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FROM THE AUA Secretary

Update on AUA2020

On March 13, the AUA announced the cancellation of the 2020 Annual Meeting in Washington, DC due to rapidly escalating COVID-19 health concerns. Over the course of nearly 120 years, the AUA has only canceled a handful of meetings, all of which were during World War I and World War II.

Cancelling the 2020 AUA Annual Meeting was one of the most difficult decisions the AUA has ever had to make, while also one of the most necessary. There is no higher priority to the AUA than the health, safety, and well-being of our staff, members, partners, volunteers, guests and the community at large.

The unprecedented public health emergency caused by the spread of COVID-19 has clearly impacted not only the AUA, but many nations, societies and individuals throughout the world. We recognize the AUA meeting is a major global event for the urology community, and preparing for it involves the time and talent of a great many of our physician volunteers, speakers and exhibitors. We are incredibly grateful for the time they have invested to date and deeply disappointed not to be able to hold the meeting as planned.

We are currently exploring opportunities for sharing AUA2020 surgical videos and other important clinical education, and we will keep you apprised of where you can find this information as it becomes available. However, the meeting abstracts will be published in the supplement to the April issue of The Journal of Urology® as scheduled.

Recognizing that this issue of AUA News has traditionally been focused on previewing the AUA meeting presentations, I am pleased to highlight several of our named and state-of-the-art lectures from the 2020 program.

Dr. Jorge Gutierrez-Aceves from Winston-Salem, North Carolina questions whether mini-percutaneous nephrolithotomy is the new standard for percutaneous nephrolithotomy. In the Confederación Americana de Urología (CAU) Lecture he compares the 2 techniques and weighs the pros and cons.

In the European Association of Urology (EAU) Lecture Dr. Alberto Briganti from Milan, Italy highlights the evolution of locally advanced and metastatic prostate cancer. Specifically, he answers questions about the optimal management of both disease states as well as the crucial issues still to be resolved.

Dr. André van der Merwe from Cape Town, South Africa discusses barriers and enablers of research in resource constrained countries in the Société Internationale D’Urologie (SIU) Lecture. He mentions common barriers such as time constraints and research which may seem peripheral and presents solutions to overcoming them.

In the John Duckett Memorial Lecture Dr. Daniel M. Green of Memphis, Tennessee discusses the long-term effects of cancer on pediatric patients. He highlights the increased risk of death for adult survivors of childhood cancer from not only the original cancer, but from nonexternal causes such as cardiac disease.

Dr. John W. Davis of Houston, Texas presents first-hand how the web and social media are used to help journal readers find what they want in The Journal of Urology® Lecture.

Dr. Keith A. Jarvi from Toronto, Ontario, Canada asks the question: “How can we expect a urologist to ‘painlessly’ (for the urologist) manage CSP [chronic scrotal pain] when the condition is little understood and many of the confounding issues are outside our areas of training and expertise?” in his state-of-the-art lecture.

A look into the future of neuromodulation for overactive bladder is presented in the state-of-the-art lecture by Dr. Philip E. V. Van Kerrebroeck of Maastricht, the Netherlands.

The AUA continues to be a leader in developing innovative, evidence-based quality education for urologists and urology health care professionals worldwide, and offers educational resources year-round through the AUA University at AUA.UANet.org.

The AUA Board of Directors and I sincerely appreciate your patience and understanding during these challenging times. The support of our members means everything to us. If you have any questions related to the AUA meeting, please visit AUA2020.org to access our Frequently Asked Questions (https://www.aua2020.org/attendee-info/aua2020-annual-meeting-faqs).

We will miss seeing all of you at the AUA meeting this year, but greatly look forward to seeing you in Las Vegas in 2021.

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Is Mini-Perc the New Standard for Percutaneous Nephrolithotomy?

Percutaneous nephrolithotomy (PCNL) is the current method of choice for renal stones larger than 2 cm and the most effective treatment alternative for stones larger than 1 cm in the lower pole. Although PCNL results in high stone-free rates, it is invasive surgery with the potential for increased blood loss, postoperative pain, infections and longer hospital stay relative to ureteroscopy and shock wave lithotripsy (SWL). In addition, the complication rate of PCNL varies widely ranging from 15% to 83%.

In recent years techniques used to create a miniaturized percutaneous tract have gained interest. The concept of mini-percutaneous nephrolithotomy (mPCNL) has emerged in an attempt to decrease blood loss and postoperative pain, while encouraging same day surgery. Minimizing the percutaneous renal access tract size seems to be a logical approach to performance of less invasive surgery.

The caliber of the tract should be adapted to the intrarenal anatomy of the patient. We need to consider better compatibility between the calyceal anatomy and caliber of the tract. A distented intrarenal system may accommodate a broad percutaneous tract, whereas a large tract in a narrow collecting system could result in tear or rupture. Therefore, a small tract should be considered in a narrow collecting system when stone burden allows.

Intraoperative and postoperative bleeding is the most common complication of conventional PCNL, with transfusion rates ranging from 2% to 23%, and blood transfusion rates between 4.9% and 7%. There is enough evidence to support the relevant role of the caliber of the tract as a predisposing factor for the risk of bleeding and, therefore, performing miniaturized access to the kidney is a reasonable approach to decrease this risk. The single most significant benefit of a miniaturized tract over the conventional tract for PCNL is the decrease in blood loss and fewer or no blood transfusions. This finding has been consistent in all contemporary mPCNL series.1–5

Progression in minimizing the percutaneous tract size has led to the development of even less invasive techniques. Tract size ranges from 14Fr to 20Fr for mPCNL, 11Fr to 13Fr for ultra-mPCNL and 4.8Fr for micro-PCNL. In our opinion the most important factor when selecting the size of the tract is to create a low pressure system using at least 3Fr to 4Fr gauge between the access sheath and the nephroscope to facilitate continuous outflow and reduce the risk of high intrarenal pressure.

Current potential indications for mPCNL include solitary stone in 1 calyx (particularly in the lower pole where flexible ureteroscopy deflection may limit success), stones in the calyceal diverticula, complimentary percutaneous tracts for multi-access PCNL, stones in pediatric patients not amenable to SWL or retrograde intrarenal surgery and initial inspection in patients with complex intrarenal anatomy before full dilatation of the tract. Nevertheless, there is a lack of consensus as to the stone size for the best outcome of mPCNL. For renal stones smaller than 2 cm, the stone-free rate of mPCNL is comparable to that of conventional PCNL. In their series Kokov et al noted that conventional PCNL and mPCNL were effective for removing renal stones up to 3.5 cm in greatest dimension with no difference in residual stone volume, postoperative analgesic use or operative time, although blood loss was significantly less in patients treated with mPCNL.3

While the main advantage of mPCNL is decrease in bleeding and the need for blood transfusion, a disadvantage of this approach is longer surgical time. There is now convincing evidence that prolonged surgical time is probably the main risk factor for postoperative infection complications and sepsis. In a recent prospective study surgical time longer than 100 minutes increased significantly the risk of sepsis post-PCNL.6 Prolonged surgical time may also increase the risk of undetected residual fragments. Several reports have emphasized the importance and clinical implications of residual fragments after different stone procedures with limited fragment clearance and higher rates of reintervention. Therefore, treating large and complex stones with mPCNL may potentially increase the risk of postoperative infection and sepsis as well as the number of reinterventions for residual stones.

So who is the right patient for mPCNL? We performed a retrospective study of 133 subjects to identify the ideal candidate for mPCNL. Mean stone size was 20±10.62 (range 6.9 to 39.4). Of the patients 68 (51%) had a single stone and 65 (49%) had stones in 2 or more locations in the kidney and upper ureter. Within 24 hours of surgery based on low dose computerized tomography and 0 mm residual fragments as the cutoff 57 patients (42.9%) were stone-free. On a ROC curve the preoperative stone burden that produced the highest combined sensitivity and specificity for predicting stone-free status was 20.25 mm (sensitivity 0.62, specificity 0.75, see figure). Again using 0 mm residual stone fragments as the cutoff, 61.3% of patients with stones smaller than 20.25 mm were free of stones compared to 24.1% of patients with larger stones. Patients with multiple stones had significantly higher rates of postoperative residual fragments (X2 (2, N = 133) = 15.3, p <0.01). There were no significant differences in stone-free rates based on age, body mass index or laterality.

Mini-PCNL is an effective method of removing renal stones with decreased risk of bleeding and postoperative transfusion. mPCNL prolongs surgical time and may increase the risk of postoperative infections when treating large complex stones. The best results with mPCNL are obtained in patients with stones smaller than 20.25 mm and single stones, as they have the greatest chance of becoming stone-free and the lowest rates of reintervention. ◆

Clinically Relevant Questions in the Management of Locally Advanced and Oligometastatic Prostate Cancer

Alberto Briganti, MD, PhD
Milan, Italy

An inverse stage migration toward higher rates of newly diagnosed locally advanced and metastatic prostate cancer (PCa) has recently been reported. Such a trend might be the result of the advent of more advanced imaging modalities as well as less intense PCa screening programs. Despite several improvements in the field, some important clinical questions remain unanswered. Among them, the optimal management of node-positive disease has certainly gained increasing attention.

Lymph nodes represent one of the most relevant sites of PCa dissemination. The rate of newly diagnosed clinically node-positive (cN1) disease has in fact exceeded 10% in some series. However, there is a paucity of data with regard to the best therapeutic approach for these men. Although the results of the STAMPEDE trial showing longer survival in men with a low metastatic burden treated with prostate radiotherapy (RT) might be considered indirect evidence of the benefit of local therapy in men with cN1 disease, disappointingly no prospective randomized trial has been conducted in this patient group. The aim would be not only to establish the role of the treatment of the primary tumor but also to assess the optimal multimodal strategy in these patients.

Currently available guidelines suggest the use of RT or radical prostatectomy (RP) in selected patients with cN1 disease. Such recommendations are mainly based on retrospective series with all known possible reverse biases. However, the studies in the literature inevitably show that local treatment (with surgery or radiation therapy) is consistently associated with a survival benefit. Nevertheless, it is possible given the heterogeneity of this patient group that not all men with de novo cN1 PCa would benefit equally from treatment of the primary. Men with lower Gleason scores and with 2 or fewer suspicious lymph nodes in the pelvis at conventional imaging had better outcomes after surgery. Whether multimodal approaches starting with surgery or radiation therapy have the same efficacy has yet to be demonstrated. Moreover, a recent exploratory analysis of the STAMPEDE trial has even tested the role of primary RT in men with nonregional positive lymph nodes (M1a) only with a reported benefit in progression-free survival and overall survival.

While these results should be interpreted as exploratory, they represent the first prospective evidence in support of the treatment of the primary in men with M1a disease only. Can these results obtained with RT be extrapolated to surgery? The answer is currently unknown. In addition to the eradication of the primary tumor, RT may indeed also act via systemic immune modulation, an effect not seen after surgery.

It must be acknowledged that virtually all these data are based on results obtained by conventional imaging modalities. The added value of up-front positron emission tomography-computed tomography (PET/CT) in the setting of individualized management of newly diagnosed node-positive disease must still be demonstrated.

Of all men diagnosed with cN1 disease at conventional imaging, approximately 70% to 80% will have pathologically confirmed nodal invasion (pN1) at pelvic lymph node dissection. The rates of pN1 disease have been rising steadily given increasing use of extended pelvic lymph node dissection at the time of RP. However, the limited robust data can guide urologists in the clinical decision making process on the optimal postoperative course.

Different approaches are currently recommended, including initial observation for those patients with undetectable prostate specific antigen and limited nodal invasion, adjuvant radiation with or without androgen deprivation therapy (ADT), or lifelong ADT. Except for the use of adjuvant lifelong ADT tested in a small and historical randomized controlled trial, the remaining options are based on retrospective single center series or population-based data.

Unfortunately, virtually all major trials testing the role of adjuvant or early salvage RT excluded men with pN1 disease. Therefore, the optimal timing of RT is currently unknown for pN1 disease, again underscoring a significant gap in the clinical research in this setting. At any rate, it is likely that the optimal multimodal approach should be tailored according to individual clinical and disease features.

Moreover, a nonnegligible proportion of men with locally advanced PCa (with or without positive lymph nodes) have detectable prostate specific antigen after surgery. Currently, no randomized controlled trial has been reported about the optimal treatment of these patients. Guidelines recommend the use of early imaging by prostate specific membrane antigen (where available) or choline PET/CT with the aim of potentially selecting the candidate for metastasis-directed therapy (MDT). While a phase 2 trial showed a benefit of PET/CT guided MDT in men with oligorecurrent PCa treated at a median of 5 years after initial diagnosis, no randomized trial has tested the role of early treatments in men with persistent disease after surgery (likely undetected at the time of treatment of the primary). Early salvage RT is still a mainstay treatment for some of these patients, especially those more likely to be affected by clinically significant but not yet systemic disease persistence.

In the setting of de novo metastatic disease there is evidence that adding the treatment of the primary with RT in men with low volume metastatic burden prolongs survival. While still searching for the optimal definition of oligometastatic PCa, several factors also need to be elucidated. Given the current lack of phase 3 prospective randomized trials including surgery as primary treatment, it is currently unknown whether such beneficial effects reported for RT can be extrapolated to RP. At a recent
In addition, it is not known whether MDT should be used in combination with the treatment of the primary. Combined use of local treatment with ablative approaches to all visible lesions is often performed without any strong underlying evidence. Remarkably the beneficial effect of local treatment reported in the STAMPEDE trial was seen only by applying RT to the prostate. Trials aiming to address this issue are currently underway.

Finally, the optimal combination of systemic and local treatments as well as the best candidate for such a combined approach are not yet fully defined. It is likely that not only imaging but also assessment of tumor biology will have major roles.

In summary, while the field of locally advanced and metastatic PCa has certainly evolved, several challenging, clinically meaningful questions remain unanswered. Prospective randomized trials are needed (and many are underway) to shed some light on these crucial issues.

Conducting Research in Resource Constrained Environments

André van der Merwe, MD
Cape Town, South Africa

Conducting research in any environment is difficult. However, in a resource constrained environment the pressure on the researcher comes from many angles such as clinical overload, poor record keeping, suboptimal treatment of common diseases, lack of research skills and rigor, personal financial concerns and research funding pressures. Funders tend to fund experienced researchers exclusively. While this situation may seem impossible, it is not.

In 2006 Dr. Richard Santucci, a well-known American reconstructive and trauma urologist, made a comment at a workshop in Maputo, Mozambique that forever changed my perception of research. He said, “You are spending the time anyway—you can just as well make a big splash!” How true those words are, especially in resource constrained environments where the general perception is one of poor quality retrospective research. While the principles outlined here are helpful in resource poor settings, the same can also be applied to well funded, large academic departments.

Barriers and Enablers of Research in Resource Constrained Countries

The first barrier is time constraints due to an overload of clinical work, leaving no room for critical thinking that will lead to a research question that will make it to a plenary in the next few years. There is also no time for protocol writing or replying to an IRB (institutional review board), no time for data collection and no time for writing a manuscript.

The enablers addressing the first barrier deserve careful attention. The most difficult and first step in research (but also one free of cost) is finding a good research question. The Internet makes reading accessible and affordable. Before deciding on a research topic, read extensively on the conditions most commonly seen at your hospital.

Start with a recent review and look for areas of ambiguity. Unless you are new to research, do not pursue a topic someone else has given you as they are not likely to give away a very good research question. Once you have decided on a broad research topic, narrow the topic down in the PICO format of patients, intervention or exposure, comparator and outcome, which will make the project manageable.

Using other protocols as a framework, being cautious not to plagiarize, can make protocol writing easier. Sample protocols may be found at www.clinicaltrials.gov and include not only randomized, controlled trials but all study types. Once protocol writing is underway it is vital to make an appointment with a statistician before submission to an IRB as this will also save time.

Time spent on your protocol is a good investment and will save you time later on. For instance, the introduction and methods sections in the protocol should be good enough to use in a publication that will follow the study. In time constrained, resource poor settings the datasheet needs to be lean, answering the research questions and objectives only. Once data are collected, the results should follow the design of the well constructed protocol toward early publication.

Novice researchers in resource poor countries should try to conduct studies with only 1 patient contact. Followup studies take more administrative time and can bias or skew data if not performed well. Writing and submitting a paper for publication can make protocol writing easier.

The second barrier that researchers from resource constrained countries often encounter is that they think their patients are not as interesting as the big benign prostate hyperplasia, prostate cancer or renal stone research presented by expert plenary speakers at international conferences. This is a misperception.

Poorly resourced researchers should look at the top few diagnoses in their area and review relevant literature and guidelines. Guideline panels have done all the work already, and if the guidelines have poor levels of evidence and low grades of recommendation on diagnoses in your area, this presents a golden opportunity. Publishing prospective, well designed studies on topics for which current guidelines lack good evidence will result in many citations and improve your academic footprint.

Another option is to use a different study design for a familiar topic. For instance, researchers can perform qualitative research to redress a common diagnosis such as prostate cancer or get the true patient perspective through qualitative in-depth interviews and a thematic analysis. They can also use retrospective databases to find cases for case-control studies. These cases are then contacted and prospectively with similar controls, which is not at all expensive.

Learning research methodology is a sure way to overcome barriers.

This approach can be explained using the blue ocean strategy. A red ocean might be qualitative prostate cancer research where the competition is fierce (and the water red with blood), while a blue ocean could be qualitative studies on the same topic that have hardly ever been explored (and the water blue without any blood).

In fact, the penile transplant study we conducted in South Africa represents exactly this strategy. We took our commonly seen ritual circumcision aphallic cases and used our knowledge of organ transplantation and microsurgery to create a new (blue water) treatment (see figure). Researchers from resource constrained areas who found blue water include Drs. S. Gueye, I. Khalif, C. Heyns, S. Kulkarni, M. Desai and J. Desai, among others.

Summary

Formulating a winning research question is key. Barriers to research in resource poor countries are potential opportunities. Remember, “You are spending the time anyway—you can just as well make a big splash!”

Figure. Penis transplants in 2014 (left) and 2017 followed blue ocean strategy applied to research in resource poor environment where common diagnoses were taken (aphallic males after ritual circumcision) and new treatment created with known therapies (knowledge of solid organ transplantation and microsurgery).
Late Effects of Treatment of Children with Cancer

Pediatric patients with cancer have a vastly improved 5-year survival rate, with roughly 85% expected to achieve this landmark. However, 5-year survivors have inferior long-term survival compared to their siblings or the U.S. population.

Adult survivors of childhood cancers have an increased risk of death compared to the general population. The standardized mortality ratio is 13.2 (95% CI 12.5–14.0) for female survivors and 6.7 (95% CI 6.4–7.0) for males. The primary cause of death during the first 30 years after diagnosis is the original cancer, but beyond 30 years of nonrecurrence, nonexternal causes such as cardiac disease, pulmonary disease and second malignant tumors exceed recurrence/progression as the most significant causes of death.

Pediatric renal malignancies and primary testis tumors are generally treated on multi-institutional protocols. These treatment regimens can include surgical procedures such as orchiectomy, cystectomy, prostatectomy, nephrectomy and retroperitoneal lymph node dissection that may produce significant late effects. Radiation therapy to the renal fossa, pelvis and/or lungs can impair fertility and pulmonary function.

Finally, chemotherapeutic agents used in curative regimens for these malignancies may include doxorubicin, cyclophosphamide, etoposide, cisplatin and bleomycin that may impact cardiac, gonadal and pulmonary function, and impair hearing and balance. Radiation therapy and chemotherapy may cause treatment related malignancies.

The prevalence of grades 3 to 5 adverse health events is 53.2% (95% CI 32.0–34.3) at 20 years after diagnosis among adult, 5-year survivors of childhood cancer. The hazard ratio for a grade 3 to 5 serious adverse outcome is 4.9 (95% CI 4.3–5.5) among 5-year Wilms tumor survivors compared to a sibling control group.

The HRs for hypertension (8.2, 95% CI 6.4–10.5), congestive heart failure (23.6, 95% CI 10.8–51.5) and renal failure (50.7, 95% CI 14.5–177.4) are all increased among 5-year survivors of Wilms tumor. The cumulative incidence of congestive heart failure was 4.4% 20 years after diagnosis among National Wilms Tumor Study participants who received doxorubicin as part of their initial therapy and 17.4% among those who received doxorubicin for an initial or subsequent relapse. Female sex, cumulative doxorubicin dose and left flank radiation therapy were each significant risk factors for congestive heart failure.

Among patients treated for rhabdomyosarcoma of the bladder who underwent partial cystectomy, the majority (73%) were reported by their physicians to have normal bladder function. However, there is no published study of a group of such patients evaluated with modern imaging and cystometrics.

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Fertility is impaired among male and female adult survivors of childhood cancer with a greater risk of impairment with exposure to increasingly high cumulative doses of alkylating agents. Men who have undergone bilateral retroperitoneal lymph node dissection are at risk for retrograde ejaculation.

Pregnancy complications and outcomes have been evaluated among survivors of Wilms tumor. Rates of hypertension complicating pregnancy (ICD 642), early or threatened abortion, and pre eclampsia are all increased among 5-year survivors of Wilms tumor. The incidence of hypertension complicating pregnancy is 4.9% among female survivors of Wilms tumor who received doxorubicin as part of their initial therapy and 17.4% among those who received doxorubicin for an initial or subsequent relapse. Female sex, cumulative doxorubicin dose and left flank radiation therapy were each significant risk factors for hypertension.

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Use of Web and Social Media Sources to Sift through Scientific Literature

John W. Davis, MD, FACS
Online Content Editor, The Journal of Urology®
Houston, Texas

Keeping up with the current literature has long been a challenge for busy physicians. While evolution of the internet and the advent of digital publishing have provided a “wealth of riches” when it comes to the availability and accessibility of scientific literature, it has also created the often time-consuming challenge of sorting through it all to find what you need.

For the last several years I and the online content assistant editors, Drs. Khurshid Ghani, Phillip Pierorazio, Angela B. Smith and Quoc-Dien Trinh, have worked closely with Journal Editor Dr. Joseph A. Smith, Jr. to continually update, expand and enhance the Journal’s web and social media presence of The Journal.

What the editors have tried to do is to transition and broaden the Journal’s reach beyond just the paper copy that is received in the mail. As a result, we are able to interact with readers on a more ongoing basis in terms of not only making them aware of what content is available in advance, but also helping them quickly and easily find the content most relevant to them.

One of the many ways to broaden the Journal’s reach and encourage interaction among readers is through increased use of social media, particularly Twitter, to highlight articles and foster dialogue between readers and the authors themselves.

Working with the online team, we go through every issue of The Journal and write tweets for the articles, which can take the form of a short summary statement highlighting a key finding or simply posing the question that the authors were attempting to answer. The tweet allows our followers to, at a glance, determine if they need to read the entire article or to simply share, re-tweet or comment on the article, and participate in a discussion on the topic.

Additionally, beyond being an easy way to explore content from The Journal, Twitter can help busy physicians find other information related to a specific topic or subspecialty through the use of what is known as “hashtagging.” With hashtagging, one can basically turn their Twitter feed into a personalized reading experience based on your specialty and/or areas of interest. To help with this, I encourage people to check out the Symplur Healthcare Hashtag Project (https://www.symplur.com/healthcare-hashtags), an initiative to create standard hashtag nomenclature across medical specialties, including urology.

Another way The Journal is using digital technology to highlight important articles and offer its readers conveniently digestible content is through increased production of podcasts on the website, which includes interviews with article authors that people can download and listen to whenever they have time.

What we know is true and what we have confirmed through surveys is that people today are doing most of their reading online, either on devices or desktops, and are less often walking around with a print copy of The Journal in their hand or in their briefcase. Understanding that, our goal at The Journal of Urology is what it has always been, which is to educate and inform our readers, and provide them with information they can apply to their practice. We are doing that by continually looking for ways to help people sift through the noise of all the publications and journals that are out there today and find what is actually useful for them.

How to Painless Scrotal Pain

Keith A. Jarvi, MD, FRCSC
Toronto, Ontario, Canada

Chronic scrotal pain (CSP) is a common yet poorly understood condition. We reported that up to 4.3% of men coming to a urology clinic for other reasons may suffer from CSP.1 Despite its high prevalence the condition remains generally poorly understood, frustrating patients and clinicians.2,4 Patients will often see multiple clinicians for treatment.

Further complicating this situation, CSP has a significant negative impact on patient quality of life and mood. More than 50% of patients with CSP report limitations to their daily activities, limited ability to work, decreased sexual activity and mood disorders (depression).1,2,5

How can we expect a urologist to “painless” (for the urologist) manage CSP when the condition is little understood and many of the confounding issues are outside our areas of training and expertise? We also suffer from a lack of well accepted guidelines to treat men with CSP.

Being part of a team of specialists in different disciplines interested in CSP is one of the most effective means to care for men with CSP while reducing stress on the urologist. A multidisciplinary approach allows patients to receive quality care and allows urologists to work within their area of expertise.

Urologists’ contributions to CSP management are important. Studies have shown that the most common identifiable causes of direct pain to the scrotal structures are mainly urological (table 1).

Urologists are often the first specialists to assess men with CSP and there is a simple algorithm for the diagnostic evaluation of men with CSP (fig. 1).2 Note that history and physical examination are critical parts of the diagnostic evaluation, while laboratory tests or diagnostic imaging are not routine components of training.

Table 1. Etiologies of CSP%

<table>
<thead>
<tr>
<th>Cause</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasectomy</td>
<td>20.61</td>
</tr>
<tr>
<td>Trauma</td>
<td>12.21</td>
</tr>
<tr>
<td>Infection</td>
<td>11.45</td>
</tr>
<tr>
<td>Hernia repair</td>
<td>4.58</td>
</tr>
<tr>
<td>Epididymal cyst</td>
<td>1.52</td>
</tr>
<tr>
<td>Other identified causes (hydrocelectomy, transurethral resection of prostate, orchectomy, donor nephrectomy)</td>
<td>6.10</td>
</tr>
<tr>
<td>Unknown</td>
<td>43.51</td>
</tr>
</tbody>
</table>

Figure 1. Diagnostic evaluation.2 US, ultrasound. CESI, Chronic Epididymitis Symptom Index. CPPS, chronic pelvic pain syndrome. G+C, gonorrhea and chlamydia.
Chronic Scrotal Pain Management

of the investigation for CSP and are reserved for men with indications for the testing.

The initial evaluation will usually identify known causes of CSP and the need for assessment with mental health professionals or medical pain specialists. Treatment for some of the specific conditions causing CSP is often successful and well within the expertise of the urologist.

Many men will have idiopathic CSP. For these men, and as a line of expertise of the urologist, often successful and well within the need for assessment with mental health.

identify known causes of CSP and the testing.

Continued from page 8

Figure 2. Conservative and medical management of CSP.

Table 2. Medical management outcomes for CSP

<table>
<thead>
<tr>
<th>Medication Class/Dosage</th>
<th>Reported Efficacy (%)</th>
<th>Common Side Effects (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsteroidal anti-inflammatory drugs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>400-600 mg Ibuprofen by mouth every 6 hrs, 500 mg naproxen by mouth twice daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26-100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse, gastrointestinal ulcers, acute + chronic renal failure (1-5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>500 mg Levofloxacin by mouth daily × 10 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofloxacin—nausea (4-8), diarrhea (2), headache (1-2), dizziness, elevated transaminases (2-3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone—gastrointestinal (3-5), hypersensitivity (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentinoids:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>300 mg Gabapentin by mouth daily, uptitrate by 300 mg/day up to max 1,800 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>61.5-75—Pts with 50% or greater improvement in symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedation, dizziness, nausea, gastrointestinal upset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCAs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 mg Nortriptyline by mouth 3 times/day, uptitrate by 10 mg daily to max 150 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>67—Pts with 50% or greater improvement in symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedation, dry mouth, dizziness, insomnia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Invasive procedures for CSP

<table>
<thead>
<tr>
<th>Intervention</th>
<th>% Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onabotulinum toxin A cord blockade</td>
<td></td>
</tr>
<tr>
<td>50 or Greater—partial or complete pain resolution at 3-mo followup</td>
<td></td>
</tr>
<tr>
<td>Pulsed radio frequency denervation</td>
<td></td>
</tr>
<tr>
<td>56-100—Partial or complete pain resolution at 3-6-mo followup</td>
<td></td>
</tr>
<tr>
<td>Microsurgical vasosvasostomy for PVPS</td>
<td></td>
</tr>
<tr>
<td>50-100—Complete pain resolution</td>
<td></td>
</tr>
<tr>
<td>Epididymectomy for PVPS + symptomatic epididymal cysts</td>
<td></td>
</tr>
<tr>
<td>10-90—Partial or complete pain resolution</td>
<td></td>
</tr>
<tr>
<td>Varicocele repair for symptomatic varicoceles</td>
<td></td>
</tr>
<tr>
<td>80-100—Partial or complete pain resolution</td>
<td></td>
</tr>
<tr>
<td>Microsurgical denervation of spermatic cord</td>
<td></td>
</tr>
<tr>
<td>71-96—Partial or complete pain resolution</td>
<td></td>
</tr>
<tr>
<td>Inguinal orchiectomy</td>
<td></td>
</tr>
<tr>
<td>20-75—Partial or complete pain resolution</td>
<td></td>
</tr>
</tbody>
</table>

Other surgeries such as removal of the epididymis or orchectomy have also been used to manage CSP. Procedures to denervate the tests by interrupting the ilioinguinal and genitofemoral nerves may be of short duration (nerve blocks using onabotulinum toxin A, radio frequency ablation or injectable anesthetics) or more permanent (microsurgical denervation of the spermatic cord).

Thus, there are simple diagnostic and treatment algorithms to help urologists manage the treatment of men with CSP. Hopefully this will help take the pain out of the management of CSP.

John Duckett Memorial Lecture

Continued from page 7

labor (ICD 644) and malposition of the fetus (ICD 652) increased with increasing radiation dose in female patients. The percentages of off-spring weighing less than 2,500 gm at birth and of those having fewer than 37 weeks of gestation also increased with radiation therapy dose. The risk of pregnancy complications was not increased among the partners of male survivors of Wilms tumor.

These risks for late adverse events support recommendations for targeted screening of long-term survivors of childhood cancers, particularly screening of cardiovascular, pulmonary and gonadal function, and supervision of pregnancies of irradiated women in high risk obstetrical clinics.


Future of Neuromodulation: Rechargeable, Implantable Percutaneous Tibial Nerve Stimulation—What Else?

Neuromodulation by stimulation of a sacral nerve (SNM) is an established, minimally invasive therapy for refractory overactive bladder and functional urinary retention, but percutaneous tibial nerve stimulation is a potential alternative.

With more than 300,000 patients with implants worldwide, SNM with a current recharge-free device (InterStim™ II) is the standard approach but is only approved for magnetic resonance imaging (MRI) of the head.1

A rechargeable and conditional MRI safe device (Axonics r-SNM™ System) has recently been introduced (fig. 1). In addition, a new InterStim device received CE marking and U.S. Food and Drug Administration approval. These devices provide full body MRI safety for 1.5 and 3 Tesla, and the clinical effectiveness appears to be similar to that of the current recharge-free device.2

The need for full body MRI safe implants is obvious, since about 50% of patients with neurostimulators will have an indication for MRI over their lifetime and up to 23% of SNM explantations are currently due to the need for MRI. Therefore, it is expected that these new technologies will enable more patients to choose SNM as the preferred therapeutic option.

And what about rechargeable systems? A rechargeable battery results in a smaller volume implantable pulse generator (IPG) and potentially more comfort for patients. Currently available SNM systems include the recharge-free Medtronic InterStim II system (14 cm³) and the rechargeable Axonics system (5.5 cm³). The emerging InterStim Micro technology (2.8 cm³) reduces the size by about 80% compared with the InterStim II (fig. 2).

However, smaller devices will not be a benefit to all patients as about 40% of the global adult population is obese. Correct implantation of a small rechargeable device with the necessity for recharges may be challenging in obese patients, since the angle and distance between the superficially implanted IPG and recharger may change between recharging sessions, thus making the recharge more cumbersome. Furthermore, the stability of the IPG inside the subcutaneous tissue could be compromised and the patient might be more likely exposed to twiddler’s syndrome.

An important aspect of rechargeable systems relates to the requirement for IPG changes. The battery life of rechargeable devices has been estimated at 15 years vs 5 to 7 years for InterStim II. As a result, rechargeable IPGs will be associated with a reduced need for reoperation. Therefore, patient life expectancy along with cognition and dexterity will be important factors when considering rechargeable devices. Additionally, the recent adoption of an optimized tined lead placement technique allows for lower amplitudes, so longer battery life can be expected from recharge-free systems.3

There are also some potential pitfalls associated with rechargeable devices. Patients must be compliant and have the cognitive capability plus the manual dexterity to recharge their IPG. Although the recharging process can be done at home without being connected to a power socket, the therapeutic noncompliance of patients can be an issue. Since a lack of compliance will lead to a loss of effectiveness and/or an increased burden for health care professionals, careful screening of candidates for a rechargeable device is imperative. Recharge-free devices require no regular or frequent interactions with the patient programmer and patients with poorer compliance may better qualify for recharge-free devices.

Another factor is disease awareness, as the psychological perception of the problem will be experienced differently between individuals with a rechargeable or a recharge-free system. One of the benefits that patients describe is the ability to forget about their medical condition once a SNM device is implanted. A recharge-free system allows the patient to set and forget the treatment, while a rechargeable system actively reminds patients of their condition every 1 or 2 weeks.

How does this discussion translate into decision making for the individual patient? Good indications for rechargeable devices are seen in technology savvy, compliant and highly motivated patients, or in patients in need of high energy stimulation with expected reduction of battery life, slim patients with insufficient fat tissue at the implant site, those with a history of pain or patients with significant infection risks for device replacements.

When assessing patient compliance for rechargeable SNM it is recommended to look at all factors that may impact therapeutic noncompliance. These include demographic factors (age, gender, education, available caregivers), psychosocial factors (motivation, attitude, health literacy, patient knowledge, physical difficulties, forgetfulness or history of good compliance), complexity of therapy maintenance (finding the right spot to recharge), potential side effects of therapy maintenance (potential discomfort due to mild heating depending on battery technology), compatibility with lifestyle (frequent traveling), lack of accessibility for therapy maintenance (frequent traveling, easy access in case of lost recharger, help line in case of technical questions), cost issues (insurance in case of lost recharger) and patient motivation.

A shared decision making process between patient and physician is

Continued on page 14
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% (0.9%); lymphopenia ERLEADA® 41% (2%), placebo 21% (2%).
• Chemistry—In the TITAN study; hyperglycemia ERLEADA® 17% (3%), placebo 12% (2%). In the SPARTAN study; hypercholesterolemia ERLEADA® 70% (0.1%), placebo 63% (0.3%); hyperglycemia ERLEADA® 70% (2%), placebo 59% (1%); hyperglycemia 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 rash (defined as covering >30% body surface area [BSA]) was 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 re-introduction 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 CYP2C9 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 (seeDosage 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-glucuronosyltransferase (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.

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 no new 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 orchectomy. Patients with a history of (i.e., 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.

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†

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

Janssen Biotech, Inc.
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Visit erleadahcp.com
ERLEADA® (apalutamide) tablets

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=1), sepsis (n=1), cardiac failure (n=1), and cerebrovascular accident (n=1). One patient in the TITAN study received ERLEADA and 2 patients treated with placebo died from cerebrovascular accident (n=1) and cardiac failure (n=1), respectively. The most frequent serious adverse reactions (≥5% in all patients treated with ERLEADA) were myocardial infarction (10%), cerebrovascular accident (3%), and cardiac failure (3%). Table 1 shows adverse reactions occurring in ≥10% on the ERLEADA arm that occurred at a significantly greater 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)

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>ERLEADA N=527</th>
<th>Placebo N=523</th>
<th>Between Arm Difference</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory Abnormality</td>
<td>ERLEADA N=527</td>
<td>Placebo N=523</td>
<td>Between Arm Difference</td>
<td>95% CI</td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White blood cell decreased</td>
<td>27.4 0.4</td>
<td>19.6 0.6</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>13 1.2 2.2</td>
<td>11 1.2 2.2</td>
<td>2%</td>
<td></td>
</tr>
</tbody>
</table>

Does not reflect fasting values

Non-metastatic Castration-resistant Prostate Cancer (nmCPRC)

In a randomized study (SPARTAN) of patients with non-metastatic castration-resistant prostate cancer, fractures occurred in 9% of patients treated with ERLEADA and in 2% 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.

Table 2: Laboratory Abnormalities Occurring ≥1% in Patients Treated with ERLEADA and/or Placebo

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>ERLEADA N=527</th>
<th>Placebo N=523</th>
<th>Between Arm Difference</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory Abnormality</td>
<td>ERLEADA N=527</td>
<td>Placebo N=523</td>
<td>Between Arm Difference</td>
<td>95% CI</td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>10 0.4 16</td>
<td>6 0.4 10</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Leukopenia</td>
<td>3 0.1 2</td>
<td>1 0.1 1</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>41 2 21</td>
<td>21 2 11</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>Chemistry</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>76 0.1 46</td>
<td>41 0.1 23</td>
<td>35%</td>
<td></td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>70 0.2 39</td>
<td>39 0.2 22</td>
<td>71%</td>
<td></td>
</tr>
</tbody>
</table>
| Does not reflect fasting values

In the combined data of two randomized, placebo-controlled clinical trials, rash (≥1%) was the most common adverse reaction, 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 (4%) versus placebo (1.5%). The onset of rash occurred at a median of 83 days of ERLEADA treatment. Rash resolved in 78% of patients within a median of 28 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 26% and 28% of patients, respectively. Of the 10 patients who had dose interruption, 5% experienced reoccurrence of rash upon reintroduction of ERLEADA.

Hypothyroidism

In the combined data of two randomized, placebo-controlled clinical trials, hypothyroidism was reported for 4% of patients treated with ERLEADA and 2% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. ERLEADA was discontinued in 25% 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 tapered or dose-adjusted (see Drug Interactions).

Table 3: Adverse Reactions in SPARTAN (nmCPRC)

<table>
<thead>
<tr>
<th>System/Status</th>
<th>ERLEADA N=361</th>
<th>Placebo N=367</th>
<th>Between Arm Difference</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>General and metabolic adverse reactions</td>
<td>23.8 0.3 5.1</td>
<td>26.4 0.4 6.4</td>
<td>-2.7%</td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue reactions</td>
<td>12.8 0.1 3.3</td>
<td>15.0 0.2 4.0</td>
<td>-2.2%</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>16 0 12</td>
<td>19 0 10</td>
<td>1%</td>
<td></td>
</tr>
</tbody>
</table>

Does not reflect fasting values

Rash

In the combined data of two randomized, placebo-controlled clinical trials, rash (≥1%) was the most common adverse reaction, 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 (4%) versus placebo (1.5%). The onset of rash occurred at a median of 83 days of ERLEADA treatment. Rash resolved in 78% of patients within a median of 28 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 26% and 28% of patients, respectively. Of the 10 patients who had dose interruption, 5% experienced reoccurrence of rash upon reintroduction of ERLEADA.
Based on animal studies, ERLEADA may impair fertility in males of reproductive potential 3 months after the last dose of ERLEADA. Males and females of reproductive potential should use effective contraception during treatment and for 3 months following the last dose of ERLEADA.

**Risk Summary**

**Pregnancy**

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. There are no data on the use of ERLEADA in pregnant women. ERLEADA is not indicated for use 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.

**Lactation**

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**

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.

**Infertility**

Based on animal studies, ERLEADA may impair fertility in males of reproductive potential. There are no 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.

**OVERDOSAGE**

There is no known specific antidote for apalutamide overdose. In the event of an overdose, stop taking ERLEADA and support 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.

**Falls and Fractures**

- Inform patients that ERLEADA is associated with an increased incidence of falls and fractures.

**Seizures**

- Inform patients that ERLEADA has been associated with an increased risk of seizures. 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.

**Rash**

- Inform patients that ERLEADA is associated with rashes and to inform their healthcare provider if they develop a rash.

**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.
- Inform patients that apalutamide is a weak inhibitor of CYP2C8, CYP2C9, and CYP3A4 in humans. Concomitant use of ERLEADA with medications that are primarily metabolized by CYP2C8, CYP2C9, or CYP3A4 can result in lower exposure to these medications. Use caution if substrates of these medications are recommended when possible or evaluate for loss of activity if medication is continued. Concomitant use of ERLEADA with medications that are substrates of UGT can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA and evaluate for loss of activity if medication is continued.
- Inform 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.

- 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.

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Androgen Deprivation Therapy and Radiotherapy in the Salvage Setting—Is Combination Therapy Better?

Should the combination of androgen deprivation therapy (ADT) and radiation therapy (RT) be used in men with biochemical failure following radical prostatectomy? Maybe not.

Central to the treatment of men with aggressive prostate cancer is integration of multimodality therapy. The best example is integration of RT with ADT for primary treatment of localized high-risk disease. In the first study to examine this paradigm Bolla et al randomized 415 men with mostly cT3 and T4 disease to 70 Gy radiotherapy with or without 3 years of concomitant goserelin. At 10-year follow-up the men in the combination arm had improved outcomes including disease-specific survival (89.7% vs 69.6%) and overall survival (58.1% vs 39.8%).

The survival benefit is not due to ADT alone. Warde et al demonstrated that the addition of radiation (65 to 69 Gy to prostate, 45 Gy to pelvic nodes) to ADT resulted in improved overall survival (74% vs 66%, p=0.033) and disease-specific survival (90% vs 79%, p=0.0001) in high-risk men. Given the strong data on combination therapy, it is not surprising that randomized trials have explored the integration of ADT and RT for salvage treatment for prostate-specific antigen (PSA) failure after radical prostatectomy.

In RTOG 9601 Shipley et al examined the impact of adding 2 years of 150 mg daily bicalutamide to salvage RT for men with positive margins or pT3 disease at prostatectomy. They found a decreased mortality from prostate cancer (5.8% vs 13.4%, p < 0.001) and improved overall survival (76.3% vs 71.3%, p < 0.001) at 12 years despite using what many regard as suboptimal ADT.

In the GETUG-AFU 16 trial Carrie et al randomized 743 men to RT vs RT plus 6 months of conventional ADT with a gonadotropin-releasing hormone agonist. With shorter follow-up than the RTOG trial, they found an improvement in progression-free survival of 64% vs 49% favoring the combination of RT plus ADT. The lack of survival advantage to date was attributed to shorter follow-up. An update at the 2019 American Society of Clinical Oncology annual meeting with 9 years of follow-up showed an improvement in metastasis-free survival but not yet overall survival.

However, recent data presented by Spratt et al at an American Society for Radiation Oncology meeting have raised concerns about combination therapy. In RTOG 9601 there was a range of pre-RT PSAs from 0.2 to 4.0 ng/ml with more than 60% having a PSA greater than 0.5 ng/ml, a level that exceeds the recommendation for salvage RT. This raised the question of whether the benefit was in the men receiving salvage RT with an appropriately low PSA.

Analysis of the subset with PSA 0.2 to 1.5 ng/ml demonstrated no benefit with an overall survival at 12 years of 76% in the men receiving RT alone and 77% in the men receiving ADT plus RT. In contrast, for the subset with PSA 1.6 to 4.0 ng/ml there was a clear benefit to the combination therapy with overall survival at 12 years of 49% in the men receiving RT alone and 74% in the men receiving ADT plus RT.

Given that early treatment is central to use of salvage RT, preferably with PSA in the range of 0.1 to 0.2 ng/ml, the combination therapy appears to have the greatest benefit in a patient population that should not routinely exist with good follow-up and prompt referral for elevated PSA. Importantly, a dose of 150 mg bicalutamide was not without risk. Patients with a PSA from 0.2 to 0.6 ng/ml had a higher other cause mortality, which was believed to be due to a 3 to 4.5 times higher risk of serious cardiac events.

Where do we go from here? The first step is to wait for maturation of the GETUG-AFU 16 trial. Clearly high dose bicalutamide use in RTOG 9601 is not the standard form of ADT used in the United States and it should not be used in this setting. The results of RTOG 9601 should not be extrapolated to other forms of ADT until the GETUG-AFU 16 matures. It is entirely possible that standard ADT with RT will prove to be superior with longer follow-up (see figure).

Standard gonadotropin-releasing hormone agonists have fewer cardiac side effects and more effectively depress testosterone. In addition, since the trigger point for salvage RT was...
Androgen Deprivation with Radiotherapy in Salvage Setting

Continued from page 14

lower in the GETUG-AFU 16 trial with a median PSA of 0.3 ng/ml, the results may better reflect the standard of care in 2020.

The second step is to adopt a risk stratified approach to the integration of RT and ADT in the salvage setting. ADT combined with RT should be considered for those with a higher grade cancer and, therefore, are at risk for micrometastatic disease. Decipher® risk assessment can identify men at increased risk for salvage RT monotherapy failure and, thus, could potentially benefit from the addition of ADT. These risk stratification strategies will be assessed in the next generation of randomized trials.

FROM THE Urology Care Foundation

Urology Care Foundation Launches Humanitarian Award and Grant Program

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

On March 13 the AUA made the difficult but necessary decision to cancel the 2020 Annual Meeting due to the global coronavirus health crisis. The disappointment pales in comparison to the impact COVID-19 is having on our family, friends, colleagues and the world.

More than 16,000 individuals from around the world attend the AUA meeting each year to share in groundbreaking research, new guidelines and the latest advances in urological medicine. It is a time when attendees descend upon our vibrant host city and take part in the many spectacular events, resources and activities the Urology Care Foundation has to offer!

It was at this venue that 2 new, exciting and important philanthropic initiatives from the Foundation were to be shared. So rather than announcing from a plenary platform, I am deeply honored to announce:

1. The Urology Care Foundation Humanitarian Award
2. The Urology Care Foundation Humanitarian Grant Program

The Urology Care Foundation Humanitarian Award

The Urology Care Foundation Humanitarian Award is designed to recognize an individual who/which has, “demonstrated commitment in improving access to quality urologic health care in underserved populations.”

We have a moral and ethical duty in society to recognize those who take part in bringing these humanitarian efforts to fruition. Although urologists may have been recognized for their work in the past, there has never been a mechanism codified in either the Foundation or the AUA to recognize this critical part of our mission as urologists until now.

The Urology Care Foundation Humanitarian Grant Program

We also will be launching a new grant program designed to support humanitarian efforts. The Urology Care Foundation Humanitarian Grant program aims to support individuals and organizations who provide direct urology care to impoverished individuals and communities in underserved areas, either within or outside the United States. In the spirit of true humanitarianism, the program supports individuals who give of themselves without expectation of renumeration, and provide services to all equally, impartially and cooperatively. In addition to direct support, the Foundation envisions this program will help encourage

new volunteer opportunities and additional support.

The new mission will not detract from, nor diminish, our Foundation’s traditional research and educational priorities. Stayed tuned for more information on both of these innovative programs in the coming weeks.

The Foundation Welcomes Dr. Ralph V. Clayman to the Board of Directors

I am also pleased to announce and welcome Dr. Ralph V. Clayman to the Urology Care Foundation Board of Directors. As a highly respected urologist with valuable leadership experience, we look forward to Dr. Clayman’s expertise and assistance with advancing our mission worldwide.

As Distinguished Professor of Urology at the University of California, Irvine, Dr. Clayman led the team that performed the world’s first laparoscopic removal of a kidney and ureter for cancer treatment. He is also co-founder of the Endourology Society and serves as the co-editor of the journal of Endourology.

I am sure you will all agree that these new initiatives are exciting and reaffirm the values that we all share.

Upper and Lower Tract Urothelial Carcinomas—Family or Friends?

Panagiotis J. Vlachostergios, MD, PhD
Brian D. Robinson, MD
Bishoy M. Faltas, MD
New York, New York

Upper tract urothelial cancers (UTUCs) constitute 10% of urothelial carcinomas (UCs). They usually present at more advanced stages and are associated with worse clinical outcomes than urothelial carcinoma of the bladder (UCB) (see Appendix).\(^1\)\(^4\)

The Cancer Genome Atlas (TCGA) study classified UCB into 5 molecular subtypes (luminal papillary, luminal infiltrated, luminal basal/squamous, neuronal).\(^5\) However, it did not include UTUC.

Additionally, our understanding of the immune milieu of UTUC is incomplete. A critical question is whether the anatomical location of urothelial carcinoma can result in 2 different diseases at the molecular level (fig. 1). In other words, can UTUC be positioned within the UC continuum or is it a disease of its own?

To answer this question, we analyzed whole exome sequencing and RNA sequencing (RNAseq) data from high grade UTUC tumors from patients at Weill Cornell Medicine (WCM), Baylor College of Medicine (BCM) and MD Anderson Cancer Center (MDA).\(^6\)\(^7\) We used whole exome sequencing and RNAseq data from UTUC tumors from TCGA cohort as a comparison,\(^7\) which enabled us to define the biological differences between UC arising from the upper and lower urinary tracts.

We found that UTUC has a distinct mutational profile compared to urothelial bladder cancer, most notably a higher prevalence of fibroblast growth factor receptor 3 (FGFR3) alterations.\(^6\) In addition, the dominant mutational process in UTUC is APOBEC induced mutagenesis. This is interesting given the recently identified association between APOBEC3 induced mutagenesis and FGFR3 S249C mutations in bladder cancer.\(^3\)

In addition, we found that the expression of several DNA repair genes, including the canonical DNA mismatch repair (MMR) genes MLH1, PMS2, MSH2 and MSH6, was significantly down-regulated in UTUC compared to UCB.\(^6\) Nevertheless, the low MMR protein levels failed to translate to microsatellite instability. In fact, UTUC has a lower tumor mutational burden (TMB) than UCB. This point is worth emphasizing, as, contrary to the prevalent notion of UTUC being a Lynch syndrome associated tumor, sporadic UTUCs (which constitute the majority of UTUCs) are not microsatellite unstable and may have a lower TMB than urothelial carcinoma of the bladder.\(^6\)

We then assessed whether the wiring of UTUC from its transcriptome follows the same framework as UCB. Previous work by Dranrauer,\(^1\)\(^6\) Choi\(^1\) and Sjödahl\(^1\)\(^6\) et al demonstrated that UCB can be grouped into intrinsic basal and luminal molecular subtypes. We asked whether UTUC recapitulates the same molecular subtypes as UCB.

When analyzing our data we discovered that the majority of UTUCs consistently cluster within the luminal subtype (UNC classifier) and luminal papillary subtype using TCGA classifiers. This finding was confirmed in UTUC tumors from 2 different data sets from 3 institutions.\(^6\)

To further confirm our results we used nonnegative matrix factorization, an unsupervised statistical method, to extract the key biological features of UTUC from our RNAseq meta-data set. This analysis demonstrated that the luminal papillary component is a stable and defining feature of UTUC.\(^6\)

Because bulk RNAseq is an aggregate of tumor and immune cell components, we used these data to define the immune contexture of UTUC. The immune microenvironment of UTUC could influence response to immune checkpoint inhibition, which is an increasingly important treatment option for urothelial cancers (including UTUC).\(^1\)\(^3\)

We selected the top 5,000 genes with the highest variability in expression across the UTUC and TCGA UCB samples to generate a 170-gene classifier that comprised the key immune genes. This classifier segregated UC into T-cell inflamed and T-cell depleted clusters regardless of anatomical origin (UTUC vs UCB). Interestingly, most UTUCs clustered in the T-cell depleted subgroup, showing down-regulation of T-cell related genes such as CD8. This finding potentially reflects lower CD8+ tumor infiltrating lymphocytes in UTUC (fig. 2).

To identify signaling pathways that could be involved in shaping the immune contexture of UTUC, we compared the expression outliers between T-cell depleted and T-cell inflamed subtypes. We noted that FGFR3 mRNA levels were high in these T-cell depleted UTUCs. Therefore, we investigated whether FGFR3 signaling is a putative driver of UTUC’s immune depleted contexture.

Using UC cell lines with constitutive activation of FGFR3 signaling we confirmed that the inhibition of FGFR3 by shRNA led to the up-regulation of genes associated with response to interferon gamma. We replicated this effect using pharmacological inhibition with the FGFR3 inhibitor erdafi tinib in UC cell lines addicted to FGFR3 signaling. We found a consistent up-regulation of interferon gamma target genes such as BST2 and IRF9. In conclusion, our recent work shows that UTUC has high FGFR3 signaling, a T-cell depleted microenvironment and a low TMB, all of which may contribute to a less robust antitumor immune response.

If FGFR3 potentially coordinates the luminal papillary and immune depleted phenotypes in UTUC, its inhibition can potentially reverse the mechanisms underlying the immune depletion we observed.

Our results provide a rationale for why FGFR3 inhibition may be particularly suited for the treatment of UTUC. This rationale is highly relevant in the context of the recent U.S. Food and Drug Administration approval of erdafi tinib for the treatment of advanced bladder cancer after progression on chemotherapy and/or immunotherapy.\(^1\)\(^4\) Trials combining FGFR3 and PD-L1 inhibitors are ongoing (NCT03123055, NCT03473743).

Therefore, we can look at this situation from 2 perspectives to answer the initial question, “UTUC and UCB—family or friends?” Since UTUC has a predominantly luminal papillary T-cell depleted contexture within the continuum of UC biology, one could argue that upper tract and lower tract UC can be viewed as family. However, like friends who might have a lot in common but still have...
key individual differences, there are some clear distinctions in their biology. A deeper understanding of the biology of UTUC will be critical for developing effective UTUC targeted therapeutic strategies.


Appendix. Differences in clinical characteristics between UTUC and UCB

<table>
<thead>
<tr>
<th>Differences</th>
<th>UTUC (vs UCB)</th>
</tr>
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<tbody>
<tr>
<td>Embryology/histology:</td>
<td>Uroplakin content, keratin expression, extracellular matrix</td>
</tr>
<tr>
<td>Risk factors:</td>
<td>+ Aristolochic acid + Germline MMR defects (Lynch) but the majority of cases are sporadic</td>
</tr>
<tr>
<td>Staging:</td>
<td>• More commonly invasive at diagnosis (60% vs 15%-25%) • More variable (no muscularis in some areas of the renal pelvis) • Stronger correlation with grade • No pT3 subclassification</td>
</tr>
<tr>
<td>Surgical management:</td>
<td>• Lymph node dissection with radical nephroureterectomy controversial</td>
</tr>
<tr>
<td>Medical treatment:</td>
<td>• Instillation therapies challenging • Neoadjuvant/adjuvant chemotherapy/immunotherapy less studied</td>
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A vegetable rich diet is often recommended to men with prostate cancer on active surveillance but hard data to support this approach are lacking. The authors conducted a randomized clinical trial at 91 U.S. urology and medical oncology clinics that enrolled 478 men 50 to 80 years old with biopsy proven prostate adenocarcinoma (International Society of Urological Pathology grade group I in those younger than 70 years and less than 2 in those 70 years old or older), stage cT2a or less and serum prostate specific antigen less than 10 ng/ml.

Patients were randomized to a counseling behavioral intervention by telephone promoting consumption of 7 or more vegetable servings daily (MEAL [Men’s Eating and Living] intervention 257) or a control group that received written information about diet and prostate cancer (241). The primary outcome was time to progression.

Among 478 patients randomized 443 eligible patients (93%) were included in the primary analysis and overall there were 245 progression events (intervention 124, control 121). There were no significant differences in time to progression (unadjusted HR 0.96, 95% CI 0.75 to 1.24; adjusted HR 0.97, 95% CI 0.76 to 1.25). The 24-month Kaplan-Meier progression-free percentages were 43.5% and 41.4% for the intervention and control groups, respectively (difference 2.1%, 95% CI -8.1 to 12.2).

The authors concluded that among men with early stage prostate cancer managed with active surveillance, a behavioral intervention that increased vegetable consumption did not significantly reduce the risk of prostate cancer progression. The findings do not support use of this intervention to decrease prostate cancer progression in this population, although the study may have been underpowered to identify a clinically important difference.
The Halstedian “see one, do one, teach one” model of surgical training has defined how generations of surgeons learned and subsequently taught how to operate. However, changes in the field and in resident surgical education are placing strain on this dogma.

During the last several decades resident exposure to complex open cases has gradually declined while endoscopic, laparoscopic and other advanced minimally invasive techniques have increasingly required mastery.1 In conjunction with the advent of work hour restrictions, this shift has created a setting in which residents increasingly graduate with doubts in their ability to perform the full scope of urological practice.2

Considering these challenges, it is critical to optimize the learning environment and make efficient educational use of available operating time. This requires a paradigm shift from the current practice where the onus of education falls solely on the learner, who is expected to passively absorb surgical competency through exposure to cases.

Furthermore, although education itself is an art, many attending surgeons are not trained educators. In an effort to optimize resident education, assessment and education, tools worth highlighting have been developed to guide attendings and residents toward targeted competency goals.

One type of tool is the perioperative briefing and debriefing, which has been shown to improve the intraoperative learning experience, especially in the identification of learning objectives.3 Through structured educational briefings and debriefings, faculty and residents can focus on the specific learning goals from each case and, thus, target the educational zone of proximal development.4

A commonly referenced model to challenge the Halstedian steps is the Zwischenberger model.5 This model comprises the 4 learning stages of Show and Tell, Smart Help, Dumb Help and No Help. In the Show and Tell phase the senior surgeon completes the operation while describing the process to the resident. The resident then performs the surgery in the Smart Help stage while the attending provides exposure and performs some critical steps of the operation. During the Dumb Help stage the resident operates mostly independently and is only interrupted if an action may cause harm. Lastly, in the No Help stage the attending simply assists while providing very little, if any, guidance. This method allows “scaffolding,” with a formal system of progression that can be documented and tracked.

Assessment of surgical competency is also a vital part of surgical education and residency training. One such assessment scale is the Ottawa Surgical Competency Operating Room Evaluation (O-SCORE), which evaluates residents’ technical, planning and communication skills.

In addition to validated questionnaires, other methods using video or app based postprocedural analyses of resident operative performance are in active development and application. These assessment tools must balance inherent time constraints with the educational value provided.

Surgical education faces pressures from multiple sources, including decreased exposure to open cases, increased case variety and less operative time in which to gain necessary skills. In response, educational and evaluative tools are being developed to enhance the learning environment. With exploration of the new strategies and tools becoming available, residents and attendings can implement those most fitting with the culture of their program. 


FROM THE Chief Executive Officer

Navigating COVID-19

Michael T. Sheppard, CPA, CAE
Linthicum, Maryland

As I write this, the world is focused on the global outbreak of coronavirus disease (COVID-19) and the AUA is no exception. Like many of you, we have actively monitored COVID-19 since January, and we share concerns about how this new virus will impact our communities and those of our colleagues around the world. The AUA is committed to the health and safety of our staff, our members, our volunteers and the community at large during this unprecedented situation.

The AUA is taking a wide range of steps to help the urology community navigate COVID-19. To date, we have instituted a number of strategies, including sharing information, virtual meetings as well as modifying AUA events and staff working arrangements, to do our part in mitigating transmission of the coronavirus. These strategic plans were made to ensure your physician leaders and our staff can continue to provide the top-notch services you expect from the AUA. I am pleased to report that we do not anticipate any disruption to member subscriptions to AUA publications, including The Journal of Urology, Urology Practice and AUANews.

Sharing Information

We believe that information is critical. Our team has developed a Coronavirus Information Center on AUAnet.org and is actively posting updates from federal agencies and regulators to help you navigate the latest news and information about COVID-19. This page also includes links to assist members who may be incorporating telehealth and telemedicine into their practices in the coming weeks and months.

Virtual Meetings for Volunteers

In March the AUA shifted all meetings of councils, committees and other volunteers to a virtual format. I’d like to thank all of the many participants who helped ensure the productivity of those meetings. We will continue to implement this strategy to gather our volunteers and leaders together in the coming months as institutions around the country manage travel restrictions related to COVID-19.

Modifying AUA events

As previously announced, the Annual Urology Advocacy Summit was postponed until later this year, and the 2020 AUA annual meeting was canceled. These decisions were made in the best interests of our attendees, and we are looking forward to a highly productive advocacy event from August 31 to September 2, 2020 in our nation’s capital. In regard to the AUA meeting, we are currently exploring ways to share the surgical videos and other important clinical information that would have been presented at the meeting. The meeting abstracts will be published in the supplement to the April issue of The Journal of Urology® as scheduled

Modifying Staff Working Arrangements

More than 150 staff members work in our offices in Maryland and Washington, DC, and other remote...
Memoriam

Datta Wagle, MD

Joseph M. Greco, MD
Buffalo, New York

The urology community has lost one of its most dedicated members. Datta Wagle, MD, AUA President (2010-2011), passed away January 24, 2020 after a brief illness. He was 83 years old.

Dr. Wagle came to Buffalo, New York from India with $8 in his pocket when he was 20 years old. He was President of the AUA Northeastern Section, New York State Urologic Society and the American Association of Clinical Urologists. He was the recipient of numerous honors, and received AUA’s Distinguished Service Award in 1999.

Throughout the years, Dr. Wagle and I shared many fond memories personally and professionally. One of his long-standing mottos to colleagues was, “be informed, be involved, and be vested in the urologic profession.” He lived his mantra.

Datta touched the lives of innumerable patients and colleagues over the years. He will be remembered for putting patients first. He was loved and admired by many. At the conclusion of his professional career in 2013 Datta retired to spend time with his family.

In addition to his wife, survivors include 4 daughters, 2 brothers, a sister and 7 grandchildren.

AUANews

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Urologist

Cambridge Health Alliance (CHA)

Cambridge Health Alliance (CHA), is a nationally recognized, award-winning public healthcare system located in the Boston metro area. We are currently recruiting a Urologist to join our existing department (3 MDs & 1 PA). CHA is comprised of three hospital campuses and an integrated network of primary and specialty outpatient care sites.

CHA is an academic affiliate of Harvard Medical School (HMS) and Tufts University School of Medicine. Incoming MD will have opportunity to teach HMS Medical Students, HMS IM residents and Tufts FM residents.

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To confidentially apply visit www.CHAproviders.org or email your CV/cover letter to Kasia Marchini at ProviderRecruitment@challiance.org.
Web Search Queries and Prostate Cancer: The Thin Line Between the Digital and Real World

Cacciamani G, Gill K, Gill IS. Lancet Oncology (April 2020)

We investigated the correlation between online Google searches-engine queries (SEQs) for PCa and metastatic PCa and its epidemiologic prevalence and variations according to U.S. Preventive Service Task Force (USPSTF) screening recommendations. SEQ trends correlate temporally and geographically with annual incidence of PCa, mPCa and PCa-mortality. This correlation increased further since the USPSTF recommendations (Fig.1a). U.S. state-by-state differences in SEQs reflect PCa-specific mortality in those states (Fig.1b). Conclusion: SEQs are a valid PCa-related public information resource and might serve as a complementary epidemiological tool. Providing accurate PCa-specific online information can deliver a valuable population-level service for patients and those related to them.

Deep Learning on Automated Performance Metrics (APMs) and Clinical Features to Predict Urinary Continence Recovery after Robot-assisted Radical Prostatectomy (RRP)


We predicted continence recovery in 100 RRP s using a trained deep learning (DL) model (DeepSurv). For 8 surgeons, robotic APMs were captured prospectively and compared to their historical RRRs (01/2015-08/2016). DeepSurv model features, ranked per importance in prediction, selected the top 4 surgeons “Group 1/APMs” versus others “Group 2/APMs”. Continence rate: 79% @ 3 mos. Continence prediction by the DL model: CI 0.6; MAE 85.9. This model ranked APMs higher than patient features. In the historical cohort, “Group 1/APM” patients had superior continence @ 3 mos (p=0.034) and 6 mos (p=0.047). Conclusions: Using APMs and patient data, the DeepSurv model was able to predict continence after RRP. Surgeons with more efficient APMs had higher continence rates.

Opioid Prescription Patterns and Opioid Usage after Vasectomy


We determined urologists’ opioid prescribing (e-survey) and patients’ post-vasectomy pain control regimens (telephone survey). 52% of urologists routinely prescribed opioids post-vasectomy; yet, 42% of men did not actually use them. Of men using opioids, 53% used ibuprofen as their primary pain med vs 93% of men not using opioids (p=0.004). Ibuprofen use correlated with using fewer opioid tablets (p=0.003). Conclusion: Opioid prescription after vasectomy is common, yet not routinely necessary. Patients using ibuprofen used less opioids.

Exercise Modulates Neuronal Activation in The Micturition Circuit: The MAPP Research Network Study


Stress exacerbates and exercise may improve symptoms of interstitial cystitis/bladder pain syndrome (IC/BPS). Animals exposed to water avoidance stress (WAS) have increased engagement of the brain micturition circuit. We evaluated the effect of voluntary exercise on the central amplification of stress-induced bladder hyperalgesia. After 10 days of WAS, W-K female rats were randomized to observation or daily exercise. Exercise animals had reduced bladder hypersensitivity, pain and frequency, with dose response. These changes correlated with brain changes in the micturition circuit (Barrington nucleus) and its control, the Periaqueductal Gray and the limbic system. Conclusion: Chronic exercise may help modify urinary symptoms in patients with IC/BPS.