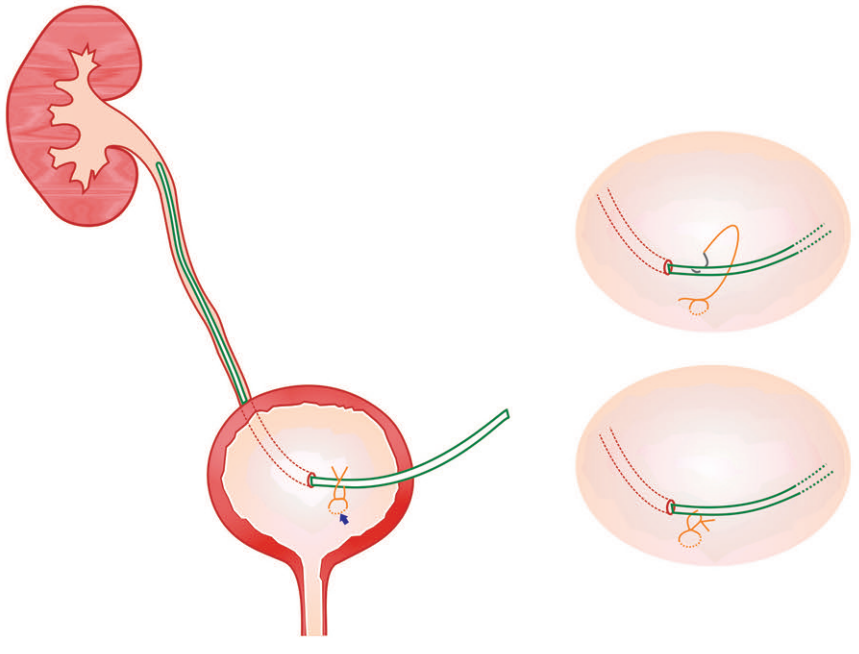


Figure 1. Illustration showing transfixation of infant feeding tube with catgut suture to bladder mucosa. Loop is created to permit some movement of tube with ureteral peristalsis. Arrow shows that suture is fixed to bladder mucosa.

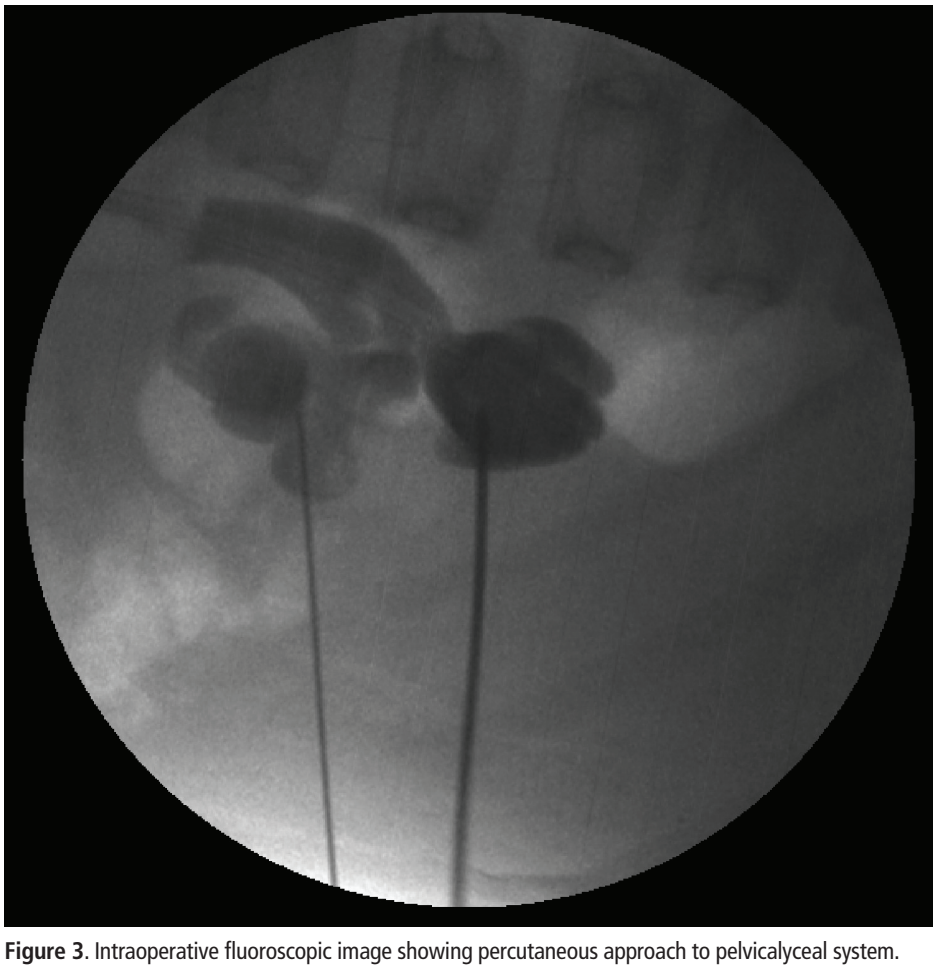


Figure 3. Intraoperative fluoroscopic image showing percutaneous approach to pelvicalyceal system. Thinner needle is to access pelvicalyceal system under ultrasound guidance and larger needle is to place guidewire under fluoroscopic guidance.

Case Report

▼ Continued from page 12

hematuria and lower urinary tract symptoms.[2] Forgotten DJS is another known complication. IFT as a ureteral splint is cheaper than DJS and can be removed easily without requiring cystoscopy (under anesthesia).

For better drainage surgeons often make extra holes in the IFT. Sometimes the suture used for transfixation passes inadvertently through this hole. The IFT may break at this point at the time of removal. In this patient a 5Fr IFT was used as a splint and was transfixed with 3-zero catgut. Passing 3-zero needle through the IFT may have made it weak, causing it to break during removal. It is possible that transfixation with thinner suture (5-zero catgut) could avoid damage of the splint. Usually, broken ureteral splints can be managed by ureteroscopy. However, because of Cohen's cross trigonal ureteral reimplantation ureteroscopy failed and a percutaneous approach was needed.

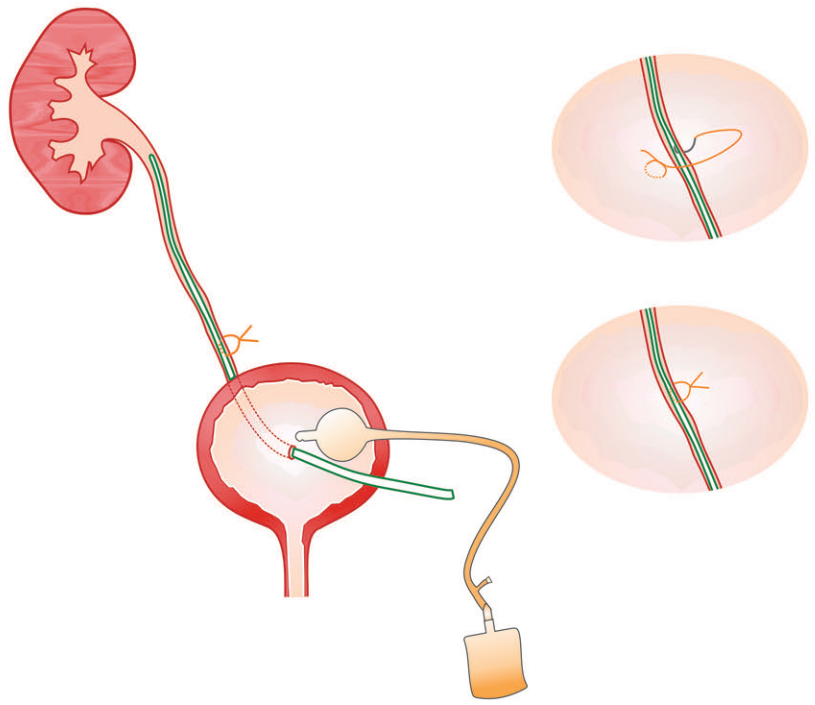


Figure 4. Illustration showing fixation of infant feeding tube to ureter. This step is often done at time of ureteral reimplantation in situation of lower ureteric injury (after hysterectomy).

IFTs are also commonly used at time of ureteral reimplantation in context of lower ureteral injury after hysterectomy or after radical cystectomy with ileal conduit. Here also the IFT is secured to the ureter with a suture passing through the ureter and the IFT (fig. 4). In this situation the IFT may also break at time of its removal. Breakage of an IFT is rare as catgut suture usually dissolves by the time the tube is removed.

Broken splint is a rare complication that may occur with an IFT. Transfixation with thinner suture would be better. Making extra holes in the IFT should be avoided. The tube should be removed gently and complete removal should be ensured. ◆

1. Finney RP: Experience with new double J ureteral catheter stent. J Urol 1978; **120**: 678.
2. Nerli RB, Magdum PV, Sharma V et al: Forgotten/retained double J ureteric stents: a source of severe morbidity in children. Afr J Paediatr Surg 2016; **13**: 32.

From the AUA Secretary

▼ Continued from page 11

a vaccine available by the end of this calendar year, or first quarter of 2021.

While Dr. Fauci stated we are far from being out of the woods, this pandemic has taught us that global collaboration and transparency are essential, good public health measures are critical to controlling an epidemic, experience with prototype pathogens and vaccine platforms can accelerate countermeasure development, and mild presentations of disease can complicate control of an epidemic.

Dr. Fauci's full presentation is available for free to AUA members at https://www.auavirtual.org/aua-live. ◆

Indocyanine Green Guidance

▼ Continued from page 10

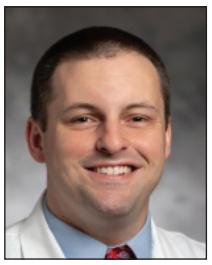
With a CK19 mRNA copy number cutoff of 250 copies per µl the authors show promising results for the improvement of intraoperative LN staging.[5] Further verifications are required, but having a potentially reliable biomarker in this field is an important step forward in terms of integration between technical development and tailored treatment for patients with PCa.

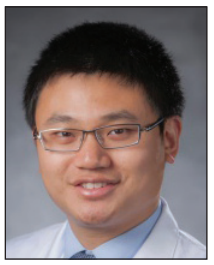
AUA 2020 Virtual Science Best Poster winner. ◆

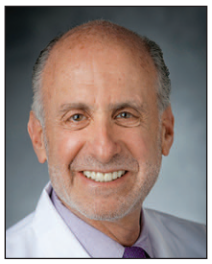
1. Fossati N, Willemse PPM, Van den Broeck T et al: The benefits and harms of different extents of lymph node dissection during radical prostatectomy for prostate cancer: a systematic review. Eur Urol 2017; **72**: 84.
2. Ramírez-Backhaus M, Mira Moreno A, Gómez Ferrer A et al: Indocyanine green guided pelvic lymph node dissection: an efficient technique to classify the lymph node status of patients with prostate cancer who underwent radical prostatectomy. J Urol 2016; **196**: 1429.
3. Briganti A, Karnes JR, Filippo L et al: Two positive nodes represent a significant cut-off value for cancer specific survival in patients with node positive prostate cancer. A new proposal based on a two-institution experience on 703 consecutive n + patients treated with radical prostatectomy. Eur Urol 2009; **55**: 261.
4. Harke NN, Godes M, Wagner C et al: Fluorescence-supported lymphography and extended pelvic lymph node dissection in robot-assisted radical prostatectomy: a prospective, randomized trial. World J Urol 2018; **36**: 1817.
5. Winter A, Engels S, Goos P et al: Detection of ck19 mRNA using one-step nucleic acid amplification (OSNA) in prostate cancer: preliminary results. J Cancer 2018; **9**: 4611.

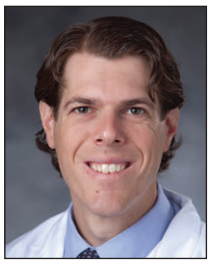
The Significant Yet Unrecognized Role of Bubble Collapse during Laser Lithotripsy


Derek Ho, PhD


Russell Terry, MD


Robert Qi, MD


Glenn Preminger, MD


Michael Lipkin, MD, MBA


Pei Zhong, PhD

Durham, North Carolina

During holmium:yttrium-aluminum-garnet (Ho:YAG) laser lithotripsy (LL) rapid vaporization of fluid at the laser fiber tip results in the formation of an elongated vapor bubble known as the Moses effect. This effect is conventionally believed to facilitate energy delivery and thus promote thermal ablation of the stone. Although variation of pulse settings on stone retropulsion and treatment outcome has been previously investigated,[1,2] the contribution of the bubble to stone damage is often neglected and remains elusive.

In this work, we present evidence supporting a direct contribution of LL induced bubble collapse as a secondary mechanism to stone damage besides the dominant photothermal mechanism widely recognized in the literature.[3,4] This new finding suggests that future development of laser technology and pulse modulation strategy should consider optimization of bubble dynamics during LL to improve stone fragmentation.

Using a clinical Ho:YAG laser lithotripter (H Solvo 35W laser, Dornier MedTech) we compared the laser pulse profile (0.8 J/pulse) measured in air (fig. 1, red line) vs in water (fig. 1, blue line) with the resultant bubble dynamics captured simultaneously by high speed imaging. A light guide (shown at the top of each high speed image frame in fig. 1) placed at 4 mm distance from the laser fiber tip was used to facilitate photodetector measurement and served to mimic a target stone. Three pulse modes (fragmenting, standard and advanced) with increasing pulse duration of 75, 150 and 200 µs, respectively, were examined.

As expected, with minimal absorption of the laser in air no significant difference in pulse energy delivered to the target stone was observed among pulse modes (fig. 2a). In contrast, the energy transmission through water to the stone was delayed by the strong absorption of the laser in water and the resultant vapor bubble formation and expansion (fig. 1) and therefore varied significantly among pulse modes. More laser energy was delivered to the "target stone by longer pulses (fig. 2b).

Next we evaluated stone damage produced by each mode (0.8 J, 10 Hz setting) in BegoStone samples from 1 to 100 pulses with the laser fiber aligned perpendicularly in contact with the stone surface. Damage craters were quantified using an optical coherence tomography system (OQ Labscope, Lumedica). Surprisingly, despite the higher energy delivery efficiency of the longer laser pulses in water the damage craters were smaller in volume than those produced by shorter pulses (fig. 3a). This counterintuitive observation indicates that there may be other potential contributing factors to stone damage in LL besides the presumably dominant photothermal mechanism.[3–5]

We hypothesized that the violent and asymmetric collapse of LL generated bubbles near a stone with potential jet impact and water hammer pressure may create sufficient mechanical stress to erode the stone surface.[6,7] To test this hypothesis we conducted 3 additional experiments. First, we eliminated the bubble contribution to stone damage by treating water saturated samples in air and found that the crater volume was significantly reduced for all modes, especially for the short pulse fragmenting mode (fig. 3b).

Second, we minimized the photothermal contribution to stone damage in water by aligning the laser fiber parallel to the stone surface at a standoff distance of 0.5 mm. A characteristic 4-crater pattern was observed following 100 pulses with the craters coinciding with the locations of the primary and daughter bubble collapse on the stone surface (fig. 4a). Furthermore, after 100 pulses the crater volume in parallel fiber alignment could reach about a third of the value produced by perpendicular fiber alignment in contact with the stone surface (fig. 4b).

Third, we performed photoelastic imaging and observed stress fields formation in the substrate resulting from the LL bubble collapse (fig. 4c). All together, these results suggest that the cavitation (ie the formation, expansion and collapse of bubbles) may represent a significant mechanism (primarily through jet impact and water hammer pressure produced at bubble collapse rather than shock wave emission in the fluid) that contributes significantly to the overall stone damage process during LL.

The role of cavitation in stone damage has traditionally been neglected during Ho:YAG laser lithotripsy, and technology for improving treatment efficiency has been primarily focused on increasing laser energy delivery to the stone.[3–5] However, our results suggest that the LL bubble may play a critical role not only in energy delivery (via the Moses effect) but also in stone damage (via the violent collapse with jet impact) that has not been previously appreciated. In particular, the evolution of damage volume with pulse number (fig. 3a) suggests a multiphase process of

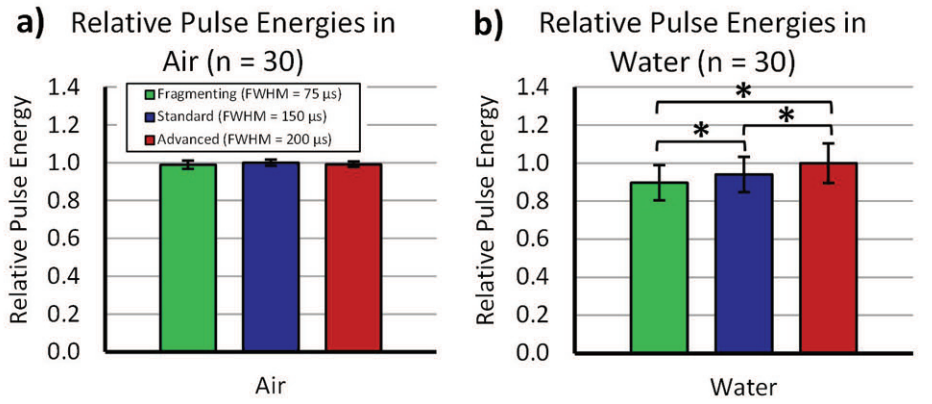


Figure 2. Relative pulse energy measurements for each treatment mode in air (*a*) and through light guide offset from LL fiber tip by 4 mm in water (*b*). Asterisk indicates p <0.05.

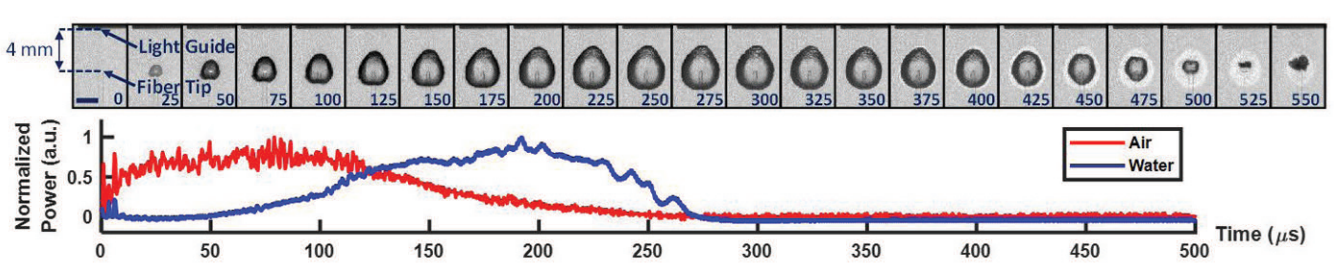


Figure 1. Still frames from high speed video of bubble expansion and collapse (corresponding time in microseconds shown in blue) for standard mode pulse in air (red) and water (blue) synced with video frames above.

▼ Continued on page 16

Modified Diuretic Drainage Time Cutoffs in Antenatal Hydronephrosis

Amr Hodhod, MD

Francis Petrella, MD

John-Paul Capolicchio, MD, FRCSC, FAAP

Montreal, Quebec, Canada

Antenatal hydronephrosis is among the most common congenital anomalies. Isolated hydronephrosis, which is dilatation of the pelvicalyceal system without ureteral dilatation, is a common type of antenatal hydronephrosis. The management of high grade (HG) isolated hydronephrosis has been changing over time. In the past most surgeons had preferred surgical intervention rather than conservative management to avoid renal function deterioration.

In the last few decades many studies have recommended a more conservative approach because most renal units with HG isolated hydronephrosis have preserved renal functions. Therefore, it is now common practice to manage HG isolated hydronephrosis with preserved function conservatively assuming a risk of eventual pyeloplasty in only 23% of cases. The most important issue is to predict whether a renal unit will eventually require surgical intervention.

Although the role of diuretic renogram is well defined and greatly accepted in adults for the management of ureteropelvic junction obstruction, the case is not the same for the pediatric population. Since the introduction of diuretic renogram there has been much debate about its usefulness in the prediction of pyeloplasty. This dilemma is caused by many factors that could affect the estimated renal function and the isotope drainage including immaturity of the renal tissue and hydration status of the patient. Despite these limitations most pediatric urologists and guidelines consider the diuretic renogram an essential tool in the assessment of HG hydronephrosis especially for those with good renal function.

Many articles have attempted to improve the utility of drainage time renogram by studying numerous parameters including gravity assisted drainage times and cortical transit time. However, these trials were not adopted by most health centers due to technical problems. Recently, the spotlight was directed again to the renogram drainage time when Sussman et al demonstrated that post-furosemide half time value ($t_{1/2}$) can be valuable in predicting pyeloplasty.[1] They found that $t_{1/2}$ less than 5 minutes was associated with nonobstructive pathology while $t_{1/2}$ more than 75 minutes perfectly predicted pyeloplasty.

Despite these promising findings there are limitations caused by the selection of patients who require surgical interventions. The first is that Sussman and coauthors found that about half of the surgical group and more than two-thirds of the conservative group had indeterminant drainage ($t_{1/2}$ 5–75 minutes). The second limitation is that the indications of pyeloplasty differ from one institution to another in

▼ Continued on page 16

Bubble Collapse during Laser Lithotripsy

▼ Continued from page 14

stone damage in LL, from an initial rapid growing phase (1 to 10 pulses) in which photothermal effect may be dominant, to a transition phase (10 to 40 pulses) in which cavitation induced damage may become increasing important, to eventually the plateau phase (40 to 100 pulses) in which continued delivery of the laser energy yields diminished return in terms of stone damage.

Further studies are warranted to dissect this complex process in order to optimize laser energy utilization in stone treatment with reduced procedural time. With the growing clinical interest in high frequency, low pulse energy Ho:YAG lasers for dusting and the introduction of the new thulium fiber lasers,[8,9] we anticipate that cavitation induced stone damage will be further accentuated because of the significantly increased total number of bubble events created during such procedures. Overall, strictly focusing on laser energy delivery efficiency and photothermal effects neglects a substantial area for potential improvement. Future development of LL systems and treatment strategies should consider optimizing the effects of cavitation in order to improve the overall treatment efficiency in stone management.

AUA 2020 Virtual Science Best Poster winner. ◆

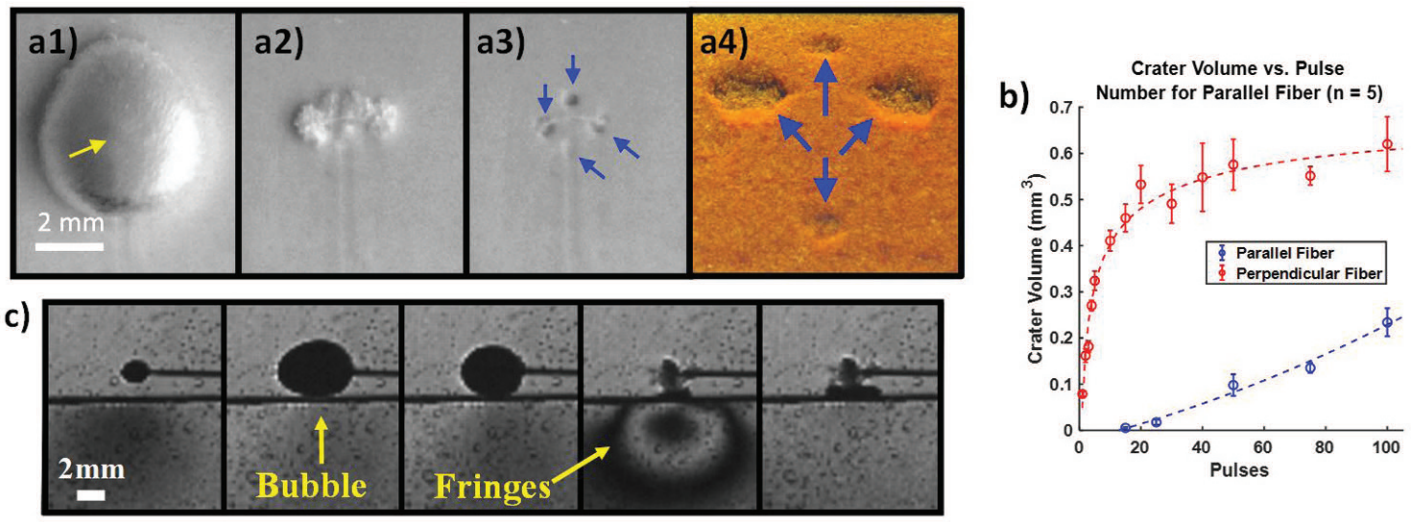


Figure 4. High speed imaging of LL bubble with parallel fiber (*a*) showing maximum bubble expansion (*a1*) with fiber tip location (yellow arrow), bubble collapse (*a2*), resulting stone craters (*a3*), optical coherence tomography 3D reconstruction of 4-crater damage pattern (*a4*) similar to that shown in a3. Crater volumes over 100 pulses (*b*) produced by LL (0.8 J and 10 Hz) with comparison between parallel (at 0.5 mm standoff distance) and perpendicular (in contact with stone surface) fiber alignment. Photoelastic imaging for parallel fiber treatment to substrate surface (*c*). Fringes indicate stress fields production by bubble collapse.

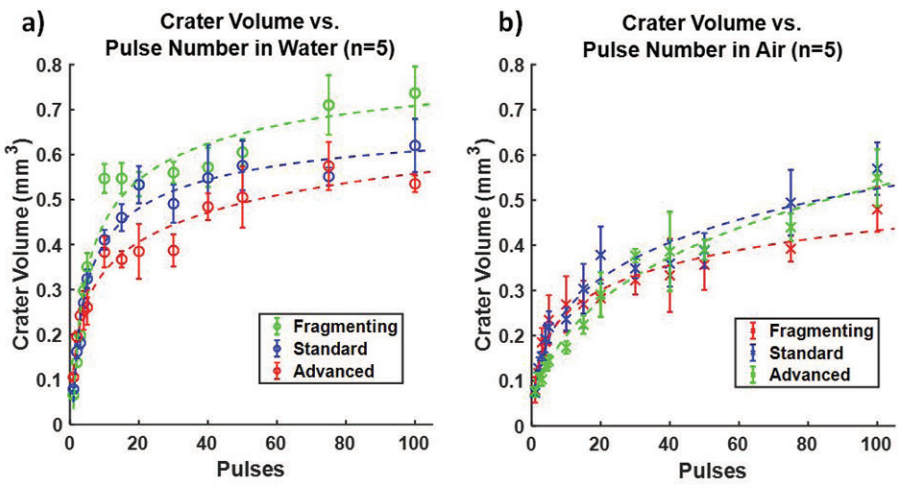


Figure 3. Crater volume of BegoStone samples produced by LL (0.8 J and 10 Hz) in water (*a*) and in air (*b*) for 3 laser pulse modes after different number of pulses (5). Laser fiber was aligned perpendicular and in contact with stone surface before treatment.

1. Aldoukhi AH, Roberts WW, Hall TL et al: Watch your distance: the role of laser fiber working distance on fragmentation when altering pulse width or modulation. J Endourol 2019; **33**: 120.
2. Elhilali MM, Badaan S, Ibrahim A et al: Use of the Moses technology to improve holmium laser lithotripsy outcomes: a preclinical study. J Endourol 2017; **31**: 598.
3. Chan KF, Vassar GJ, Pfefer TJ et al: Holmium:YAG laser lithotripsy: a dominant photothermal ablative mechanism with chemical decomposition of urinary calculi. Lasers Surg Med 1999; **25**: 22.
4. Vassar GJ, Chan KF, Teichman JM et al.: Holmium: YAG lithotripsy: photothermal mechanism. J Endourol 1999; **13**: 181.
5. Aldoukhi AH, Roberts WW, Hall TL et al: Holmium laser lithotripsy in the new stone age: dust or bust? Front Surg 2017; **4**: 57.
6. Crum LA: Cavitation microjets as a contributory mechanism for renal calculi disintegration in ESWL. J Urol 1988; **140**: 1587.
7. Zhong P, Chuong CJ and Preminger G: Propagation of shock waves in elastic solids caused by cavitation microjet impact. II: Application in extracorporeal shock wave lithotripsy. J Acoust Soc Am 1993; **94**: 29.
8. Traxer O and Keller EX: Thulium fiber laser: the new player for kidney stone treatment? A comparison with Holmium:YAG laser. World J Urol 2020; **38**: 1883.
9. Matlaga BR, Chew B, Eisner B et al: Ureteroscopic laser lithotripsy: a review of dusting vs fragmentation with extraction. J Endourol 2018; **32**: 1.

Antenatal Hydronephrosis Draining Time Cutoffs

▼ Continued from page 15

the absence of a gold standard. In our retrospective cohort we tried to validate the modified drainage cutoff while also analyzing the utility of the Global Washout (GW). GW is another renogram parameter that represents the percentage of excreted isotope to the amount taken up by the kidney.

In order to do this we retrospectively reviewed patients who had prenatally detected high grade isolated hydronephrosis from 2004 to 2014. Patients were divided into a pyeloplasty group and a conservative management group. All included patients underwent technetium 99m mercaptoacetyltriglycine (MAG-3) renogram where furosemide was injected after 0 minutes of isotope injection. As proposed by Sussman et al we categorized $t_{½}$ into the 3 groups of less than 5 minutes, greater than 75 minutes and 5–75 minutes (indeterminant group). We used the receiver operating characteristic (ROC) to evaluate the ability of $t_{½}$ and GW in predicting surgical intervention.

In our cohort we collected 142 patients including 84 patients (88 renal units) in the pyeloplasty group and 58 patients (59 renal units) in the control group. A renal unit (1.1%) in the pyeloplasty group had a $t_{½}$ less than 5 minutes whereas 26.2% (23) had $t_{½}$ greater than 75 minutes ($p < 0.001$). In the control group 47.5% (28) of units had $t_{½}$ less than 5 minutes and none had $t_{½}$ greater than 75 minutes ($p < 0.001$). The ROC curve showed that a $t_{½}$ of 5 minutes is associated with 97.7% sensitivity and 50.8% specificity whereas a $t_{½}$ greater than 75 minutes is associated with 100% specificity and 26.1% sensitivity. Analysis of the GW using a ROC curve revealed that a cutoff of 50% GW has 100% specificity and 54.7% sensitivity for pyeloplasty. Notably, the modified drainage cutoff values exist only in 35% of our patients. In the remaining 65% with indeterminant drainage GW was able to successfully predict the line of management in 37% of such units.

According to our results we can conclude that the modified $t_{½}$ criteria is a valid predictor of pyeloplasty in antenatally detected isolated hydronephrosis. Unfortunately, the $t_{½}$ cutoffs of 5 and 75 minutes were beneficial in the prediction of management in only slightly more than a third of renal units. Using GW in addition to $t_{½}$ is beneficial in the predication of management. Therefore, we believe that renogram findings such as GW in addition to the modified drainage time cutoffs would be more beneficial in predicting pyeloplasty.

AUA 2020 Virtual Science Best Poster winner. ◆

1. Sussman RD, Blum ES, Sprague BM et al: Prediction of clinical outcomes in prenatal hydronephrosis: importance of gravity assisted drainage. J Urol 2017; **197**: 838.

Evidence-Based YouTube Streaming Video Intervention in Men's Health




Kassandra E. Zaila, MD | Vadim Osadchiy, MD | Sriram V. Eleswarapu, MD, PhD | Jesse N. Mills, MD

Los Angeles, California

Patients are turning to online streaming video services at alarming rates for health related educational content, profoundly influencing their understanding of pathology, diagnosis and treatment of various health conditions. YouTube, the most popular online video sharing platform, is bridging the gap between communication and knowledge among users and is reaching more than 2 billion diverse users globally. Researchers warn that despite the unprecedented level of access to information, non-evidence-based material and misinformation are widely disseminated on YouTube.[1] The field of urology is not immune. Streaming videos often predate guidelines based care and offer urological information that is biased, commercialized or misinformative.

Recently, streaming videos focused on men's heath have proliferated on YouTube. However, reliable content produced by trained health professionals remains scarce. As a way to combat this lack of reliable data, our large, university-based health system has created a series of evidence-based men's health streaming videos on YouTube. We sought to evaluate the popularity and reach of 6 such videos focused on male factor infertility, men's health and Peyronie's disease. All videos feature a board certified urologist with fellowship training in andrology. Using YouTube analytics viewership characteristics were evaluated to better understand video popularity and reach.

Across the 6 evidence-based men's health streaming videos we found that on average there were 107,747 lifetime views with viewership ranging from 1.2 to 3,124 views per month across 47 countries (table 1). The figure depicts the view counts across the lifespan of each video and highlights that not all videos perform equally over time. Despite a peak viewership of the streaming video "Movember & why you should support men's health" close to the initial release date with decreasing viewership thereafter, all other videos have had rising view counts since the initial release date.

Table 1. Overall YouTube metrics for all 6 men's health streaming videos

	Mean	Range
Video duration (min:sec)	39:41	29:06 to 51:39
No. lifetime views	107,747	303 to 391,812
Watch time (min)	478,791	1,153 to 1,469,613

Warren and colleagues recently showed that YouTube videos featuring physicians were of significantly higher quality and less biased but had lower viewership compared to videos not featuring a physician.[2] While being cognizant that

▼ Continued on page 18

YouTube Intervention in Men's Health

▼ Continued from page 17

prior videos featuring physicians may have had their challenges with successful viewership, our data demonstrate that a health system approach can have tremendous global reach despite not all videos being equally successful in attaining high viewership numbers.

While noting the impressive reach and popularity of our videos, social media analytics tools grant the opportunity to provide granular feedback that can be acted on to enhance video content and viewership including data on watch time and audience retention rate. The mean video duration of all videos was 39 minutes and 41 seconds (39:41), and total watch time was 2.9 million minutes. The total watch time for each video ranged from 1,153 minutes to 1.46 million minutes.

Of note, although video duration ranged from 29:07 to 51:40, actual mean watch time by viewers ranged from 3:45 to 8:30 accounting for an audience retention rate as low as 9%. However, there is no indication that longer videos had lower audience retention rates. In order to optimize future men's health videos other considerations such as content and user engagement may need to be taken into account to increase viewership and retention.

Additionally, users are accessing our health system videos at greater rates through organic traffic via direct YouTube search than through non-organic sources (eg clicking paid advertisements). This increased rate of YouTube search is consistent with the rising trend of individuals directly seeking health information online. Alarmingly, YouTube's algorithm ranks and orders videos based on higher user engagement and popularity regardless of the quality of video content. In doing so the algorithm plays an important role in deciding which content is more readily available to individuals.

Table 2. Video specific YouTube metrics

Video Title	Days Since Upload	Mean Views per Day	Mean Watch Time (min:sec)	Total Video Duration (min:sec)	Audience Retention (%)
"Optimizing male fertility"	1,300	6	5:36	51:40	11
"Vasectomy reversal: Fertility options after vasectomy"	1,297	18	6:19	41:17	15
"3 steps to better men's health"	1,053	5	8:30	39:00	22
"Movember & why you should support men's health"	998	0.3	4:59	29:07	17
"Insight into Peyronie's disease: Cause and treatment for penis curvature"	745	292	5:21	36:41	15
"Improving fertility in men with poor sperm count"	502	781	3:45	40:19	9

Having a clearer understanding of how to better optimize the YouTube algorithm can aid in enhancing user engagement with our videos and can propagate their success. For example, a component that determines ranking by YouTube's search algorithm is the congruency between viewer keyword queries and the keywords tagged by the health system videos.[3] Future investigations should focus on better understanding viewer keyword queries to improve search engine optimization and ensure greater engagement with reliable video content.

Overall, our data demonstrate that video content created by an academic health system has the potential to have extensive reach and popularity. The outcomes of this study signal that the integration between content platforms and health systems can significantly influence the dissemination of accurate and reliable men's health content. As patients increasingly turn to the Internet for health information, health systems and urologists could find it beneficial to leverage high impact social media platforms such as YouTube to share evidence-based urological content.

An expanded version of this work has been published in *Translational Andrology and Urology.*[4]

AUA 2020 Virtual Science Best Poster winner. ◆

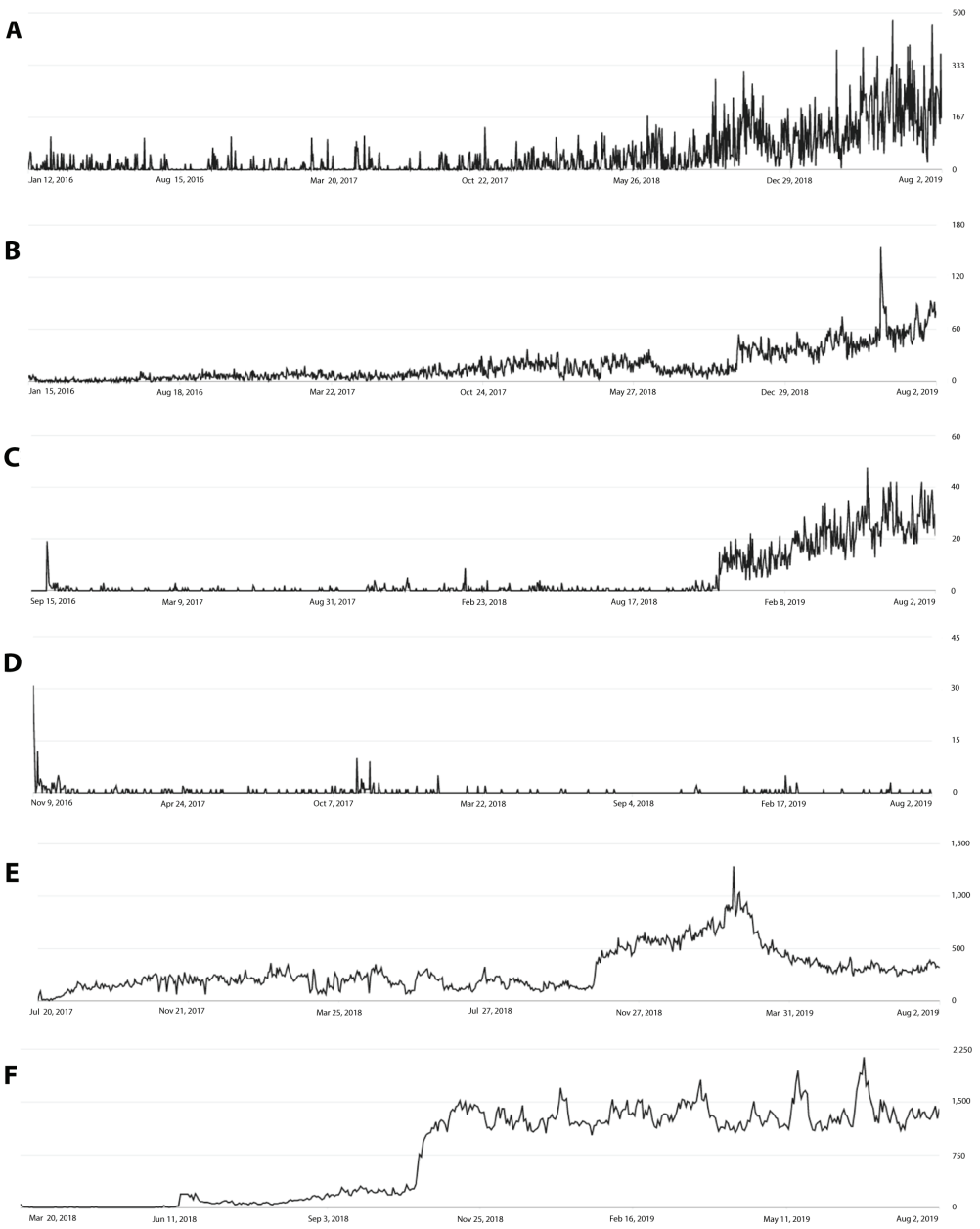


Figure. YouTube video viewer trends comparing number of views across video lifetime, with trends for "Optimizing male fertility" (*A*), "Vasectomy reversal: Fertility options after vasectomy" (*B*), "3 steps to better men's health" (*C*), "Movember & why you should support men's health" (*D*), "Insight into Peyronie's disease: Cause and treatment for penis curvature" (*E*) and "Improving fertility in men with poor sperm count" (*F*).

1. Loeb S, Sengupta S, Butaney M et al: Dissemination of misinformative and biased information about prostate cancer on YouTube. Eur Urol 2019; **75**: 564.
2. Warren C, Shah T, Ward B et al: Evaluation of YouTube videos on male hypogonadism. J Sex Med, suppl., 2020; **17**: S62.
3. Cooper P: How Does the YouTube Algorithm Work? A Guide to Getting More Views. Hootsuite 2019. Available at https://blog.hootsuite.com/how-the-youtube-algorithm-works/. Accessed February 8, 2020.
4. Zaila KE, Osadchiy V, Anderson AS et al: Popularity and worldwide reach of targeted, evidence-based internet streaming video interventions focused on men's health topics. Transl Androl Urol 2020; **9**: 3.

The Emerging Role of Androgens in Reconstructive Urology

Matthias D. Hofer, MD, PhD
Chicago, Illinois

Tissue viability relies on adequate perfusion and limited perfusion can lead to tissue injury including cell death, tissue atrophy or replacement by less metabolically active cells such as fibrocytes resulting in scar formation. This is predominantly important in a postoperative context where wound healing and tissue regeneration is dependent on adequate perfusion. Hence, smoking status, radiation and the presence of diabetes, all of which are associated with (micro-) angiopathies, are complicating factors for any surgery.

The dermatological literature had identified the benefit of estrogen supplementation to increase angiogenesis in dermal wounds, and the use of topical estrogen is common to regenerate vaginal mucosa that has atrophied in response to low estrogen levels. However, the role of androgens for tissue homeostasis and regeneration has been less clearly defined. Pediatric urologists have long supplemented androgens to prepubertal boys prior to hypospadias repairs in order to promote penile growth facilitating the surgery and also to improve outcomes. However, there has been a dispute about the benefit of this practice as an increase in postoperative complications was also observed.

Early work from our group has found in animal experiments that testosterone supplementation in an androgen naïve system such as prepubertal rats increases the inflammatory response after a surgical intervention, in this case a urethroplasty, which may be responsible for an increase in early fistula formation and poor healing in general. While we had also found an increase in tissue angiogenesis, our study interval of 30 days was not long enough to analyze an overall benefit derived from improved angiogenesis and tissue perfusion. Interestingly, in these early studies we noted that in an androgen deprived environment (castrated rats) androgen receptor expression was absent in periurethral tissue, thereby eliminating any androgen mediated angiogenesis, raising the concern that long-term androgen deprivation may be associated with urethral atrophy.

Indeed, we would shortly thereafter find a clinical correlate for our hypothesis. We saw that the rate of artificial urinary sphincter (AUS) erosions appeared to be increased in patients with low testosterone levels. In a subsequent clinical study we were able to demonstrate that hypogonadism conferred a nearly fifteenfold risk of AUS erosions with 90% of men with hypogonadism experiencing erosion within 6 years of AUS insertion.[1] Notably, up to half of the men undergoing AUS placement were found to have low serum testosterone[2] which is greater than twice the prevalence of hypogonadism seen in randomly selected men more than 70 years old in the community emphasizing the scale of this issue. AUS erosions are reported to be as high as 20% and while being the gold standard treatment for male incontinence this may explain why there appears to be some hesitancy among urologists to proceed with AUS implantation for incontinent men.

In urethral tissue from hypogonadal men we found significantly decreased periurethral vascularity and associated reduction in expression of androgen receptor (AR) and angiopoietin-1 receptor (TIE-2) which led us to believe that in hypogonadal men impaired androgen mediated angiogenesis promotes urethral atrophy which subsequently increases the risk for AUS cuff erosions (similar to radiation and prior urethral surgery which all decrease urethral blood supply).[3] This in turn raised the question of whether androgen resupplementation in the form of testosterone replacement therapy (TRT) would be able to mitigate this effect restoring urethral vascular perfusion.

Unlike other risk factors for AUS erosion such as prior radiation therapy, hypogonadism could be reversible with testosterone supplementation thus possibly lowering the erosion rate significantly. Before using this approach clinically we

▼ Continued on page 20

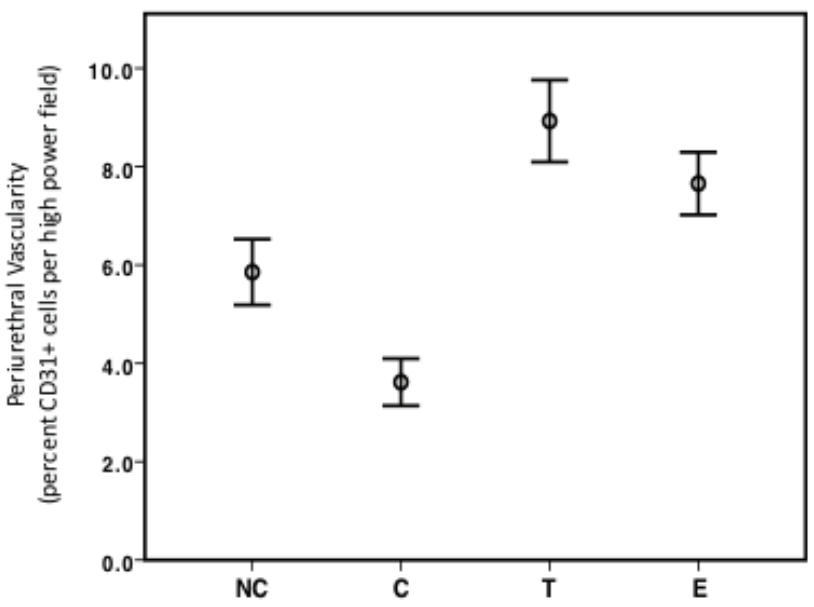


Figure 1. Testosterone and estrogen supplementation significantly increase tissue vascularity as measured by number of CD31 positive cells (marker of endothelial cells). *NC*, noncastrated control rat. *C*, castrated and nonsupplemented rat. *T*, castrated rat with testosterone supplementation. *E*, castrated rat with estrogen supplementation.

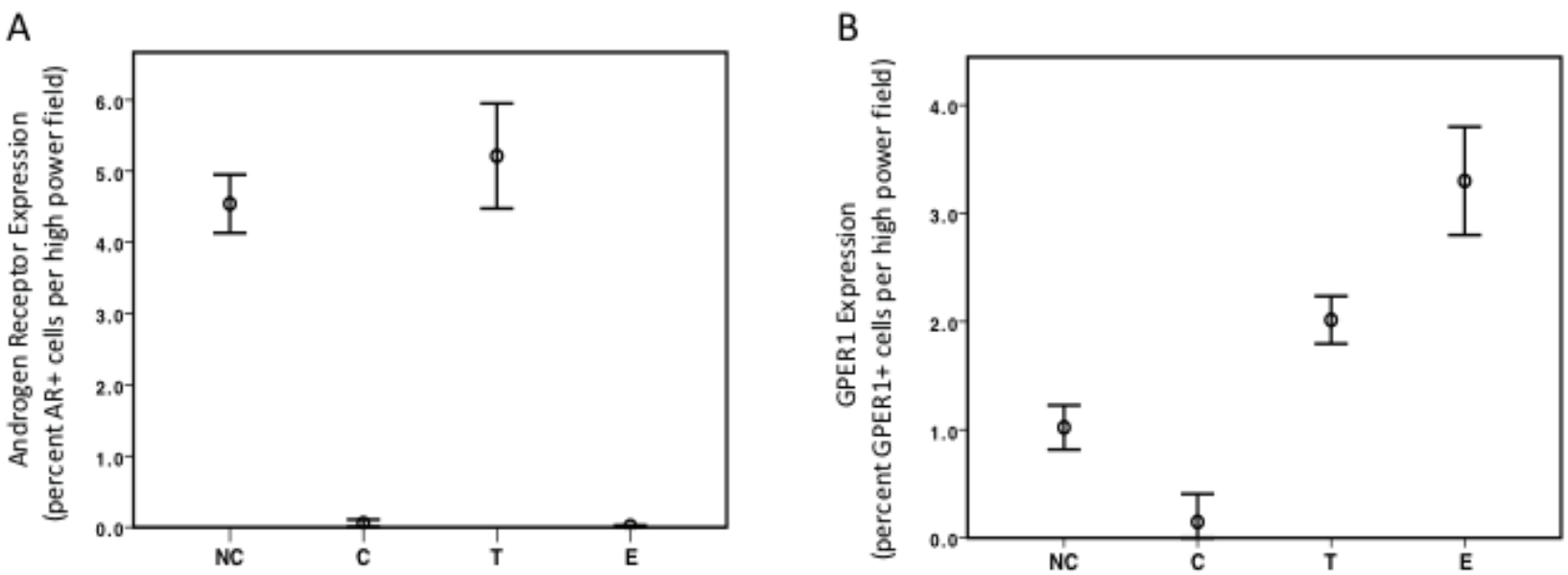


Figure 2. Testosterone supplementation increases AR expression to physiological levels while AR expression is virtually 0 in absence of testosterone (*A*). Estrogen supplementation is associated with upregulation of expression of membrane bound estrogen receptor GPER1 which is also increased in rats receiving testosterone supplementation (*B*). *NC*, noncastrated control rat. *C*, castrated and nonsupplemented rat. *T*, castrated rat with testosterone supplementation. *E*, castrated rat with estrogen supplementation.

Androgens in Reconstructive Urology

▼ Continued from page 19

first wanted to analyze the effect of TRT on urethral vascularity in a rat model as a preclinical study. As TRT can be contraindicated in some men (eg those with detectable prostate specific antigen levels after prostate cancer therapy) we also analyzed the effects of estrogen supplementation in this model.

In this study we found that testosterone and estrogen supplementation in castrated rats led to a significant increase in angiogenesis and periurethral vascularity (fig. 1).[4] In addition, testosterone administration was able to restore androgen receptor expression to the level of noncastrated control rats suggesting generally a reversibility of the effects encountered in association with hypogonadism (fig. 2, *A*).

Our findings demonstrate that the urethral changes in association with low testosterone levels are reversible and that testosterone and estrogen replacement therapy would be appropriate.

Another interesting result was that mechanistically the angiogenetic effects of testosterone supplementation appear to occur via upregulation of TIE-2, an androgen responsive angiopoietin receptor. This could potentially represent a target for further pharmacological therapy circumventing the testosterone-androgen receptor axis in men in whom testosterone administration is contraindicated.

Looking at the mechanics of estrogen induced angiogenesis we were initially not able to find an upregulation of the (nuclear) estrogen receptor in animals receiving estrogen supplementation. However, we found that the membrane bound estrogen receptor GPER1 was upregulated suggesting this to be the target of estrogen. Although this receptor has been found to require the presence of larger amount of estrogens for activation than the nuclear estrogen receptor, resupplementation at physiological levels was sufficient for restoring angiogenesis.

Our findings demonstrate that the urethral changes in association with low testosterone levels are reversible and that testosterone and estrogen replacement therapy would be appropriate. Given the high predominance of low testosterone in patients receiving an AUS and the fifteenfold higher risk of AUS erosion, resupplementation of testosterone or estrogen would be a promising approach to mitigate this risk. The next step in our research endeavor of analyzing the effects of androgens on the urethra is to use the results from our animal studies clinically, and we are currently resupplementing testosterone to select patients with low testosterone at high risk of erosion (such as having had a prior erosion).

In summary, low testosterone affects many aspects of the male body including the urethra, and this can lead to severe consequences such as the increased risk of AUS erosions. However, increasingly understanding the role of androgens for tissue homeostasis allows us to use testosterone supplementation to mitigate these effects, the effectiveness of which we have found in our recent animal experiments, paving the way to introduce this approach clinically. ◆

1. Hofer MD, Morey AF, Sheth K et al: Low serum testosterone level predisposes to artificial urinary sphincter cuff erosion. Urology 2016; **97**: 245.
2. McKibben MJ, Fuentes J, Shakir N et al: Low serum testosterone is present in nearly half of men undergoing artificial urinary sphincter placement. Urology 2018; **118**: 208.
3. Hofer MD, Kapur P, Cordon BH et al: Low testosterone levels result in decreased periurethral vascularity via an androgen receptor-mediated process: pilot study in urethral stricture tissue. Urology 2017; **105**: 175.
4. Yura EM, Bury MI, Chan Y et al: Reversing urethral hypovascularity through testosterone and estrogen supplementation. (Unpublished data)

Office and Surgical Technologies

Bodo Knudsen, MD, FRCSC
Columbus, Ohio

This month I have the pleasure of writing the inaugural column for a new feature in AUA*News* entitled "Office and Surgical Technologies." The goal of the column is to highlight new technologies that are being used in clinical and ambulatory settings to help urologists improve efficiency and deliver better patient care. While some columns may highlight specific equipment that can aid with this end, the goal is to keep the subject matter broad so other things such as software innovations and best practices may also be featured. The goal is to keep the column practical and informative. I am also open to exploring any suggestions you as the reader have regarding topics. Please feel free to reach out to me directly at bodo.knudsen@osumc.edu.

New Single Use Cystoscope

Single use flexible ureteroscopes have been used for several years now in the operating room during surgical stone cases. However, ureteroscopy is a far less commonly performed procedure in the clinic setting. In contrast, cystoscopy with stent removal in the office setting is performed in most urology practices, traditionally with a reusable rigid or flexible cystoscope and a stent grasper. More recently a single use option has become available called Isiris® (Coloplast, see figure). The device is similar in appearance to a flexible cystoscope but houses an integrated stent grasper. It is not meant to be used for surveillance cystoscopy, but rather for stent removal. It connects to a small proprietary portable monitor that acts as the signal processor and display. The overall footprint is much smaller than a standard cystoscopy tower setup. The image quality and vision have been deemed on par with reusable devices.[1]

The question then is why would a urologist incorporate a single use stent removal device into the office setting? I would suggest there are 2 potential reasons, the first being cost certainty. We recently evaluated our costs of performing cystoscopy and stent removal in our outpatient setting in the benign clinic at the Ohio State University Wexner Medical Center. Our model included the purchase cost of the reusable flexible cystoscopes, repair contracts, processing and sterilization costs, and associated labor.

With this model we determined our cost per stent removal with a reusable cystoscope was $161.85. The cost at the time of this study for a single use cystoscope with integrated stent grasper was $200.00. Therefore, the cost was close, but slightly higher for the disposable device, but this was based on a large volume of procedures. It was only after performing 705 or more stent removals a year that the reusable device became more cost efficient.[2] Furthermore, while we currently have our repair costs managed through a large institutional service and repair contract, some practices may not have this option or elect not to participate in such a plan. This can lead to unanticipated costs should scope failure occur prematurely.

A second benefit is flexibility in the clinic where the stent removal procedures are performed. As practices grow there may be a finite number of dedicated procedure rooms for the urologists to use or a limited number of reusable cystoscopes available. Furthermore, sterilization of the reusable cystoscope takes time and human resources. Along with always being available, the Isiris platform is small and mobile. While it can be used in a standard procedure suite, it can also be easily moved into a smaller standard patient examination room. This allows for procedures in rooms in which they have not been traditionally performed, freeing up the dedicated procedure suites for other activities.

I anticipate we will continue to see the growth of single use products in the decade to come. Thoughtful evaluation of costs and practice patterns are needed to determine their benefit as well as any potential negative impact such as environmental waste. The right devices have the potential to be cost effective and improve efficiencies. ◆

Figure.

1. Talso M, Emiliani E, Baghdadi M et al: The new grasper-integrated single use flexible cystoscope for double J stent removal: evaluation of image quality, flow and flexibility. World J Urol 2017; **35**: 1277.
2. Beebe S, Jenkins L, Posid T et al: Single-use grasper integrated flexible cystoscope for stent removal: a micro-costing analysis-based comparison. J Endourol 2020; doi:10.1089/end.2020.0144.

Oncologic Outcomes Following Organ Sparing Surgery for Penile Carcinoma

Andrea Kokorovic, MSc, MD, FRCSC **Curtis Pettaway, MD**

Houston, Texas

Penile cancer is a rare malignancy with only 2,200 cases expected in the United States this year.[1] The traditional management of penile cancer involves organ amputation with partial or total penectomy. These procedures provide excellent oncologic outcomes. However, they are associated with significant functional and cosmetic concerns. Radiotherapy also plays a role, but it is associated with significant treatment related adverse events and may result in higher rates of recurrence.[2]

The adaptation of organ sparing surgery (OSS) has been made possible by multiple recent reports that challenge the requirement for a traditional 2 cm margin following tumor excision.[3–5] Based on newer data it appears that a 1 mm margin may in fact be sufficient.[5] Therefore, OSS has taken on a larger role in the surgical treatment of this rare disease. OSS procedures include laser ablation, Moh's microsurgery, glans resurfacing, wide local excision and glansectomy (partial or total), among others.

We presented our experience with OSS for penile cancer at the American Urological Association 2020 virtual annual meeting with updated results reported here. We described the outcomes of 129 patients undergoing OSS at our institution during a 22-year period. The median age was 61 years old, and 65.1% of our cohort presented with pathological Tis (pTis) or T1a or less disease. Organ sparing procedures in our series were diverse and included wide local excision, partial or total glansectomy, laser ablation monotherapy and laser ablation therapy combined with OSS. The most commonly performed procedure was laser therapy combined with OSS (38.8%). We achieved negative margins intraoperatively with frozen section margins and laser therapy for residual pTis or dysplasia. With this approach we only had 1 positive margin on final pathological analysis in this series.

Using a variety of techniques we found low rates of recurrence with only 17 patients (13.2%) presenting with local recurrence at a median followup of 28 months. The median time to local recurrence was 21 months. We only identified 3 patients with a regional recurrence and none with distant metastases following OSS. Of local recurrences 88.2% were identified within 5 years of surgery, and there was no detrimental impact on overall survival compared to patients without recurrences. Importantly, 76.5% of patients presenting with local recurrence were successfully treated with further penile preservation (OSS or partial penectomy).

We sought to identify risk factors associated with local recurrence. Several clinical factors were examined to predict risk including lesion location, clinical nodal stage, procedure type, grade, pT stage and pN stage. On univariate analysis we identified pathological T stage as the only predictor for local recurrence. Specifically, patients with pTa or pT1a disease had worse recurrence-free survival than those with pTis or pT1b disease or greater (p=0.008). To further delineate this relationship we grouped OSS procedures into excisional vs laser or laser combination and determined that laser treatment of any type was associated with increased local recurrence (p=0.0346). Patients in the pTa/pT1a group were more likely to undergo laser or laser combination therapy than an excisional procedure alone compared to the pT1b or greater group and similar to those in the pTis group (p=0.0087). Importantly, we found that patients with pTa/pT1a disease treated with any laser therapy had worse local recurrence-free survival than those treated with an excisional procedure (p=0.03).

Traditional penile amputation is associated with a detrimental impact on quality of life for patients with penile cancer.[3] Therefore, OSS is an attractive alternative approach to treating this rare malignancy. With recent reports suggesting a 2 cm margin is not necessary for oncologic control, the indications for OSS are expected to evolve over time.[4-6] In keeping with this, several groups have reported on their experiences with OSS and the results overall suggest an increased rate of local recurrence with OSS compared to amputation.[7-11] However, this does not appear to negatively impact overall survival as most recurrences can be salvaged with further surgical treatment. Importantly, in our series we found that laser or laser combination therapy in patients with invasive disease was associated with worse local recurrence-free survival compared to an excisional strategy.

In conclusion, our data demonstrate that OSS using a variety of surgical techniques where negative margins were achieved provided long-term effective local control for localized penile cancer. Most local recurrences can be successfully treated with further penile preserving strategies, and long-term followup is essential. Laser monotherapy or combination therapy should be used with caution in patients with invasive disease. ◆

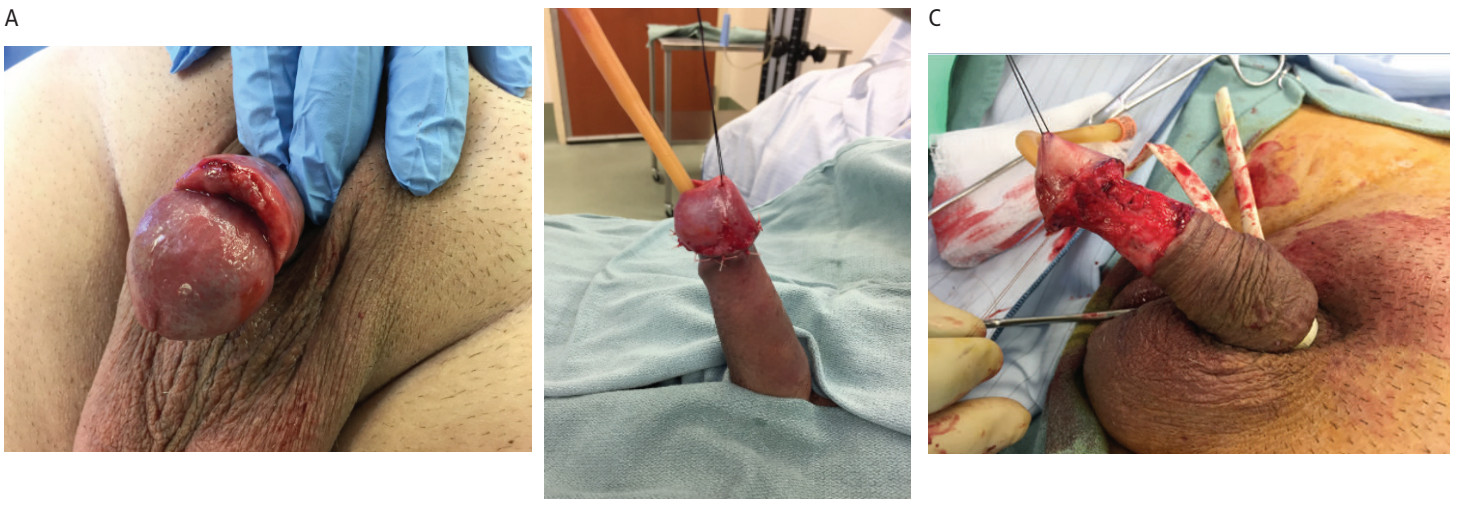


Figure. 54-year-old male with history of biopsy proven T1b squamous carcinoma involving dorsal aspect of foreskin at junction of glans penis (*A*). Patient underwent partial glansectomy with circumcision with excellent cosmesis (*B,C*) and is without evidence of disease at 22 months after procedure.

1. American Cancer Society: Cancer Facts & Figures 2020. Atlanta, Georgia: American Cancer Society 2020.
2. Solsona E, Bahl A, Brandes SB et al: New developments in the treatment of localized penile cancer. Urology, suppl., 2010; **76**: S36 .
3. Kieffer JM, Djajadiningrat R, van Muilekom E et al: Quality of life for patients treated for penile cancer. J Urol 2014; **192**: 1105.
4. Agrawal A, Pai D, Ananthakrishnan N et al: The histological extent of the local spread of carcinoma of the penis and its therapeutic implications. BJU Int 2000; **85**: 299.
5. Minhas S, Kayes O, Hegarty P et al: What surgical resection margins are required to achieve oncological control in men with primary penile cancer? BJU Int 2005; **96**: 1040.
6. Sri D, Sujenthiran A, Lam W et al: A study into the association between local recurrence rates and surgical resection margins in organ-sparing surgery for squamous penile cell cancer. BJU Int 2018; **122**: 576.
7. Feldman AS and McDougal WS: Long-term outcome of excisional organ sparing surgery for carcinoma of the penis. J Urol 2011; **186**: 1303.
8. Veeratterapillay R, Sahadevan K, Aluru P et al: Organ-preserving surgery for penile cancer: description of techniques and surgical outcome. BJU Int 2012; **110**: 1792.
9. Philippou P, Shabbir M, Malone P et al: Conservative surgery for squamous cell carcinoma of the penis: resection margins and long-term oncological control. J Urol 2012; **188**: 803.
10. Baumgarten A, Chipollini J, Yan S et al: Penile sparing surgery for penile cancer: a multicenter, international retrospective cohort. J Urol 2017; **199**: 1233.
11. Leijte JA, Kirrander P, Antonin N et al: Recurrence patterns of squamous cell carcinoma of the penis: recommendations for follow-up based on a two-centre analysis of 700 patients. Eur Urol 2008; **54**: 161.

17-Hydroxyprogesterone: A Serum Biomarker of Intratesticular Testosterone

Thiago Fernandes Negris Lima, MD

Miami, Florida

Ranjith Ramasamy, MD

Premal Patel, MD

Winnipeg, Manitoba, Canada

Testosterone deficiency (TD) is diagnosed with low circulating testosterone (T) in combination with symptoms such as low libido, erectile dysfunction and low energy.[1] Several medications such as selective estrogen receptor modulators (clomiphene citrate [CC]), gonadotropins (human chorionic gonadotropin [hCG]), aromatase inhibitors (anastrozole) and testosterone therapy (TT) can be used to treat TD.[1]

TT is known to cause a decrease in fertility. Therefore, for patients desiring to preserve fertility hCG and CC should be used instead. Monitoring T and evaluating symptoms is important in establishing the success of the treatment. However, measurement of serum T can be imprecise, varying from sample to sample and lab to lab, thereby underscoring the need to evaluate another representative serum biomarker.

Studies of testicular biopsy specimens in men have also found an intratesticular testosterone (ITT) to serum T gradient of roughly a hundredfold.[2,3] However, serum T to ITT correlation is not reliable and can vary among men receiving medications that alter serum ITT, making serum T a poor serum biomarker to titrate these therapies. Additionally, it is impractical to perform testicular aspiration for ITT evaluation. Seeking different methods to assess ITT Amory et al showed that serum 17-hydroxyprogesterone (17-OHP), an intermediate in the production of T from cholesterol through the steroid biosynthesis pathway, had good correlation with aspirated ITT and serum 17-OHP in men treated with human chorionic gonadotropin.[4]

Based on the mechanism of action of hCG, CC and TT, we hypothesized that serum 17-OHP levels for men receiving hCG and/or CC would be similar or higher than our control group (fertile men with T greater than 300 ng/dl). Alternatively, men receiving TT would have suppressed serum 17-OHP levels as compared to baseline due to negative feedback on the hypothalamus–pituitary–gonadal axis.

To test our hypothesis between July 2018 and March 2019 we conducted a cross-sectional analysis of 17-OHP values within 42 fertile men, 30 men receiving hCG/CC and 21 men receiving TT. We showed that all men had normal range (300–1,000 ng/dl) levels of serum T, but serum 17-OHP was found to be lower in men receiving testosterone replacement therapy (TRT) as compared to fertile men (controls) or those receiving hCG/CC (fig. 1).[5]

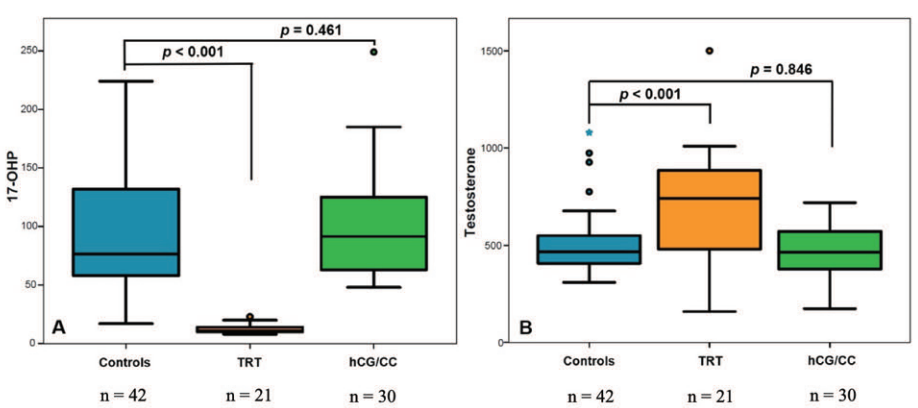


Figure 1. Cross-sectional analysis of serum 17-OHP and T concentrations in fertile controls and men receiving hCG/CC or TRT.

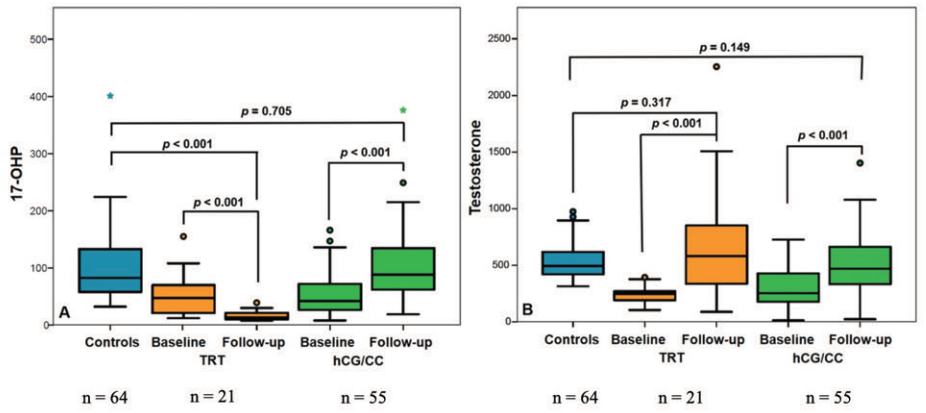


Figure 2. Prospective comparison of serum 17-OHP and T between baseline and followup measurements within men receiving TRT or hCG/CC and fertile controls.

We subsequently conducted a prospective study comparing 55 men treated with agents that increase ITT, either CC or hCG; 21 men treated with agents known for decreasing ITT, such as several types of exogenous TRT; and 64 fertile men who presented at the andrology clinic with complaints other than infertility or testosterone deficiency. When analyzing serum 17-OHP change over a 3-month period from baseline to followup, men who received TT had a significant reduction of 17-OHP to undetectable levels while those treated with hCG/CC presented with a significant increase reaching levels similar to fertile men (fig. 2).[5]

We believe that the measurement of 17-OHP levels may be useful in several clinical scenarios. Firstly, if men with hypogonadotropic hypogonadism or anabolic steroid abuse are seeking to initiate spermatogenesis, 17-OHP levels may be able to indicate when adequate ITT levels are achieved to initiate and support spermatogenesis. Secondly, for men on TT who desire fertility, 17-OHP may be used to ensure maintenance of ITT levels for spermatogenesis. Thirdly, 17-OHP levels can be used to guide hCG/CC therapy for men with oligospermia. In addition, it may identify men with impaired sperm production who may not benefit from hormonal manipulation (ie men with normal ITT pretreatment with oligozoospermia and possible Sertoli cell dysfunction).[3,5]

In conclusion administration of exogenous T resulted in nearly undetectable levels of serum 17-OHP while hCG/CC therapy improved 17-OHP levels in hypogonadal men. Serum 17-OHP was a reliable marker in determining ITT levels in followup therapy, and its use may allow a more precise followup with patients using therapies that alter ITT. Conversely, serum T was not associated with 17-OHP and should not be used to titrate medical therapy for hypogonadal men.

Future studies will need to answer a few questions. What levels of 17-OHP are necessary for spermatogenesis? What cutoff level of 17-OHP better predicts semen improvement parameters after medical therapy? And what levels of serum 17-OHP should be considered normal in the fertile male population?

AUA 2020 Virtual Science Best Poster winner. ◆

1. Carrasquillo R, Chu K and Ramasamy R: Novel therapy for male hypogonadism. Curr Urol Rep 2018; **19**: 63.
2. McLachlan RI, O'Donnell L, Stanton PG et al: Effects of testosterone plus medroxyprogesterone acetate on semen quality, reproductive hormones, and germ cell populations in normal young men. J Clin Endocrinol Metab 2002; **87**: 546.
3. Patel A, Patel P, Bitran J et al: Can serum 17-hydroxyprogesterone and insulin-like factor 3 be used as a marker for evaluation of intratesticular testosterone? Transl Androl Urol, suppl., 2019; **8**: S58.
4. Amory JK, Coviello AD, Page ST et al: Serum 17-hydroxyprogesterone strongly correlates with intratesticular testosterone in gonadotropin-suppressed normal men receiving various dosages of human chorionic gonadotropin. Fertil Steril 2008; **89**: 380.
5. Lima TFN, Patel P, Blachman-Braun R et al: Serum 17-hydroxyprogesterone is a potential biomarker for evaluating intratesticular testosterone. J Urol 2020; **204**: 551.

How Do I Do Office Cystoscopic Fulguration?

Alexander P. Kenigsberg, MD
New York, New York

Yair Lotan, MD
Dallas, Texas

Bladder cancer is associated with a high risk of recurrence and progression to muscle invasive disease. Due to these risks urologists appropriately recommend cystoscopic surveillance for these patients. However, standard office white light surveillance cystoscopy (WLC) is not without its nuances and is far from a perfect surveillance modality.

Many patients with intermediate or high risk bladder cancer receive intravesical therapy to reduce the risk of recurrence per guideline recommendations.[1] Intravesical therapies and the consequent treatment effect on the urothelium create a diagnostic dilemma for urologists. The common finding of a red patch presents a particular challenge as there is a particular fear of missing carcinoma in situ (CIS).

Swinn et al found that only 12% of red patches biopsied in bladder cancer surveillance patients actually represented malignancy,[2] and subsequent studies have shown that the vast majority of red patches biopsied with rigid or flexible cystoscopy are of benign or inflammatory etiology.[3] Another study found that equivocal lesions in patients with prior bladder cancer had a 33% cancer rate as opposed to papillary lesions which were 84% cancerous.[4]

Evidence demonstrates that WLC can miss CIS and small and recurrent tumors relative to blue light cystoscopy (BLC),[5,6] and that the adjunctive testing of cytology is insufficiently sensitive to salvage this modality.[7] A prospective cohort at our institution and USC has demonstrated high sensitivity of in-office cystoscopy biopsy in blue light positive lesions for CIS and nonmuscle invasive bladder cancers, particularly in blue light positive/white light negative lesions.[8]

Comparative studies have demonstrated a cost benefit to in-office cystoscopic biopsies,[9,10] particularly for lesions smaller than 1 cm in size, and shown that patients can tolerate the procedure. Some studies have found that a single operating room transurethral resection of bladder tumor can cost between $3,000 and $6,000.[11] Furthermore, in-office biopsy has the benefit of helping patients avoid the risks of general anesthesia. The cognitive effects of general anesthesia can disproportionately manifest in elderly patients who comprise the majority of bladder cancer diagnoses.[12]

Some practitioners may have hesitation about the notion of in-office biopsies from an oncologic perspective. Complete tumor resection and/or ablation is considered a cornerstone of management in endoscopic treatment of bladder cancer, which has an effect on recurrence-free and progression-free survival.[13] Studies addressing this issue even prior to the widespread use of blue light cystoscopy have found comparable oncologic outcomes between in-office biopsy and fulguration in patients with lesions smaller than 1 cm with low concern for muscle invasive disease.[10] Furthermore, immediate periprocedural intravesical chemotherapy can still be given to these patients as recommended in the guidelines. Most urologist offices are well equipped to administer intravesical therapy and to do so with some regularity. There is a theoretically lower risk of complications with intravesical therapy in this setting than in the perioperative setting given the use of a small biopsy forceps rather than a cutting resection loop, which could perforate the bladder.

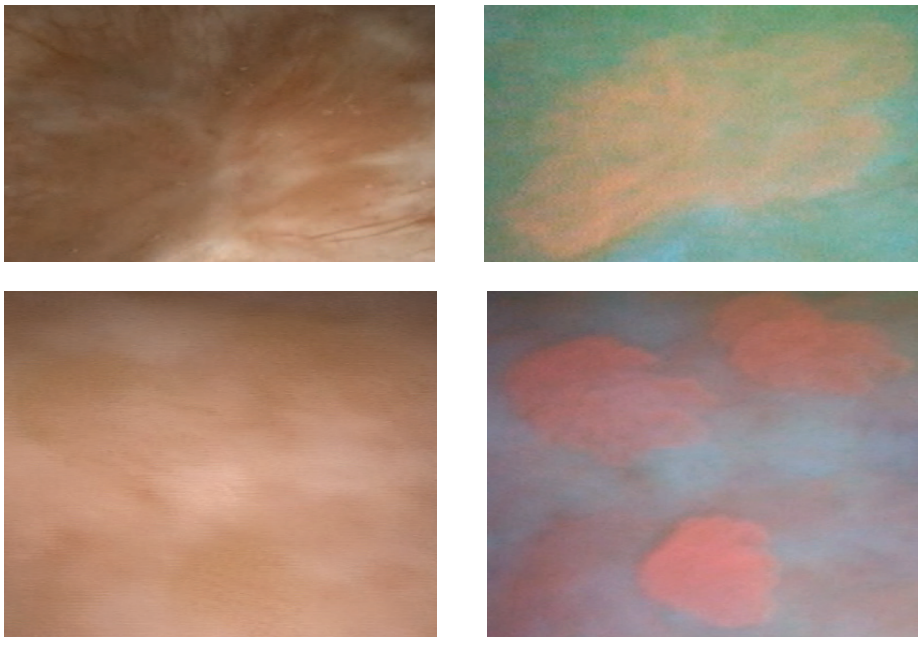


Figure 1. Cystoscopic lesions viewed under WLC (left) and BLC (right).

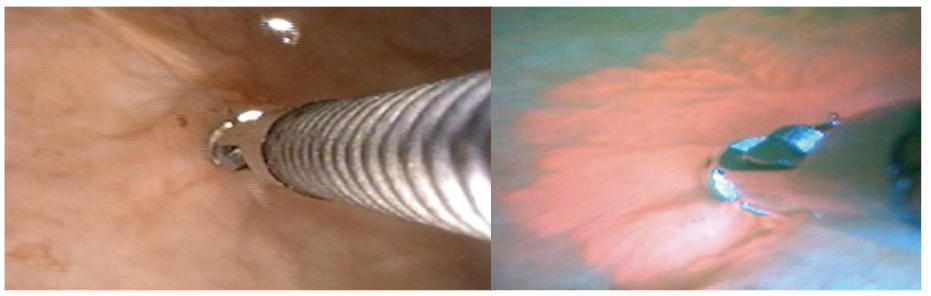


Figure 2. Flexible cystoscopic biopsies performed under WLC (left) and BLC (right).

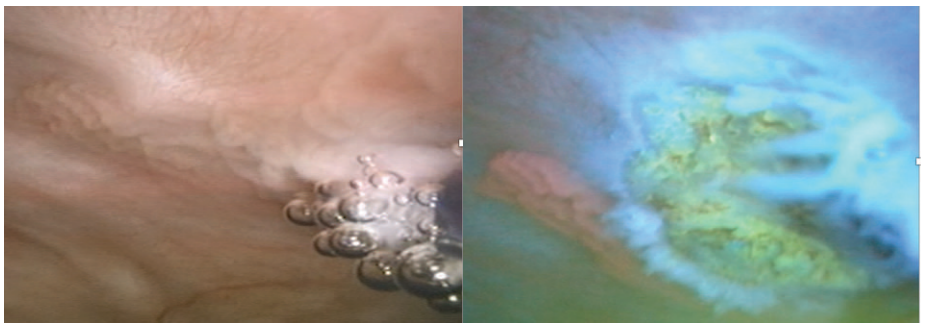


Figure 3. Evaluating areas adjacent to biopsy site under WLC (left) and BLC (right).

For a well selected patient in-office cystoscopic biopsy and fulguration have significant benefits. But the question remains for many urologists of how to set up practices to optimally perform in-office biopsies. In our practice the patient is checked in and screened similarly to any patient undergoing cystoscopy. If the biopsy is performed with blue light flexible cystoscopy they arrive 1 hour before cystoscopy and hexaminolevulinate is instilled per established protocols.[6] We also instill 10 cc of 1% lidocaine solution at this time and allow it to dwell while the patient is returned to the waiting room.

After 1 hour the patient voids, and is brought to the procedure room and draped in the usual fashion for office cystoscopy with a 16Fr flexible cystoscope. Sterile water is the preferred fluid for the procedure. A systematic WLC is performed followed by a systematic BLC. Lesions that are indeterminate on white light can be immediately viewed under blue light settings to evaluate for areas of enhancement under blue light (fig. 1).

Flexible cold cup biopsy forceps can be used through the cystoscope to biopsy under WLC or BLC settings (fig. 2). We then remove the cystoscope with the biopsy forceps still in place out of the scope to avoid losing the specimen in the working channel. If there are several papillary lesions the cystoscope is reinserted and the lesions removed sequentially. A flexible bugbee cautery is then introduced through the working channel and used to fulgurate the biopsy sites. The energy setting used for coagulation is 20W.

Transitioning between WLC and BLC can allow the urologist to determine if there are remaining adjacent areas that must be cauterized at this time (fig. 3). A repeat systematic WLC and BLC can be performed after all lesions are believed to have been addressed to ensure completeness of the fulguration. The urologist may then empty the bladder slowly under direct vision to ensure adequate hemostasis. If there is a plan to instill intravesical chemotherapy a sterile catheter

▼ Continued on page 25

Office Cystoscopic Fulguration

▼ Continued from page 24

is inserted after the procedure and the chemotherapy is instilled.

Given oncologic, cost, safety and tolerability findings, office biopsy is an important option for many patients on bladder cancer surveillance, particularly those with red patches in whom tissue diagnosis is necessary to distinguish between benign/inflammatory lesions and high grade disease such as CIS. Furthermore, this technique is useful for patients with low grade noninvasive bladder cancers with small papillary tumors. However, patient selection is critical. If there is a larger tumor burden the small amount of tissue sampled may be insufficient for diagnosis or staging. While office biopsy will often yield lamina propria it is not an optimal staging modality and muscle is rarely obtained. In addition, while it is largely tolerated it can be quite uncomfortable for those with bladder neck and trigone lesions. These patients may prefer an anesthetic.

Despite its limitations office biopsy is feasible, cost-effective, oncologically reasonable and has a low risk of complications. Early experience with blue light flexible cystoscopy in this setting has improved detection of high grade disease and improves office biopsy and fulguration. Further studies are needed to evaluate cost and determine the optimal patient for office blue light cystoscopy, biopsy and fulguration. ◆

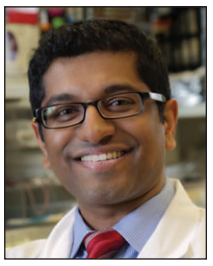
1. Chang SS, Boorjian SA, Chou R et al: Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline. J Urol 2016; **196**: 1021.
2. Swinn MJ, Walker MM, Harbin LJ et al: Biopsy of the red patch at cystoscopy: is it worthwhile? Eur Urol 2004; **45**: 471.
3. Nkwam N, Trecarten S, Momcilovic S et al: Isolated red patches seen during endoscopic surveillance of bladder cancer: incidence of malignancy and when should we biopsy? J Endourol 2018; **32**: 324.
4. Svatek RS, Lee D and Lotan Y: Correlation of office-based cystoscopy and cytology with histologic diagnosis: how good is the reference standard? Urology 2005; **66**: 65.
5. Jocham D, Witjes F, Wagner S et al: Improved detection and treatment of bladder cancer using hexaminolevulinate imaging: a prospective, phase III multicenter study. J Urol 2005; **174**: 862.
6. Daneshmand S, Patel S, Lotan Y et al: Efficacy and safety of blue light flexible cystoscopy with hexaminolevulinate in the surveillance of bladder cancer: a phase III, comparative, multicenter study. J Urol 2018; **199**: 1158.
7. Freifeld Y and Lotan Y: Effect of blue light cystoscopy on contemporary performance of urine cytology. BJU Int 2019; 124: 251.
8. Lotan Y, Chaplin I, Ahmadi H et al: Prospective evaluation of blue light flexible cystoscopy with hexaminolevulinate in non-muscle-invasive bladder cancer. BJU Int 2020; doi:10.1111/bju.15166.
9. Park DS, Hwang JH, Gong IH et al: An analysis of the efficacy, safety, and cost-effectiveness of fulguration under local anesthesia for small-sized recurrent masses: a comparative analysis to transurethral resection of bladder tumors in a matched cohort. J Endourol 2013; **27**: 1240.
10. Al Hussein Al Awamlh B, Lee R, Chughtai B et al: A cost-effectiveness analysis of management of low-risk non-muscle-invasive bladder cancer using office-based fulguration. Urology 2015; **85**: 381.
11. Svatek RS, Hollenbeck BK, Holmang S et al: The economics of bladder cancer: costs and considerations of caring for this disease. Eur Urol 2014; **66**: 253.
12. Wu L, Zhao H, Weng H et al: Lasting effects of general anesthetics on the brain in the young and elderly: "mixed picture" of neurotoxicity, neuroprotection and cognitive impairment. J Anesth 2019; **33**: 321.
13. Babjuk M, Bohle A, Burger M et al: EAU guidelines on non-muscle-invasive urothelial carcinoma of the bladder: update 2016. Eur Urol 2017; **71**: 447.

Measuring the Impact of a Physician Led Collaborative on the Quality of Prostate Cancer Care: 7 Years of Making MUSIC

Mahin Mirza, MPH
Ann Arbor, Michigan

Susan Linsell, MSA
Ann Arbor, Michigan

Ji Qi, MS
Ann Arbor, Michigan



Arvin George, MD
Ann Arbor, Michigan

Khurshid Ghani, MBChB, MS, FRCS
Ann Arbor, Michigan

James Montie, MD
Ann Arbor, Michigan

David Miller, MD, MPH
Ann Arbor, Michigan

Richard Sarle, MD
Lansing, Michigan

Beginning in 2012 the Michigan Urological Surgery Improvement Collaborative (MUSIC) endeavored to build on the success of the Collaborative Quality Initiatives program of Blue Cross Blue Shield of Michigan and improve the quality of urological care for patients in Michigan with an initial focus on prostate cancer (PCa).

MUSIC is comprised of more than 250 urologists representing 90% of urologists in Michigan. Prospective data collection began in 2012 with more than 77,000 patients with prostate biopsy and more than 44,000 patients with PCa in the registry to date. From 2012 to 2018 efforts to improve PCa care included reducing prostate biopsy related infectious hospitalizations, optimizing the use of radiographic staging (ie computerized tomography [CT] scan and/or bone scan) for men with newly diagnosed PCa, enhancing treatment appropriateness for patients with favorable risk PCa (ie Gleason 3+3 or low volume Gleason 3+4) and establishing the MUSIC patient reported outcomes (PRO) program, an electronic infrastructure for measuring and improving long-term urinary and sexual functional outcomes after radical prostatectomy (RP).

Physician led collaboratives can positively contribute to better health care.[1,2] Through the years MUSIC has proved itself to be successful in its efforts. In the investigation of prostate biopsy related hospitalizations across diverse urology practices MUSIC discovered that most of the events resulted from serious infections with fluoroquinolone resistant bacteria. To address this issue and reduce the risk of infection due to fluoroquinolone resistant bacteria MUSIC developed 2 prophylactic pathways.

The first pathway involved rectal swab cultures before prostate biopsy to identify the presence of any fluoroquinolone resistant organisms and to allow the subsequent tailoring of antibiotic prophylaxis with culture directed agents. The second pathway uses augmented antibiotics to broaden coverage in the event a patient harbors fluoroquinolone resistant organisms. MUSIC also created a prostate biopsy checklist that helps to capture patient risk factors that may increase the risk for a complication after biopsy. For patients who have a greater risk of infection a urologist ideally could modify the timing, dosing and route of prophylactic antibiotic administration to further reduce the risk of infection.

As a result of these combined efforts from 2012 to 2018 the overall rate of prostate biopsy

▼ Continued on page 26

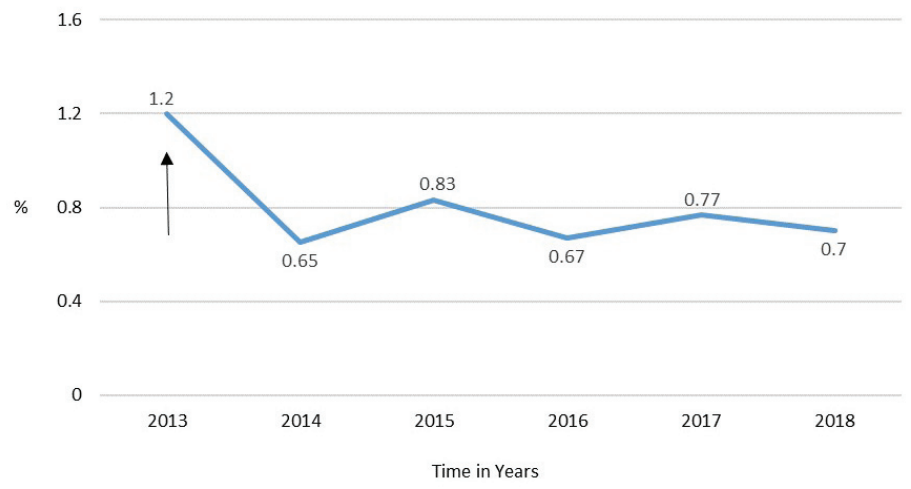


Figure 1. Biopsy related infectious hospitalizations.

Measuring Impact of MUSIC

▼ Continued from page 25

related infectious hospitalizations decreased from 1.2% before intervention to 0.7% after intervention (p <0.001) representing the avoidance of 280 hospitalizations (fig. 1). The next initiative for prostate biopsy is to increase the use of transperineal biopsies in the office under local anesthesia to further reduce infection rates while ensuring that PCa detection remains high.

In an effort to optimize the radiographic staging of newly diagnosed patients with localized PCa MUSIC provided feedback on current performance, reviewed current guidelines and disseminated best practices.[3] For patients with low risk PCa when radiographic staging is non-indicated (ie prostate specific antigen 20 or less, Gleason less than 8 or clinical T stage less than cT3) the use of bone scan and CT scan decreased from 16.4% to 5.9% (p <0.001). This change resulted in approximately 1,750 patients avoiding inappropriate imaging. For patients with intermediate and high risk PCa MUSIC developed and implemented statewide specific, evidence-based appropriateness criteria for staging bone scan and/or CT scan.

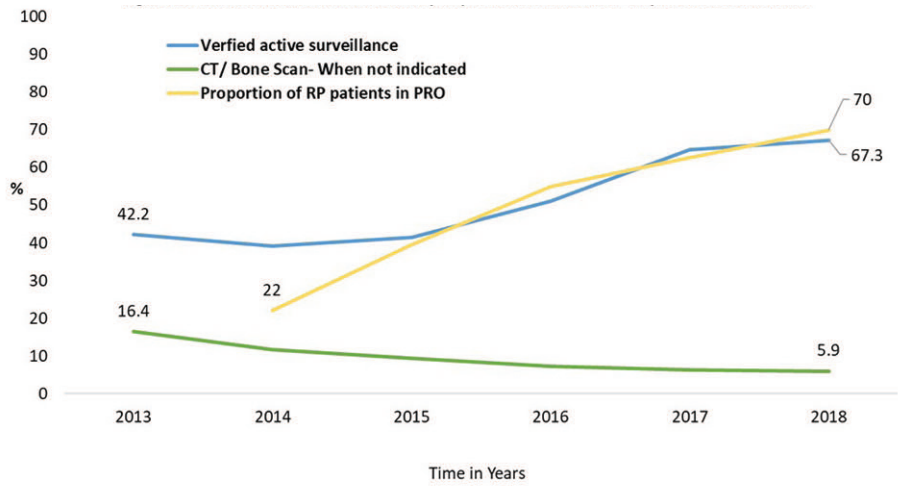


Figure 2. MUSIC prostate related quality improvement initiatives' improvement over time.

In other work MUSIC developed a systematic approach or roadmap for the management of men with favorable risk, early stage PCa and recommended that these men consider active surveillance as a management option.[4] For patients with favorable risk PCa verified active surveillance from 2013 to 2018 increased from 42.2% to 67.3% (p <0.001), equivalent to 1,600 patients avoiding initial definitive treatment where its benefits are less apparent.

With regard to improving patient outcomes after RP the PRO program provides an innovative infrastructure for assessing functional status and health related quality of life before and after RP. The proportion of patients who had undergone RP enrolled in PRO from 2014 to 2018 increased from 22.0% to 70.0% (p <0.001), and MUSIC has PRO data on more than 8,700 men after radical prostatectomy (fig. 2).

By collecting clinically credible data, comparing performance among our peers, sharing best practices with collaborative learning and implementing changes in clinical behavior, MUSIC is enhancing the quality, value and outcomes of care for patients with prostate cancer in Michigan. ◆

1. Luckenbaugh AN and Auffenberg GB: Leveraging the clinical collaborative model to drive value improvement. Curr Opin Urol 2018; **28**: 348.
2. Luckenbaugh AN, Miller DC and Ghani KR: Collaborative quality improvement. Curr Opin Urol 2017; **27**: 395.
3. Hurley P, Dhir A, Gao Y et al: A statewide intervention improves appropriate imaging in localized prostate cancer. J Urol 2017; **197**: 1222.
4. Auffenberg GB, Lane BR, Linsell S et al: A roadmap for improving the management of favorable risk prostate cancer. J Urol 2017; **198**: 1220.

A Bench Model for Measuring Intrapelvic Pressure during Ureteroscopy



Anuj U. Patel, MD **Jeffrey Plott, PhD** **Khurshid R. Ghani, MBChB, MS, FRCS**

Ann Arbor, Michigan

Flexible ureteroscopy (URS) with laser lithotripsy to treat upper urinary tract stones is a mainstay of endourological practice. During these procedures irrigation allows for distension of the collecting system and visualization through stone debris. Sometimes high irrigation flow rates may be necessary to ensure sufficient visibility, especially when performing a dusting laser technique.

When performing URS without a ureteral access sheath higher pressure irrigation conditions may raise the intrapelvic pressure (IPP), which is becoming a recognized risk factor for pain and infectious complications.[1,2] Infectious complications are thought to occur through pyelovenous backflow, which has been shown to occur at a minimum pressure of 40 cmH_2O, a value that can be easily surpassed during flexible URS.[3] As such, understanding the variation of IPP during URS under different conditions is a continuing unmet need with the potential to improve clinical care.

To date, studies of IPP have been conducted in a number of model types including mathematical, in vitro, ex vivo porcine, in vivo porcine, ex vivo human and in vivo human kidney models.[4] Each model type has advantages and disadvantages (fig. 1). Of these, in vitro models are valuable due to their ability to permit easy, replicable and repeated bench testing without the need for tissue handling. However, past studies of in vitro models lacked realistic intrarenal anatomy and were also unable to quantitatively match IPPs of in vivo kidneys, making them limited in application. Our objective was to create an anatomically accurate in vitro kidney model that can provide IPP profiles similar to in vivo conditions. This type of model can permit bench studies of new techniques and technologies and their impact on IPP.

We modified an anatomical, synthetic kidney ureter model obtained from Simagine Health (Seattle, Washington). This model's anatomy was constructed from computerized tomography data of a patient that were digitally recreated and 3D printed into a mold around which the model was constructed. As a result the model's intrarenal anatomy is quite realistic and

▼ Continued on page 28

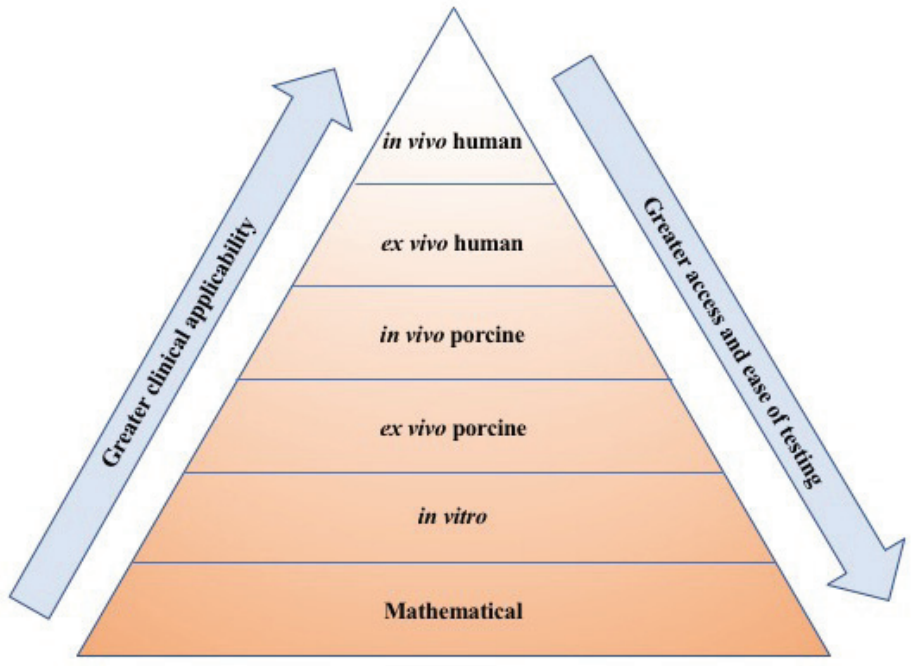


Figure 1. Advantages and disadvantages of different types of models used to study IPP.

RADIOLOGY *Corner*

Bull's Eye Sign after Renal Trauma

Sorena Keihani, MD, MSCI

Jeremy B. Myers, MD, FACS
Associate Editor, AUANews

Salt Lake City, Utah

Case Presentation

A 33-year-old man was transferred to the emergency department with hypotension and tachycardia after crush injury to his abdomen and pelvis. After initial fluid and blood product resuscitation computerized tomography (CT) scan showed multiple injuries including splenic, colon and left renal lacerations. A grade IV renal injury with segmental devascularizations and urinary extravasation was diagnosed. Extravasation of urine down the sheath of the ureter with lack of intraluminal contrast material created a bull's eye appearance on the delayed phase of the CT scan (fig. 1).[1] This suggested complete ureteropelvic junction (UPJ) disruption, which was confirmed upon retrograde ureteropyelography (fig. 2, *A*) and coiling of the ureteral stent outside of the renal pelvis.

The patient underwent laparotomy for management of concomitant injuries and the decision was made for early surgical repair of the UPJ disruption using a parachute end-to-end anastomosis technique with ureteral stent placement. Followup retrograde pyelography and renal function scan at 8 months showed well-healed UPJ (fig. 2, *B*) and differential renal function of 35% for the injured kidney. Creatinine level at 3 years after injury was 1.1 mg/dl.

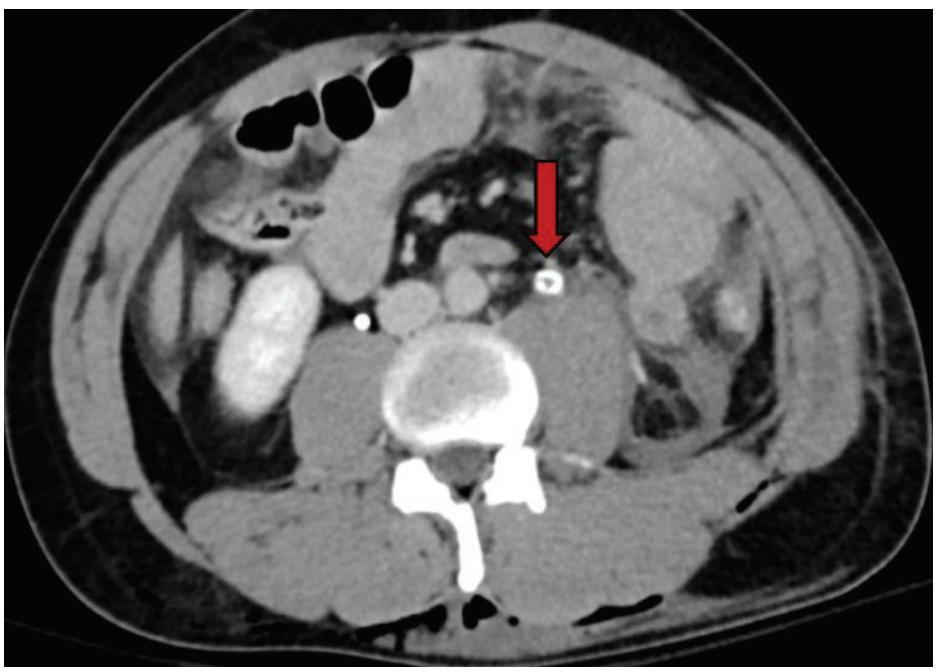


Figure 1. Bull's eye sign in complete UPJ disruption. Periureteral extravasation of contrast material during delayed excretory phase with lack of intraluminal contrast material in ipsilateral ureter distal to injury.

Discussion

Ureteral injury and UPJ disruption are rare injury patterns after blunt abdominal trauma. A delayed excretory phase CT scan with adequate contrast excretion into the collecting system is required for accurate diagnosis of collecting system injuries.[2] Lack of contrast material in the ureteral lumen with extravasation of the contrast around the ureter on the injured side creates the bull's eye sign on the CT scan.[1] This radiological finding is highly suggestive of complete disruption of the UPJ and warrants further assessment with retrograde imaging for early diagnosis.

Complete UPJ disruptions are often missed during the initial assessment given the presence of multiple concomitant injuries and also lack of hematuria in about a third of cases.[3] Late diagnosis is associated with higher complication and nephrectomy rates.[4] Although most cases of urinary extravasation and partial ureteral injuries can be managed conservatively or using a ureteral stent, a bull's eye appearance is more suggestive of complete disruption and the possible need for open interventions.

The AUA urotrauma guidelines are vague on management of UPJ disruptions but recommend early ureteral injury repair for stable patients and nephrostomy tube placement with delayed repair in unstable patients.[5] However, fibrotic tissue formation from urine leak can make accessing the renal hilum and the transected ureter challenging for a delayed repair.

Differential diagnoses include partial ureteral or renal pelvis injuries and blood clots in the collecting system. Filling defects from intraluminal blood clots can mimic a bull's eye appearance (fig. 3) but intraluminal contrast can usually be seen distal to the filling defect and can be differentiated from UPJ disruption using retrograde ureteropyelography.

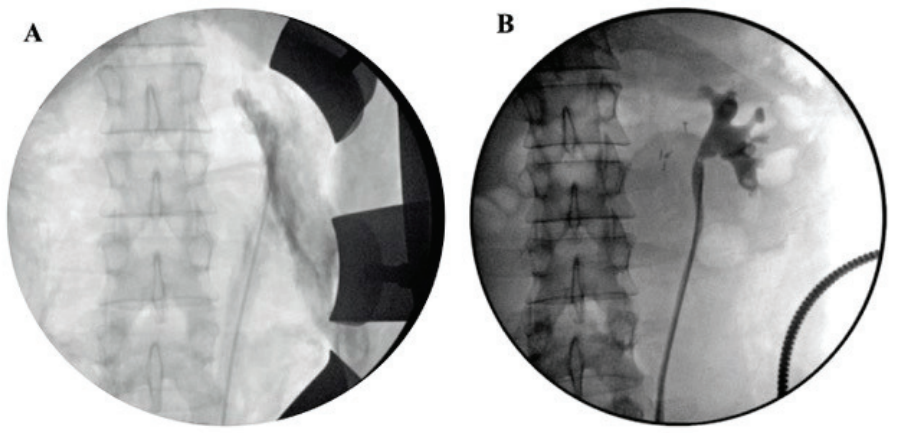


Figure 2. Retrograde ureteropyelography before repair showing complete UPJ disruption with contrast extravasation (*A*) and 8-month followup after repair showing well-healed patent UPJ (*B*).

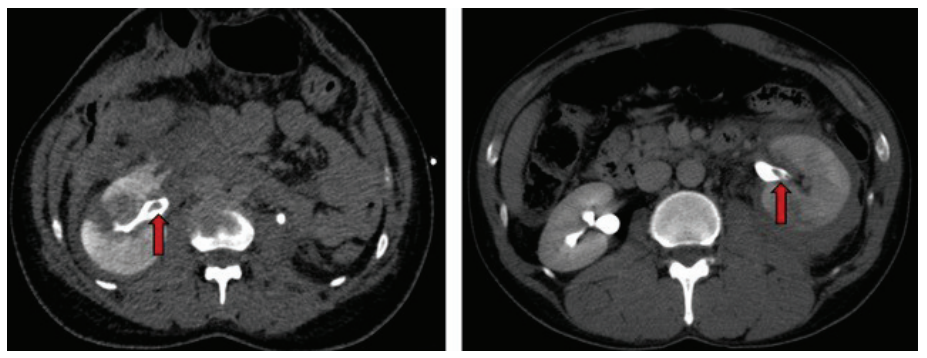


Figure 3. Blood clots in collecting system after renal trauma in 2 patients mimicking bull's eye sign. In both cases distal parts of ureters were visualized with intraluminal contrast material (not shown).

Conclusion

Periureteral urinary extravasation with lack of intraluminal contrast in the distal ipsilateral ureter can be seen as the bull's eye sign in the excretory phase of a CT scan. This finding can help in early identification of complete UPJ disruption and should trigger obtaining retrograde ureteropyelography imaging for further assessment and potentially early intervention. ◆

1. Donnenfeld SR, Keihani S, Young JB et al: The bull's-eye sign: a hallmark radiologic sign of complete ureteropelvic junction disruption after blunt renal trauma. Urol Case Rep 2018; **17**: 91.
2. Keihani S, Anderson RE, Hotaling JM et al: Diagnosis and management of urinary extravasation after high-grade renal trauma. Nat Rev Urol 2019; **16**: 54.
3. Ekeh AP, Patterson L, Anderson G et al: Isolated traumatic disruption of the ureteropelvic junction in a patient with a solitary kidney. J Trauma 2002; **52**: 167.
4. Boone TB, Gilling PJ and Husmann DA: Ureteropelvic junction disruption following blunt abdominal trauma. J Urol 1993; **150**: 33.
5. Morey AF, Brandes S, Dugi DD 3rd et al: Urotrauma: AUA guideline. J Urol 2014, **192**: 327.

Intrapelvic Pressure during Ureteroscopy

▼ Continued from page 26

allows for ureteroscopic maneuvering. Additionally, the silicone material from which this model is made allows for greater flexibility than previously studied in vitro models made from plastic.

As in vivo kidneys experience ureteral irrigant outflow during URS we hypothesized that simulating and controlling this fluid outflow would be critical to creating realistic IPPs. We achieved this by modifying the kidney model. First, we partially occluded the distal ureter with silicone to allow for a fluid tight seal around inserted ureteroscopes and ureteral access sheaths (UASs). We also added a screw type Tuohy-Borst valve through a hole created in the renal pelvis. We then placed a fiber optic pressure sensor through the Tuohy-Borst valve until reaching the renal pelvis (fig. 2). With these changes we were able to control the rate of irrigant fluid outflow through the Tuohy-Borst valve by loosening and tightening the valve and could calibrate the fluid outflow to provide a pressure reading equivalent to what occurs in in vivo human kidneys during URS.

With the model calibrated we studied IPP by measuring IPPs with a ureteroscope in the model and a laser fiber inserted through the working channel under varying irrigation pressures from 61 to 193 cmH_2O without and with different size UASs (11/13Fr, 13/15Fr). Consistent with clinical findings we found that increasing irrigation pressure and/or decreasing UAS size resulted in higher IPP values (fig. 3).

We then compared our data to prior in vivo and ex vivo studies of IPP that used similar experimental conditions and found that values from the model were similar to published data. Specifically, we found that IPP surpassed 40 cmH_2O at irrigation pressures 153 cmH_2O or greater when a UAS is not used. Use of an 11/13Fr or 13/15Fr UAS kept IPP 40 cmH_2O or less for irrigation pressures up to 193 cmH_2O. In short, our model redemonstrates that in order to keep IPP low clinicians should use a UAS and/or low irrigation pressures.

A distinct advantage of this model is the realistic intrarenal anatomy, which can allow for study of how IPP is influenced by ureteroscopic maneuvering, intermittent irrigation boluses and instrumentation such as basketing and laser lithotripsy. While in vitro studies of IPP cannot replace in vivo studies, this model could allow for a standardized approach to bench testing of new technologies aimed at measuring and mitigating rises in IPP during URS. In the future we hope to improve upon the model by exploring materials with more realistic tissue compliance as well as developing a more streamlined calibration method. ◆

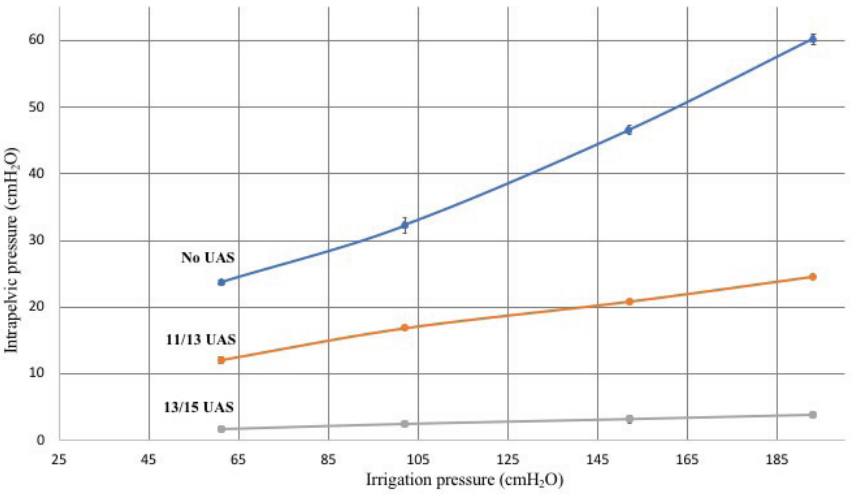


Figure 3. IPP measurements at varying irrigation pressures and UAS conditions.

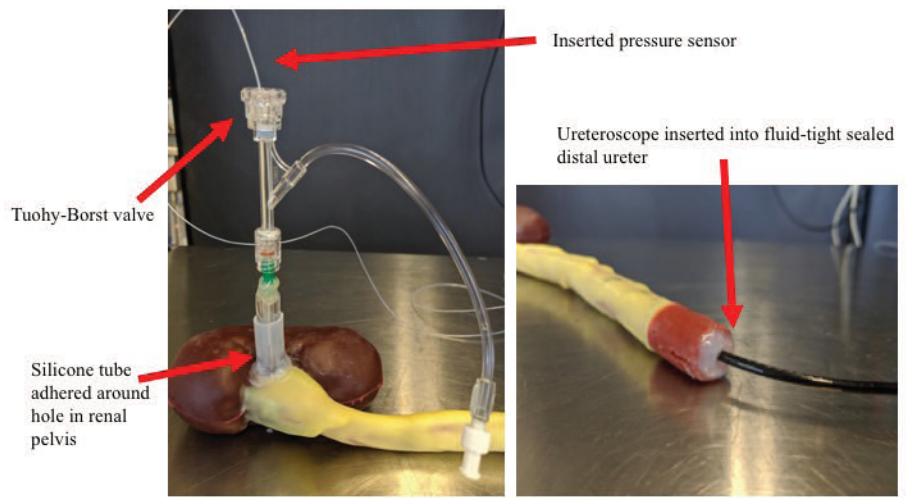


Figure 2. Modifications made to kidney model.

1. Tokas T, Skolarikos A and Nagele U: Pressure matters: intrarenal pressures during normal and pathological conditions, and impact of increased values to renal physiology. World J Urol. 2019; **37**: 125.
2. Alsyouf M, Abourbih S, West B et al: Elevated renal pelvic pressures during percutaneous nephrolithotomy risk higher postoperative pain and longer hospital stay. J Urol 2018; **199**: 193.
3. Doizi S, Letendre J, Cloutier J et al: Continuous monitoring of intrapelvic pressure during flexible ureteroscopy using a sensor wire: a pilot study. World J Urol 2020; doi:10.1007/s00345-020-03216-w.
4. Tokas T, Herrmann TRW and Nagele U: Pressure matters 2: intrarenal pressure ranges during upper-tract endourological procedures. World J Urol 2019; **37**: 133.

Global Surgery in Urology Training: A Resident Perspective

Devang Sharma, MD
Charlottesville, Virginia

There is an unmet need for global surgery experiences for U.S. urology residents. Graduating medical students are increasingly seeking global health experience during residency as a way to augment their surgical learning. Unfortunately, few urology programs formally offer these opportunities as part of their training program.[1] When urology trainees do find opportunities they are most commonly external through the generous efforts of charities or organizations such as IVUmed (International Volunteers in Urology). Furthermore, even though these experiences provide significant educational benefit they are not recognized by the ACGME (Accreditation Council for Graduate Medical Education).[2] These barriers limit the number of urology residents who receive the tremendous benefits of global surgery exposure.

Global surgery experiences provide several notable benefits including gaining unique surgical experience, developing a cost conscious approach to care, building

▼ Continued on page 29

Figure 1. Global Surgical Expedition May 2019 team.

Global Surgery in Urology Training

▼ Continued from page 28

relationships with mentors and colleagues, mitigating burnout, and planting the seed for future international volunteerism. I had the good fortune of being part of 2 international surgical trips to Belize during my training at the University of Virginia and share my perspectives from these experiences (fig. 1). These trips were made possible by the generosity and support of my mentor, Dr. David Rapp, and Global Surgical Expedition (GSE), a charity he founded in 2012 with the goal of delivering surgical care to those in need and fostering the next generation of medical volunteers. Leadership and support from my training program was also critical as they formally offered the international experience as an integrated part of my residency.

The surgical experience in Belize included a robust volume, diversity of cases and advanced pathology. In 1 week we saw a 150-patient walk-in clinic and performed about 30 surgeries including a diverse representation of oncology (radical nephrectomy, orchiectomy, penectomy), reconstruction (perineal urethrostomy, urethroplasty), female urology (fascial slings, sacrocolpopexy) and stone/prostate disease (open pyelolithotomies and ureterolithotomies, transurethral resection of prostate, cystolithotomy, diverticulectomy; fig. 2). As a trainee at a rural academic center serving Appalachia I was no stranger to advanced pathology and complex cases. Still, I would hardly call that a typical workweek in Charlottesville. Tackling challenging cases without the benefit of a blood bank, intensive care unit, surgical colleagues, fluoroscopy or lasers helped me build confidence and gain appreciation for resources that are taken for granted in modern training. Operating with fewer resources necessitates diligent preparation for contingencies, thinking several steps ahead and adapting to changes on a moment's notice—all critical skills in the growth and development of a surgeon.

Practicing a cost conscious approach comes out of necessity when resources are limited. Our patients in Belize would often travel for hours and pay cash to get a computerized tomography scan. As providers, plain film and a sunny window were the closest we got to reading rooms and 3-dimensional reconstructions (fig. 3). Discovering that you can make do without these advanced technologies often with only a thorough history and physical exam was a refreshing realization. Honing these fundamental skills and gaining a new perspective on what is truly necessary helps lay a foundation for stewardship in our medical system where resources are abundant and costs are exorbitant.

Mentorship is one of the greatest takeaways from training and can be strengthened during international experiences. Traditional hierarchy fades, a more personal relationship grows and fond memories are formed. Whether this is a result of pursuing a common altruistic goal, sharing the struggles and rewards of working in an underserved community or sharing a cold beverage after a hard day's work is a topic for future research.

Burnout is an all too prevalent ailment in medical training today. Despite a week of surgeries often lasting late into the night I returned from Belize invigorated and refreshed. Teamwork in health care was never more apparent to me as traditional roles were less important (fig. 4). Attendings held mops, residents helped recover patients, anesthesiologists still did Sudoku puzzles. Families were surgical nurses, physical therapists and discharge coordinators. Patients were healthy and compliant, and our international colleagues were collaborating by our sides throughout.

Figure 2. Kidney, ureters, bladder x-ray showing large right ureteral stone (*left*), removal of stone via open ureterolithotomy (*center*) and gross specimen (*right*).

Figure 3. Review of outside images.

The net result was care that was personal, compassionate and patient centered.

My global health experience left me wanting more. Accordingly, I was back in Belize with GSE in a new role early in my fellowship, this time to conduct research assessing the financial impact of urological conditions on these patients and communities. By continuing a commitment to service I hope to transform these positive experiences into career-long volunteerism. There is a paucity of data on international surgical training in urology, but experience in global health settings during plastic and orthopedic surgery residency has been shown to be predictive of future international service.[3] By creating opportunities for global health in urology residency we not only help trainees achieve ACGME core competencies but, more importantly, we foster the future of international service, collaboration and research. ◆

This article is part 2 in a 2-part series on global health experiences as a critical part of resident education. Part 1 appeared in the August issue.

Figure 4. Team approach to repair of posterior urethral disruption.

1. Hau DK, Smart LR, DiPace JI et al: Global health training among U.S. residency specialties: a systematic literature review. Med Edu Online 2017; **22:** 1.
2. Badlani G: International volunteerism and global responsibility. Transl Androl Urol 2017; **6:** 258.
3. Murthy P, Malik RD, McCammon KA et al: Perspectives on international urological volunteerism: a survey of IVUmed resident scholar alumni. Urol Pract 2017; **4:** 176.

FROM THE *AUA Science & Quality Council*

Quality Reporting through the Merit-based Incentive Payment System

David F. Penson, MD, MPH
Chair, AUA Science and Quality Council
Nashville, Tennessee

Traditional fee for service payment systems are shifting to a system based on value and quality. To reward high value, high quality care the Centers for Medicare & Medicaid Services (CMS) developed the Quality Payment Program (QPP). While there are 2 arms to the QPP an overwhelming majority of urologists use the Merit-based Incentive Payment System (MIPS) arm, which focuses on the 4 performance categories of quality, improvement activities, promoting interoperability and cost. Providers receive a score based on their performance in each reporting category, and the combined overall score determines the Medicare payment adjustment for the provider.

In the 2020 Physician Fee Schedule Final Rule CMS details the changes to MIPS for the 2020 reporting year. The most significant updates are seen in the cost category while the remaining 3 have only minimal changes.

The cost category makes up 15% of a participant's total MIPS score and focuses on 2 areas, the resources clinicians use to provide patient care and Medicare expenses per beneficiary during an episode of care. While this remains unchanged from 2019 the attribution methodology was revised. Such a change should benefit urologists who previously were attributed some patients despite having no input into the costs incurred by those patients as the new 2020 methodology corrects this misalignment.

CMS continues to add additional specialty specific, episode based measures to the cost category. In 2020 this will include the Renal or Ureteral Stone Surgical Treatment measure, the first cost measure directly related to urology. The specifications for the new cost measures have not yet been released. However, CMS intends to publicize this information before the close of 2020.

Looking to 2021 CMS is working to simplify reporting through MIPS Value Pathways (MVPs), which is a program designed to align reporting and collect measures and activities across all 4 performance categories. The core of MVPs will be based on a combination of administrative claims measures and specialty or condition specific measures that will streamline reporting, reduce complexity and burden, and improve measurement. In addition to simplifying MIPS and ultimately achieving better clinical outcomes and lowering costs for patients, CMS believes that MVPs will create a more cohesive and meaningful participation experience, improve value, reduce clinician burden and assist with the transition from MIPS reporting to Advanced Alternative Payment Model reporting.

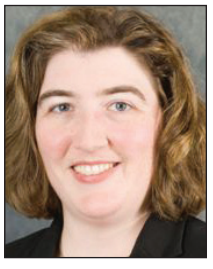
Education in the upcoming year will be a key factor to success in 2021. Throughout the course of 2020 CMS will offer a number of educational programs and products. Additionally, CMS will work with stakeholders to develop the measures and activities for future use in MVPs. The AUA will continue discussions with CMS regarding forthcoming measures and events, and welcomes member input in order to advise CMS on how best to aid urologists.

For further information on successful reporting in 2020 the AUA has identified the top 10 takeaways from the 2020 MIPS updates, which can be found on the AUA website along with the 2020 MIPS Toolkit at https://www.auanet.org/practice-resources/patient-safety-and-quality-of-care/2020-mips-toolkit. For more information on MIPS, including COVID-19 updates, visit qpp.cms.gov or contact CMS at QPP@CMS.hhs.gov or 866-288-8292. AUA Quality staff can be reached at Quality@auanet.org or 410-689-3925. ◆

FROM THE *AUA Judicial & Ethics Committee*

Website Rules of the Road

Christian O. Twiss, MD, FACS
AUA Judicial & Ethics Committee Chair
Tucson, Arizona



Diane E. Bieri, Esq.
AUA General Counsel
Linthicum, Maryland

Need a weather report? The hours of your favorite restaurant? Basic information on benign prostatic hyperplasia, overactive bladder or prostate cancer? For many patients the first source is the Internet.

While studies indicate that health care professionals remain the preferred and most trusted sources of medical information, we know that people are increasingly turning to the web for additional information. Naturally, many urologists and their institutions capitalize on this trend, creating or contributing to educational websites filled with clear, accurate medical information and eye catching graphics. This begs the question, What ethical rules should AUA members keep in mind when posting health related content on the web?

First, protect your patients' privacy. HIPAA (Health Information Portability and Accountability Act) applies in cyberspace the same way it does in the brick and mortar world. Websites or apps that store or transmit protected health information (PHI) must be HIPAA compliant. This includes using appropriate encryption, working with HIPAA compliant vendors under business associate agreements and ensuring that PHI is only accessible to authorized individuals. If you are unsure of the requirements it is wise to consult an expert (there are specialized attorneys and consultants with expertise in this area) and/or your organization's privacy officer.

Second, know your audience. When communicating with your own patients through a private portal you know their history and can reference specific symptoms or treatments. However, if you are posting on a website–your own or someone else's–visible to the general public, be careful to offer only general information and not medical advice. Websites should not substitute for professional medical care.

Third, be a credible source. As in all communications with patients and consumers your online communications should be clear, accurate and supported by published scientific evidence. Provide information that clarifies complex terms and concepts and helps patients and caregivers make informed judgments about health information, products or services provided by your practice or institution.

Finally, respect your own and others' original content. In this high speed, digitized world it may seem as though anything posted on a website can be reposted at will. Typically, this is not the case. Remember that you have exclusive rights in the form of a copyright for anything that you write, record, draw or photograph yourself. No one can repost your original content without your permission. Likewise, you should not repost on your own website articles, podcasts, drawings, graphics or photographs created by others without first obtaining creator permission.

So how can you share useful information posted on a website or in a blog that you did not create yourself? Posting a direct link to content on other sites is generally acceptable. For example, AUA members may link to the Urology Care Foundation website (urologyhealth.org) to share materials that help educate patients on a variety of urological conditions and treatments.

In some cases you may want to ask for permission to repost the content on your site with full credit to the original source. Doing so may require you to sign a license agreement and pay a fee to the original author. Most websites publicize their policies on linking and reposting, so it is always best to check individual website policies (often included under the "About Us" heading) for specific rules before linking to or reposting content. ◆

HAVE YOU *Read?*

Daniel Shoskes, MD
Cleveland, Ohio

Haas CR, Li G, Hyams ES et al: Delayed decompression of obstructing stones with urinary tract infection is associated with increased odds of death. J Urol 2020; doi:10.1097/JU.0000000000001182.

Antibiotics do not penetrate obstructed spaces, the fundamental principle of surgical infectious disease. We all know upper tract obstruction with urinary tract infection (UTI) is an emergency, but with modern antibiotics what impact does delayed decompression have on mortality? The authors used the National Inpatient Sample from 2010 to 2015, and all patients aged 18 years or older with ICD-9 diagnosis of UTI who had a ureteral stone or kidney stone with hydronephrosis (311,100) were identified.

Two weighted sample multivariable logistic regression models assessed predictors of the primary outcome of death in the hospital and secondly predictors of delayed decompression. After controlling for patient demographics, comorbidity and disease severity delayed decompression significantly increased odds of death by 29% (OR 1.29, 95% CI 1.03–1.63, p=0.032). Delayed decompression was more likely to occur with weekend admissions, nonwhite race and lower income demographic.

The authors conclude that while the overall risk of mortality is low in patients with obstructing upper urinary tract stones and UTI a delay in decompression increased odds of mortality by 29%. The increased likelihood of delay associated with weekend admissions, minority patients and lower socioeconomic status suggests opportunities for improvement.

de Jonge SW, Boldingh QJJ, Solomkin JS et al: Effect of postoperative continuation of antibiotic prophylaxis on the incidence of surgical site infection: a systematic review and meta-analysis. Lancet Infect Dis 2020; doi:10.1016/S1473-3099(20)30084-0.

While not specific to urology, surgical site infections remain a constant morbidity risk. While many intraoperative interventions can lower the incidence, antibiotic use beyond the time of surgery seems protective but is not evidence based. In this meta-analysis the authors searched MEDLINE®, Embase®, CINAHL®, CENTRAL® and WHO® regional medical databases for randomized controlled trials (RCTs) on postoperative antibiotic prophylaxis that were published from 1990 to 2018. RCTs comparing the effect of postoperative continuation vs discontinuation of antibiotic prophylaxis on the incidence of surgical site infection in patients undergoing any surgical procedure with an indication for antibiotic prophylaxis were eligible. The primary outcome was the effect of postoperative surgical antibiotic prophylaxis continuation vs its immediate discontinuation on the occurrence of surgical site infection. They identified 83 relevant RCTs of which 52 with 19,273 participants were included in the primary meta-analysis.

The pooled relative risk (RR) of surgical site infection with postoperative continuation of antibiotic prophylaxis vs its immediate discontinuation was 0.89 (95% CI 0.79–1.00) with low heterogeneity in effect size between studies (τ^2=0.001, χ^2 p=0.46, I^2=0.7%). Subgroup analysis showed a significant association between the effect estimate and adherence to best practice standards of surgical antibiotic prophylaxis. The RR of surgical site infection was reduced with continued antibiotic prophylaxis after surgery compared with its immediate discontinuation in trials that did not meet best practice standards (0.79, 95% CI 0.67–0.94) but not in trials that did (1.04, 95% CI 0.85–1.27, p=0.048). Whether studies adhered to best practice standards explained all variance in the pooled estimate from the primary meta-analysis.

The authors conclude that there is no conclusive evidence for a benefit of postoperative continuation of antibiotic prophylaxis over its discontinuation. When best practice standards were followed postoperative continuation of antibiotic prophylaxis did not yield any additional benefit in reducing the incidence of surgical site infection.

Shore ND, Saad F, Cookson MS et al: Oral relugolix for androgen-deprivation therapy in advanced prostate cancer. N Engl J Med 2020; 382: 2187-2196.

Androgen ablation has been the mainstay for initial therapy of metastatic prostate cancer for decades and is usually begun with injectable luteinizing hormone releasing hormone agonists. Relugolix is a new oral gonadotropin releasing hormone antagonist that the authors tested against leuprolide. The authors randomly assigned patients with advanced prostate cancer in a 2:1 ratio to receive relugolix (120 mg orally once daily) or leuprolide (injections every 3 months), respectively, for 48 weeks. The primary end point was sustained testosterone suppression to castrate levels (less than 50 ng/dl) through 48 weeks. Secondary end points included noninferiority with respect to the primary end point, castrate levels of testosterone on day 4 and profound castrate levels (less than 20 ng/dl) on day 15.

A total of 622 patients received relugolix and 308 received leuprolide. Of men who received relugolix 96.7% (95% CI 94.9–97.9) maintained castration through 48 weeks as compared with 88.8% (95% CI 84.6–91.8) of men receiving leuprolide. The difference of 7.9% (95% CI 4.1–11.8) showed noninferiority and superiority of relugolix (p <0.001 for superiority). All other key secondary end points showed superiority of relugolix over leuprolide (p <0.001). The percentage of patients with castrate levels of testosterone on day 4 was 56% with relugolix and 0% with leuprolide. In the subgroup of 184 patients followed for testosterone recovery the mean testosterone levels 90 days after treatment discontinuation were 288.4 ng/dl in the relugolix group and 58.6 ng/dl in the leuprolide group. Among all patients the incidence of major adverse cardiovascular events was 2.9% in the relugolix group and 6.2% in the leuprolide group (HR 0.46, 95% CI 0.24–0.88).

The authors conclude that relugolix achieved rapid, sustained suppression of testosterone levels that was superior to that of leuprolide, with a 54% lower risk of major adverse cardiovascular events. ◆

PRACTICE *Tips & Tricks*

How are You Living Your Dash?

Neil H. Baum, MD
New Orleans, Louisiana

I was recently jogging by a cemetery and paused to look at a few tombstones. Every stone had the name of the departed, the date of birth and the date of death. The dates of birth and death were different for each person, but every tombstone had a dash between those dates.

Let's dissect these 3 marks that appear on every tombstone. The first is the birth date. On the day you were born your parents likely invited a few people to your home to meet you and celebrate your entry into this world. Similarly, on the day you die a few dozen people will show up to share a few comments about you with your family. Truth be told, the size of your funeral will likely be determined by the weather!

The symbol on every tombstone is the dash between those dates. The dash represents the life in between those important dates in a man's or woman's life. This short, straight line is the essence of your time on earth. It is your contribution to the world and how you will really be remembered. The world likely will not remember the day you were born or the day you died, but it will remember what you did with your dash.

Or do you want your tombstone to say you were a great doctor, a

▼ Continued on page 32

FROM THE *AUA Research Council*

Improving Diversity and Inclusion in AUA Research Scholar Awards

Aria F. Olumi, MD
Chair, AUA Research Council
Boston, Massachusetts

Socioeconomic status has been shown to be a predictor of health similar to risk factors like smoking, physical activity, hypertension and diabetes.[1] Many population heath studies have shown that using zip codes or subway stations can serve as indicators of individual average life expectancy, highlighting that location of residence can be an indirect surrogate for overall well-being.

Similarly, educational achievements are directly linked to underlying socioeconomic status. A study by the National Center for Education Statistics (https://bit.ly/3jzNQvK) of 2002 high school sophomores found that 10 years later there is a significant difference in obtaining a bachelor's degree between high vs low socioeconomic households of 60% vs 29%, respectively (see figure).[2] Continuing along similar trends students from low socioeconomic backgrounds who attend college have a much lower likelihood of choosing a science, technology, engineering or math (STEM) major, which reflects another challenge in recruitment to medical and graduate schools and urology training.

Underrepresented minorities comprise a significant proportion of the low socioeconomic group and as a result face an uphill battle in attainment of a higher educational degree, which is important to promising careers and obtaining favorable economic outcomes. The National Institutes of Health have recognized the need to encourage and enable biomedical scientists from disadvantaged backgrounds and has made special efforts to promote the scientific progress of these individuals.[3] As an example, principal investigators can request supplemental funds to enhance diversity, and facilitate recruitment and training of promising scientists from diverse backgrounds and underrepresented groups.[4]

The AUA Office of Research has been proactive to improve engagement of underrepresented minorities in our council, grant review committees and research grant applicants as outlined in an earlier issue of AUANews.[5] Furthermore, we are grateful that the SUO (Society of Urologic Oncology) has created a new endowment, its fourth endowment in partnership with UCF (the Urology Care Foundation) and the AUA, and designated it for underrepresented minorities and women in urologic oncology research. We applaud SUO's forward thinking in creating this opportunity for our research community that will aid our efforts in improving the diversification of our research workforce, provide higher impact research and improve patient care. We look forward to working with the AUA and UCF Boards of Directors to continue our efforts in promoting diversity and inclusion, which is an important initiative at the Office of Research. ◆

1. Stringhini S, Carmeli C, Jokela M et al: Socioeconomic status and the 25 x 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1.7 million men and women. Lancet 2017; **389**: 1229.
2. National Center for Education Statistics: Postsecondary Attainment: Differences by Socioeconomic Status. National Center for Education Statistics 2015. Available at https://nces.ed.gov/programs/coe/indicator_tva.asp.
3. Lauer M: Expanding NIH's Definition of Socio-Economic Disadvantaged to be More Inclusive and Diversify the Workforce. National Institutes of Health 2019. Available at https://nexus.od.nih.gov/all/2019/11/26/expanding-nihs-definition-of-socio-economic-disadvantaged-to-be-more-inclusive-and-diversify-the-workforce/.
4. National Institutes of Health: Research Supplements to Promote Diversity in Health-Related Research (Admin Supp - Clinical Trial Not Allowed). National Institutes of Health 2020. Available at https://grants.nih.gov/grants/guide/pa-files/PA-20-222.html.
5. Olumi AF: Workforce diversity is necessary for urological research. AUANews 2019; **24**: 27, issue 3.

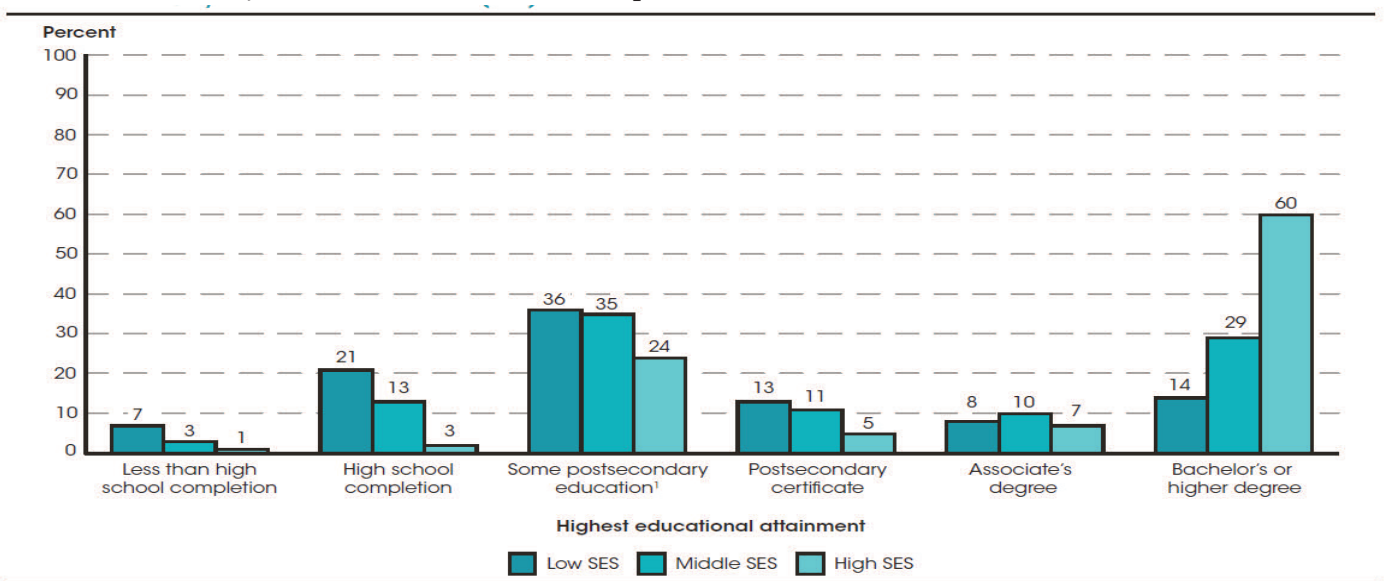


Figure. Percentage distribution of highest level of educational attainment of spring 2002 high school sophomores in 2012 by socioeconomic status (SES). Source: National Center for Education Statistics.

Practice Tips & Tricks

▼ Continued from page 31

great healer and a great clinician? Or perhaps you would like your dash to represent that you were a devoted husband/wife/father/mother/grandparent, a friend to all, an inspiration to all, that you spread love everywhere you went, gave to the community, the region and the world, kept your word, or were a role model to everyone.

Among the best books I have read is *When Bad Things Happen to Good People* by Rabbi Harold Kushner.[1] He writes, "I never met a man on his death bed who said 'I wish I would have spent one more day at the office.'" Perhaps this sentence might be written for doctors to say, "I never met a man on his death bed who said, 'I wish I would have provided medical care for one more patient.'" I think most of us on our death beds will likely say, "I wish I would have spent one more day with my family and friends."

When I have given thought to my own dash I would hope it would say, "Here lies Neil, who learned the importance of balance between his personal life and his professional life." For a significant part of my life I was focused on my career and really did not have a balanced life. After reading Rabbi Kushner's book I took to heart what might be said on my deathbed, and I made a real effort to find the balance between my career and my life with my family. So you might reflect on how you are living your dash and how you want to be remembered.

The bottom line is that I ask, "Have you thought about your dash? What do you want to have others remember about you between those two dates–the day you were born and the day that you left this world?" I wish my fellow urologists a balanced life between career and family, and that you live your dash. ◆

1. Kushner H: When Bad Things Happen to Good People (2nd Anchor Books edition). New York, New York: Anchor Books 2007.

FROM THE *Chief Executive Officer*

Membership Matters

Michael T. Sheppard, CPA, CAE
Linthicum, Maryland

As the COVID-19 pandemic continues to impact physicians, health care providers and patients, a sense of community is more important than ever before. Here at the AUA, we pride ourselves on our members and the community we have been building together for decades.

Our mission to promote the highest standards of urological clinical care through education, research and the formulation of health care policy continues to ring true even in these unprecedented times, and we stand prepared to invest in our mission and deliver on our promise to our members.

Now more than ever, the AUA is proud to serve as the world's premier urological association, and to provide our members with the tools, resources and education to advance the specialty. Your membership in the American Urological Association ensures that you have access to:

The latest clinical standards and research. From our journals – *The Journal of Urology*® and *Urology Practice* – to our clinical practice guidelines and white papers and *AUANews*, we help ensure our members stay abreast of the newest information impacting patient care.

An extensive array of online education and worldwide educational events. In addition to our Annual Meeting, the AUA also offers more online education than any other urological association. Our AUA *University* makes it easier than ever for our members to obtain the learning they need.

An extensive network of peers from around the globe. In 2019 the AUA celebrated a major milestone in membership growth, with more than 2,200 new members. In March 2020 our membership exceeded 23,000!

Relevant practice resources. From videos and engaging and informative patient guides to posters and patient magazines, the Urology Care Foundation provides members with a plethora of educational materials.

Valuable funding opportunities. Committed to supporting urological research through education, advocacy and funding, the AUA provides the urological community with a number of awards to foster ongoing and critical urological research.

Opportunities to make a difference. Whether you choose to advocate with lawmakers or volunteer for global philanthropic programs, we have you covered.

From practicing urologists to trainees and medical students, as well as advanced practice providers, researchers and more, AUA members represent an incredible breadth of urological health care professionals. Together, I have no doubt that our community will continue to support innovative advancements, provide best in class patient care and work to navigate the ongoing global health crisis as a specialty united. ◆

Walt Whitman, John Mahay and Urotrauma in the American Civil War

Michael W. Witthaus, MD
Rochester, New York

Eric Mathews, MD
Rochester, New York

Marni Rabinowitz
Pittsford, New York

Ronald Rabinowitz, MD
Rochester, New York

Steven Hudak, MD
Dallas, Texas

"Thus in silence in dreams' projections,
Returning, resuming, I thread my way
through the hospitals; The hurt and
wounded I pacify with soothing hand,
I sit by the restless all the dark night –
some are so young; Some suffer so much
– I recall the experience sweet and sad"
–Walt Whitman, *The Wound Dresser* (1865)[1]

American Poet and Volunteer Nurse

Walt Whitman (1819–1892, fig. 1) was a visionary American poet who inspired innovation within the literary landscape, choosing to preserve real, complex life with poetic imagery. He also chose to volunteer as a nurse during the American Civil War, daring to confront the violent, painful reality of war's aftermath with precision and unflinching honesty. In 1862 as Walt Whitman was caring for his mother in Brooklyn, New York, he read the *New York Herald* listing the Union casualties from clashes south of Washington, D.C. Fearing for his brother's safety he quickly boarded a train for Fredericksburg, Virginia.

He found his brother alive, but he also found himself outside of a hospital with a heap of amputated feet, legs, arms and hands. After journeying through the rooms visiting the weak and wounded soldiers Whitman was compelled to settle in Washington, D.C., where he spent his days and nights tending to soldiers as a volunteer nurse.[2]

"I onward go, I stop,
With hinged knees and steady hand to
dress wounds,
I am firm with each, the pangs are sharp
yet unavoidable,
One turns to me his appealing eyes–poor
boy! I never knew you,
Yet I think I could not refuse this moment
to die for you, if that would save you."
–Walt Whitman, The Wound Dresser (1865)[1]

American Civil War: Urotrauma

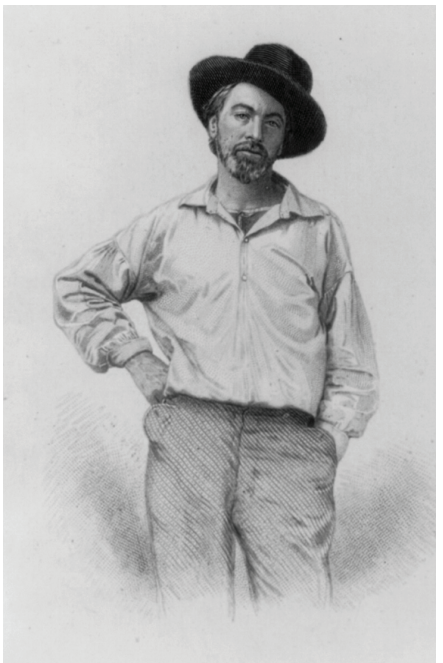


Figure 1. Walt Whitman in 1854 (courtesy of United States Library of Congress).

During the American Civil War injuries were predominantly caused by low explosive weaponry and infrequently resulted in genitourinary (GU) trauma. Fewer than 1% of traumatic injuries resulted in GU injuries, totaling nearly 1,500 cases, but 22% of these cases were fatal.[3]

However, injury to the urethra or external genitalia had a much lower mortality rate, partly due to diverting urine by perineal urethrostomy or suprapubic cystostomy.[4] Antibiotics would not be fully implemented in battlefield medicine until 1942, and battlefield triage would not be fully implemented by Army Medical Director Jonathon Letterman until September 1862.

The Second Battle of Bull Run, August 29, 1862

The Second Battle of Bull Run left the Union Army of the Potomac retreating in the early days of the American Civil War (fig. 2). Of those retreating to Washington, D.C., Private John Mahay of the 101st New York suffered a penetrating injury through the pelvis (fig. 3).[5] The bullet fractured his pelvis and perforated his bladder, leaving a wound that drained pus, urine, blood and bone fragments from his urethra. He would later confront chronic fistulas, pain, bladder stones and infection.

A Poet at the Bedside

Private Mahay was one of Whitman's first and favorite patients with numerous writings and correspondences between them. As Mahay initially languished from his injuries, they gradually became chronic. Whitman was known to visit him for his care and supply him with candy to improve his morale. Whitman wrote, "the water came out of the wound, by slow but

▼ Continued on page 34

Urotrauma in American Civil War

▼ Continued from page 33

steady quantities, for many weeks – so that he lay almost constantly in a sort of puddle."[1]

"One scene at his bedside will suffice for the agonies of nearly two years. The bladder had been perforated by a bullet going entirely through him– The water ran out of his eyes from the intense pain, and the muscles of his face were distorted, but he uttered nothing except a low groan now and then. Hot moist cloths were applied, and relieved him somewhat. Poor Mahay, a mere boy in age, but old in misfortune."

–Walt Whitman, Specimen Days (1882)[1]

Mahay's wounds would never heal. Mahay died on October 24, 1863 after 14 months of chronic urological care. Several urinary stones were removed from Mahay's bladder on autopsy (fig. 4), which remain in the NMHM (National Museum of Health and Medicine) to this day.

Figure 2. Second Battle of Bull Run, August 29, 1862 (courtesy of United States Library of Congress).

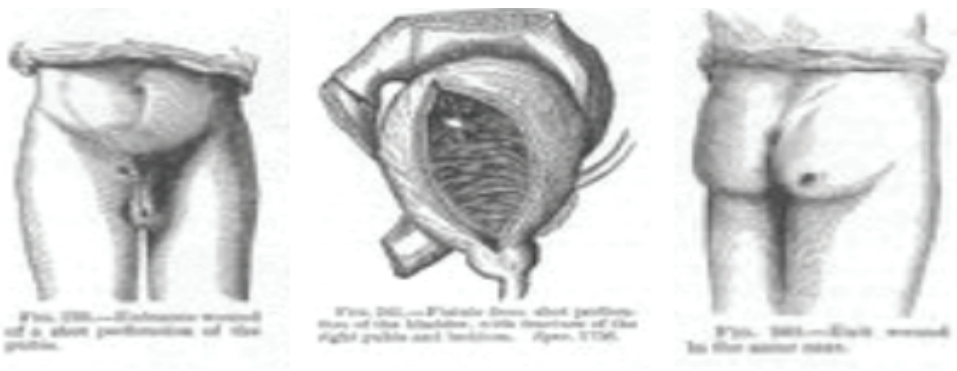


Figure 3. Private John Mahay, who sustained penetrating GU injury during Second Battle of Bull Run (courtesy of NMHM).

Figure 4. Several bladder stones removed from Private John Mahay (courtesy of NMHM).

Walt Whitman's Civil War writings chose to confront reality with honesty, precision and eloquence. His commitment to John Mahay's care during the Civil War underscores the essential human aspects of acute and chronic urological care following traumatic injury.

"The sun bursts through in unlooked-for directions,
Strong thoughts fill you and confidence, you smile,
You forget you are sick, as I forget you are sick,
You do not see the medicines,
You do not mind the weeping friends, I am with you,
I exclude others from you, there is nothing to be commiserated,
I do not commiserate, I congratulate you."

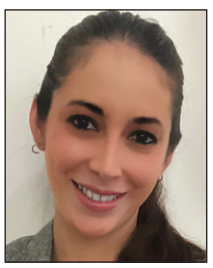
–Walt Whitman, Leaves of Grass (1860) Excerpt from "To One Shortly to Die"[1]

AUA 2020 Virtual Science Best Poster winner. ◆

1. Whitman W and Schmidgall G: Walt Whitman: Selected Poems, 1855-1892: A New Edition. 1st Stonewall Inn ed. New York, New York: St. Martin's Press 2000.
2. Whitman W: Life and Letters, Correspondence: Walt Whitman to Martha Whitman, 2–4 January 1863. The Walt Whitman Archive. Available at https://whitmanarchive.org/biography/correspondence/tei/loc.00759.html. Accessed August 3, 2019.
3. Herr HW: Urological injuries in the Civil War. J Urol 2004; **172**: 1800.
4. Herr HW and McAninch JW: Urethral injuries in the Civil War. J Urol 2005; **173**: 1090.
5. Barbian L, Sledzik PS and Reznick JS: Remains of war: Walt Whitman, Civil War soldiers, and the legacy of medical collections. Mus Hist J 2012; **5**: 7.

AUA *Residents & Fellows Committee News*

Residency in a Pandemic Time: What a Resident Feels



Ana Vidal Brandt, MD
Residents & Fellows Committee Representative, Mexico
Mexico City, Mexico

Starting a medical residency is among the most awaited achievements for a recently graduated MD when we finally will be able to specifically study the specialty to which we will dedicate the rest of our lives.

During this challenging stage workload and study increase, and the level of responsibility with our patients rises. As residents we want to spend that time in the best possible way to achieve success, understanding it as a function of persistence and willingness to work to the maximum for as long as possible. Besides, community needs and expectations constantly change, prompting us to adapt to new situations.

Among unexpected incidents the COVID-19 pandemic has been one of the most challenging situations with a profound impact on medical care and negative consequences to educational programs globally. In many hospitals and institutions around the world a significant number of urologists have focused part of their practices on the management of patients with COVID-19.[1] In general this process has rapidly led to a substantial decrease in the clinical and surgical practice of urology in all centers. In this context the training of urology residents has also been seriously affected. However, we must bear in mind that in times of contingency and isolation our role as urologists in training must adapt to the stage of the epidemiological emergency.

Certainly, this pandemic impairs the educational process of all residents in many ways. First, sudden cancellation of surgeries and procedures reduces learning opportunities to a minimum, representing an unprecedented challenge for academic and health institutions. Second, the long awaited last year of residency is probably most compromised by these circumstances, with reduced daily urological practice and lower routine exposure to clinical and surgical training activities. This has been recently confirmed by reports from Italy showing that performance of surgical procedures was dramatically reduced mainly for last year residents, being the most affected by the pandemic of COVID-19.[2] This is of major concern for young urologists who are about to start their own real world experience but with the uncertainty of an incomplete training.

On the other hand this contingency has represented an opportunity to rediscover the essence of medicine and remember why we chose this path. It is an excellent time for all health workers to join and support one another to fight this health problem regardless of specialty.

In the near future the additional challenge will be to resume care of nonCOVID-19 patients with urological pathologies, especially for patients 60 years or older, many of them with comorbidities that increase the risk to develop complications from COVID-19.[3] ◆

1. Pelayo-Nieto M, Linden-Castro E, Gómez-Alvarado MO et al: [Has the COVID-19 pandemic impacted urological practice in Mexico?]. Rev Mex Urol 2020; **80**: 1.

FROM THE *Urology Care Foundation*

Empowering the Fight against Prostate Cancer

Harris M. Nagler, MD, FACS
President, Urology Care Foundation
New York, New York

The Urology Care Foundation empowers men to make informed decisions about prostate cancer screening, care and treatment in a multitude of ways. While our unwavering commitment to fight this disease takes place year-round, September is Prostate Cancer Awareness Month, a time when we intensify our efforts to raise awareness about this important disease and generate support for those affected worldwide.

The Foundation is committed to funding and advancing research through the generous support of donors like you. We have provided more than $34 million in funding to help nearly 900 of the brightest minds conduct innovative urology research. One day our research may help cure or prevent prostate cancer.

I would like to highlight some of the researchers we have helped support during their journeys.

Charles Brendler, MD

Dr. Brendler is a Foundation Research Scholar who made major contributions to the field of prostate cancer research, particularly regarding the technique of radical prostatectomy, and helped identify the genes associated with prostate cancer risk and lethality.

Stephen J. Freedland, MD

Dr. Freedland is a Distinguished Professor of Urology at Cedars-Sinai in Los Angeles and inaugural recipient of the Urology Care Foundation Rising Stars in Urology Research Award. With Foundation support, he studied the impact of diet on prostate cancer growth. This work resulted in promising data leading to an initial clinical trial.

Simpa Salami, MD, MPH

Dr. Salami's research is focused on developing optimal paradigms for early detection of prostate cancer and accurately stratifying patients into risk categories. His goal is to improve active surveillance and treatment response for men around the world fighting this disease.

Michael M. Shen, PhD

As we know, cancer is a complex disease that develops, evolves and responds to treatment in different ways that can vary unpredictably among patients. Dr. Shen has teamed with several Foundation funded researchers to study this therapeutic dilemma. Dr. Shen's laboratory specializes in research on stem cells to better understand prostate cancer.

Patient Education

September is an important month in the Foundation's commitment to educating patients while encouraging men to know their prostate cancer risk and talk to their doctor. Educating those at risk, and those already suffering from urological conditions, including prostate cancer, is key to our mission.

Capitalizing on our carefully crafted library of educational resources, based on the AUA's clinical practice guidelines, the Foundation has built an easily navigable hub of prostate cancer materials for patients. Our resources are available in many different types of media and languages. Some of these offerings include:

- The Localized Prostate Cancer Patient Guide
- The Prostate Health Playbook
- A collection of videos and podcasts with easy-to-understand prostate cancer facts and stories.

Please be sure to send your patients to UrologyHealth.org/PCInfoCenter and ensure they receive these trusted resources during this crucial awareness month. ◆

FROM THE *AUA Education Council*

A New Self-Assessment Study Program App

Victor W. Nitti, MD
Chair, AUA Education Council
Los Angeles, California

2020 is a year we will all remember. As health care practitioners we had to learn to practice in a new way in a new environment, and with new challenges and barriers. As we have adapted to these changes we have also been exposed on a large scale to new ways of acquiring information and learning. As lifelong learners we now have almost instantaneous access to incredible amounts of information.

As education, learning and access to information have evolved the AUA has remained viligant. And with that we are excited to announce a significant change to one of the AUA's most popular products, the AUA Self-Assessment Study Program (SASP)! The AUA SASP is getting a major upgrade in 2021. Available in January the SASP will be offered as a mobile app. The app will not only be more convenient, but will also allow users to:

- Engage in test and practice modes
- Choose to receive all questions at once or in spaced intervals
- Sort questions by topic area and pull questions from multiple years
- Tag questions to review which will allow for the creation of a personalized deck

The SASP mobile app will also include leaderboards and links to other AUA resources including the AUA Guidelines and Core Curriculum. When you purchase the new app all of your previous years of questions will be available to you in 1 convenient location. This content will also be accessible online from a desktop as needed.

As part of this new product launch the AUA is offering new ways to purchase the SASP. New for 2021 you can purchase the app and then for a small additional fee also purchase the book. The AUA is also offering a brand new Resident Combo rate for SASP and Update Series, and a volume discount for Residency Programs.

The new SASP app will join several other AUA educational apps. If you were not aware, the following apps are available for download:

- The AUA *University* mobile app is a quick, easy way to access information on the go. From the app homepage, you have direct access to all AUA *University* podcasts, the Core Curriculum and for subscribers, the Update Series Lessons and new audiobooks.
- The AUA Guidelines at a Glance
- The AUA Oral Board Study Guide
- The AUA Medical Student Curriculum

For more information on all AUA apps, go to https://www.auanet.org/education/auauniversity/education-products-and-resources/app-store.

If it has been a while since you visited AUA *University*, your login has not changed. If you have any issues, please contact the AUA Customer Service Department at 800-908-9414 or 410-689-3917, or via customerservice@auanet.org.

If you have any ideas or suggestions for the AUA Office of Education, we welcome your feedback. Please send us an email at education@auanet.org. ◆

BEST HOSPITALS
U.S.News & WORLD REPORT
NATIONAL
UROLOGY
2020-21

USC Urology Nationally Ranked #9

Exceptional.

The University of Southern California is proud that USC Urology is, once again, among the top urology programs in the country. This distinction is based on our physicians' clinical expertise, your patient experiences and, most importantly — your health and safety. We take the toughest cases and provide exceptional care. That's the Keck Effect.

(800) USC-CARE • urology.KeckMedicine.org

Keck Medicine of USC

BEYOND EXCEPTIONAL MEDICINE™