American Urological Association

AUA NEWS

JUNE 2020 | THE OFFICIAL NEWSMAGAZINE OF THE AMERICAN UROLOGICAL ASSOCIATION | VOLUME 25 | ISSUE 6

INSIDE THIS ISSUE

FROM THE *AUA President*

Inaugural Address

Scott K. Swanson, MD
Scottsdale, Arizona

It is my honor and privilege to serve as the 116th President of the American Urological Association (AUA). As the world's oldest urological association, the AUA has helped to advance and shape a legacy of diversity and excellence within the specialty for more than a century, and I am deeply honored to assume the leadership of this extraordinary organization.

As I reflect on my travels and interactions with many of you over the past year as President-Elect, I am reminded of the commitment we all have to the profession of urology and improving patients' lives, of the commonalities and unique character of the urology community, as well as the similarity of challenges we face, regardless of our country of origin. Even with the geographic and professional diversity among our membership, we all share a common mission: to advance urology and promote the highest standards of urological clinical care.

During the last several months I have watched as the global landscape has evolved into nothing any of us has seen before. In December my wife Connie and I were planning some family ski trips. I was excited about attending the AUA's Advocacy Summit. I was looking forward to attending the AUA Annual Meeting in Washington, D.C. and I was making plans for a grand motorcycle ride home to Arizona from the Annual Meeting, with stops in Michigan, Wisconsin and Colorado. Clinics were full, operating schedules were robust and hospitals were on diversion. We may have complained, but we were silently proud.

Today, we find ourselves in the midst of a perfect storm. Physicians are working hard in the face of this global COVID-19 pandemic. Many are practicing – or preparing to practice – at the edge, or outside of their standard scope of work, yet are ready to give the all-out effort required to save lives. Residents and trainees are finding themselves on the front lines of this outbreak, anxious, maybe a little frightened, but quickly realizing why they chose a career in medicine – and beginning to realize their graduation ceremony may not include the pomp and circumstance they once envisioned.

Those who have been furloughed or, like me, "offered" pay cuts, are ready and able to step in and make a difference when the currently restrictive operative experience returns with a significantly greater volume of cases, and when the need to socially distance from colleagues and family, as well as virtually connect, calm and care for patients through telemedicine, has become the norm.

Based on the AUA's long history of strong, disciplined fiscal stewardship, the AUA remains well positioned both financially, and as an organization, to weather the impact COVID-19 is having on the economy. While not all interact daily with members, the AUA headquarters staff, under

▼ Continued on page 3

PRACTICE *Tips & Tricks*

Tele-Etiquette: Dos and Don'ts of Telemedicine

Neil H. Baum, MD
New Orleans, Louisiana

Coronavirus has changed the playing field and methodology of caring for patients. We no longer will be seeing all of our patients in our offices and conducting physical examinations or touching patients. Now for first time there are codes and reimbursements that make it possible to be compensated for virtual care.

Just as there are proper behaviors expected of physicians who are face-to-face with patients, there is a code of behavior for telemedicine. Here are a few suggestions for making your telemedicine visits more meaningful and professional.

Have a nondistracting background. I gave several virtual lectures

▼ Continued on page 4

NON-PROFIT ORG.
U.S. POSTAGE
PAID
PERMIT NO. 161
LANCASTER, PA

American Urological Association
1000 Corporate Boulevard
Linthicum, Maryland 21090

GET THE ADVANTAGE OF SPEED

UROLOGY'S ALL-IN-ONE EHR

GUARANTEED TO INCREASE YOUR EFFICIENCY

and Bottom Line in less than ***90 days!***

Our ***Advantage SMART Practice***® EHR and practice management solution uses real-time data to make every part of your workflow faster.

EHR | PM | TELEHEALTH

AUA SI | PATIENT ENGAGEMENT | RCM | MIPS

WWW.COMPULINKADVANTAGE.COM/UROLOGYEHR | 805.716.8688

compulink

From the AUA President

▼ Continued from page 1

the leadership of Chief Executive Officer Mike Sheppard, is a group of dedicated and responsible individuals who clearly deserve recognition for their professionalism, adaptability and enormous contributions to our member experience during this time of crisis, as well as before and after.

It is in times like these that we are reminded of our strength as a global community and the continuity of our enduring values. We realize these times are what create new chapter headings in our AUA narrative. Our book is thick with nearly 120 years of stories, and together we will embark on writing compelling new chapters for urology.

Education

Urology is a bold specialty and the AUA has been remarkably successful in harnessing that boldness in pursuit of academic excellence. It has used its competitive advantage of allowing and even encouraging innovation to propel us forward in sometimes unexpected and dramatic ways. In today's changing environment the AUA continues to bring a global perspective to all its educational programs and activities. While COVID-19 has resulted in the cancellation or rescheduling of several AUA events this year, your association remains committed to providing quality, evidence-based education for urologists and urological health care providers worldwide, throughout all stages of their careers.

Whether offering instructional courses, hands-on courses, online education and now virtual learning opportunities, the AUA remains at the forefront for tapping into the innovative spirit of our specialty and developing the rich educational activities you have come to expect. This summer the AUA will employ the latest technologies to effectively deliver a virtual experience, creating a new, multimedia reinvention of the AUA Annual Meeting aimed at connecting and educating our global community. Through the combined talents of our Board Secretary, Dr. John Denstedt, coupled with the expertise of current Education Chair Dr. Victor Nitti and incoming Chair Dr. Jay Raman, we will continue to provide educational resources throughout the world and shape our future for generations to come.

Research

Urology research is critical to moving our specialty forward. The research we pursue in urology and other areas of medicine helps to generate new knowledge, new connections and new insights into patient care. We work to understand the origins of disease and explore the molecular code that is equally essential to our humanity. As an association, we continue to invest in our remarkable young scientists as they focus on the future and dare to take risks to shape new ways for preventing, diagnosing and treating urological conditions and disease.

Working together, Research Council Chair-Elect Dr. Stephen Kaplan and current Chair Dr. Aria Olumi will continue to advance research across the full spectrum of urological disease, as well as increase and diversify funding opportunities worldwide. Collectively, they will help to develop and implement new initiatives to facilitate the advancement of urological research and reduce the burden of urological disease.

Advocacy

As a leading advocate for the specialty of urology, the AUA works on behalf of you and your patients to ensure critical interests are promoted to a wide array of decision makers. Whether contacting lawmakers on Capitol Hill, at the state level, or federal officials within government agencies, their sole purpose is dedication to the practice of urology and urological health. As many can attest, today's health care landscape is rapidly evolving. With increasing demands and ever changing regulations, it can be quite overwhelming. However, the AUA is working to stay abreast of these changes and develop strategies to help guide us through these unprecedented times.

The AUA remains focused on its advocacy agenda, which includes such initiatives as physician reimbursement, access to care and urology/cancer research funding, to name a few. Now is the time to make a difference. Reach out to your lawmakers at the local and national levels to advocate for the interests of urologists and preserve our specialty. Attend the Annual Urology Advocacy Summit in the fall, which is a great opportunity for members to gather in Washington, D.C. and on Capitol Hill and help carry urology's messages to lawmakers. Whether contacting lawmakers on Capitol Hill or federal officials in government agencies, we are supporting and defending the practice of urology.

Mission Driven

I am humbled to follow on the heels of such dedicated and impressive leadership. I am grateful to Dr. John Lynch for his leadership and outstanding contributions and I thank him for his tireless service to the AUA and Urology Care Foundation. Please also join me in thanking Dr. Robert Flanigan, who recently completed his term as our Immediate Past President, as well as the "old guard" with whom I am honored to have served when I was Western Section Representative, namely Drs. Frederick Gulmi, Roger Schultz and Chandru Sundaram, who completed their terms as representatives for the Mid-Atlantic, New York and North Central Sections, respectively.

I would also take a moment to welcome the following individuals to the AUA Board of Directors: Dr. Raju Thomas, President-Elect; Dr. Thomas Stringer, Treasurer-Elect; Dr. Kurt McCammon, Mid-Atlantic Section Representative; Dr. Reza Ghavamian, New York Section Representative and Dr. James Ulchaker, North Central Section Representative.

I look forward to serving you over the next year and will be working with a distinguished group of individuals, including members from our Board of Directors, our councils, committees, volunteers and AUA staff. Each is ready and willing to serve you, our members.

If you have not already figured it out, you are a member of a remarkable association, one rooted in purpose, guided by enduring values and determined to lead. Over the next year, and with your help, I will work hard to keep our organization at the forefront of this changing health care arena and ensure the AUA remains the premier urological association, advancing urology and providing support to members and communities throughout the world. ◆

MEDISUITE

MediSuite Pharmacy

Cary, NC

Mail Order Pharmacy

Specializing in generic urology medications

Sildenafil • Tadalafil • Abiraterone • Silodosin • Clomiphene

www.Medisuite.com

On all eRx systems (search under "mail order" in your EMR) – including Epic

Licensed to ship medications to 44 states and D.C.

All prices include home delivery

Phone: 919.200.6952 Email: info@medisuiterx.com Fax: 919.200.6951

Practice Tips & Tricks

▼ Continued from page 1

with a background showing books and files, which was off-putting. Viewers were looking at the titles of my books and not me. Be aware of the background and make it as plain and bland as possible. Check the lighting to minimize glare and reflections.

Ensure that the visit is private and that there is no noise from your staff if you are in your office or from family members if you are working from home. No files or other papers or reports should be present that are not pertinent to the patient. Your mobile phone should be turned off.

Dress for success. We should dress like physicians. This includes a shirt, tie and white lab coat. An alternative is to wear a scrub top with a white coat.

Be on time. With a virtual visit your patients are expecting this. Many of your patients are working remotely and have other calls and meetings to attend, or they are helping their children with online school assignments, so it is imperative that you be on time for the telemedicine visit.

Review patient complaints and charts before the virtual appointment, just as with an in-office visit. Doing so allows you to look at the camera and not at charts or other papers on your desk.

Always maintain eye contact with patients by looking into the webcam instead of their on-screen faces.

Give the visit your undivided attention. That means no e-mails or other forms of multitasking. Do not eat or drink coffee during the visit.

Conclude by asking patients if all of their questions have been answered.

After answering all of their questions be certain they understand your recommendations and know about their medications and when to schedule the next virtual visit.

Finally, ask for feedback at the end of the virtual visit in order to improve your next appointment.

The bottom line is that there are no golden rules that physicians can follow to make virtual visits successful. However, you can demonstrate empathy and caring even if you cannot touch the patient. Perhaps a few of these suggestions will help you improve your connectivity using virtual health care. If you have any ideas to enhance the virtual visit, please let me hear from you. I can be reached at doctorwhiz@gmail.com. ◆

AUA NEWS

June 2020
Volume 25 | Issue 6

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

Associate Editors
Sam S. Chang, MD
Nashville, Tennessee
Amy E. Krambeck, MD
Indianapolis, Indiana
Jeremy B. Myers, MD
Salt Lake City, Utah
David F. Penson, MD, MPH
Nashville, Tennessee
David Rapp, MD
Charlottesville, Virginia
Hossein Sadeghi-Nejad, MD, CM
Hackensack, New Jersey
Aseem Shukla, MD
Philadelphia, Pennsylvania

Spanish Edition Editor
Alejandro Remigio Rodriguez, MD
Rochester, New York

Executive Editor
Patricia Banks, Executive Vice President
Marketing, Communications, Publications & Member Engagement
American Urological Association
1000 Corporate Boulevard
Linthicum, Maryland 21090

Managing Editor
Dorsey Mills
Publications Department
American Urological Association
1000 Corporate Boulevard
Linthicum, Maryland 21090

Production
Cenveo Publisher Services
3575 Hempland Rd
Lancaster, Pennsylvania

National Sales Manager
The Walchli Tauber Group
2225 Old Emmorton Road, Suite 201
Bel Air, MD 21015
Phone: 443-512-8899 ext. 101

American Urological Association
2020–2021 AUA Officers

President
Scott K. Swanson, MD, FACS
President-elect
Raju Thomas, MD, FACS, FRCS, MHA
Immediate Past President
John H. Lynch, MD, FACS
Secretary John D. Denstedt, MD, FRCSC, FACS, FCAHS
Treasurer David F. Green, MD, FACS

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. Copyright © 2020 by American Urological Association Education and Research, Inc.. No part of this publication may be reproduced in any form or language without written permission from the publisher. 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.

Disclaimer: The statements and opinions contained in the articles in **AUA*News*** are solely those of the individual authors and contributors and not of the American Urological Association. The appearance of advertisements in **AUA*News*** is not a warranty, endorsement or approval of the products or services advertised or of their effectiveness, quality or safety. The content of this publication may contain discussion of off-label uses of some of the agents mentioned. Please consult the prescribing information for full disclosures of approved uses. The American Urological Association disclaims responsibility for any injury to persons or property resulting from any ideas or products referred to in the articles or advertisements.

How Early Should Early Salvage Radiation Be Performed?

Xinglei Shen, MD

Ronald Chen, MD, MPH

Kansas City, Kansas

For patients with prostate cancer with adverse pathological features on the radical prostatectomy specimen there has long been a debate on the relative benefits and harms of adjuvant radiation treatment (RT) for undetectable prostate specific antigen (PSA) vs salvage RT for patients with detectable PSA.

It has been well-established that patients with these adverse pathological features have a high risk of residual disease after prostatectomy.[1] However, some have proposed that early salvage RT may offer oncologic outcomes similar to those of adjuvant therapy while minimizing overtreatment for those cured by surgery alone. The recent report of 3 randomized trials provides high quality data to inform this debate.

RAVES (Radiotherapy – Adjuvant Versus Early Salvage),[2] RADICALS (Radiation Therapy and Androgen Deprivation Therapy in Treating Patients Who Have Undergone Surgery for Prostate Cancer)[3] and GETUG-AFU 17 compared adjuvant to early salvage RT for patients with adverse pathological features on the radical prostatectomy specimen. RAVES and RADICALS were presented in 2019 at the ASTRO (the American Society for Radiation Oncology) and ESMO (European Society for Medical Oncology) meetings, respectively. At 5 to 8 years of followup there was no difference in biochemical event-free survival between adjuvant and early salvage radiation. In the preplanned ARTISTIC meta-analysis (which also included the GETUG AFU 17 trial) the estimated potential absolute difference in biochemical event-free survival at 5 years between the adjuvant and early salvage radiation approaches was 1%.[4]

It should be noted that these studies have not been published. The process of peer review and providing further details on the study design and results are critically important for clinicians and researchers in fully evaluating whether and how these trials should impact clinical practice.

Nevertheless, if these results hold true and early salvage RT becomes increasingly adopted, "how early should early salvage radiation be performed" is an important and practical clinical question. The AUA defines biochemical recurrence after surgery as PSA 0.2 ng/ml or greater confirmed on a second reading. This cutoff partly reflects the lower sensitivity of historical tests. However, with more sensitive PSA tests now widely available, is there a clinical reason to wait for salvage therapy in a patient known to be at high risk for residual cancer, and with rising PSA (even if less than 0.2 ng/ml)?

The best data to address this question come from a large multi-institutional cohort of 2,460 patients who received salvage RT.[5] Based on variations in clinical practice the patients were referred for and received salvage RT at various PSA levels after radical prostatectomy. Patients who received salvage RT at PSA less than 0.2 ng/ml had the best long-term oncologic outcomes. Five-year freedom from biochemical failure rates were directly correlated with PSA at salvage RT, at 71% (PSA 0.01 to 0.2 ng/ml), 63% (PSA 0.21 to 0.5 ng/ml), 54% (PSA 0.51 to 1.0 ng/ml) and 43% (PSA 1.01 to 2.0 ng/ml). Importantly, 10-year distant metastasis rates were also correlated with PSA at time of treatment, at 9% (PSA 0.01 to 0.2 ng/ml), 15% (PSA 0.21 to 0.50 ng/ml), 19% (PSA 0.51 to 1.0 ng/ml) and 20% (PSA 1.01 to 2.0 ng/ml). The effect of PSA on biochemical control and distant metastasis remained significant when stratified by Gleason score.

For a patient whose prostate cancer was of sufficient clinical significance to warrant radical prostatectomy, these results are not surprising. When residual disease is detectable earlier salvage treatment leads to better outcomes. These data suggest that the historical PSA cutoff of 0.2 ng/ml after radical prostatectomy may no longer represent the optimal guidance regarding salvage therapy for every patient in modern times.

There are 2 important issues to emphasize when interpreting the results of these recent randomized trials. First, they compared adjuvant RT to early salvage RT. In the RADICALS trial the trigger for early salvage radiation was a PSA greater than 0.1 ng/ml and 2 consecutive rises, or 3 consecutive PSA rises without a threshold level, whereas in the RAVES trial the trigger was PSA 0.2 ng/ml or greater. Median PSA at salvage radiation in both trials was 0.2 ng/ml. The safety and efficacy of waiting for PSAs beyond these low levels were not studied, and it would be incorrect for clinicians to inform patients that any salvage timing is equivalent to adjuvant therapy.

Second, patients enrolled in these trials had favorable characteristics. In general, 73% to 91% had Gleason 7 or less disease, median preoperative PSA was 7.4 to 7.9 ng/ml and only 19% to 21% had seminal vesicle invasion. Currently many clinicians may suggest active surveillance rather

▼ Continued on page 6

Developing a Registry for Focal Therapy of Prostate Cancer

Patrick Lewicki, MD
New York, New York

Art Sedrakyan, MD, PhD
New York, New York

Jim C. Hu, MD
New York, New York

Michael A. Gorin, MD
Baltimore, Maryland

Recent improvements in prostate imaging and biopsy technology have stimulated interests and efforts in partial prostate gland ablation (PGA), or focal therapy, for clinically localized prostate cancer. Additionally, patient demand for a treatment paradigm that may minimize biopsies while avoiding the adverse effects of whole gland treatment is well recognized.

Previously, American men had traveled abroad for high intensity focused ultrasound (HIFU) until the U.S. Food and Drug Administration (FDA) approval of this technology for prostate ablation in 2015. Together these factors have fueled increased use of HIFU as well as other ablative technologies such as cryotherapy for PGA.

Accumulation of high quality prospective evidence on the efficacy and safety of PGA has proven difficult for a multitude of reasons. Dozens of clinical trials for prostate cancer have closed prematurely in recent years due to failed recruitment and lack of patient or physician equipoise, among other reasons. Regarding trial design, oncologic end points such as metastasis-free and cancer specific survival in men with low or favorable intermediate risk disease would take years to develop.

Moreover, there is controversy in terms of appropriate patient selection for PGA with respect to tumor grade, volume, location and magnetic resonance imaging characteristics. There is also no consensus regarding treatment or surveillance protocols. Additional hurdles in study design include the challenge of posttreatment prostate specific antigen interpretation and biopsy strategy. This lack of consensus hampers the generalizability of any single study's results.

These challenges beg for evidence collection beyond the context of randomized controlled trials. The FDA has acknowledged a similar need in other areas of medicine and has published guidance on the use of real-world data (eg, data collected as part of a registry) to support regulatory decisions. The concept is not a loosening of evidentiary standards but rather was established by the FDA to outline what constitutes data of suitable quality in a broader context.

The SPARED (Study of Prostate Ablation Related Energy Devices) registry was developed over a series of meetings as part of the Medical

▼ Continued on page 7

Decreasing Opioid Use for Female Pelvic Medicine and Reconstructive Surgery



Meenakshi Davuluri, MD, MPH **Shirly Solouki, MD** **Nitya Abraham, MD**

The Bronx, New York

Opioid overdoses killed more than 47,600 people in 2017. These deaths commonly involved prescription opioids at a rate 45.2% higher than in the previous year.[1] Physicians, including urologists, have recognized their role in curbing this epidemic.

In recent years numerous studies have been published in the urology literature describing optimal postoperative opioid needs within oncology, endoscopic surgery and female pelvic medicine and reconstructive surgery (FPMRS). The AUA published its own position statement on opioid use to help guide urologists on prescription practices.[2] This statement encourages urologists to adequately address pain while increasing awareness of opioid overprescription. Recommendations include using the lowest dose and potency narcotics, optimizing nonnarcotic alternatives and providing patient education regarding proper disposal of unused tablets.

To understand how we can decrease opioid prescriptions in FPMRS it is imperative to examine postoperative opioid prescription and usage patterns. We recently demonstrated that patients used an average of 10 opioid tablets following FPMRS surgery despite being prescribed a range of 12 to 17 opioid tablets.[3] As a result more than 50% of patients had excess opioid tablets with 90% reporting not disposing of them. These excess tablets and lack of proper opioid disposal can increase the potential for opioid misuse and abuse.

Multimodal analgesia is key to minimizing narcotic requirements for postoperative pain control and has been widely promoted as part of enhanced recovery after surgery protocols at many institutions. First, the appropriate use of oral nonnarcotic medication should be implemented. For 28 to 72 hours after FPMRS we recommend 650 mg acetaminophen every 6 hours alternating with nonsteroidal anti-inflammatory drugs (NSAIDs, ie ibuprofen, ketorolac) every 6 hours, with 5 mg oxycodone immediate release only as needed for breakthrough pain (0 to 10 tablets prescribed). After 2 or 3 days the acetaminophen and NSAIDs can be taken as needed.

In addition, randomized controlled trials have shown that the perioperative use of gabapentin can decrease the time frame for which opioids are required postoperatively.[4] Therefore, this medication can be considered if there are no contraindications. Stool softeners such as docusate sodium or sennosides are prescribed to counteract any constipation associated with the narcotics and minimize straining after surgery.

As we continue to study the amount of narcotics needed to provide patients with appropriate postoperative pain control there are simultaneous efforts to explore adjunct methods of multimodal analgesia. Some of the tools available to surgeons in the operating room are local anesthetics including pudendal nerve and transversus abdominal plane (TAP) blocks.

The pudendal nerve provides major sensory innervation to the external genitalia and pelvic floor. Local anesthetic is injected transvaginally or transcutaneously into the pudendal nerve using the ischial spine or ischial tuberosity as landmarks, respectively. This block can be easily administered once the patient is placed in dorsal lithotomy position and does not increase the surgical time.

Use of this block in vaginal colporrhaphy was shown to decrease postoperative pain and opioid requirements. A study demonstrated that pudendal nerve block significantly reduced morphine requirements 4 hours after surgery (52% in control arm vs 22% in pudendal block arm).[5] These analgesic effects were seen up to 48 hours after surgery.

The TAP block has not been studied in FPMRS cases but it has shown promise in gynecologic surgery. The TAP block consists of administration of local anesthetic superior to the transversus abdominis muscle, blocking the T6-L1 sensory nerves and making it appropriate for transabdominal surgery such as robotic sacrocolpopexy and rectus fascia sling surgery.

The TAP block has been shown to be as effective as a spinal block with a superior safety profile, eliminating complications such as hypotension and dural puncture. Additionally, it is an effective way to decrease postoperative narcotic pain requirements, delirium and length of stay.[6] The TAP block may be an underused tool in FPMRS and should be considered given its potential benefit and minimal impact on surgical workflow in the operating room. TAP or pudendal blocks can be performed on a case by case basis depending on patient factors and surgeon expertise.

In conclusion, urologists can continue minimizing opioid use after FPMRS by using nonopioid analgesics, prescribing the minimum number of opioids necessary based on data in the literature and exploring alternative analgesic approaches like pudendal or TAP blocks in the operating room. Information about safe disposal of narcotics should be given to every patient.

This multimodal approach seeks to offer optimal postoperative pain control while decreasing the potential diversion of opioids into the community where they can be misused. After implementing these guidelines at our institution we have improved our ability to address patient postoperative pain needs while limiting the amount of narcotics prescribed. ◆

1. Scholl L, Seth P, Kariisa M et al: Drug and opioid-involved overdose deaths – United States, 2013–2017. MMWR Morb Mortal Wkly Rep 2019; **67**: 1419.
2. Solouki S, Plummer M, Agalliu I et al: Opioid prescribing practices and medication use following urogynecological surgery. Neurourol Urodyn 2019; **38**: 363.
3. AUA Board of Directors: AUA Position Statement: Opioid Use. American Urological Association 2019. Available at https://www.auanet.org/guidelines/opioid-use.
4. Hah J, Mackey SC, Schmidt P et al: Effect of perioperative gabapentin on postoperative pain resolution and opioid cessation in a mixed surgical cohort: a randomized clinical trial. JAMA Surg 2018; **153**; 303.
5. Rouholamin S, Jabalameli M and Mostafa A: The effect of preemptive pudendal nerve block on pain after anterior and posterior vaginal repair. Adv Biomed Res 2015; **4**: 153.
6. Shahait M and Lee DI: Application of TAP block in laparoscopic urological surgery: current status and future directions. Curr Urol Rep 2019; **20**: 20.

Timing of Early Salvage Radiation

▼ Continued from page 5

than radical prostatectomy for these patients. In addition, the RADICALS trial allowed patients whose only risk factor was Gleason 7 to 10 disease or preoperative PSA 10 ng/ml or greater.

Therefore, results from these trials do not clearly apply to patients with more aggressive prostate cancers (high risk disease, node positive or multiple adverse pathological risk factors)[6] who make up a large portion of those treated with radical prostatectomy today. For these patients with aggressive prostate cancers who are not well represented in the recently reported trials, adjuvant RT should still be discussed with the patient as an important consideration.

The optimal treatment for patients after radical prostatectomy remains an active area of research. Multiple clinical trials have provided high level evidence to guide current clinical practice and more data will emerge to continue to refine the optimal timing of radiation after prostatectomy. ◆

1. Swanson GP, Hussey MA, Tangen CM et al: Predominant treatment failure in postprostatectomy patients is local: analysis of patterns of treatment failure in SWOG 8794. J Clin Oncol 2007; **25**: 2225.
2. Kneebone A, Fraser-Browne C, Delprado W et al: A phase III multi-centre randomised trial comparing adjuvant versus early salvage radiotherapy following a radical prostatectomy: results of the TROG 08.03 and ANZUP "RAVES" Trial. Int J Radiat Oncol Biol Phys, suppl., 2019; **105**: S37.
3. Parker C, Clarke NW, Cook A et al: Timing of radiotherapy (RT) after radical prostatectomy (RP): first results from the RADICALS RT randomised controlled trial (RCT) [NCT00541047]. Ann Oncol, suppl., 2019; **30**: v883.
4. Vale CL, Brihoum M, Chabaud S et al: LBA48_PR - Adjuvant or salvage radiotherapy for the treatment of localised prostate cancer? A prospectively planned aggregate data meta-analysis. Ann Oncol, suppl., 2019; **30**: v883.
5. Tendulkar RD, Agrawal S, Gao T et al: Contemporary update of a multi-institutional predictive nomogram for salvage radiotherapy after radical prostatectomy. J Clin Oncol 2016; **34**: 3648.
6. Fossati N, Karnes RJ, Cozzarini C et al: Assessing the optimal timing for early salvage radiation therapy in patients with prostate-specific antigen rise after radical prostatectomy. Eur Urol 2016; **69**: 728.

Focal Therapy of Prostate Cancer Registry

▼ Continued from page 5

Device Epidemiology Network with a focus on addressing the need for real-world data on PGA for localized prostate cancer.[1,2] The stakeholders include FDA officers, academic and community urologists, and industry partners, among others.

A necessary first step was to establish consensus regarding enrollment, clinical variables to capture, and whether to incorporate new technologies beyond HIFU and cryotherapy.[3] A Delphi process consisting of several rounds of surveys and conference calls was used to reach consensus on patient and treatment characteristics as well as oncologic, functional and safety outcomes to be included in the registry.

The group agreed to include data for all approved medical devices for prostate ablation as this would allow benchmarking of technologies to each other. Moreover, it was decided to collect data on whole gland ablation and PGA. Finally, consensus was reached on the use of validated quality of life instruments to capture urinary and sexual function outcomes including ejaculate volume, which is an important consideration for some patients.

The multi-institutional SPARED registry launched earlier this year and several sites have already contributed prospectively collected real-world data. Additionally, discussions for partnership with professional societies are underway to encourage more widespread participation in the project. SPARED leadership hope to incorporate data from the United States and abroad into the registry. Data from academic and community centers are welcome.

Furthermore, Dr. Hu leads PC CONCEPT (Prostate Cancer Comparative Outcomes of New Conceptual Paradigms for Treatment), which will capture additional data to inform comparative effectiveness of new treatments such as PGA and stereotactic body radiation as well as traditional options.[4] In parallel to this prospective registry a FDA led multispecialty conference on trial design has given way to a proposed randomized trial for PGA with alternative end points (upgrade on biopsy and repeat or salvage therapy).[5]

Through these incremental advances the accumulation of PGA evidence will define ideal patient selection and outcomes and inform men with prostate cancer, their loved ones, providers, payers and policymakers regarding the effectiveness of PGA. ◆

1. Medical Device Epidemiology Network: SPARED. Medical Device Epidemiology Network 2020. Available at http://mdepinet.org/spared-2/. Accessed April 20, 2020.
2. Gross MD, Sedrakyan A, Bianco FJ et al: SPARED collaboration: patient selection for partial gland ablation in men with localized prostate cancer. J Urol 2019; **202**: 952.
3. Golan R, Bernstein A, Sedrakyan A et al: Development of a nationally representative coordinated registry network for prostate ablation technologies. J Urol 2018; **199**: 1488.
4. Hu JC and Chen RC: Prostate Cancer Comparative Outcomes of New Conceptual Paradigms for Treatment. Patient-Centered Outcomes Research Institute 2019. Available at https://www.pcori.org/research-results/2019/prostate-cancer-comparative-outcomes-new-conceptual-paradigms-treatment-pc. Accessed April 20, 2020.
5. Weinstock C, Suzman D, Kluetz P et al: Development of treatments for localized prostate cancer in patients eligible for active surveillance: U.S. Food and Drug Administration Oncology Center of Excellence Public Workshop. J Urol 2020; **203**: 115.

The Era of Radiation Survivorship: Victims of Our Own Success

Bradley A. Erickson, MD
Iowa City, Iowa

Matthew Grimes, MD
Madison, Wisconsin

The introduction of radiotherapy revolutionized the treatment of pelvic malignancies where surgery can be technically difficult and associated with significant morbidity. Increased use of pelvic radiotherapy has cured millions of patients, although sometimes at the cost of devastating urological morbidity due to radiation toxicity. As urologists we are charged with helping these patients, and must understand the pathophysiology of radiation injury, recognize the increasing burden of genitourinary (GU) radiation toxicity and wield techniques to prevent, mitigate and manage these injuries.

How Does Radiation Injure Tissue?

The goal of radiotherapy is selective destruction of cancer cells while minimizing toxicity to normal tissue. Ionizing radiation is so named because the high energy particles overcome the binding energy of electrons, knocking them out of their orbits to create ions. These ions cause cell death in 3 ways.

First, ionizing radiation directly damages cellular DNA, causing strand breaks and/or base damage. This mechanism preferentially kills cancer cells as they are rapidly dividing and less able to repair DNA damage compared to normal cells. Second, radiation interacts with intracellular water to produce reactive oxygen species causing cell death via direct oxidative damage and activation of cell-mediated immunity. This mechanism is less selective and forms the basis for acute radiation toxicity. Lastly, radiotherapy alters gene expression which may provide the basis for development of delayed toxicity.

Radiation toxicity occurs when healthy cells are destroyed or injured. Radiation toxicity is proportional to the dose received, which varies between tissue types. This variability is accounted for in calculation of the absorbed dose which is expressed in units called gray (Gy).[1] Radiation oncologists use 2 important mechanisms to mitigate radiation toxicity, fractionation and targeting.

Fractionation of radiation treatment means that the total dose of radiotherapy is delivered in several smaller treatments. For example, prostate cancer radiotherapy is typically 80 Gy but is delivered in 40 treatments (fractions) of 1.8 to 2.0 Gy each. Fractionation maximizes the killing of cancer cells and minimizes normal cellular death as noncancer cells are better able to repair DNA damage and rebound between fractions.

The goal of improved targeting is delivery of the desired dose to the tumor while minimizing the dose received by adjacent tissues. The details of these techniques are beyond the scope of this discussion but are the rationale for radiation modalities such as stereotactic body radiation therapy, intensity modulated radiation therapy and proton therapy.

The Era of Survivorship

Approximately 15% of all radiotherapy is used in the treatment of pelvic malignancies. Radiation is an effective means of cancer control achieving robust long-term survival. This causes a happy problem. An estimated 4.5 million cancer survivors who received pelvic radiotherapy are at risk for treatment toxicity. Genitourinary radiation toxicity is classified as acute or delayed and graded in severity from 0 to 5 by the Radiation Therapy Oncology Group with grade 3 or higher complications typically requiring surgical intervention.[2]

Acute toxicity is generally proportional to absorbed dose, follows a predictable course and resolves in 2 to 6 weeks after treatment. As urologists we most frequently encounter the delayed toxicity of radiotherapy following prostate cancer treatment (see figure). For patients with prostate cancer the incidence of delayed grade 2 or greater GU toxicity is 15% to 20% and grade 3 or greater is 3% to 6%. This translates into 900,000 survivors with grade 2 or greater toxicity and 270,000 survivors with grade 3 or greater toxicity from prostate cancer treatment alone.[3] The burden of this toxicity is high as patients with grade 3 or greater urinary adverse events typically require surgical intervention.

What are the Solutions?

As urologists we are often faced with the challenge of treating patients who are cancer-free but experience delayed toxicity from radiotherapy. In this setting tissue injury has already occurred and we manage the sequelae of injury using the same techniques as in nonradiated cases, although with generally lower success.

Treatments to reverse or mitigate the effects of radiation injury are lacking. The most commonly used and only U.S. Food and Drug Administration approved example is hyperbaric oxygen for radiation cystitis. Hyperbaric oxygen increases the partial pressure of oxygen in tissue that promotes angiogenesis, progenitor cell mobilization and improved wound healing. Hyperbaric oxygen therapy is effective for the management of radiation cystitis. However, the specialized equipment and required frequency of treatments can create significant barriers to delivery.

Conceptually, the best way to reduce radiation toxicity is to prospectively identify patients at high risk for severe toxicity and direct them toward alternative treatments. The extreme

▼ Continued on page 8

Era of Radiation Survivorship

▼ Continued from page 7

heterogeneity of radiation toxicity suggests a genetic basis for susceptibility to injury, which is supported by animal studies.[4] Further elucidation of the genetic changes responsible for increased toxicity may enable prospective identification of these patients and allow avoidance of radiotherapy or at least improved counseling regarding the risks of treatment.

In lieu of these tools we focus on reducing the effective dose delivered to nontumor tissues and/or delivering chemo-sensitizing agents to improve selective cell death of cancer cells. Examples of this approach include intravesical instillation of glycosaminoglycans before radiotherapy to avoid radiation cystitis and the use of hydrogel spacers placed between the rectum and prostate to reduce gastrointestinal toxicity during prostate radiotherapy. While effective, these techniques can be costly and logistically burdensome.

In summary, while the absolute incidence of severe GU toxicity following pelvic radiotherapy is low the widespread use of this modality has created a large and growing cohort of cancer survivorships burdened with this toxicity. As urologists it is incumbent on us to consider the potential impact of this morbidity when using pelvic radiotherapy in treatment of our patients with cancer and to be well prepared to manage these situations when they arise. As scientists it is critical to understand the mechanisms underlying radiation toxicity and to organize efforts to treat and prevent urological complications in this ever growing cohort of cancer survivors. ◆

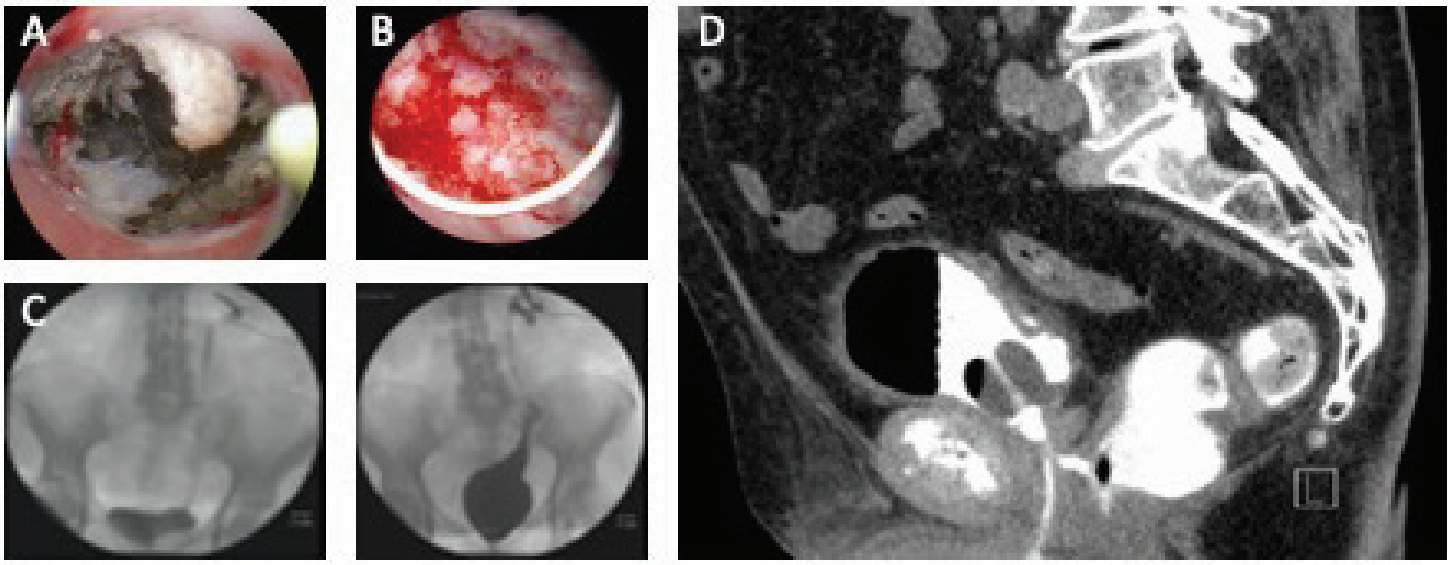


Figure. Examples of severe toxicity following pelvic radiotherapy. *A*, bladder neck contracture with stone formation and radionecrosis following adjuvant radiotherapy for prostate cancer. *B*, cystoscopic appearance of radiation cystitis. *C*, preoperative (left) and postoperative (right) antegrade nephrostograms of radiation associated ureteral stricture repaired with Boari flap and ureteral reimplantation. *D*, computerized tomography cystogram demonstrating rectourethral fistula following primary radiotherapy for prostate cancer.

1. Brenner DJ and Hall EJ: Computed tomography–an increasing source of radiation exposure. N Engl J Med 2007; **357**: 2277.
2. Cox JD, Stetz J and Pajak TF: Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 1995; **31**: 1341.
3. Mak RH, Hunt D, Efstathiou JA et al: Acute and late urinary toxicity following radiation in men with an intact prostate gland or after a radical prostatectomy: a secondary analysis of RTOG 94-08 and 96-01. Urol Oncol 2016; **34**: 430.
4. Zwaans BMM, Wegner KA, Bartolone SN et al: Radiation cystitis modeling: a comparative study of bladder fibrosis radio-sensitivity in C57BL/6, C3H, and BALB/c mice. Physiol Rep 2020; **8**: e14377.

Real-World Implementation of a Shared Decision Aid for Localized Prostate Cancer

Jonathan Bergman, MD, MPH
Los Angeles, California

Christopher S. Saigal, MD, MPH
Los Angeles, California

David F. Penson, MD, MPH
Nashville, Tennessee

Shared decision making (SDM) is a goal promoted in most professional society guidelines, particularly for the management of preference sensitive conditions like localized prostate cancer.[1] However, actualizing that goal remains elusive, and none of the guidelines espousing shared decision making delineates how to implement it across populations.

Decision aids are electronic or paper tools intended to facilitate implementation of SDM. Even when a decision aid is working in one environment, scaling its use in a wide array of clinical settings is often difficult. Additionally, in order for decision aids to be clinically useful, updating them with contemporaneous data is vital to reflect clinical practices that affect the coetaneous patient being counseled.

PCORI (Patient-Centered Outcomes Research Institute) funded a project on how to optimize effective decision aid use in men with prostate cancer in different care settings. The care settings include 2 academic medical centers (UCLA Health and Vanderbilt University Medical Center) and 1 public hospital (Olive View UCLA Medical Center).

The software based decision aid WiserCare has been shown to improve decisional quality, key aspects of SDM and patient perceptions of physicians.[2] WiserCare delivers a decision analysis to patients regarding treatment options by personalizing the clinical evidence on treatment outcomes in light of their own clinical factors. However, the outcomes data used in WiserCare's algorithms must be updated as evidence changes regarding topics like survival in active surveillance or quality of life outcomes after robotic surgery.

An earlier PCORI funded project, CEASAR (Comparative Effectiveness Analysis of Surgery and Radiation for Localized Prostate Cancer), reported recent population based data on outcomes of care.[3] Getting those data to patients and physicians for use in decision making can be challenging. However, the new PCORI project funded incorporation of CEASAR data into the WiserCare data models so they could be used in routine care. Data from CEASAR were successfully incorporated into models to predict sexual, urinary and bowel function related outcomes of treatment by age, baseline function, comorbidities and other factors.

Minority representation is more robust in CEASAR than in previous data sets, and functional outcomes are often worse in African American men compared with Caucasians.[4] Using these data in WiserCare's software allows for better prediction and counseling for those men in an example of the power of the approach.

The overall Net Promoter Score was 93% for the doctor relationship and 91% for hospital, both strikingly high (fig. 1). Net Promoter Scores are based on how likely the patient is to recommend the doctor or hospital to a friend or family member, and are tied to service line growth. For reference, Apple®'s Mac® has one of the highest Net Promoter Scores in its industry at 76. Decisional Conflict scores (fig. 2) were strikingly low at all sites, indicating that men left the consultation with greater confidence in their choice (these scores are significantly improved from baseline scores at one site). Satisfaction with Care was high across all sites (fig. 3).

The PCORI grant aims to use the methods of implementation science research to document specific tactics needed for SDM programs to succeed in different environments (eg between an academic

▼ Continued on page 9

Shared Decision Aid for Localized Prostate Cancer

▼ Continued from page 8

medical center and a county hospital). Practice changes related to implementation were tailored to the specific needs of each population and, therefore, differed significantly among the 3 sites. Leadership at the Los Angeles County Department of Health Services (LAC-DHS) places a premium on equity, ensuring that patients across LAC-DHS receive similar care regardless of point of entry. Thus, while WiserCare was only available at one of the county hospitals (Olive View), the intervention was offered to patients across the entire health system, which serves over 700,000 unique patients annually.

As specialty and primary care are integrated and buttressed by eConsult, cross clustered scheduling was readily feasible and transportation was provided to patients with significant travel distance. A Spanish language version of the decision aid was also key to scaling. At UCLA the intervention unearthed a common problem among many tertiary referral centers. Patients often arrived for second opinion consultations without their pathology slides or reports. Therefore, a process was initiated to inquire about and upload these items at the point of referral scheduling. At Vanderbilt, during the intervention period there was an increase in the number of patients who saw urology and radiation oncology on the same visit day.

Our multisite effort represents the next phase in shared decision making, which is broad implementation of models that shape differently for disparate patients and populations, responding to unique needs and evolving to best serve each individual. If these efforts can be expanded throughout the country, they will represent a step towards maximizing our ability to empower each man with prostate cancer to knowledgeably navigate the disease and his life.

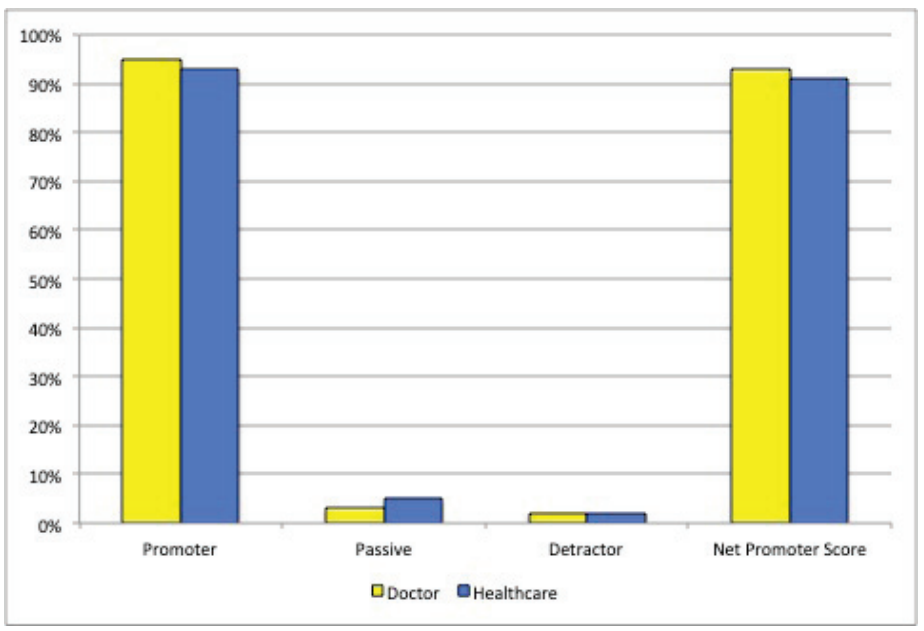


Figure 1. Net Promoter Scores.

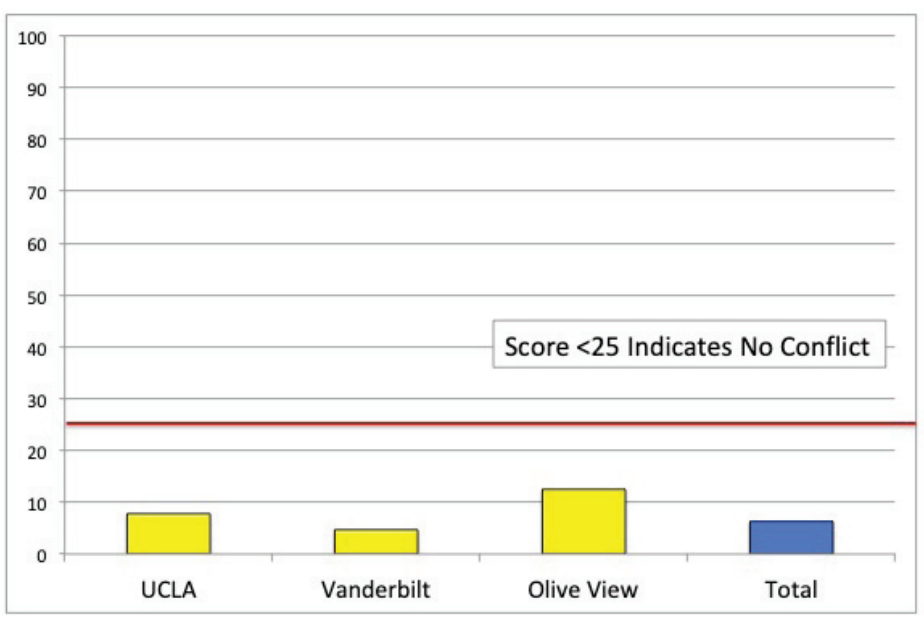


Figure 2. Decisional conflict by institution.

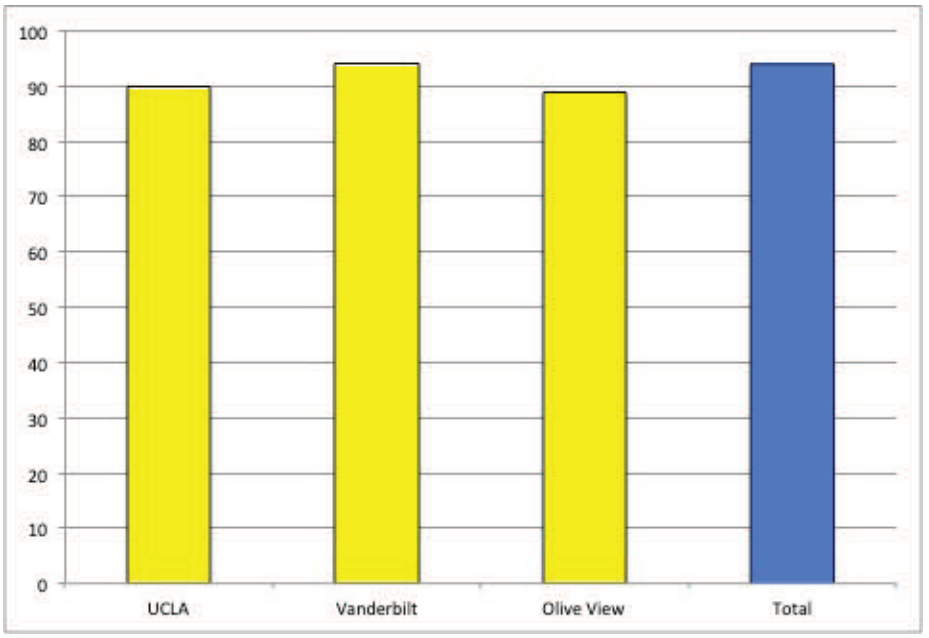


Figure 3. Satisfaction with care by institution.

Many men struggle with making "the right choice" in this setting, and each choice has downstream risks.

However, as noted psychologist Ellen Langer, PhD has advised, although these men cannot control the outcomes of any treatment they choose, they can control the process they use to decide.[5] She succinctly paraphrases her philosophy for optimal decision making as, "Don't make the right decision; make the decision right." ◆

1. Sanda MG, Cadeddu JA, Kirkby E et al: Clinically localized prostate cancer: AUA/ASTRO/SUO guideline. Part I: risk stratification, shared decision making, and care options. J Urol 2018; **199**: 683.
2. Peña A, Qian Z, Lambrechts S et al: Evaluation of implementation outcomes after initiation of a shared decision-making program for men with prostate cancer. Urology 2019; **132**: 94.
3. Avulova S, Zhao Z, Lee D et al: The effect of nerve sparing status on sexual and urinary function: 3-year results from the CEASAR study. J Urol 2018; **199**: 1202.
4. Gandaglia G, Bray F, Cooperberg MR et al: Prostate cancer registries: current status and future directions. Eur Urol 2016; **69**: 998.
5. Langer E: The illusion of calculated decisions. In: Beliefs, Reasoning, and Decision Making. Essex, United Kingdom: Psychology Press 2013: pp 43-64.

Ureteroscopic Dusting versus Mini-Percutaneous Nephrolithotomy




Ron Golan, MD **Ojas Shah, MD** **Eric Ballon-Landa, MD** **Roger Sur, MD**

New York, New York San Diego, California

The AUA/Endourological Society surgical management of stones guideline primarily uses size criteria and stone location to guide procedure selection for renal stones, recommending percutaneous nephrolithotomy (PCNL) for stone burden larger than 2 cm and shock wave lithotripsy (SWL) or endoscopic techniques (ureteroscopy [URS] or PCNL) for stones 2 cm or smaller depending on location.[1]

Therefore, the surgeon treating a patient with a 2 cm renal stone must account for several factors when selecting the appropriate procedure. We discuss the merits of URS vs mini-PCNL (MIP) for the 2 cm renal stone. Mini-PCNL is a modification of standard PCNL that uses a smaller caliber access sheath (smaller than 24Fr).

Ureteroscopy

URS is the workhorse procedure for the urologist and among the most commonly performed procedures in urological surgical training. It is a well tolerated outpatient procedure with limited morbidity, negligible blood transfusion requirement and rapid recovery. The procedure can be safely performed in patients requiring anticoagulation or antiplatelet therapy, or in patients with physical or anatomical anomalies limiting percutaneous access. Although published series comparing URS to PCNL suggest a higher need for re-treatment and lower stone-free rates (SFRs), these studies were performed without the newer high powered lasers (100 to 120W) that improve the efficiency of stone dusting.[2]

Stone dusting techniques have been shown to decrease operation times and reduce short-term disposable costs with low complication and repeat procedure rates in short-term followup.[3] To date, these newer laser techniques have not been well studied against standard or mini-PCNL, an area ripe for future study. High success rates with relatively low morbidity via URS for intermediate size stones have also led to many centers increasing their treatment size threshold to stone burdens larger than 2 cm, either by patient choice or in those not suitable for PCNL.

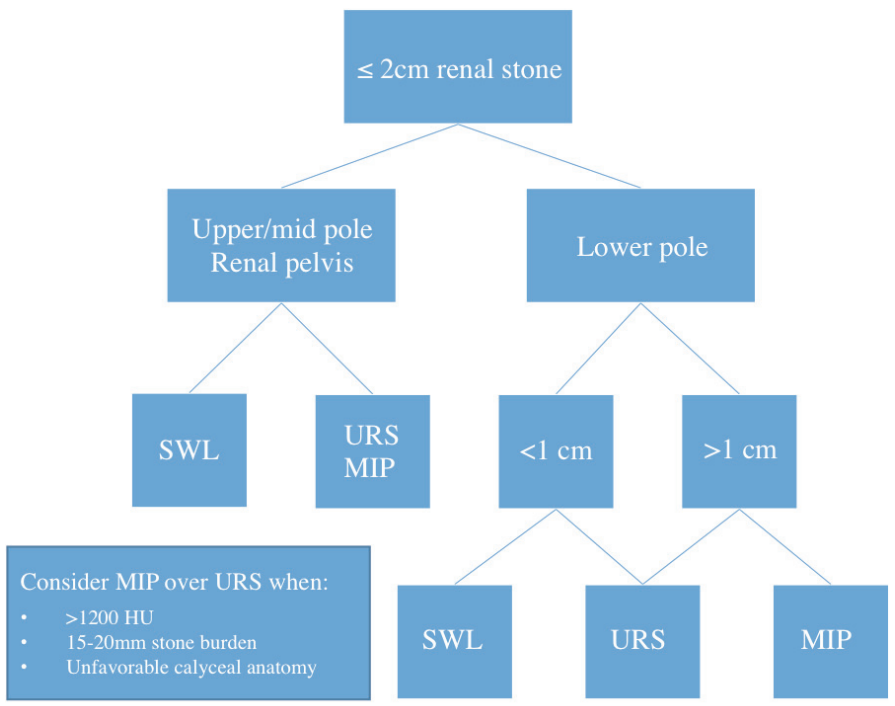


Figure. Flow chart for management of renal stone 2 cm or smaller.

Reusable or single use ureteroscopes are also widely available in the United States, and multiple technological advancements have allowed for simultaneously decreased scope diameter, improved image quality and preserved deflectability to allow the surgeon to access all areas of the collecting system.

Multiple international series have also demonstrated decreased length of stay (LOS) for URS compared to mini-PCNL (2.5 vs 4 days, p <0.01). However, this is less of an issue in the U.S. since the majority of URS is performed as an outpatient procedure.[2] The shorter LOS compared to PCNL is a major benefit of URS, although there is an increasing number of publications suggesting that outpatient PCNL, including mini-PCNL, can be safely performed in carefully selected patients.

Finally, radiation exposure with URS is substantially lower than with PCNL even when ultrasound guided percutaneous access is used. When also considering the impact of ionizing radiation from imaging and procedures, limiting radiation exposure is a valuable goal for the patient and surgeon.

Considering the procedure familiarity, ready access to high quality ureteroscopes, high success rates, low major complication rates and lower radiation exposure, URS should be recommended as first line treatment in stones up to 2 cm in size.

Mini-PCNL

Robust evidence supports that standard PCNL leads to higher stone-free rates for stones 2 cm or larger as well as lower pole renal stones larger than 1 cm (more than 90% SFR across numerous studies) compared to URS, although PCNL is associated with higher morbidity, pain and blood loss. Because of these limitations mini-PCNL was introduced to achieve similar SFRs without the morbidity of standard PCNL.

Compared to standard PCNL, mini-PCNL offers the advantage of lower blood loss (as well as transfusion rates) due to a smaller caliber renal access sheath at the trade-off of longer operation times. SFRs for single access mini-PCNL may be equivalent to standard PCNL, especially for stones smaller than 2 cm.[4]

Many definitions of mini-PCNL exist, including ultra-mini (11 to 13Fr) and micro (5Fr) access technologies with variability in practice patterns and use. This creates heterogeneity in the analysis of mini-PCNL and difficulty in interpreting and, thus, generalizing the data. This fact notwithstanding, mini-PCNL provides a higher SFR compared to URS at 89.3% and 80.1%, respectively (OR 2.01, 95% CI 1.53–2.64, p <0.01).[2] Additionally, it carries a favorable side effect profile similar to URS. Like URS, mini-PCNL uses holmium laser for stone fragmentation, although pneumatic or ultrasonic devices can also be deployed through larger mini-PCNL scopes.

We use a 17.6Fr sheath Karl Storz MIP nephroscope and holmium laser energy. The scope is large enough to evacuate 3 to 4 mm stone fragments and narrow enough in profile permitting torqueing to reach most calyces via a single access tract. Moreover, the nephroscope design permits trapping of stones and a vacuum cleaner effect that efficiently washes out most fragments without need for baskets or ancillary devices.

In conjunction with ultrasound guided renal access we are able to reduce ionizing radiation to patients. In 57 consecutive cases we demonstrated an average 44 second decrease in fluoroscopy time for the access portion alone (66 vs 22 seconds, p <0.001; unpublished data). In our initial series of 61 cases (mean stone size 2.2 cm) 63% of patients were discharged home on the same day (unpublished data).

When might the clinician favor mini-PCNL over URS? We propose the following algorithm for renal stones (see figure). Recognizing relative equivalence between URS and mini-PCNL, mini-PCNL can be considered in mid or upper calyceal stones or renal pelvis, particularly when a case has subtle nuances that prolong or challenge flexible ureteroscopic stone removal such as durile stones (Hounsfield units [HU] greater than 1,200) and larger stones (15 to 20 mm) that necessitate longer procedure times. Similarly, mini-PCNL may be preferred for lower pole stones in these former conditions with the 2 additional indications of unfavorable lower pole calyx (acute angle; thin, long infundibulum) and larger lower pole stones 10 to 20 mm.

Conclusions

Our clinical experience and evidence

▼ Continued on page 12

Long-Term Evidence for Treatment for Peyronie's Disease

Irwin Goldstein, MD
San Diego, California

Peyronie's disease (PD) is a tunica albuginea wound healing disorder characterized by collagen rich plaque formation. It may cause erect penile curvature associated with pain, psychological and physical symptoms, difficulties with sexual intercourse and relationship difficulties. Treatment options not yet evaluated in large, randomized, placebo controlled clinical trials include oral pentoxifylline, traction devices, intralesional injections of interferon α-2b and calcium channel blockers, and reconstructive surgery.

Collagenase clostridium histolyticum (CCH), which selectively targets type I and III collagen abundant in PD plaques, is the only injectable medication approved by the U.S. Food and Drug Administration for the treatment of adult men with a palpable plaque and dorsal and/or lateral penile curvature of 30 degrees or more at the start of therapy.[1] Two large, 12-month, double-blind, placebo controlled clinical trials[2] and 2, 9-month, open label studies[3,4] established clinical safety and efficacy of CCH for the treatment of PD. However, because long-term followup efficacy and safety data had not yet been assessed, counseling patients about expectations for long-term outcomes had been challenging.

The first ever long-term prospective study was conducted with patients with PD previously treated in clinical trials with CCH.[5] Conducted up to 5 years after initial injection, the study assessed long-term outcomes data concerning penile curvature deformity, clinical symptoms, patient reported outcomes, long-term safety and the immunogenicity profile of CCH. The patients previously participated in either of the pivotal 12-month, double-blind, placebo controlled clinical trials or in 1 of 2, 9-month, open label studies. They received no additional CCH treatment and were followed once yearly for up to 5 years.

At each visit data were obtained concerning flaccid penile examination to record number of plaques, location and consistency, length of the stretched flaccid penis, degree and direction of curvature of erect penis following intracavernosal vasoactive agent administration, and responses to outcome questionnaires such as the Peyronie's Disease Questionnaire (PDQ). In this questionnaire domains examined include bother, psychological and physical symptoms, and penile pain. The International Index of Erectile Function domains examine erectile and orgasmic function, sexual desire, satisfaction with intercourse and overall satisfaction.

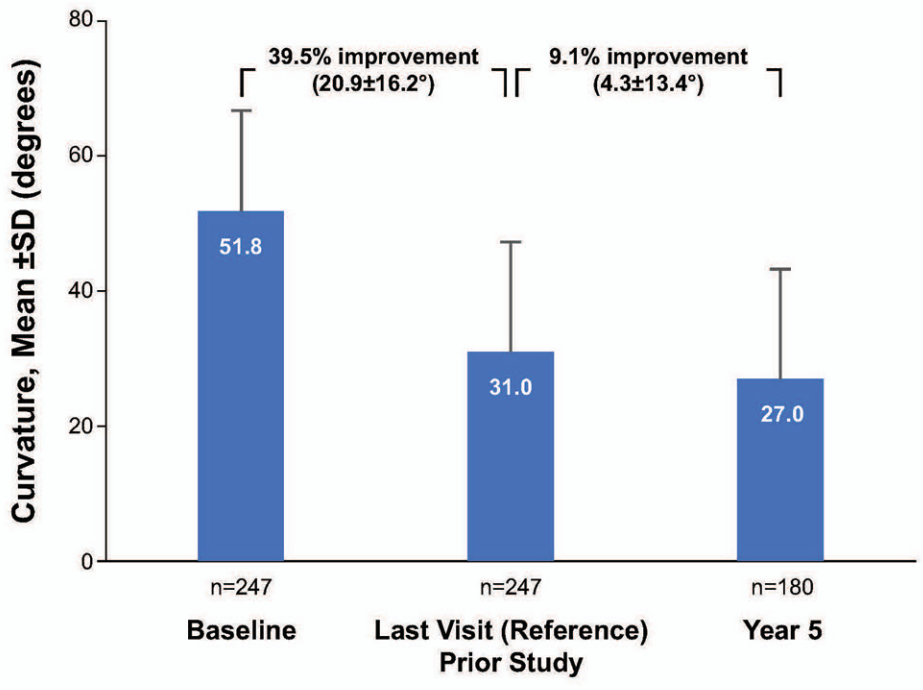


Figure 1. Mean improvement in penile curvature.[5]

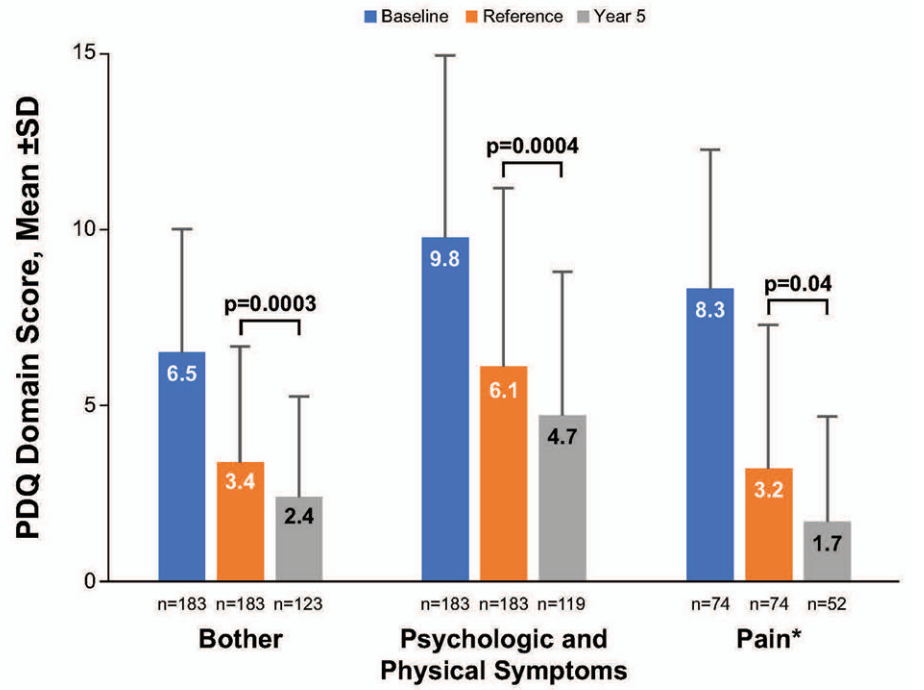


Figure 2. Mean improvement in PDQ domain scores.[5] Asterisk indicates evaluated only in patients with baseline pain score 4 or greater.

In addition, adverse events occurring since the previous visit were recorded and blood samples were collected for measurement of total and neutralizing antibodies to clostridial collagenase types I (AUX-I) and II (AUX-II).

Of the 280 patients enrolled 204 (73%) completed the study through year 5. From baseline to last visit in the previous studies patients (247) had already experienced mean penile curvature decrease from 51.8 ± 15.0 degrees to 31.0 ± 16.1 degrees (improvement of 20.9 ± 16.2 degrees or 39.5%, fig. 1). At year 5 (180) despite no additional treatment in this period there was an additional 9.1% improvement in mean penile curvature compared with the last visit in the previous studies (4.3 ± 13.4 degrees, 95% CI 2.3–6.2, p <0.02). In addition, improvement in penile length was maintained over the course of the followup study (year 5 mean change from baseline 0.6 ± 2.4 cm, p=0.004).

From baseline to the last visit in previous studies patients (183) experienced mean PDQ bother domain score improvement from 6.5 ± 3.5 to 3.4 ± 3.3. At year 5 there was additional improvement to a score of 2.4 ± 2.9 (p=0.0003, fig. 2). Mean PDQ psychological and physical symptoms domain, and PDQ pain domain scores outcomes also indicated continued improvement during the 5-year followup period.

Adverse events were reported in 17.5% (49 of 280) of patients, but none was considered treatment related. No long-term safety issues were identified up to 5 years after CCH treatment. Long-term immunogenicity profiling showed a decreasing trend in the number of anti-AUX-I and anti-AUX-II seropositive patients at years 4 and 5 after CCH treatment.

This study extends the followup period and reports on the long-term (5 years) efficacy, safety and tolerability profile of CCH in adult men treated for PD. A key outcome of this long-term study was that the statistically significant increase from baseline in penile lengthening observed after CCH treatment in the previous studies was maintained during the 5 years of followup. Penile shortening over time can be an issue after surgical treatment for PD,[6] but these data suggest that CCH treatment provides durable, stable improvement in penile length posttreatment that does not decrease during at least 5 years of followup.

During these same 5 years of followup without further surgical or medical treatments for PD there were also continued improvements in the areas of penile curvature and PD symptoms as measured by the PDQ, including PD related bother, pain, and psychological and physical symptoms. Additionally, at year 5 mean improvements reported during previous clinical studies were maintained as assessed by the International Index of Erectile Function questionnaire and in penile plaque consistency scores for previously treated plaques. At year 5 no additional safety signals were identified. ◆

▼ Continued on page 12

Ureteroscopic Dusting vs Mini-Percutaneous Nephrolithotomy

▼ Continued from page 10

from the literature support the use of URS (with dusting techniques) and mini-PCNL for the treatment of intermediate size (2 cm) renal stones. Each has potential benefits in exchange for minor trade-offs. Developing proficiency in both techniques may permit urologists to enhance patient care, improve stone-free rates, decrease morbidity in stone treatment and individualize treatment to optimize outcomes via a shared decision making approach with patients. ◆

1. Assimos D, Krambeck A, Miller NL et al: Surgical management of stones: American Urological Association/Endourological Society guideline. J Urol 2016; **196**: 1153.
2. Davis NF, Quinlan MR, Poyet C et al: Miniaturised percutaneous nephrolithotomy versus flexible ureteropyeloscopy: a systematic review and meta-analysis comparing clinical efficacy and safety profile. World J Urol 2018; **36**: 1127.
3. Matlaga BR, Chew B, Eisner B et al: Ureteroscopic laser lithotripsy: a review of dusting vs fragmentation with extraction. J Endourol 2018; **32**: 1.
4. Feng D, Hu X, Tang Y et al: The efficacy and safety of miniaturized percutaneous nephrolithotomy versus standard percutaneous nephrolithotomy: a systematic review and meta-analysis of randomized controlled trials. Investig Clin Urol 2020; **61**: 115.

Peyronie's Disease Treatment

▼ Continued from page 11

1. Endo Pharmaceuticals: Xiaflex® (collagenase clostridium histolyticum) for injection, for intralesional use prescribing information. Malvern, Pennsylvania: Endo Pharmaceuticals Inc 2019.
2. Gelbard M, Goldstein I, Hellstrom WJ et al: Clinical efficacy, safety and tolerability of collagenase clostridium histolyticum for the treatment of Peyronie disease in 2 large double-blind, randomized, placebo controlled phase 3 studies. J Urol 2013; **190**: 199.
3. Goldstein I, Knoll LD, Lipshultz LI et al: Changes in the effects of Peyronie's disease after treatment with collagenase Clostridium histolyticum: male patients and their female partners. Sex Med 2017; **5**: e124.
4. Levine LA, Cuzin B, Mark S et al: Clinical safety and effectiveness of collagenase clostridium histolyticum injection in patients with Peyronie's disease: a phase 3 open-label study. J Sex Med 2015; **12**: 248.
5. Goldstein I, Lipshultz LI, McLane M et al: Long-term safety and curvature deformity characterization in patients previously treated with collagenase clostridium histolyticum for Peyronie's disease. J Urol 2020; **203**: 1191.
6. Ralph D, Gonzalez-Cadavid N, Mirone V et al: The management of Peyronie's disease: evidence-based 2010 guidelines. J Sex Med 2010; **7**: 2359.

AUA Practice Managers' Network

OPTIMIZE YOUR PRACTICE WITH A SUBSCRIPTION TO THE PMN!

PMN PERKS:

AUA Coding Hotline
PMN Online Community
PMN Monthly Email Newsletter
AUA Policy & Advocacy Brief
DISCOUNTS on conferences, seminars and products

Subscribe today at AUAnet.org/PMN

American Urological Association

Update on Renal Trauma Management

Sorena Keihani, MD, MSCI

Jeremy B. Myers, MD, FACS

Salt Lake City, Utah

With a paradigm shift toward more conservative management of renal trauma, most hemodynamically stable patients are managed nonoperatively or with the help of endovascular procedures to control bleeding. Within this new standard of care most patients with high grade renal trauma (HGRT) are good candidates for nonoperative management and nephrectomy is reserved for patients in extremis and those with unsalvageable renal injuries.

Given the overall rarity of renal trauma, for years our knowledge was based on the information from the National Trauma Data Bank® (NTDB) or single center studies with a limited sample size often using retrospective data spanning decades when management trends underwent marked change. The Multi-Institutional Genito-Urinary Trauma Study (MiGUTS) was created to bridge this knowledge gap and provide contemporary analysis of current renal trauma management.[1]

The project gathered HGRT data from 21 level 1 trauma centers across the United States (fig. 1). Phase 1 focused on contemporary management patterns and the development of a nomogram for predicting bleeding interventions, and phase 2 concentrated on external validation of this predictive tool (fig. 2). Several important findings from the MiGUTS study are outlined here.

Radiologic Predictors of Renal Bleeding

With advancements and widespread use of imaging technologies the majority of trauma cases are initially evaluated with computerized tomography (CT). The inclusion of radiographic findings can provide information that is pivotal for accurately recognizing injury patterns (eg parenchymal, vascular and collecting system injuries) and helping clinical decision making.

For example, presence of vascular contrast extravasation (VCE) is an important indicator of active bleeding and the possible need for early interventions usually with an endovascular approach. VCE is typically seen as a contrast blush with pooling of contrast

▼ Continued on page 16

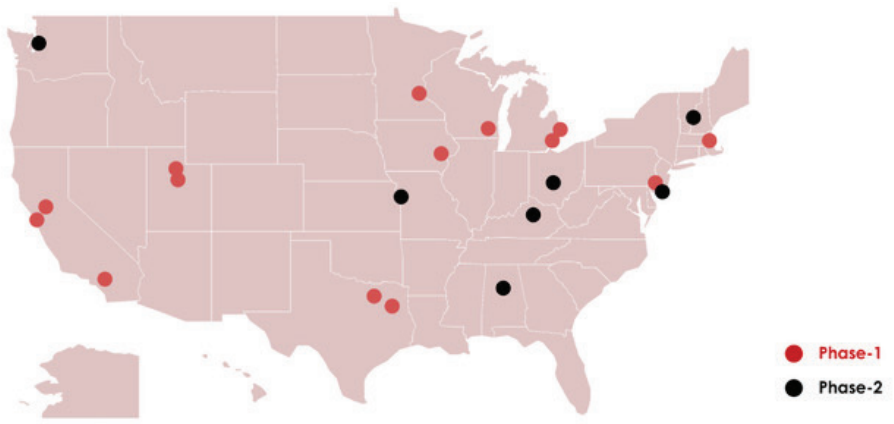


Figure 1. Participating level 1 trauma centers in MiGUTS.

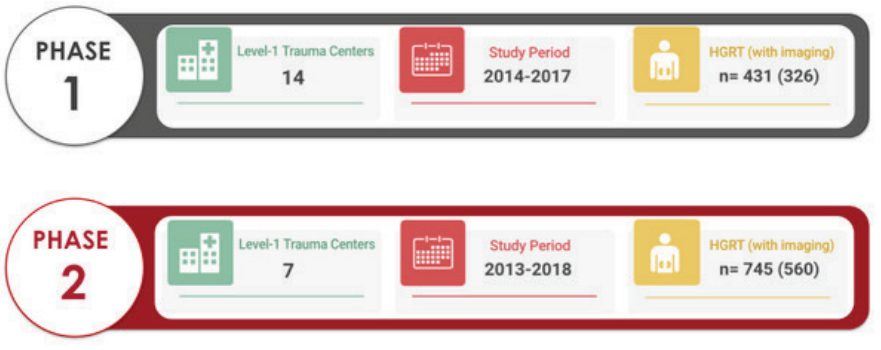


Figure 2. MiGUTS phases 1 and 2.

Erleada® (apalutamide) 60 mg tablets

Start early with ERLEADA®

For your patients with metastatic prostate cancer who will be starting ADT or have recently initiated ADT*

In the TITAN study† in patients with metastatic castration-sensitive prostate cancer (mCSPC):

ERLEADA® + ADT reduced the risk of death by 33% vs placebo + ADT[1]

(Median overall survival was not estimable in either arm; HR=0.67; 95% CI: 0.51, 0.89; *P*=0.0053)

INDICATION

ERLEADA® (apalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with:

- Metastatic castration-sensitive prostate cancer (mCSPC)
- Non-metastatic castration-resistant prostate cancer (nmCRPC)

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Ischemic Cardiovascular Events—In a randomized study (SPARTAN) of patients with nmCRPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA® and 3% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA® and 2% of patients treated with placebo. Across the SPARTAN and TITAN studies, 6 patients (0.5%) treated with ERLEADA® and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event. Patients with current evidence of unstable angina, myocardial infarction, or congestive heart failure within 6 months of randomization were excluded from the SPARTAN and TITAN studies.

Ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA®. Monitor for signs and symptoms of ischemic heart disease. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Consider discontinuation of ERLEADA® for Grade 3 and 4 events.

Fractures—In a randomized study (SPARTAN) of patients with nmCRPC, fractures occurred in 12% of patients treated with ERLEADA® and in 7% of patients treated with placebo. In a randomized study (TITAN) of patients with mCSPC, fractures occurred in 9% of patients treated with ERLEADA® and in 6% of patients treated with placebo. Evaluate patients for fracture risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

Falls—In a randomized study (SPARTAN), falls occurred in 16% of patients treated with ERLEADA® compared with 9% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Falls occurred in patients receiving ERLEADA® with increased frequency in the elderly. Evaluate patients for fall risk.

Seizure—In 2 randomized studies (SPARTAN and TITAN), 5 patients (0.4%) treated with ERLEADA® and 1 patient treated with placebo (0.1%) experienced a seizure. Permanently discontinue ERLEADA® in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with ERLEADA®. Advise patients of the risk of developing a seizure while receiving ERLEADA® and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others.

Embryo-Fetal Toxicity—The safety and efficacy of ERLEADA® have not been established in females. Based on its mechanism of action, ERLEADA® can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA® *[See Use in Specific Populations (8.1, 8.3)]*.

ADVERSE REACTIONS

Adverse Reactions—The most common adverse reactions (≥10%) that occurred more frequently in the ERLEADA®-treated patients (≥2% over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture.

Laboratory Abnormalities—All Grades (Grade 3-4)

- **Hematology**—In the TITAN study: white blood cell decreased ERLEADA® 27% (0.4%), placebo 19% (0.6%). In the SPARTAN study: anemia ERLEADA® 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA® 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA® 41% (2%), placebo 21% (2%)
- **Chemistry**—In the TITAN study: hypertriglyceridemia ERLEADA® 17% (3%), placebo 12% (2%). In the SPARTAN study: hypercholesterolemia ERLEADA® 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA® 70% (2%), placebo 59% (1%); hypertriglyceridemia ERLEADA® 67% (2%), placebo 49% (0.8%); hyperkalemia ERLEADA® 32% (2%), placebo 22% (0.5%)

Rash—In 2 randomized studies, rash was most commonly described as macular or maculopapular. Adverse reactions of rash were 26% with ERLEADA® vs 8% with placebo. Grade 3 rashes (defined as covering >30% body surface area [BSA]) were reported with ERLEADA® treatment (6%) vs placebo (0.5%).

The onset of rash occurred at a median of 83 days. Rash resolved in 78% of patients within a median of 78 days from onset of rash. Rash was commonly managed with oral antihistamines, topical corticosteroids, and 19% of patients received systemic corticosteroids. Dose reduction or dose interruption occurred in 14% and 28% of patients, respectively. Of the patients who had dose interruption, 59% experienced recurrence of rash upon reintroduction of ERLEADA®.

Hypothyroidism—In 2 randomized studies, hypothyroidism was reported for 8% of patients treated with ERLEADA® and 2% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. Elevated TSH occurred in 25% of patients treated with ERLEADA® and 7% of patients treated with placebo. The median onset was at the first scheduled assessment. There were no Grade 3 or 4 adverse reactions. Thyroid replacement therapy, when clinically indicated, should be initiated or dose-adjusted.

DRUG INTERACTIONS

Effect of Other Drugs on ERLEADA®—Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties. No initial dose adjustment is necessary; however, reduce the ERLEADA® dose based on tolerability *[see Dosage and Administration (2.2)]*.

Effect of ERLEADA® on Other Drugs—ERLEADA® is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9 in humans. Concomitant use of ERLEADA® with medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or evaluate for loss of activity if medication is continued. Concomitant administration of ERLEADA® with medications that are substrates of UDP-glucuronosyl transferase (UGT) can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA® and evaluate for loss of activity.

P-gp, BCRP, or OATP1B1 Substrates—Apalutamide is a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. Concomitant use of ERLEADA® with medications that are substrates of P-gp, BCRP, or OATP1B1 can result in lower exposure of these medications. Use caution if substrates of P-gp, BCRP, or OATP1B1 must be co-administered with ERLEADA® and evaluate for loss of activity if medication is continued.

cp-50507v2

Please see Brief Summary of full Prescribing Information for ERLEADA® on subsequent pages.

*All patients who enrolled in the TITAN study started ADT for mCSPC ≤6 months prior to randomization.

†**Study Design:** TITAN was a phase 3, multicenter, randomized, double-blind, placebo-controlled trial of patients with mCSPC (N=1052). Patients had *de novo* mCSPC or relapsed metastatic disease after initial diagnosis of localized disease. All patients in the TITAN trial received a concomitant GnRH analog or had a bilateral orchiectomy. Patients with visceral (ie, liver or lung) metastases as the only sites of metastases were excluded. Patients were randomized 1:1 to receive ERLEADA® 240 mg orally once daily + ADT or placebo orally once daily + ADT. The dual primary endpoints were overall survival and radiographic progression-free survival.[1,2]

References: 1. ERLEADA® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for metastatic castration-sensitive prostate cancer. *N Engl J Med.* 2019;381(1):13-24. doi: 10.1056/NEJMoa1903307.

ADT = androgen deprivation therapy; CI = confidence interval; HR = hazard ratio; TITAN = Targeted Investigational Treatment Analysis of Novel Antiandrogen.

Janssen Biotech, Inc.

Janssen Oncology

PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Erleada® (apalutamide) 60 mg tablets

Visit erleadahcp.com

© Janssen Biotech, Inc. 2020 02/20 cp-94338v2

Brief Summary of Prescribing Information for ERLEADA® (apalutamide)

ERLEADA® (apalutamide) tablets, for oral use

See package insert for Full Prescribing Information

INDICATIONS AND USAGE

ERLEADA is indicated for the treatment of patients with

- Metastatic castration-sensitive prostate cancer (mCSPC)
- Non-metastatic castration-resistant prostate cancer (nmCRPC)

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Ischemic Cardiovascular Events

Ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA. Monitor for signs and symptoms of ischemic heart disease. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Consider discontinuation of ERLEADA for Grade 3 and 4 events.

In a randomized study (SPARTAN) of patients with nmCRPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA and 3% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA and 2% of patients treated with placebo. Across the SPARTAN and TITAN studies, 6 patients (0.5%) treated with ERLEADA and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event. Patients with current evidence of unstable angina, myocardial infarction, or congestive heart failure within six months of randomization were excluded from the SPARTAN and TITAN studies.

Fractures

Fractures occurred in patients receiving ERLEADA. Evaluate patients for fracture risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

In a randomized study (SPARTAN) of patients with non-metastatic castration-resistant prostate cancer, fractures occurred in 12% of patients treated with ERLEADA and in 7% of patients treated with placebo. Grade 3-4 fractures occurred in 3% of patients treated with ERLEADA and in 1% of patients treated with placebo. The median time to onset of fracture was 314 days (range: 20 to 953 days) for patients treated with ERLEADA. Routine bone density assessment and treatment of osteoporosis with bone-targeted agents were not performed in the SPARTAN study.

In a randomized study (TITAN) of patients with metastatic castration-sensitive prostate cancer, fractures occurred in 9% of patients treated with ERLEADA and in 6% of patients treated with placebo. Grade 3-4 fractures were similar in both arms at 2%. The median time to onset of fracture was 56 days (range: 2 to 111 days) for patients treated with ERLEADA. Routine bone density assessment and treatment of osteoporosis with bone-targeted agents were not performed in the TITAN study.

Falls

Falls occurred in patients receiving ERLEADA with increased frequency in the elderly *[See Use in Specific Populations]*. Evaluate patients for fall risk.

In a randomized study (SPARTAN), falls occurred in 16% of patients treated with ERLEADA compared to 9% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure.

Seizure

Seizure occurred in patients receiving ERLEADA. Permanently discontinue ERLEADA in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with ERLEADA. Advise patients of the risk of developing a seizure while receiving ERLEADA and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others.

In two randomized studies (SPARTAN and TITAN), five patients (0.4%) treated with ERLEADA and one patient treated with placebo (0.1%) experienced a seizure. Seizure occurred from 159 to 650 days after initiation of ERLEADA. Patients with a history of seizure, predisposing factors for seizure, or receiving drugs known to decrease the seizure threshold or to induce seizure were excluded. There is no clinical experience in re-administering ERLEADA to patients who experienced a seizure.

Embryo-Fetal Toxicity

The safety and efficacy of ERLEADA have not been established in females. Based on its mechanism of action, ERLEADA can cause fetal harm and loss of pregnancy when administered to a pregnant female *[see Clinical Pharmacology (12.1) in full Prescribing Information]*. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA *[see Use in Specific Populations]*.

ADVERSE REACTIONS

The following are discussed in more detail in other sections of the labeling:

- Ischemic Cardiovascular Events *[see Warnings and Precautions]*.
- Fractures *[see Warnings and Precautions]*.
- Falls *[see Warnings and Precautions]*.
- Seizure *[see Warnings and Precautions]*.

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 most common adverse reactions (≥ 10%) that occurred more frequently in the ERLEADA-treated patients (≥ 2% over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture.

Metastatic Castration-sensitive Prostate Cancer (mCSPC)

TITAN, a randomized (1:1), double-blind, placebo-controlled, multi-center clinical study, enrolled patients who had mCSPC. In this study, patients received either ERLEADA at a dose of 240 mg daily or placebo. All patients in the TITAN study received a concomitant gonadotropin-releasing hormone (GnRH) analog or had prior bilateral orchiectomy. The median duration of exposure was 20 months (range: 0 to 34 months) in patients who received ERLEADA and 18 months (range: 0.1 to 34 months) in patients who received placebo.

Ten patients (2%) who were treated with ERLEADA died from adverse reactions. The reasons for death were ischemic cardiovascular events (n=3), acute kidney injury (n=2), cardio-respiratory arrest (n=1), sudden cardiac death (n=1), respiratory failure (n=1), cerebrovascular accident (n=1), and large intestinal ulcer perforation (n=1). ERLEADA was discontinued due to adverse reactions in 8% of patients, most commonly from rash (2%). Adverse reactions leading to dose interruption or reduction of ERLEADA occurred in 23% of patients; the most frequent (>1%) were rash, fatigue, and hypertension. Serious adverse reactions occurred in 20% of ERLEADA-treated patients and 20% in patients receiving placebo.

Table 1 shows adverse reactions occurring in ≥10% on the ERLEADA arm in TITAN that occurred with a ≥2% absolute increase in frequency compared to placebo. Table 2 shows laboratory abnormalities that occurred in ≥15% of patients, and more frequently (>5%) in the ERLEADA arm compared to placebo.

Table 1: Adverse Reactions in TITAN (mCSPC)

	ERLEADA N=524		Placebo N=527	
System/Organ Class Adverse reaction	**All Grades %**	**Grade 3-4 %**	**All Grades %**	**Grade 3-4 %**
General disorders and administration site conditions				
Fatigue[1,3]	26	3	25	2
Musculoskeletal and connective tissue disorders				
Arthralgia[3]	17	0.4	15	0.9
Skin and subcutaneous tissue disorders				
Rash[2]	28	6	9	0.6
Pruritus	11	<1	5	<1
Vascular disorders				
Hot flush	23	0	16	0
Hypertension	18	8	16	9

[1] Includes fatigue and asthenia

[2] Includes rash, rash maculo-papular, rash generalized, urticaria, rash pruritic, rash macular, conjunctivitis, erythema multiforme, rash papular, skin exfoliation, genital rash, rash erythematous, stomatitis, drug eruption, mouth ulceration, rash pustular, blister, papule, pemphigoid, skin erosion, dermatitis, and rash vesicular

[3] Per the Common Terminology Criteria for Adverse Reactions (CTCAE), the highest severity for these events is Grade 3

Additional adverse reactions of interest occurring in 2%, but less than 10% of patients treated with ERLEADA included diarrhea (9% versus 6% on placebo), muscle spasm (3% versus 2% on placebo), dysgeusia (3% versus 1% on placebo), and hypothyroidism (4% versus 1% on placebo).

Table 2: Laboratory Abnormalities Occurring in ≥ 15% of ERLEADA-Treated Patients and at a Higher Incidence than Placebo (Between Arm Difference > 5% All Grades) in TITAN (mCSPC)

	ERLEADA N=524		Placebo N=527	
Laboratory Abnormality	**All Grades %**	**Grade 3-4 %**	**All Grades %**	**Grade 3-4 %**
Hematology				
White blood cell decreased	27	0.4	19	0.6
Chemistry				
Hypertriglyceridemia[1]	17	3	12	2

[1] Does not reflect fasting values

Non-metastatic Castration-resistant Prostate Cancer (nmCRPC)

SPARTAN, a randomized (2:1), double-blind, placebo-controlled, multi-center clinical study, enrolled patients who had nmCRPC. In this study, patients received either ERLEADA at a dose of 240 mg daily or a placebo. All patients in the SPARTAN study received a concomitant gonadotropin-releasing hormone (GnRH) analog or had a bilateral orchiectomy. The median duration of exposure was 16.9 months (range: 0.1 to 42 months) in patients who received ERLEADA and 11.2 months (range: 0.1 to 37 months) in patients who received placebo.

Eight patients (1%) who were treated with ERLEADA died from adverse reactions. The reasons for death were infection (n=4), myocardial infarction (n=3), and cerebral hemorrhage (n=1). One patient (0.3%) treated with placebo died from an adverse reaction of cardiopulmonary arrest (n=1). ERLEADA was discontinued due to adverse reactions in 11% of patients, most commonly from rash (3%). Adverse reactions leading to dose interruption or reduction of ERLEADA occurred in 33% of patients; the most common (>1%) were rash, diarrhea, fatigue, nausea, vomiting, hypertension, and hematuria. Serious adverse reactions occurred in 25% of ERLEADA-treated patients and 23% in patients receiving placebo. The most frequent serious adverse reactions (>2%) were fracture (3%) in the ERLEADA arm and urinary retention (4%) in the placebo arm.

Table 3 shows adverse reactions occurring in ≥10% on the ERLEADA arm in SPARTAN that occurred with a ≥2% absolute increase in frequency compared to placebo. Table 4 shows laboratory abnormalities that occurred in ≥15% of patients, and more frequently (>5%) in the ERLEADA arm compared to placebo.

Table 3: Adverse Reactions in SPARTAN (nmCRPC)

	ERLEADA N=803		Placebo N=398	
System/Organ Class Adverse reaction	**All Grades %**	**Grade 3-4 %**	**All Grades %**	**Grade 3-4 %**
General disorders and administration site conditions				
Fatigue[1,4]	39	1	28	0.3
Musculoskeletal and connective tissue disorders				
Arthralgia[4]	16	0	8	0
Skin and subcutaneous tissue disorders				
Rash[2]	25	5	6	0.3

ERLEADA® (apalutamide) tablets

Table 3: Adverse Reactions in SPARTAN (nmCRPC) (continued)

	ERLEADA N=803		Placebo N=398	
System/Organ Class Adverse reaction	**All Grades %**	**Grade 3-4 %**	**All Grades %**	**Grade 3-4 %**
Metabolism and nutrition disorders				
Decreased appetite[5]	12	0.1	9	0
Peripheral edema[6]	11	0	9	0
Injury, poisoning and procedural complications				
Fall[4]	16	2	9	0.8
Fracture[3]	12	3	7	0.8
Investigations				
Weight decreased[4]	16	1	6	0.3
Vascular disorders				
Hypertension	25	14	20	12
Hot flush	14	0	9	0
Gastrointestinal disorders				
Diarrhea	20	1	15	0.5
Nausea	18	0	16	0

[1] Includes fatigue and asthenia

[2] Includes rash, rash maculo-papular, rash generalized, urticaria, rash pruritic, rash macular, conjunctivitis, erythema multiforme, rash papular, skin exfoliation, genital rash, rash erythematous, stomatitis, drug eruption, mouth ulceration, rash pustular, blister, papule, pemphigoid, skin erosion, dermatitis, and rash vesicular

[3] Includes rib fracture, lumbar vertebral fracture, spinal compression fracture, spinal fracture, foot fracture, hip fracture, humerus fracture, thoracic vertebral fracture, upper limb fracture, fractured sacrum, hand fracture, pubis fracture, acetabulum fracture, ankle fracture, compression fracture, costal cartilage fracture, facial bones fracture, lower limb fracture, osteoporotic fracture, wrist fracture, avulsion fracture, fibula fracture, fractured coccyx, pelvic fracture, radius fracture, sternal fracture, stress fracture, traumatic fracture, cervical vertebral fracture, femoral neck fracture, and tibia fracture

[4] Per the Common Terminology Criteria for Adverse Reactions (CTCAE), the highest severity for these events is Grade 3

[5] Includes appetite disorder, decreased appetite, early satiety, and hypophagia

[6] Includes peripheral edema, generalized edema, edema, edema genital, penile edema, peripheral swelling, scrotal edema, lymphedema, swelling, and localized edema

Additional clinically significant adverse reactions occurring in 2% or more of patients treated with ERLEADA included hypothyroidism (8.1% versus 2% on placebo), pruritus (6.2% versus 2% on placebo), and heart failure (2.2% versus 1% on placebo).

Table 4: Laboratory Abnormalities Occurring in ≥ 15% of ERLEADA-Treated Patients and at a Higher Incidence than Placebo (Between Arm Difference > 5% All Grades) in SPARTAN (nmCRPC)

	ERLEADA N=803		Placebo N=398	
Laboratory Abnormality	**All Grades %**	**Grade 3-4 %**	**All Grades %**	**Grade 3-4 %**
Hematology				
Anemia	70	0.4	64	0.5
Leukopenia	47	0.3	29	0
Lymphopenia	41	2	21	2
Chemistry				
Hypercholesterolemia[1]	76	0.1	46	0
Hyperglycemia[1]	70	2	59	1
Hypertriglyceridemia[1]	67	2	49	0.8
Hyperkalemia	32	2	22	0.5

[1] Does not reflect fasting values

Rash

In the combined data of two randomized, placebo-controlled clinical studies, rash associated with ERLEADA was most commonly described as macular or maculo-papular. Adverse reactions of rash were reported for 26% of patients treated with ERLEADA versus 8% of patients treated with placebo. Grade 3 rashes (defined as covering > 30% body surface area [BSA]) were reported with ERLEADA treatment (6%) versus placebo (0.5%).

The onset of rash occurred at a median of 83 days of ERLEADA treatment. Rash resolved in 78% of patients within a median of 78 days from onset of rash. Rash was commonly managed with oral antihistamines, topical corticosteroids, and 19% of patients received systemic corticosteroids. Dose reduction or dose interruption occurred in 14% and 28% of patients, respectively. Of the patients who had dose interruption, 59% experienced recurrence of rash upon reintroduction of ERLEADA.

Hypothyroidism

In the combined data of two randomized, placebo-controlled clinical studies, hypothyroidism was reported for 8% of patients treated with ERLEADA and 2% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. Elevated TSH occurred in 25% of patients treated with ERLEADA and 7% of patients treated with placebo. The median onset was at the first scheduled assessment. There were no Grade 3 or 4 adverse reactions. Thyroid replacement therapy was initiated in 5% of patients treated with ERLEADA. Thyroid replacement therapy, when clinically indicated, should be initiated or dose-adjusted *[see Drug Interactions]*.

DRUG INTERACTIONS

Effect of Other Drugs on ERLEADA

Strong CYP2C8 or CYP3A4 Inhibitors

Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties (sum of unbound apalutamide plus the potency-adjusted unbound N-desmethyl-apalutamide). No initial dose adjustment is necessary however, reduce

the ERLEADA dose based on tolerability *[see Dosage and Administration (2.2) in full Prescribing Information].* Mild or moderate inhibitors of CYP2C8 or CYP3A4 are not expected to affect the exposure of apalutamide.

Effect of ERLEADA on Other Drugs

CYP3A4, CYP2C9, CYP2C19 and UGT Substrates

ERLEADA is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9 in humans. Concomitant use of ERLEADA with medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or evaluate for loss of activity if medication is continued. Concomitant administration of ERLEADA with medications that are substrates of UDP-glucuronosyl transferase (UGT) can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA and evaluate for loss of activity *[see Clinical Pharmacology (12.3) in full Prescribing Information].*

P-gp, BCRP or OATP1B1 Substrates

Apalutamide was shown to be a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. At steady-state, apalutamide reduced the plasma exposure to fexofenadine (a P-gp substrate) and rosuvastatin (a BCRP/OATP1B1 substrate). Concomitant use of ERLEADA with medications that are substrates of P-gp, BCRP, or OATP1B1 can result in lower exposure of these medications. Use caution if substrates of P-gp, BCRP or OATP1B1 must be co-administered with ERLEADA and evaluate for loss of activity if medication is continued *[see Clinical Pharmacology (12.3) in full Prescribing Information].*

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

The safety and efficacy of ERLEADA have not been established in females. Based on its mechanism of action, ERLEADA can cause fetal harm and loss of pregnancy *[see Clinical Pharmacology (12.1) in full Prescribing Information].* There are no human data on the use of ERLEADA in pregnant women. ERLEADA is not indicated for use in females, so animal embryo-fetal developmental toxicology studies were not conducted with apalutamide.

Lactation

Risk Summary

The safety and efficacy of ERLEADA have not been established in females. There are no data on the presence of apalutamide or its metabolites in human milk, the effect on the breastfed child, or the effect on milk production.

Females and Males of Reproductive Potential

Contraception

Males

Based on the mechanism of action and findings in an animal reproduction study, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA. *[see Use in Specific Populations].*

Infertility

Males

Based on animal studies, ERLEADA may impair fertility in males of reproductive potential *[see Nonclinical Toxicology (13.1) in full Prescribing Information].*

Pediatric Use

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

Geriatric Use

Of the 1327 patients who received ERLEADA in clinical studies, 19% of patients were less than 65 years, 41% of patients were 65 years to 74 years, and 40% were 75 years and over.

No overall differences in effectiveness were observed between older and younger patients.

Of patients treated with ERLEADA (n=1073), Grade 3-4 adverse reactions occurred in 39% of patients younger than 65 years, 41% of patients 65-74 years, and 49% of patients 75 years or older. Falls in patients receiving ERLEADA with androgen deprivation therapy was elevated in the elderly, occurring in 8% of patients younger than 65 years, 10% of patients 65-74 years, and 19% of patients 75 years or older.

OVERDOSAGE

There is no known specific antidote for apalutamide overdose. In the event of an overdose, stop ERLEADA, undertake general supportive measures until clinical toxicity has been diminished or resolved.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Ischemic Cardiovascular Events

- Inform patients that ERLEADA has been associated with ischemic cardiovascular events. Advise patients to seek immediate medical attention if any symptoms suggestive of a cardiovascular event occur *[see Warnings and Precautions].*

Falls and Fractures

- Inform patients that ERLEADA is associated with an increased incidence of falls and fractures *[see Warnings and Precautions].*

Seizures

- Inform patients that ERLEADA has been associated with an increased risk of seizure. Discuss conditions that may predispose to seizures and medications that may lower the seizure threshold. Advise patients of the risk of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Inform patients to contact their healthcare provider right away if they experience a seizure *[see Warnings and Precautions].*

Rash

- Inform patients that ERLEADA is associated with rashes and to inform their healthcare provider if they develop a rash *[see Adverse Reactions].*

Dosage and Administration

- Inform patients receiving concomitant gonadotropin-releasing hormone (GnRH) analog therapy that they need to maintain this treatment during the course of treatment with ERLEADA.
- Instruct patients to take their dose at the same time each day (once daily). ERLEADA can be taken with or without food. Each tablet should be swallowed whole.
- Inform patients that in the event of a missed daily dose of ERLEADA, they should take their normal dose as soon as possible on the same day with a return to the normal schedule on the following day. The patient should not take extra tablets to make up the missed dose *[see Dosage and Administration (2.1) in full Prescribing Information].*

Embryo-Fetal Toxicity

- Inform patients that ERLEADA can be harmful to a developing fetus. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA. Advise male patients to use a condom if having sex with a pregnant woman *[see Warnings and Precautions].*

Infertility

- Advise male patients that ERLEADA may impair fertility and not to donate sperm during therapy and for 3 months following the last dose of ERLEADA *[see Use in Specific Populations].*

Manufactured by:
Janssen Ortho LLC
Gurabo, PR 00778

Manufactured for:
Janssen Products, LP
Gurabo, PR 00778

© 2019 Janssen Pharmaceutical Companies

cp-50510v2

Renal Trauma Management Update

▼ Continued from page 12

material around the kidney in the early phase of contrast enhanced CT. Although not all patients with VCE will eventually need interventions to control bleeding, it serves as an early and highly predictive clue to identify those patients at higher risk.

Most HGRT cases are also associated with some degree of hematoma around the kidney. Hematoma characteristics such as size and degree of hematoma extension are additional useful predictors to define high risk patients. Hematoma rim distance (HRD, the distance between the kidney border and the hematoma rim in the horizontal plane of CT) provides a simple and fairly reproducible measure of bleeding severity. According to the MiGUTS findings a HRD of 3.5 cm or greater provided the best distinction for undergoing bleeding interventions (sixfold risk increase).[2]

When combined with pararenal extent of hematoma (for bleeding that extends vertically down into the pelvis or horizontally across the midline) these findings can provide invaluable information about which patients are more likely to benefit from vigilant monitoring or bleeding control interventions. MiGUTS is one of the first studies to have a large enough cohort for a controlled analysis and found all of these factors to be highly associated with interventions for renal hemorrhage.[2]

Timing of Excretory Imaging

Accurate grading of renal injuries usually requires obtaining delayed excretory phase images to assess for collecting system injuries and urinary extravasation. These images are typically obtained 2 to 15 minutes after contrast injection (fig. 3). A 10-minute delay is considered standard and also recommended by the AUA urotrauma guidelines to allow contrast excretion and adequate visualization of the collecting system.[3]

In our MiGUTS analysis timing of the excretory phase was an independent predictor of urinary extravasation diagnosis after controlling for injury severity, active bleeding and shock.[4] Importantly, about a third of patients with HGRT did not undergo excretory phase imaging as part of initial renal injury assessment, which is discordant with AUA guidelines.

Median time between early and delayed phase of CT was only 4 minutes in the cohort, which potentially led to 12% of patients having inconclusive excretory phase images and multiple patients with missed diagnosis of urinary extravasation. The optimal time between the early and delayed phase of the contrast CT for diagnosis of urinary extravasation was 9 minutes, roughly translating to a 10-minute delay from the time of contrast injection.[4]

Taken together the adherence to the guidelines for obtaining delayed excretory phase images and allowing adequate time from contrast injection were an important area for process improvement even at level 1 trauma centers participating in the study.

Development of a Renal Bleeding Nomogram

A nomogram is a graphical tool that combines multiple variables based on traditional statistical methods (such as logistic and Cox regressions) to predict an outcome. Nomograms have been used in many areas of medicine and in urology they are best known for predicting outcomes of prostate cancer.[5]

In the MiGUTS project a number of important clinical and radiographic variables were combined to build a nomogram to predict the risk of undergoing bleeding control interventions (ie nephrectomy, renal repair, renal angioembolization and renal packing) (fig. 4).[6] This nomogram provided high accuracy in predicting bleeding interventions and was validated using external data with an excellent discrimination according to the AUC of 0.88 (95% CI 0.85–0.92).

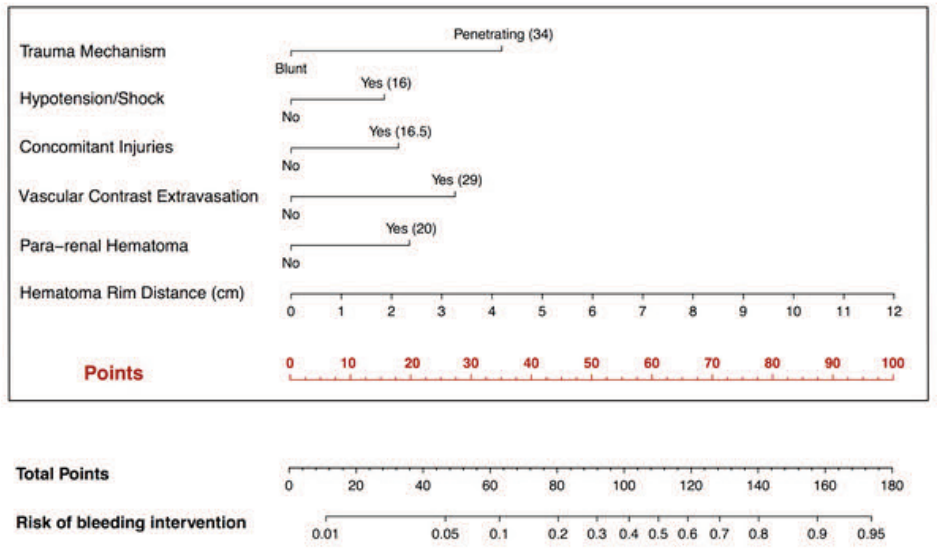


Figure 4. Renal trauma nomogram for prediction of undergoing bleeding control interventions.

Although such predictive tools cannot provide a simple and definitive answer in the complex context of managing a trauma case, they can be used to guide management decisions to encourage conservative management when the probability of interventions is low (eg in the absence of hemodynamic instability and VCE, and with small confined hematomas).

They can also suggest closer followup and proactive approaches in patients who are at higher risk (eg those presenting in shock, and with large hematomas and VCE upon imaging). More importantly, although undergoing interventions in a retrospective study is not synonymous with needing interventions, the nomogram can be used as a guide for patients who do not need intervention or transfer from lower tier trauma centers.

In MiGUTS the primary aim is to use multicenter, prospective, robust data to develop a higher level of evidence to support and revise renal trauma management guidelines and improve the care of patients with renal trauma. The collaborative nature of this study has been embraced by the urology and trauma surgical communities, which was pivotal in moving the project forward. In addition, the trial was supported by the Multi-Institutional Trials Committee of the American Association for the Surgery of Trauma.[7]

Successful organization and completion of the MiGUTS project show the feasibility of multi-institutional and multidisciplinary collaborations in the field of urological trauma, and pave the way for future prospective studies in a field that still has many clinically important but unanswered questions. ◆

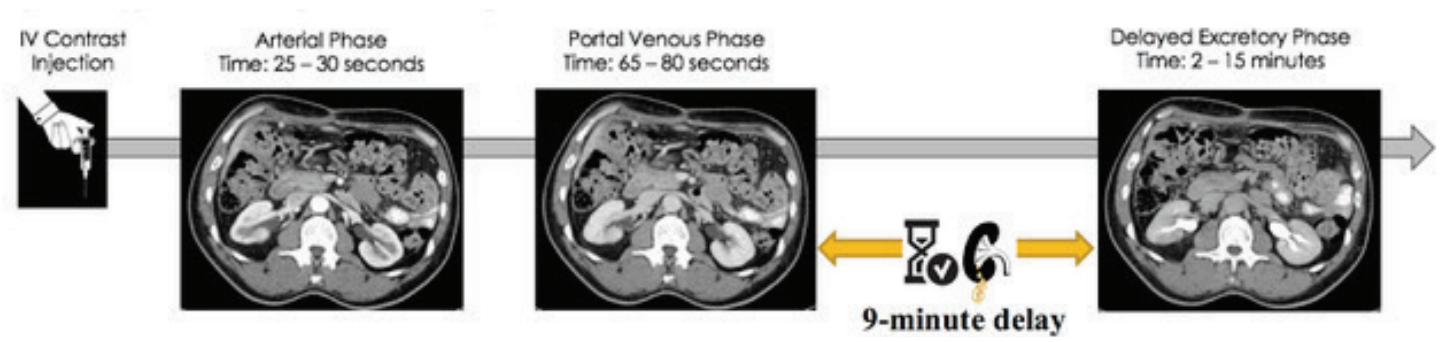
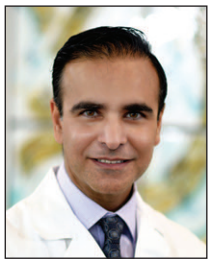


Figure 3. Typical trauma CT protocol and recommended delay time based on MiGUTS data.

1. Meyers JB, Keihani S, Anderson RE et al: Genito-Urinary Trauma Study (MiGUTS). The Trauma and Urologic Reconstructive Network of Surgeons 2020. Available at http://www.turnsresearch.org/page/genito-urinary-trauma-study-miguts-renal.
2. Keihani S, Putbrese BE, Rogers DM et al: The associations between initial radiographic findings and interventions for renal hemorrhage after high-grade renal trauma: results from the Multi-Institutional Genitourinary Trauma Study. J Trauma Acute Care Surg 2019; **86**: 974.
3. Morey AF, Brandes S, Dugi DD 3rd et al: Urotrauma: AUA guideline. J Urol 2014; **192**: 327.
4. Keihani S, Putbrese B, Rogers D et al: Optimal timing of delayed excretory phase CT scan for diagnosis of urinary extravasation after high-grade renal trauma. J Trauma Acute Care Surg 2019; **86**: 274.
5. Bianco FJ Jr: Nomograms and medicine. Eur Urol 2007; **50**: 884.
6. Keihani S, Rogers DM, Putbrese BE et al: A nomogram predicting the need for bleeding interventions after high-grade renal trauma: results from the American Association for the Surgery of Trauma Multi-Institutional Genito-Urinary Trauma Study (MiGUTS). J Trauma Acute Care Surg 2019; **86**: 774.
7. Multi-Institutional Trials Committee: Multi-Institutional Studies. The American Association for the Surgery of Trauma 2020. Available at https://www.aast.org/Research/MultiInstitutionalStudies.aspx.

Adding to the AUA Testosterone Guidelines—What is Missing?



Mohit Khera, MD
Houston, Texas

In 2018 the American Urological Association published its first testosterone guidelines regarding the diagnosis and management of patients with hypogonadism.[1] These guidelines are the most comprehensive and informative published to date.

However, there are several areas in the guidelines that need further clarification or supplementation. These areas include benign prostatic hyperplasia (BPH), management of erythrocytosis, the use of free testosterone and the optimal testosterone cutoff to diagnose testosterone deficiency (TD), and the appropriate testosterone target range for patients once testosterone therapy (TTh) is initiated.

The AUA testosterone guidelines do not address the use or impact of testosterone in men with BPH. Many urologists are still concerned that TTh will worsen lower urinary tract symptoms (LUTS). This concern is also fueled by the fact that current package inserts of testosterone products state, "patients with BPH treated with androgens are at an increased risk for worsening of signs and symptoms of BPH."

However, there is currently no convincing data to support this claim. In fact, DeLay and Kohler found that long term TTh either had no effect on LUTS or actually improved LUTS over time.[2] Other studies have also noted improvements in voided volumes and postvoid residuals in men on TTh.[1] Therefore, patients should be counseled appropriately regarding TTh for those with BPH and LUTS.

The AUA testosterone guidelines address the management of hypogonadism and erythrocytosis. The guidelines recommend intervening when the hematocrit increases above 54%, which is consistent with numerous other testosterone guideline recommendations. However, it is important to realize that there is no compelling data to support the conclusion that the hematocrit cutoff of 54% is associated with an increased medical risk when erythrocytosis is caused by TTh.

In addition, therapeutic phlebotomy is not mentioned as first line therapy. Many patients prefer therapeutic phlebotomy instead of decreasing testosterone dosage. Therapeutic phlebotomy is effective and quickly returns the hematocrit to within normal range. Finally, it should be emphasized that an option for men using injectable testosterone in whom erythrocytosis develops is to switch to a different testosterone formulation such as a testosterone gel, which has a lower rate of erythrocytosis.

The AUA testosterone guidelines provide an excellent framework for diagnosing TD, but there is debate on the testosterone threshold at which symptoms resolve. The guidelines indicate 300 ng/dL as a reasonable cutoff to diagnose TD. However, many other societies offer a range of thresholds from 264 to 350 ng/dL.[3] Numerous experts recognize that a threshold of 300 ng/dL may be too stringent and that many men who would actually benefit from TTh will not qualify based on this cutoff.

The guidelines do not recommend using free testosterone measurements as the primary diagnostic method for testosterone deficiency. Free testosterone, not total testosterone, is the most biologically active component and has been shown to better correlate with symptoms.[4] There is also wide inter-individual variability with sex hormone binding globulin (SHBG) levels among men, and some with normal testosterone levels will have low free testosterone levels.

The AUA testosterone guidelines do not offer clear recommendations on when or how to use free

▼ Continued on page 18

2020 AWARD WINNERS

RAMON GUITERAS AWARD
William J. Catalona, MD
For outstanding leadership in demonstrating the value of PSA testing and surgical management of prostate cancer

HUGH HAMPTON YOUNG AWARD
Stephen Y. Nakada, MD
For enduring leadership and pioneering studies of urolithiasis, minimally invasive surgery and renal preservation

GOLD CYSTOSCOPE AWARD
Thomas Chi, MD
For outstanding research into the cause of urolithiasis and innovations in surgical techniques for kidney stone removal

LIFETIME ACHIEVEMENT AWARD
William F. Gee, MD
For a lifetime of service advancing the goals and mission of the AUA

VICTOR A. POLITANO AWARD
Gopal H. Badlani, MD
For exemplary clinical, translational, and basic science research on the treatment of stress urinary incontinence

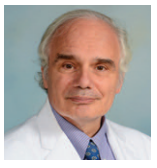
WILLIAM P. DIDUSCH ART & HISTORY AWARD
Michael E. Moran, MD
For extensive written contributions on urologic history and dedicated service as museum curator

GOLD-HEADED CANE AWARD
Daniel J. Culkin, MD, MBA
For tireless advocacy encouraging outreach to underserved rural populations and patients with spinal cord injuries

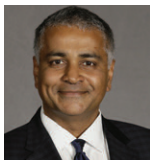
DISTINGUISHED CONTRIBUTION AWARD
Timothy D. Averch, MD
For contributions to AUA initiatives including quality improvement, simulation, e-learning and health policy

DISTINGUISHED CONTRIBUTION AWARD
Lawrence S. Ross, MD
For contributions to the field of reproductive medicine and for many years of dedicated service to the AUA

DISTINGUISHED CONTRIBUTION AWARD
J. Christian Winters, MD
For outstanding leadership and contributions to the field of incontinence and voiding dysfunction

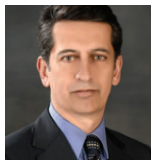


DISTINGUISHED SERVICE AWARD
Dean G. Assimos, MD
For voluminous, substantive contributions to the educational resources of the AUA



DISTINGUISHED SERVICE AWARD
Manoj Monga, MD
For innovative and impactful service as AUA Secretary to the benefit of urologists and patients worldwide

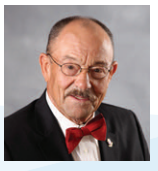
DISTINGUISHED SERVICE AWARD
Aaron Spitz, MD
For more than twelve years of outstanding service to the AMA and organized medicine on behalf of urology



PRESIDENTIAL CITATION
Jaime A. Cajigas, MD
For excellence in advancing AUA education, membership and collaborations with Sociedad Colombiana de Urología

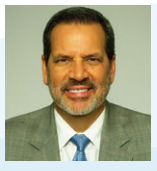
PRESIDENTIAL CITATION
Brendan M. Fox, MD
For leadership and outstanding contributions in advancing the AUA's strategic goals

PRESIDENTIAL CITATION
Stanley J. Kandzari, MD
For an outstanding career devoted to the education of urology residents



PRESIDENTIAL CITATION
Carl A. Olsson, MD
For outstanding contributions as the inaugural editor of *Urology Practice*

PRESIDENTIAL CITATION
Gail S. Prins, PhD
For leadership, determination and success in advancing the breadth of urologic research and advocacy



PRESIDENTIAL CITATION
Kevin A. Wohlfort
For over 30 years of distinguished executive leadership and outstanding contributions in advancing AUA's mission

American Urological Association
Advancing Urology™

FROM THE *AUA Secretary*

Impact of COVID-19 on Urology

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

The COVID-19 pandemic is rapidly shifting how urologists live and practice. From the halting of elective surgeries and clinical trials to the cancellation of urological meetings around the globe, urologists are learning to adapt to a new normal as we navigate these unprecedented times.

In March the AUA made the difficult decision to cancel its 2020 Annual Meeting in Washington, D.C. Thanks to the steadfast dedication of our physician and researcher leadership, and the collective commitment of our speakers, we will be leveraging the latest technologies to bring some of the best science from AUA2020 right to your computer. The AUA Virtual Experience will be free for all AUA members and will include:

- AUA Live – A Two-Day Virtual Education Experience June 27-28
- AUA Summer School – Live Instructional Course Webinars
- Research Weekend
- And more!

As we continue to find new ways to use technology during this time, it seems inevitable that electronic education will be a part of our future. While virtual activities cannot always replace the depth and breadth of in-person meetings, it allows us to connect and educate our global community, advance our specialty and improve the care of the patients we serve.

Another COVID-19 impact on urology is that institutions and governing bodies have requested urologists postpone and/or cancel elective surgeries and procedures to help preserve personal protective equipment, save resources for the care of patients with COVID-19 and protect our health care workers.

This unprecedented public health emergency has impacted our colleagues in many nations, societies and organizations throughout the world. Our longstanding friendships and robust partnerships with urological societies around the world are more important than ever at this time. We are communicating regularly with all of our global partners to discuss next steps for educational programming that may have been canceled or postponed. We are also working with them to host virtual leadership meetings and regularly checking in to ensure the safety of our friends.

I would also like to acknowledge the incredible work of the AUA staff members who, from home, continue to support the membership under the leadership of a strong executive team led by Chief Executive Officer Mike Sheppard. The organization continues to move forward in a positive way with normal day-to-day operations, planning and the added complexity of new virtual programs.

While the impact of this pandemic can be felt everywhere, from our patients and colleagues to our research and education, this pandemic is also bringing people, communities and nations together. Urology is already a very tight-knit community around the world, and this time will serve to bring us even closer together for the missions that we have of patient care, teaching and research. As we navigate these new challenges, the AUA will be there to support you as best we can. ◆

AUA Testosterone Guideline Additions

▼ Continued from page 17

testosterone. Several other guidelines have advocated using free testosterone for symptomatic hypogonadism when total testosterone is between 230 and 317 ng/dL or 300 and 350 ng/dL.[5] Many experts would offer TTh to symptomatic men who have a low free testosterone (calculated less than 100 pg/mL or direct less than 1.5 ng/dL) even if total testosterone is normal.[6]

The AUA testosterone guidelines recommend a testosterone treatment goal of 450 to 600 ng/dL. However, the goal of TTh should also be focused on symptomatic improvement and not only on serum testosterone values. Although some men may experience symptomatic improvement at testosterone levels of 400ng/dL, others may not experience symptomatic improvement until they achieve higher testosterone levels such as 600 to 900 ng/dL. This difference can be explained by wide inter-individual variability of CAG repeats in the androgen receptor gene and as well as in SHBG levels. Therefore, TTh dosing should be individualized and adjusted until symptoms are relieved while still maintaining serum testosterone concentrations within the normal range.

In summary, the AUA testosterone guidelines are the most comprehensive and informative testosterone guidelines published to date. Further considerations when interpreting the guidelines include testosterone's effect on BPH, erythrocytosis, diagnosis of TD using free testosterone, and 300 ng/dL as a cutoff and the appropriate testosterone treatment goal range. ◆

1. Mulhall JP, Trost LW, Brannigan RE et al: Evaluation and Management of Testosterone Deficiency: AUA Guideline. J Urol 2018; **200**: 423.
2. DeLay KJ and Kohler TS: Testosterone and the prostate: artifacts and truths. Urol Clin North Am 2016; **43**: 405.
3. Morgentaler A, Traish A, Hackett G et al: Diagnosis and treatment of testosterone deficiency: updated recommendations from the Lisbon 2018 International Consultation for Sexual Medicine. Sex Med Rev 2019; **7**: 636.
4. Antonio L, Wu FC, O'Neill TW et al: Low free testosterone is associated with hypogonadal signs and symptoms in men with normal total testosterone. J Clin Endocrinol Metab 2016; **101**: 2647.
5. Wang C, Nieschlag E, Swerdloff R et al: ISA, ISSAM, EAU, EAA and ASA recommendations: investigation, treatment and monitoring of late-onset hypogonadism in males. Int J Impot Res 2009; **21**: 1.
6. Morgentaler A, Traish AM and Khera M: A critique of the AUA guidelines on testosterone deficiency. J Sex Med, suppl., 2019; **pii**: S1743.

Seeking Early Career Success: Beyond "Busy"

Steven J. Hudak, MD
Chair, AUA Young Urologists Committee
Fort Worth, Texas

Kyle A. Richards, MD
Chair-Elect, AUA Young Urologists Committee
Springfield, Massachusetts

It goes without saying that the COVID-19 pandemic has already changed our personal and professional lives in countless ways. The unfortunate but necessary cancellation of the 2020 AUA Annual Meeting is a notable example. Over the last couple of months, leveraging the latest and most innovative technologies, the best science from the AUA has been released virtually. While nothing can replace the massive scope of the annual meeting, these efforts work to ensure that our community continues to receive the critical education needed to advance our specialty and improve the care of the patients we serve.

Unfortunately, nothing can take the place of the networking opportunities that were lost with the cancellation of the annual meeting. We have missed out on our annual opportunity to share well deserved free time with new friends and old. In the past, conversations with friends and colleagues at the annual meeting would often revolve around an assessment of one's level of "busyness."

For example, we would frequently answer the question, "How's your practice?" in one of several familiar ways. Recent graduates might have replied, "It's going okay. I'm trying to get busy." Young urologists in their first 2 or 3 years of practice commonly reply, "Doing well—getting busy." A few years later this changes to, "Going great! Really busy." At some point, though, the zenith of "busy" was apparently surpassed, ultimately leading to the response, "Way too busy. I need another partner!"

Why has "busy" become an index of success so commonly shared among friends and colleagues while conversing at the annual meeting and in other professional settings? The dictionary definition of busy is "having a great deal to do." In the modern medical climate (urology and otherwise) the ever increasing demands of patient loads, hospitals, employers, administrators and payers have made certain that each one of us is "busy" from the first day we begin practice.

Since the COVID-19 pandemic has taken hold in the United States "busy" has taken on an entirely different tone altogether with outpatient clinics transforming into telehealth platforms and elective surgeries exchanged for frontline coronavirus care for some or outright idleness for others. I suspect many of us have at times felt a sense of emptiness, confusion and perhaps even a lack of purpose when we find ourselves not busy. Why have we as a profession and as a society developed this obsession with "busy" as an end point that we relentlessly strive to reach? Why not a more laudable goal?

Perhaps we use the term "busy" because it has so many surrogates that can be easily measured, like patients seen, cases performed, relative value units earned, nights of call taken, meetings attended, presentations given, manuscripts submitted etc. Thus, when we say, "I'm busy," it is perhaps, intended or unintended, a humblebrag meaning "I'm essential and successful, and the busier I become the more successful I will be." Is this really how we want to communicate with one another, especially in an era when physician burnout and moral injury have become so pervasive?

Perhaps an equally important question to ask is whether there is a point at which the pressure to increase clinical volume comes at the cost of a decrease in the quality of care delivered. While workload will always be important, the quest for a successful and fulfilling career in any specialty should focus primarily on quality. For urologists this equates to quality of encounters with patients in the office, quality of surgical outcomes and quality of research activities. It should also refer to the quality of our own health and wellness, which have been irrefutably shown to influence patient care.

Many of us chose urology because we relentlessly seek such quality and the positive impact it can have on patients' lives. Making a positive impact on patients enriches our own lives and deepens our connection to the careers to which we were called. The pursuit of high quality will always guarantee we stay busy, but an intentional focus on quality over "busy" will help us ensure that the quality of care we provide is not lost into the insatiable abyss of "busy."

While the COVID-19 pandemic has caused (and unfortunately may continue to cause) an unprecedented degree of hardship for our practices, our families and our society as a whole, perhaps a positive that can come from this is time and energy to reflect on how we perceive and measure success during the first decade of our career.

It is the greatest hope of the AUA Young Urologists Committee that we will all emerge from this pandemic with a hardened resolve to weather the storm of "busy" and achieve the highest quality outcomes in our personal and professional lives. ◆

FROM THE *AUA Science & Quality Council*

The 2020 AUA Annual Census

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

In February 2014 the AUA Board of Directors approved the AUA's Data Strategic Plan, which covers a matrix of well designed data programs that work together to build a comprehensive data repository in urology with the goal of supporting evidence-based research and decision making.

One such program is the AUA Annual Census that has been conducted yearly since its initial launch at the 2014 AUA Annual Meeting. Six annual reports detailing practicing urologists in the United States have been published to date. Additional reports describing comparisons of practicing urologists and urology residents in the U.S. and around the globe are also freely available through the AUA website.

Urology currently stands as the only surgical specialty with workforce information consistently collected, analyzed and published each year. Using state-of-the-art statistical techniques the AUA Annual Census reports on workforce characteristics divided by geographic areas within the United States. The AUA Annual Census is considered a reliable and accessible source of information about the urology workforce and patterns of practice, positioning it as a valuable tool for the AUA membership.

The AUA Annual Census is designed not only to identify practice characteristics and longitudinal variations through base questions asked annually, but also to delve into emerging topics through new questions collected from specialty leadership and the urology community that vary year to year. As such, not only does the census provide accurate information on the number of practicing urologists in the United States including demographic, geographic, training and practice characteristics, but it also covers emergent topics important to the urology community such as professional burnout, physician compensation and telemedicine.

Such systematic collection of data enables the AUA to detect and track important workforce trends in the field of urology and to provide tools to anticipate potential future challenges. Some important longitudinal trends noted since the publication of the first census report include growth in the number of female practicing urologists and a shift in practice settings for urologists from private practice to hospital or other institutional settings.

Furthering the AUA mission to promote the highest standards of urological clinical care through education, research and the formulation of health care policy, the census reports are widely used by urologists, researchers and health policy decision makers to inform clinical practice, scientific research, advocacy efforts and member focused educational programs. The AUA continues to support its membership by providing AUA public use micro Census data sets and additional opportunities for researchers to present findings at various AUA annual meetings, and sectional and society conferences. The AUA also encourages collaboration between the association and its constituent partners through census question development and broad knowledge dissemination.

The 2020 AUA Annual Census will launch in May 2020 and will remain online through the end of September 2020. All members of the urological community are encouraged to participate. ◆

Is Adjuvant Chemotherapy after Prostatectomy Beneficial?

Leonard G. Gomella, MD, FACS
Philadelphia, Pennsylvania

In an attempt to improve disease control for high risk prostate cancer, numerous clinical trials have added either androgen deprivation or chemotherapy to definitive local therapy. Neoadjuvant and adjuvant strategies have been investigated in high risk disease for radical prostatectomy and radiation therapy. Androgen deprivation therapy has become a standard of care in the management of high risk prostate cancer treated with external beam radiation with strong evidence for using this combined treatment in the postoperative radical prostatectomy setting.

With the identification of high risk disease following radical prostatectomy, such as locally advanced disease or high Gleason grade, previous clinical studies have supported the use of adjuvant androgen deprivation only in the presence of nodal metastasis. Without evidence of nodal metastasis at the time of radical prostatectomy adjuvant androgen deprivation has not been practice changing. To date, neoadjuvant studies in high risk disease before radical prostatectomy have been inconclusive.

The CHAARTED (Chemo-Hormonal Therapy versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer) and STAMPEDE (Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy) trials demonstrated that docetaxel chemotherapy improved survival in men with high risk metastatic hormone sensitive prostate cancer.[1] Before these results were observed docetaxel chemotherapy with prednisone was limited to the hormone resistant metastatic setting. These positive studies moved chemotherapy earlier in the course of progressive prostate cancer and led to renewed interest in chemotherapy in combination with definitive local therapy for high risk prostate cancer.

It has been hypothesized that docetaxel could improve survival and other outcomes in men with non-metastatic high risk prostate cancer. Several studies have now been published using adjuvant chemotherapy following radical prostatectomy.

The phase 3 Scandinavian Prostate Cancer Group 12 (SPCG-12) trial was an international study of 459 men with high risk disease.[2] The investigators defined high risk as 50% or greater risk of progression based on nomograms using standard clinical features such as pT2 margin positive or pT3a Gleason score 4+3 or greater, pT3b or lymph node positive disease and Gleason score 3+4 or greater.

Patients were randomized postoperatively to 6 cycles of docetaxel without prednisone every 3 weeks or observation. There was no significant difference in time to biochemical recurrence, defined as a PSA greater than 0.5 ng/ml, or survival in the 2 arms of the trial. Survival in the docetaxel arm was 43 months vs 46 in the surveillance arm. Docetaxel without combined androgen deprivation did not significantly improve biochemical disease-free survival after radical prostatectomy.[2]

A VA (Veterans Affairs) Cooperative group study has just reported on added adjuvant chemotherapy to standard of care in high risk prostate cancer with docetaxel and prednisone vs observation.[3] Androgen deprivation was not used in either arm to limit cell cycle arrest that might reduce the impact of docetaxel on cycling cells. The study fell short on the accrual with less than half of the total intended patients enrolled. The primary end point was progression-free survival with secondary end points of overall, prostate cancer specific and metastasis-free survival, and time to androgen deprivation therapy.

The results did not show statistically significant improvement in progression-free survival, for the intent to treat population as a whole. However, some subgroups such as African American men, T3b or greater disease and Gleason grade 7 or lower had a statistically significant improvement in progression-free survival compared with the standard of care group. The progression-free survival benefit of docetaxel increased to almost 2 years in the African American subgroup. The common adverse events thought to be related to chemotherapy included neutropenia (43%), hyperglycemia (20%) and fatigue (5%), with febrile neutropenia at 2%. A followup of the VA trial is planned using genomics to further define treatment effect and target populations for chemotherapy.

As noted, radiation therapy plus long-term androgen suppression is now a standard treatment option for patients with high risk localized prostate cancer. NRG Oncology RTOG 0521 randomly assigned men to receive long-term androgen suppression plus radiation with or without adjuvant docetaxel chemotherapy.[4] For patients with high risk nonmetastatic prostate cancer, chemotherapy improved overall survival from 89% to 93% at 4 years with improved disease-free survival and a reduction in distant metastasis. While not a radical prostatectomy study, it is the first trial to suggest a potential benefit using adjuvant docetaxel chemotherapy in high risk prostate cancer.

Upcoming high risk prostate cancer adjuvant studies will involve next generation androgen receptor pathway blockers such as abiraterone, enzalutamide and apalutamide with each tested alone or in combination with radiation therapy. These evolving studies follow the concept of moving agents with a benefit in advanced disease to earlier disease states. Precision medicine using genomic analysis and other means may provide insight on the patients who will respond to these specific interventions. In the future these predictive strategies could impact adjuvant treatment decisions, leading to increased intensity treatments where appropriate and de-escalation of treatment for others with lower risk.

In reply to the question initially posed, "is adjuvant chemotherapy after prostatectomy beneficial?" the answer is uncertain. Postoperative docetaxel chemotherapy appears to benefit at best a small subset of patients. Based on current data chemotherapy following radical prostatectomy remains investigational. Perhaps next generation androgen receptor pathway blockers and other novel agents will move the use of adjuvant therapy following high risk radical prostatectomy ahead. ◆

1. Kinsey EN, Zhang T and Armstrong AJ: Metastatic hormone-sensitive prostate cancer: a review of the current treatment landscape. Cancer J 2020; **26**: 64.
2. Ahlgren GM, Flodgren P, Tammela TLJ et al: Docetaxel versus surveillance after radical prostatectomy for high-risk prostate cancer: results from the prospective randomised, open-label phase 3 Scandinavian Prostate Cancer Group 12 Trial. Eur Urol 2018; **73**: 870.
3. Lin DW, Shih MC, Aronson W et al: Veterans Affairs Cooperative Studies Program Study #553: chemotherapy after prostatectomy for high-risk prostate carcinoma: a phase III randomized study. Eur Urol 2020; **77**: 563.
4. Rosenthal SA, Hu C, Sartor O et al: Effect of chemotherapy with docetaxel with androgen suppression and radiotherapy for localized high-risk prostate cancer: the randomized phase III NRG Oncology RTOG 0521 Trial. J Clin Oncol 2019; **37**: 1159.

Treatment of Atypical Peyronie's Disease

Farouk M. El-Khatib, MD

Faysal A. Yafi, MD, FRCSC

Irvine, California

Peyronie's disease (PD) manifests as fibrosis of the tunica albuginea and can have a significant impact on male sexual function and quality of life.[1] Although underreported, PD is estimated to affect 3% to 10% of the general population and is clinically divided into acute or chronic phase. Pain and evolving plaque characterize the acute phase, usually lasting between 6 and 12 months. In contrast, resolution of pain and deformity stabilization mark the transition to the chronic phase, which generally occurs in 12 to 18 months.[1]

Most commonly, presentations include a palpable plaque and a dorsal and/or lateral curvature. Less commonly, men may present with an atypical presentation such as ventral curvature, penile indentation, hourglass deformity and/or multiplanar curvature.[2] Medical and surgical treatments are currently available for the management of PD but there are few data regarding the management of atypical disease. We discuss the latest updates in the literature on the treatment of atypical PD.

Injection therapy

Historically, intralesional injections of verapamil and interferon alpha-2b have demonstrated safety and efficacy for the management of atypical PD. Berookhim et al investigated verapamil use and found 40% improvement in ventral curvatures.[3] Stewart et al demonstrated that no difference existed in the response rate or absolute change in curvature between dorsal and ventral curvatures when interferon alpha-2b was used.[4]

Intralesional injection of collagenase Clostridium histolyticum (CCH, the only U.S. Food and Drug Administration approved medical therapy for PD) is currently not indicated per label for the management of atypical PD. However, a retrospective study of 65 men evaluated the safety and efficacy of CCH in patients with atypical presentation. Using a modified treatment protocol a mean decrease in penile curvature of 15.0 to 20.0 degrees was found in this cohort.[2] Minor adverse effects such as ecchymosis resolved completely 2 weeks after treatment.

Similarly, in another study of 74 men with PD 42 (57%) were deemed to have an atypical presentation and their outcomes were assessed based on treatment received.[5] Patients who underwent intralesional CCH injection had a mean improvement in curvature of -13.5 ± 5.7 degrees (33.1% ± 10.4%) with a mean number of injections of 6.4 ± 3.0, compared to -45.0 ± 10.8 degrees (85.5% ± 17.5%) in those who underwent surgery (see table).

All men in both groups reported high satisfaction with outcomes. Furthermore, in the subset of men who presented with indentation or hourglass deformity 11 of 17 (64%) reported subjective improvement in narrowing/indentation after receiving CCH injections. Of note, 1 patient in the CCH cohort experienced a penile fracture, which required surgical repair.[3]

Surgery

Plaque incision/partial excision and grafting with elevation of the urethra may be performed for patients with ventral PD. Alternatively, plication may be formed through a penile degloving incision. However, as described by Reddy et al dorsal plication may also alternatively be performed through a small vertical dorsal incision without the associated morbidity of penile degloving or urethral elevation.[6]

For patients with an indentation and/or hourglass deformity, a Y (for unilateral indentation) or double Y (for hourglass) incision is recommended to correct for penile wasting. However, Reed-Maldonado et al recently described a novel tunica sparing surgical technique labeled as extratunical grafting (ETG) for these patients with PD and indentation and/or hourglass deformity.[1] For 4 years 36 men underwent the ETG procedure due to difficulty with sexual intercourse or unappealing penile appearance.

With this technique a ventral longitudinal penile skin incision was performed followed by dissection between the dartos and Buck's fascia (see figure). The dissection was circumferential or focal if the patient had an hourglass deformity or an indentation, respectively, while the neurovascular bundle remained intact. The exposed tunical defect was then covered by a cadaveric fascia and sutured into position with multiple interrupted absorbable sutures to achieve the desired outcome.

The graft was presoaked in an antibiotic solution, chemically processed and gamma irradiated. This study highlighted the graft material Tutoplast Suspend®. At a mean 21-month followup all patients reported satisfactory resolution of their penile deformity and 2 men (12%) experienced hypoesthesia.[1]

Conclusions

Atypical PD presents a challenging

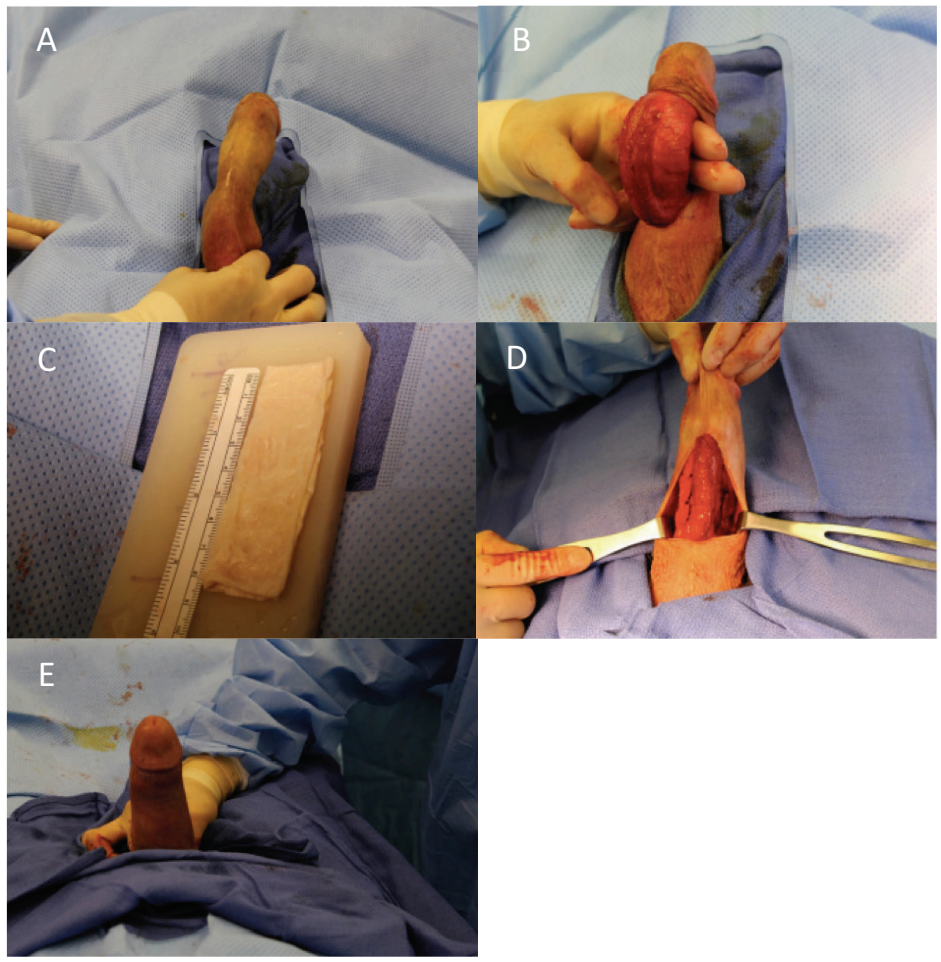


Figure. Steps of ETG procedure. *A*, intraoperative image after intracorporeal injection with 60 mg papaverine. Examination reveals dorsolateral penile curvature with a midshaft hourglass deformity. *B*, through ventral longitudinal incision dissection is carried to level between dartos and Buck's fascia in location of deformity. Neurovascular bundle is not dissected. *C*, graft material is folded to double thickness, and measured and cut to fit deformity. *D*, graft is wrapped around penis shaft and positioned appropriately. Interrupted sutures are placed adjacent to urethra on both sides to secure graft. *E*, final outcome is assessed with erection before skin closure.

Table. Treatment outcomes in men presenting with atypical PD receiving CCH injections.

	No.	Degrees Penile Curvature before CCH (degrees)	Degrees Penile Curvature after CCH (±SD)	Degree Improvement ± SD	% Improvement ± SD	p Value
Indentation	17	51.3 ± 14.6	30.9 ± 11.2	20.3 ± 8.1	39 ± 14	0.0001
Multiplanar	7	36.7 ± 7.6	20.8 ± 1.4	15.8 ± 8.0	42 ± 12	0.0001
Ventral	5	40.0 ± 7.1	21.3 ± 1.8	18.8 ± 8.8	46 ± 14	0.0004
Hourglass	6	45.0 ± 21.8	27.5 ± 20.5	17.5 ± 4.3	44 ± 20	0.1825

▼ Continued on page 23

FROM THE *Urology Care Foundation*

Advancing Urological Health through Research, Resources and Initiatives

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

June is Men's Health Month and is an important time to recognize triumphs in the Urology Care Foundation's effort to advance men's urological health. The Foundation is committed to funding and fostering the development of researchers on the vanguard of basic and clinical research so that medicine can be improved for all. Since 1975 the Urology Care Foundation has supported more than 850 outstanding young scientists with more than $34 million in research funding.

Making a Difference

During the last 40 years we have supported the journeys of top research scholars to drive lasting improvements in the lives of urology patients and their families. Two areas of investigation of particular importance for men's health include prostate cancer and male sexual dysfunction.

Prostate cancer will develop in 1 in 9 men. Our commitment to battle this disease to decrease its burden on patients and their families is stronger than ever. Areas of investigation of critical importance are detection of disease and understanding ways to mitigate disease progression. Foundation scholars who have focused their talent on this issue include Drs. Simpa Salami and Stephen J. Freedland.

Dr. Simpa Salami became the first recipient of the SPORE (Specialized Programs of Research Excellence) Research Scholar Award in 2016. Working at the University of Michigan, Dr. Salami's research focuses on developing optimal paradigms for early detection of prostate cancer and accurately stratifying patients into risk categories to improve active surveillance and treatment response.

Dr. Stephen J. Freedland is a Distinguished Professor of Urology at Cedars-Sinai in Los Angeles. He was an inaugural recipient of the Urology Care Foundation Rising Stars in Urology Research Award in 2005. With support from the Foundation, he tested whether various diets could slow prostate cancer growth and discovered a very low carbohydrate diet reduced tumor growth.

Male sexual dysfunction affects as many as 30 million men around the world. Erectile dysfunction, or ED, is the most common sexual problem that men report to their doctor. Dr. Arthur L. Burnett is one of our scholars the Foundation has recognized as a thought leader in this area of medicine.

Dr. Burnett has become a world-renowned expert in sexual medicine. His Foundation supported research on nitric oxide and carbon monoxide as mediators of the urogenital system was critical to the development of medications to treat erectile dysfunction. Dr. Burnett is now a Distinguished Professor of Urology and Director of the Basic Science Laboratory in Neuro-Urology at Johns Hopkins University.

Patient Education Resources

With everything from fact sheets and brochures to videos and podcasts, the Foundation is proud to offer multiple forms of patient education and information about prostate cancer, sexual function, male infertility, bladder cancer, benign prostatic hyperplasia and many more conditions potentially affecting the nearly 3.7 billion men throughout the world.

I encourage you to take advantage of this extraordinary member benefit and order your free patient education materials today by visiting www.UrologyHealth.org. ◆

AUA RESIDENTS & FELLOWS *Committee News*

Should I Pursue a Fellowship?

Scott Greenberg, MD
New England Section Representative, AUA Residents & Fellows Committee

Katherine Rotker, MD

Worcester, Massachusetts

During the last 2 decades it has become increasingly common for graduating residents to pursue urology fellowships, adding years of continued urological training before starting an autonomous career. Reviewing the AUA Census from 2016, less than 27% of urologists older than 65 years were fellowship trained compared to approximately 32% between 55 and 64 years, approximately 43% between 45 and 54 years, and nearly 60% less than 45 years old.

In the most recent resident census from 2016 to 2018 more than 50% of the 700+ respondents planned to pursue or were already matched to a fellowship with an additional 22% uncertain, leaving only a quarter of residents with no desire to continue training through fellowship. Additionally, through an anonymous survey Han et al found more than 64% of applicants to the University of Florida in 2017 expected to pursue fellowship training.[1] Today's urology residents are clearly leaning toward a longer duration of training than those from decades past, but what has led to this clear paradigm change for urology learners?

Numerous factors could be posited for this increase in fellowship training, including further training in a specific area, desire for specific cases in practice, pursuit of an academic career, job market competition, program expectations, future income and the availability of more fellowship opportunities. Unfortunately, there are limited data on the influencing factors driving individuals to pursue additional years of training. The most recent AUA resident census only evaluated whether those seeking additional training did so because of "type of surgical cases" (54%), "nature of clinical and medical problems" (34%) or "other" (11%).

Additionally, there is a lack of robust data on outcomes for those who complete fellowship. For example, are nonfellowship trained individuals able to achieve a similar skill set to their fellowship trained colleagues? Is it more difficult to obtain an academic position without fellowship training? Do fellowship trained urologists earn more?

There have been some early endeavors to answer these questions on outcome differences between fellowship and nonfellowship trained urologists. Omidele et al found no difference in robot-assisted partial nephrectomy outcomes performed by fellowship and nonfellowship trained urologists.[2] Kasabwala et al published data in 2014 on more than 850 urologists in academic programs, demonstrating no difference in h-index between fellowship and nonfellowship trained urologists, but that department chairpersons were more often fellowship trained (70%).[3]

Finally, Langston et al evaluated the economic impact of training and career decisions on urologist career earnings.[4] They found pediatric fellowship trained urologists earn approximately $28,000 per year less on average than their adult urology counterparts and that academic urologists make slightly less over a career than their private practice counterparts. However, other fellowship trained urological specialist earnings were not investigated in this study.

So the question stands: "Should I pursue a fellowship?" Unfortunately, the answer remains nuanced. More longitudinal research is needed to identify the motivating factors behind resident choice to pursue fellowship training and the benefits or repercussions with regard to job opportunities and earnings. With improved knowledge of motivating factors and outcomes for those who pursue fellowships we can provide future urology residents with more data to help aid informed decision making regarding their future training and careers. ◆

1. Han J, Rabley A, Vlasak A et al: Career expectations and preferences of urology residency applicants. Urology 2019; **123**: 44.
2. Omidele OO, Davoudzadeh N and Palese M: Fellowship and subspecialization in urology: an analysis of robotic-assisted partial nephrectomy. Urology 2019; **130**: 36.
3. Kasabwala K, Morton CM, Svider PF et al: Factors influencing scholarly impact: does urology fellowship training affect research output? J Surg Educ 2014; **71**: 345.
4. Langston JP, Kirby EW, Nielsen ME et al: Economic impact of training and career decisions on urological surgery. J Urol 2014; **191**: 755.

HAVE YOU *Read?*

Daniel Shoskes, MD
Cleveland, Ohio

Cooney L and Balcezak T: Cognitive testing of older clinicians prior to recredentialing. JAMA 2020; 323: 179-180.

We recognize that pilots can be too old to fly, but what about physicians and especially surgeons? In this opinion piece the authors describe the process at Yale that now requires a neurological and ophthalmological examination of all applicants for reappointment to the medical staff who are 70 years old or older. A cognitive screening battery of tests was developed and designed to balance brevity with broad coverage of abilities relevant to clinical practice.

The instrument was constructed to account for the cognitive decline and neurodegeneration commonly associated with aging. The precise battery of tests was confidential so that the clinicians could not prepare for the test. Individuals with substantial deficits on the screening test were asked to undergo comprehensive testing, or if the committee determined that the results of the screening tests demonstrated very substantial cognitive deficits were directly evaluated for their ability to practice clinical medicine. In the end a substantial proportion (12.7%) of clinicians 70 years old or older were found to have impaired cognition, raising concerns about their clinical abilities.

This is not an easy problem to address, but with the aging urology workforce it is one that we must approach with transparency and objective data.

Saad F, Doros G, Haider KS et al: Differential effects of 11 years of long-term injectable testosterone undecanoate therapy on anthropometric and metabolic parameters in hypogonadal men with normal weight, overweight and obesity in comparison with untreated controls: real-world data from a controlled registry study. Int J Obes (London) 2020; doi: 10.1038/s41366-019-0517-7.

Obesity is a growing problem worldwide with multiple associated comorbidities. The authors evaluated effects of testosterone (T) therapy (Th) in men with T deficiency with normal weight, overweight and obesity on anthropometric and metabolic parameters compared with untreated men. Hypogonadal men (823) with total T of 12.1 nmol/l or less (about 350 ng/dl) (age 60.6±7.0 years) participated in an ongoing registry study. Among these men 474 (57.6%) were obese, 286 (34.8%) overweight and 63 (7.7%) normal weight. T undecanoate injections were administered to 428 men and 395 remained untreated.

Long-term TTh in hypogonadal men regardless of weight at baseline produced improvements in body weight, waist circumference and body mass index. Furthermore, TTh decreased fasting blood glucose and HbA1c and improved lipid profiles. Gradual decreases in blood pressure (systolic and diastolic) and pulse pressure occurred in men treated with T in each group. Marked reductions in mortality and major cardiovascular events were recorded in men receiving TTh.

The authors conclude that TTh produces reductions in weight, waist circumference and body mass index. There were 77 (19.5%) deaths in the untreated groups and 23 (5.4%) in the T groups. Based on these findings the authors suggest that long-term TTh in overweight and obese hypogonadal men produces progressive and sustained clinically meaningful weight loss and that TTh may contribute to reductions in mortality and incident major adverse cardiovascular events.

Vrooman OPJ, van Balken MR and van Koeveringe GA: The effect of continuous positive airway pressure on nocturia in patients with obstructive sleep apnea syndrome. Neurourol Urodyn 2020; 39: 1124-1128.

Obstructive sleep apnea can have multiple effects on symptoms in urology including erectile dysfunction and lower urinary tract symptoms. In this study the authors examined the prevalence of nocturia in patients with obstructive sleep apnea syndrome (OSAS) who received continuous positive airways pressure (CPAP) treatment as well as the effect of CPAP treatment on nocturia. All patients who were referred to the pulmonology department of a large teaching hospital in the Netherlands and received a CPAP mask for OSAS were interviewed and invited to take part in the study.

Of the 274 patients included in the study 190 were male and 84 were female, and mean age was 60.3 years. Of all patients 64 (23.4%) reported no nocturia episodes before CPAP and 210 (76.4%) reported 1 or fewer nocturia episodes. Treatment of OSAS with CPAP reduced nocturia with 1 or more episodes per night in 42.3% of the patients. Clinically relevant nocturia (2 or more voids per night) was reduced from 73.0% to 51.5%. There were no significant gender differences.

The authors conclude that the prevalence of nocturia in patients diagnosed with OSAS is 75.8% in both sexes. After CPAP treatment almost half of patients experienced a decrease in nocturia frequency of 1 or more voids. Clinically relevant nocturia was reduced by a third after CPAP. Thus, CPAP not only reduced the number of voids during the night but also improved the associated quality of life. ◆

Atypical Peyronie's Disease

▼ Continued from page 21

situation to physicians due to its presentation, lack of approved treatment options and surgical complexity. Data presented in this summary suggest that indications for CCH should be extended to include these aforementioned presentations. Similarly, less invasive options such as nondegloving plication for ventral PD and extratunical grafting for indentation and hourglass deformity offer newer alternatives with lower morbidity. ◆

1. Reed-Maldonado AB, Alwaal A and Lue TF: The extra-tunical grafting procedure for Peyronie's disease hourglass and indent deformities. Transl Androl Urol, suppl., 2018; **7**: S1.
2. Cocci A, Di Maida F, Russo GI et al: How atypical penile curvature influence clinical outcomes in patients with Peyronie's disease receiving collagenase *Clostridium histolyticum* therapy? World J Mens Health 2020; **38**: 78.
3. Berookhim B, Chevinsky M, Jakubowski C et al: Ventral intralesional verapamil injections for Peyronie's disease: feasibility and safety. Presented at the 20th Annual Fall Meeting of the Sexual Medicine Society of North America, Miami, Florida, November 20-23, 2014.
4. Stewart CA, Yafi FA, Knoedler M et al: Intralesional injection of interferon-α2b improves penile curvature in men with Peyronie's disease independent of plaque location. J Urol 2015; **194**: 1704.
5. El-Khatib FM, Osman M, Towe M et al: Treatment related outcomes for patients with atypical Peyronie's disease (abstract MP65-17). J Urol, suppl., 2019; **201**: e956.
6. Reddy RS, McKibben MJ, Fuchs JS et al: Plication for severe Peyronie's deformities has similar long-term outcomes to milder cases. J Sex Med 2018; **15**: 1498.

TAKE THE 2020
AUA | ANNUAL CENSUS
AUAnet.org/TakeCensus
American Urological Association
Advancing Urology™

Guidelines for the Urological Management of Spina Bifida for Adult Patients

Neha R. Malhotra, MD **M. Chad Wallis, MD**

Salt Lake City, Utah

With improvements in care more patients with spina bifida are surviving longer into adulthood. A paucity of dedicated adult spina bifida clinics has led to more patients with spina bifida being seen in general adult urology clinics. Here we review recommendations from the Spina Bifida Association (2018)[1] and the European Association of Urology guidelines on neuro-urology (2016)[2] to familiarize the general urologist.

A careful history and physical examination should be obtained at the first visit and updated yearly. The focused history should elucidate prior bladder management and relevant surgical interventions, which may require outside records or interviewing a caregiver. The abdomen should be examined for scars and stomas. Latex precautions should be taken for all patients with spina bifida.

Lower Tract Management

Bladder function is impaired in nearly all patients with spina bifida.[1] When seeing patients for incontinence the urologist must remember the primary goal of renal function preservation. Secondary goals should include continence, freedom from urinary tract infections (UTIs) and independence. The majority of patients manage their bladder with clean intermittent catheterization (CIC), while some may spontaneously void and others may be incontinent and diaper dependent.[2] Feasible goals for social continence should be developed together with the patient. Indwelling catheters should be avoided.[1]

Assessment of the bladder requires urodynamics to assess for capacity, compliance, leak point pressure (LPP), detrusor overactivity and detrusor sphincter dyssynergia (DSD). If the patient has no recent urodynamics a baseline set should be obtained. A patient can then be followed clinically based on changing incontinence, recurrent UTIs or changes on upper tract imaging. A frequency volume chart should be obtained, which can be used to help a patient understand the relationship among fluid intake, bladder volume and leakage to manage their catheterization regimen to maximize social continence.

Patients with hostile bladders (high grade reflux, detrusor LPP greater than 40 mm Hg or DSD) should be placed on CIC and antimuscarinics. Prophylactic antibiotics should be considered in patients with recurrent UTIs or high grade reflux. OnabotulinumtoxinA (Botox®) intradetrusor injection can be used for patients with hostile bladder despite CIC and maximal antimuscarinics. Injections can be performed in office. However, patients with lesions above T6 should be monitored for autonomic dysreflexia.

Some patients may continue to have hostile bladder or unacceptable incontinence due to poor capacity and compliance despite maximal medication management and/or chemodenervation. Augmentation cystoplasty should be considered for this population. Urologists should ensure patient ability to catheterize per urethra or should discuss creation of a continent catheterizable channel.

Compliance with scheduled catheterization is imperative to prevent rupture. Following augmentation, regular bladder irrigation is recommended to decrease symptomatic UTIs and bladder stone formation. Patients should have annual chemistries and vitamin B12 levels tested. Routine cystoscopy is not indicated but should be performed in patients with gross hematuria, recurrent symptomatic UTIs, increasing incontinence or pelvic pain.

If the patient has incontinence secondary to low LPP procedures to increase outlet resistance may be considered. These procedures include bladder neck reconstruction, urethral lengthening, bladder neck slings and artificial urinary sphincters. Success rates are modest and complication rates are high with bladder neck procedures. Urologists should consider referral to reconstructive specialists.

Mid urethral slings can be considered and have shown good success with few complications.[1] Urethral bulking agents have shown poor efficacy and are not recommended as primary treatment. Sacral neuromodulation and posterior tibial nerve stimulation have shown limited efficacy and are not recommended.

Recurrent UTIs are a common problem for patients with spina bifida, particularly those who perform CIC. It is important to distinguish asymptomatic bacteriuria from a symptomatic UTI. Patients should be counseled not to treat positive cultures in the absence of symptoms. Some patients may require daily antibiotic prophylaxis, while others do well with self start therapy. Ideally, long-term oral antibiotics should be avoided.[1] Antibiotic irrigation can be used for patients who continue to have infections despite oral antibiotic prophylaxis. Imaging and cystoscopy may be considered in cases of recurrent infections with the same organism.

Upper Tract Surveillance

All patients with spina bifida should undergo yearly surveillance ultrasound and renal function assessment. Serum creatinine may not accurately represent renal function. Consider checking cystatin C levels as well. Patients with chronic kidney disease should be referred to nephrology.

Prostate Cancer Screening

Prostate specific antigen (PSA) testing and digital rectal examination should be performed in concordance with standard guidelines, taking into account the estimated life expectancy of the patient. PSA results should be considered in light of urinalysis and urine culture results and free PSA or repeat total PSA should be considered.[3] If biopsy is recommended consider magnetic resonance imaging guidance and a transperineal technique as well as pretreating patients who catheterize with culture specific antibiotics.

Sexual Function and Fertility

Men and women with spina bifida have high rates of sexual dysfunction. While taking the history it is important to elucidate sexual dysfunction including issues with pain, arousal, orgasm, and erection and ejaculation in men. Patients with spina bifida experience higher than average rates of sexual abuse. As such, it is important to verbalize aspects of the genital examination and respect boundaries, but still openly discuss sexual function and fertility.

While men with spina bifida have lower fertility rates, pregnancy is possible. In general, patients with lower level lesions have higher rates of sexual function. Impaired fertility for men with spina bifida is multifactorial and may be caused by failure of spermatogenesis and/or failure of sperm transport secondary to erectile or ejaculatory dysfunction.[4] Phosphodiesterase inhibitors are the first line treatment for erectile dysfunction.

Women with spina bifida have essentially normal rates of fertility. Patients with spina bifida interested in having children should be counseled on the heritability of spina bifida. In couples with a partner with spina bifida the female partner should take 4 mg folic acid daily starting 3 months before pregnancy.

Contraception should be discussed with all patients with spina bifida. Due to concerns regarding thrombosis and immobility hormonal contraception is to be avoided and condoms are the mainstay of contraception. All patients with spina bifida should be counseled on the use of polyurethane or polyisoprene nonlatex condoms. Due to decreased sensation and concern for incidental trauma women with spina bifida should always use lubricant at the time of intercourse.[5]

Cesarean section is recommended in women who have had bladder neck reconstruction or urinary sphincter placement. A urologist should be available at the time of delivery, especially in cases of augmentation cystoplasty and catheterizable stomas. Pelvic organ prolapse occurs at higher rates and younger ages even in nulliparous patients with spina bifida and may result in dyspareunia or difficulty with intercourse.[3] Urologists should offer repair for patients with bothersome symptoms but not repair asymptomatic prolapse. ◆

1. Groen J, Pannek J, Castro Diaz D et al: Summary of European Association of Urology (EAU) guidelines on neuro-urology. Eur Urol 2016; **69**: 324.

2. Wiener JS, Suson KD, Castillo J et al: Bladder management and continence outcomes in adults with spina bifida: results from the National Spina Bifida Patient Registry, 2009 to 2015. J Urol 2018; **200**: 187.

▼ Continued on page 25

FROM THE *Chief Executive Officer*

Welcome, New Board Members

Michael T. Sheppard, CPA, CAE
Linthicum, Maryland

Each year in May, the AUA has the distinct honor of welcoming new members of our Board of Directors and bidding farewell to those members whose terms have been completed. The Board plays a critical role in helping the AUA achieve its mission and works tirelessly to advance urology around the world. I'd like to take this opportunity to recognize our incoming – and outgoing – Board members.

Dr. Scott K. Swanson will lead the Board as the 2020-2021 President, having served in the President-Elect role since May 2019. Dr. Swanson has a long history of leadership within the AUA, having served previously as the Western Section Representative to the AUA Board and as president of the Western Section. He is a consultant in the Department of Urology at the Mayo Clinic in Scottsdale, Arizona, and was the first urologist on the 42-physician staff when the Mayo Clinic opened in Arizona in 1987. Prior to joining the Mayo Clinic staff, Dr. Swanson served in the U.S. Air Force from 1971 to 1987.

Dr. Raju Thomas was welcomed to the Board and will serve in the role of President-Elect through May 2021. Dr. Thomas is a past president of the AUA Southeastern Section, received the AUA Distinguished Service Award in 2016, and has served on the Urology Care Foundation Board of Directors. He has the distinction of being the first to introduce urologic laparoscopy in 1991 and was the first surgeon in the U.S. Gulf South to perform robotic surgery. In the aftermath of Hurricane Katrina in 2005, Dr. Thomas rescued – and rebuilt – the Department of Urology at Tulane University in New Orleans. He continues to chair Tulane's Department of Urology, where he also directs the department's residency program.

This year we also welcomed to the Board our new Treasurer-Elect, Dr. Thomas F. Stringer. In his year in this position, Dr. Stringer will work with AUA Treasurer Dr. David Green in preparation for taking over in 2021. Dr. Stringer is a past president of both the AUA's Southeastern Section and the Florida Urological Society, and served as the Southeastern Section Representative to the AUA Board from 2014 to 2019. He also served on the AUA's Finance, Bylaws and Investment committees, and was Chair of the AUA Compensation Committee.

In addition to our new officers, we are also pleased to announce the following new Section Representatives to the Board who will begin their 2-year terms this year.

The new Mid-Atlantic Section Representative is Dr. Kurt McCammon, a past president of the Society of Genitourinary Reconstructive Surgeons and the current Chair of the IVUmed Board. Dr. McCammon is the Devine Chair in Genitourinary Reconstructive Surgery and Chairman and Professor of the Department of Urology at Eastern Virginia Medical School, where he also serves as the Urology Residency Program Director and fellowship director of the adult and pediatric genitourinary reconstructive surgery program.

Dr. Reza Ghavamian will represent the New York Section. He is a past president of the section and is a graduate of the AUA's Leadership Program. He is the Eastern Regional Director of Urology for Northwell Health in New York, a Professor of Urology at the Zucker School of Medicine at Hofstra/Northwell, and the Chairman of Urology at Northwell's Huntington Hospital.

The North Central Section will be represented by Dr. James Ulchaker, past president of the section as well as the Ohio Urological Society and the Cleveland Urological Society. Dr. Ulchaker previously chaired multiple AUA committees and served as the 2011 AUA Gallagher Health Policy Scholar. He is the Vice Chairman of the Department of Urology at the Cleveland Clinic.

As always, we would like to extend our sincerest appreciation to our 4 departing Board members and recognize them for their service to the AUA.

Dr. Robert Flanigan completed his term as Immediate Past President, having previously served as Secretary (2006-2011), President-Elect (2017-2018) and President (2018-2019). He is a past president of the AUA North Central Section as well as the American Board of Urology, the Society of Urologic Oncology, the Society of University Urologists and the Society of Pelvic Surgeons. He is also the founder and first president of the Society of Urologic Chairpersons and Program Directors, one of the 2 groups that together formed the Society of Academic Urology.

Dr. Roger Schultz completed his term as the Mid-Atlantic Section Representative, a position he has held since 2016. Prior to representing his Section to the Board, he served as secretary, treasurer and president of the section, and served on the AUA's Practice Management, Coding and Reimbursement, Finance and Compensation committees.

Dr. Frederick Gulmi completed his term as the New York Section Representative, serving from 2016 to 2020. Dr. Gulmi has served the AUA and his Section in a number of capacities, including as secretary and president of his section, as Vice Chairman for Resident Education for the National Urology Ultrasound Faculty of the AUA, and as a reviewer for *The Journal of Urology®*.

Dr. Chandru Sundaram has represented the North Central Section since 2015. Prior to representing his Section on the AUA Board, he served as president of the North Central Section, and is a former member of the AUA Education Council and past chair of the AUA's Laparoscopic, Robotic and New Surgical Technology Committee. He is a 2009 graduate of the AUA's Leadership Program.

For more information about AUA leadership, please visit https://www.AUAnet.org/about-us/aua-governance/board-of-directors. ◆

Urological Management of Adult Spina Bifida

▼ Continued from page 24

3. Spina Bifida Association: Guidelines for the Care of People with Spina Bifida, 4th ed. Spina Bifida Association 2018. Available at https://www.spinabifidaassociation.org/wp-content/uploads/Guidelines-for-the-Care-of-People-with-Spina-Bifida-2018.pdf. Accessed April 5, 2020.
4. Deng N, Thirumavalavan N, Beilan JA et al: Sexual dysfunction and infertility in the male spina bifida patient. Transl Androl Urol 2018; **7**: 941.
5. Forsell D: [Sexuality in Spina Bifida Clinical Guidelines - Adult 2018]. The Swedish Follow-Up Programme for Spinal Dysraphism and Hydrocephalus (MCCUP) 2018. Available at http://mmcup.se/wp-content/uploads/2018/08/Kap-13-Sexualitet.pdf. Accessed April 7, 2020.

EFFECTIVE AND ALWAYS AVAILABLE

So you can do more of your best work

Ambu® aScope™ 4 Cysto
SINGLE-USE CYSTOSCOPE

- Excellent imaging and smooth maneuverability
- Consistent performance every time
- Eliminates reprocessing and repairs

Schedule A Demo Today
at **ambuusa.com/cysto**

Ambu
Ideas that work for life