Social Media and Men’s Health: Current State and Strategies for Improving Physician Impact

Rapid Growth in Social Media Use
Social media include networks and technologies that allow sharing of information. Up to 72% of U.S. adults use social media as of February 2021, an upward trend that involves not only younger age groups, but also adults over the age of 65 with 45% using at least 1 social media site. Among practicing urologists and urology trainees, global surveys show use by 87.9% and 99.4%, respectively. The wide adoption of these networks highlights their potential as a forum for engaging with patients, colleagues and other stakeholders.

The Upside
Social networks have great potential in further advancing clinical care, research and education related to men’s health. All of the major urological meetings have a presence on social media, allowing broader dissemination of important new research and practice updates to a global audience. Urologists are increasingly using these networks for clinical crowdsourcing and live case discussions that can provide valuable global insights for managing challenging clinical scenarios.

Telemedicine Implementation for Stone Disease in the Post-COVID-19 Era

The COVID-19 pandemic has led to the reshaping of health care systems and simultaneous shifting of economic resources to treat critically ill COVID-19 patients. In many countries, patients treated and followed up in urological settings are facing a significant delay of their appointments since the tertiary centers either became hospitals dedicated to COVID-19 patients or face-to-face consultations have been postponed in accordance with curfew requirements.

Telemedicine is defined as the “provision of healthcare services...
INDICATIONS
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
Cerebrovascular and 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 5% of patients treated with placebo. Across the SPARTAN and TITAN studies, 5 patients (0.8%) treated with ERLEADA® and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event. Patients with history of unstable angina, myocardial infarction, congestive heart failure, stroke, or transient ischemic attack within 6 months of randomization were excluded from the SPARTAN and TITAN studies.

- In the SPARTAN study, cerebrovascular events occurred in 4.7% of patients treated with ERLEADA® and 0.8% of patients treated with placebo. In the TITAN study, cerebrovascular events occurred in 1.9% of patients treated with ERLEADA® and 2.1% of patients treated with placebo. Across the SPARTAN and TITAN studies, 3 patients (0.2%) treated with ERLEADA®, and 2 patients (0.2%) treated with placebo died from a cerebrovascular event.

Cerebrovascular and ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA®, monitor for signs and symptoms of ischemic heart disease and cerebrovascular disorders. 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 2.1% of patients treated with placebo. In the TITAN study, fractures occurred in 12% of patients treated with ERLEADA® and 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 two 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 females with male partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA®.

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, reduced appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture.

- 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% (0.8%); lymphopenia ERLEADA® 41% (2%), placebo 21% (2%).

- Chemistry — Consider 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 (SPARTAN and TITAN), 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 (SPARTAN and TITAN), 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 CYP3A4 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**

CYP3A4, CYP2C9, and UGT Substrates — ERLEADA® is a strong inducer of CYP3A4 and CYP2C9, and a weak inducer of CYP2C9 in humans. Concomitant use of ERLEADA® with medications that are primarily metabolized by CYP3A4, CYP2C9, 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.

AP = androgen deprivation therapy; AR = androgen receptor; C1 = confidence interval; CT = computed tomography; GnRH = gonadotropin-releasing hormone; HR = hazard ratio; mCSPC = metastatic castration-sensitive prostate cancer; MFS = metastasis-free survival; mCRPC = metastatic castration-resistant prostate cancer; PSA = prostate-specific antigen; pFS = progression-free survival; SPARTAN = Selective Prostate Androgen Receptor Targeting with Apalutamide; TITAN = Targeted Investigation of Treatment Activity of Novel Andrologics.

**Study Design**: TITAN was a phase 3, multicenter, randomized, double-blind, placebo-controlled trial of patients with mCSPC (N=1052). Patients had newly diagnosed mCSPC or relapsed metastatic disease after an initial diagnosis of localized disease. 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 or placebo orally once daily. All patients in the TITAN trial received a concomitant GnRH analog or had a prior bilateral orchiectomy. The dual primary endpoints were overall survival and pFS. All patients who enrolled in the TITAN study started ADT for mCSPC ≥6 months prior to randomization.

**Study Design**: SPARTAN was a phase 3, multicenter, randomized, double-blind, placebo-controlled trial of patients with nmCRPC (N=1207). Patients had a PSA doubling time <10 months and serum testosterone levels ≤50 ng/dL. All patients enrolled were confirmed to be non-metastatic by blinded central imaging review. Patients had a history of surgery, predispensing factors for surgery, or receiving drugs known to decrease the seizure threshold or to induce seizures were excluded. Patients were randomized 2:1 to receive ERLEADA® 240 mg orally once daily or placebo orally once daily. All participants in the SPARTAN trial received a concomitant GnRH analog or had a bilateral orchiectomy. The primary endpoint was metastasis-free survival (MFS), defined as the time from randomization to the time of first evidence of blinded independent central review-confirmed distant metastasis, defined as new bone or soft tissue lesions or enlarged lymph nodes above the iliac bifurcation, or death due to any cause, whichever occurred first. Secondary endpoints were time to metastasis, progression-free survival, time to symptomatic progression, overall survival, and time to initiation of cytotoxic chemotherapy. All patients in the SPARTAN study, conventional imaging (technetium-99m bone scans and CT scans) was used to confirm that patients were non-metastatic at screening for induction. Patients with pelvic lymph nodes <2 cm in short axis (N1) located below the iliac bifurcation at screening were allowed in the study. All patients in SPARTAN had a PSA doubling time <10 months at study entry.

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

ERLEADA® (apalutamide) tablets

**INDICATIONS AND USAGE**

ERLEADA is indicated for the treatment of patients with:
- Metastatic castration-sensitive prostate cancer (mCSPC) after a progresseson of Taxane-based chemotherapy and/or hormone-refractory disease
- Metastatic castration-resistant prostate cancer (mCRPC) after a progression on enzalutamide or abiraterone
- Non-metastatic castration-resistant prostate cancer (nmCRPC)

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

Cerebrovascular and Ischemic Cardiovascular Events

Cerebrovascular and ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA. Monitor for signs and symptoms of ischemic heart disease and cerebrovascular disorders. Consider discontinuation of ERLEADA for Grade 2 or higher cerebrovascular or ischemic cardiovascular events.

In a randomized study (SPARTAN) of patients with mCRPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA and 3% of patients treated with placebo. Across the SPARTAN and TITAN studies, 5 patients (0.5%) treated with ERLEADA and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event.

In the SPARTAN study, cerebrovascular events occurred in 4.7% of patients treated with ERLEADA and 0.9% of patients treated with placebo. [see Clinical Trials Experience]. In the TITAN study, cerebrovascular events occurred in 5 patients (0.5%) treated with ERLEADA and 2 patients (0.2%) treated with placebo who died from cerebrovascular events. Patients with history of unstable angina, myocardial infarction, congestive heart failure, stroke, transient ischemic attack, or history of cerebrovascular disease were excluded. There is no clinical experience in re-administering ERLEADA to patients who experienced a cerebrovascular or ischemic cardiovascular event.

**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 or without bone-targeted agents were not performed in the study.

In a randomized study (TITAN) of patients with non-metastatic castration-resistant prostate cancer, fractures occurred in 9% of patients treated with ERLEADA and in 6% of patients treated with placebo. Grade 3 fractures were similar in both arms: 2% in the ERLEADA arm and 2% in the placebo arm. The median time to the onset of fracture was 58 days (range: 2 to 111 days) for patients treated with ERLEADA. Routine bone density assessment and treatment of osteoporosis with or without bone-targeted agents were not performed in the 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. Perioperative discontinuation of ERLEADA is recommended when administering anesthetic agents. Seizures have occurred in patients who received anesthetic agents (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 adverse reactions are considered more frequent with the long-acting formulation of apalutamide compared to the short-acting formulation. See hypertriglyceridemia.

**ADVERSE REACTIONS (continued)**

The following adverse reactions are considered more frequent with the long-acting formulation of apalutamide compared to the short-acting formulation. See hypertriglyceridemia.

**ADVERSE REACTIONS**

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. At the time of progression, patients were switched to a concomitant study evaluating the safety of apalutamide releasing hormone (GnRH) analog or had prior bilateral orchiectomy. The median duration of exposure was 28 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 (4%) who were treated with ERLEADA died from adverse reactions. The reasons for death were ischemic cardiovascular events (2 patients, 1.0% each), sudden cardiac death (1 patient, 0.5%), cerebrovascular events (2 patients, 1.0% each), and large intestine ulcer and sepsis (1 patient, 0.5%). ERLEADA was discontinued due to adverse reactions in 8% of patients, most commonly from rash (2%). Adverse reactions leading to dose interruption or reduction occurred in 23% of patients; the most frequent (>5%) were rash, diabetes, fatigue, anemia, and leucopenia. Additional adverse reactions occurred in 2% of patients treated with ERLEADA. The median time to onset of rash was 83 days (range: 7 to 162 days) for patients treated with ERLEADA.

**Rash**

Rash occurred in patients receiving ERLEADA. Evaluate patients for rash for frequency and severity. Rash is a common adverse reaction in patients receiving ERLEADA.

In a randomized study (TITAN) of patients with non-metastatic castration-resistant prostate cancer, rash occurred in 12% of patients treated with ERLEADA and in 3% of patients treated with placebo. The median time to the onset of rash was 314 days (range: 20 to 953 days) for patients treated with ERLEADA. Routine bone density assessment and treatment of osteoporosis with or without bone-targeted agents were not performed in the study.

In a randomized study (SPARTAN) of patients with nmCRPC, rash occurred in ≥15% of patients, and more frequently (>5%) in the ERLEADA treated patients 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 1: Adverse Reactions in TITAN (mCSPC)**

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>All Grades</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatologic and connective tissue disorders</td>
<td>17</td>
<td>4.0</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>28</td>
<td>7.0</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>23</td>
<td>5.0</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>All Grades</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic and nutritional parameters</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>Cardiac and respiratory parameters</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>Hematologic parameters</td>
<td>17</td>
<td>11</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>All Grades</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologic parameters</td>
<td>23</td>
<td>9.0</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>25</td>
<td>9.0</td>
</tr>
<tr>
<td>Metabolic and nutritional parameters</td>
<td>12</td>
<td>9.0</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>All Grades</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematologic parameters</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>Metabolic and nutritional parameters</td>
<td>17</td>
<td>11</td>
</tr>
</tbody>
</table>

**Additional information**

Additional clinical significance adverse reactions occurred in ≥2% of patients treated with ERLEADA included hyperglycemia (8% versus 2% on placebo), pruritus (8% versus 2% on placebo), and heart failure (3% versus 0% on placebo).

**Table 5: Additional Adverse Reactions Occurring in ≥15% ERLEADA-Treated Patients and at a Higher Incidence than Placebo (Between Arm Difference > 5% All Grades) in SPARTAN (nmCRPC)**

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>All Grades</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic and nutritional parameters</td>
<td>17</td>
<td>11</td>
</tr>
</tbody>
</table>

**Tissue and organ abnormalities**

**Co-administration of Other Medications**

**Effect of Other Drugs on ERLEADA**

**Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the blood levels of apalutamide.**

**Drug Interactions**

**Strong CYP3A4 or CYP450 Inhibitors**

Co-administration of a strong CYP3A4 or CYP450 inhibitor is predicted to significantly decrease the exposure of apalutamide. Co-administration of strong inhibitors can lead to an increased risk of adverse reactions. The ERLEADA dose based on tolerability [see Doseage and Administration.
There is no known specific antidote for apalutamide overdose. In the event of an overdose, stop receiving ERLEADA with androgen deprivation therapy was elevated in the elderly, occurring in 8% of younger than 65 years, 41% of patients 65-74 years, and 49% of patients 75 years or older. Falls in patients 3 months after the last dose of ERLEADA.

In clinical studies, 19% of patients were less than 65 years, Pediatric Use

Based on animal studies, ERLEADA may impair fertility in males of reproductive potential 3 months after the last dose of ERLEADA. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months following the last dose of ERLEADA. 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].

Contraception

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. 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. Advise male patients to use a condom if having sex with a pregnant woman [see Warnings and Precautions].

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Infertility

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Social Media and Men’s Health
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“recruiting” viewers and advancing education.

The Downside
Numerous studies have highlighted the variable quality of information on social networks. A recent review of studies assessing the reliability of YouTube videos on men’s health topics found that the majority of the videos were unreliable, with only a few studies finding mostly reliable information on their chosen topic (see Table). As an example, a study on prostate cancer videos demonstrated that among the first 150 YouTube videos featuring prostate cancer, the benefits of treatment were more commonly presented than the harms. Importantly, more than three-quarters of these videos reaching more than 6 million viewers contained biased and/or inaccurate content either within the video itself or in the accompanying comments. Other instances of inaccurate or unreliable information presented in the same review paper include erectile dysfunction, male infertility, benign prostatic hyperplasia and male hypogonadism (see Table). The quality of urological health content and information on social networks other than YouTube is similarly suboptimal. We recently examined TikTok videos on prostate cancer and noted that most included casual content designed to raise awareness or share a story without factual information. Disappointingly, nearly half of the 17% with “objective information” contained misinformation.

Strategies for Physicians
Patients who perceive worse communication with their physician are more likely to seek health information on social networks. Due to the critical importance of the patient-physician relationship, we advocate greater emphasis on communication skills throughout medical education. The time constraints of the encounter familiar to clinicians in busy clinical practices and the increased acceptance of telehealth are a call to urologists for creating audiovisual content that address the most common questions related to men’s health office visits and procedures. This will in turn provide clinicians with a reliable source for referring patients outside of the clinical encounter and reach a broad audience. For example, a recent study looking at the impact of 6 videos created by a large university-based health system found that their videos reached more than 600,000 viewers across 47 different countries. All practicing urologists should expect that their patients will seek additional information through the internet and that there is a significant risk of exposure to misinformation. Therefore, urologists should be proactive in directing patients and their families to high quality content that may be created by themselves or other reliable sources (eg Urology Care Foundation, Prostate Cancer Foundation, Sexual Medicine Society of North America). The content should be regularly updated to consider the rapidly evolving field and culturally appropriate for diverse audiences. It should also be free of jargon and created at the recommended reading level for consumer health information. Free resources through the YouTube Creator Academy are available to help content creators with this process. ≤

Table. Summary of selected research on men’s health information on YouTube.

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Disease Studied</th>
<th>Key Findings</th>
<th>Reliability Method Used</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gul et al (2019)</td>
<td>Premature Ejaculation</td>
<td>Majority of videos contained reliable information</td>
<td>DISCERN Score Criterion (average)</td>
<td>3.55 out of 5 (Reliable Group)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No significant association between number of views and reliability</td>
<td></td>
<td>0.25 out of 5 (Unreliable Group)</td>
</tr>
<tr>
<td>Fode et al (2020)</td>
<td>Erectile Dysfunction</td>
<td>Majority of videos were unreliable</td>
<td>DISCERN Score Criterion (median)</td>
<td>2.0 out of 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No significant association between number of views and reliability</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Videos created by medical institutions were more reliable (p=0.0002)</td>
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<tr>
<td></td>
<td></td>
<td>Videos that advertised a specific treatment product were less reliable</td>
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<tr>
<td></td>
<td></td>
<td>(p=0.0001)</td>
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<td></td>
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<tr>
<td>Ku et al (2020)</td>
<td>Male Infertility</td>
<td>Graded videos into four categories A, B, C, and D (A highest, D lowest)</td>
<td>Content Density Score (from questionnaire based on AUA best practices)</td>
<td>A=4 videos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>based on content density score</td>
<td></td>
<td>B=17 videos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Majority of videos were created by health care organizations</td>
<td></td>
<td>C=12 videos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minority of videos received the highest grade</td>
<td></td>
<td>D=9 videos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Highest grade only went to healthcare providers/organizations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preliminary study by</td>
<td>Peyronie’s Disease</td>
<td>Majority of videos were of acceptable quality as a patient education resource</td>
<td>DISCERN Score Criterion (average)</td>
<td>3.1 out of 5</td>
</tr>
<tr>
<td>authors</td>
<td></td>
<td>About 1% of videos featured a board-certified urologist</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Majority of videos were of acceptable quality as a patient education resource</td>
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<tr>
<td></td>
<td></td>
<td>No significant difference in reliability score between videos featuring</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>physicians and those that did not</td>
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<tr>
<td></td>
<td></td>
<td>Videos featuring physicians had less views on average than videos that were</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>not (p=0.037)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warren et al (2021)</td>
<td>Male Hypogonadism</td>
<td>Majority of videos were unacceptable as a patient education resource</td>
<td>DISCERN Score Criterion (average)</td>
<td>2.4 out of 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Videos featuring physicians were more reliable (p=0.01) but had fewer</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>average views than videos that did not</td>
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</tr>
<tr>
<td>Loeb et al (2019)</td>
<td>Prostate Cancer</td>
<td>More YouTube videos described benefits than harms</td>
<td>DISCERN Score Criterion (median)</td>
<td>3.0 out of 5</td>
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<tr>
<td></td>
<td></td>
<td>YouTube videos with worse information were viewed more than videos</td>
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<tr>
<td></td>
<td></td>
<td>with better information</td>
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<td>YouTube videos posted by physicians and professional organizations</td>
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<td></td>
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<td>contained higher quality information but were viewed less than videos</td>
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<td></td>
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<td>posted from other sources</td>
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<td></td>
<td></td>
<td>The majority of videos studied contained potentially biased or</td>
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<td></td>
<td></td>
<td>misinformative content within the video or comment section</td>
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<tr>
<td>Betschart et al (2020)</td>
<td>Benign Prostatic Hyperplasia</td>
<td>Majority of videos were created by health care professionals but also had</td>
<td>DISCERN Score Criterion (median)</td>
<td>2.0 out of 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>commercial bias and provided inaccurate information</td>
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<td>Most prevalent topic was the overall treatment procedure</td>
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<td></td>
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<td>Only videos covering bipolar enucleation, holmium enucleation, TURP, and</td>
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<td></td>
<td></td>
<td>patient education videos had an acceptable median reliability score</td>
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</tr>
</tbody>
</table>

over physically separate environments via Information and Communications Technology.14

Telemedicine has been implemented to facilitate access to health care services for patients living in remote or rural areas or in settings with limited availability of services, such as in military camps or prisons.

Kidney stone disease is a highly prevalent clinical condition associated with modern lifestyle and metabolic syndrome, with a lifetime prevalence of nearly 10%.6 Considering the high probability of recurrence, with more than 50% of patients experiencing another episode within the next 5 to 10 years and the possibility of surgical intervention rising up to 26.6%,3 the followup of these patients seems imperative. Recent reports point out the promising functionality of telemedicine in the field of urolithiasis (see Appendix).

The experience of setting up a virtual stone telephone clinic during the span of a 6-year period has shown that telemedicine is applicable and cost-effective for the followup of both asymptomatic patients with renal calculi and high-risk stone formers.4 Patients went imaging prior to telemedicine consultation or intervention. During a median followup duration of 12 months, 290 patients were enrolled in the virtual clinic, with only 2 (0.7%) choosing to return to face-to-face consultations, while only 8 (2.8%) patients did not attend the arranged appointments. The direct savings form salaries were calculated at nearly £26 per appointment (93%) compared to face-to-face meeting, without considering work days lost or travel and parking expenses.

Dietary modifications and medical treatment tailored to specific metabolic abnormalities of recurrent stone formers can drastically reduce recurrence, but both initial 24-hour urine metabolic assessment and compliance with prescribed regimen are surprisingly low.5,6 Gasparini et al evaluated the feasibility of telemedicine services to enhance the compliance and followup in patients under medical treatment for recurrent stone disease and found that 11.8% of patients did not comply with the telephone based program at 12 months and another 12.4% for duration more than 12 months.3 More interestingly, 80% of patients completed a followup 24-hour test at 1 year of followup, with most of patients experiencing improvement in the urinary parameters affecting stone recurrence after complying with most of dietary modifications suggested during the telemedicine consultations.7

Telemedicine, either via telephone consultations or through virtual meetings using relevant technology, proved to be effective in several circumstances regarding stone disease, such as remote assessment of computerized tomography (CT) scan images for identification of hydronephrosis8 or for postpercutaneous nephrolithotripsy followup using the Skype application with both physicians and patients reporting high levels of satisfaction.9 Ong et al evaluated the efficacy of telemedicine in patients with ureteric colic without complications such as infection/fever, severe pain or hydronephrosis8. Consultations were performed via telephone instead of face-to-face meetings over a 3-year period. Most patients (93.1%) were satisfied with the service provided, while the need for direct meeting was reduced by 71.1%, either due to normal CT scan (46.2%) or missing scan appointments (24.9%).10

The application of telemedicine has been studied before the occurrence of COVID-19 pandemic. Limited technological infrastructure and appropriate medical staff experience, high costs of implementation and reluctance of both patients and physicians in fear of losing direct contact resulted in scarce use from a few centers. However, more than 1 year has passed since encountering the novel coronavirus and the potentials of telemedicine now seem very enticing. Avoidance of direct contact not only drastically reduces the risk of virus contamination, but also saves time and monetary resources both for patients and health care systems. The risk of disease progression is also diminished since when the indication exists patients are referred for face-to-face consultation and receive appropriate management.

A major drawback of this type of patient encounter is the inability to perform proper physical examination, which is essential in many circumstances. However, applications are under validation for caregivers to perform basic clinical examination under physician guidance. The easier access to personal sensitive data and the need for implementing secure algorithms and software in order to protect patient data should also be overemphasized during use of telemedicine services, especially when performing medical examination.

In conclusion, the use of telemedicine regarding stone disease has gained wider attention in the post-COVID-19 era and is feasible, cost-effective and acceptable both by patients and physicians. As long as appropriate protective measures are implemented, patients with kidney stone disease could benefit from such virtual encounters, saving time and money and thereby optimizing health care resources.

### Appendix. Studies reporting telemedicine use in urolithiasis-related settings.

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Study design</th>
<th>Primary outcome</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aydogdu1/2019</td>
<td>Randomized controlled trial</td>
<td>Patient and physician satisfaction</td>
<td>Both patients and physicians were satisfied with the telemedicine services</td>
</tr>
</tbody>
</table>
| Gasparini1/2019 | Prospective | Feasibility of providing dietary advice, metabolic evaluations and appropriate medical therapy to recurrent stone formers via pharmacist-staff driven telemedicine consultation | • 99% compliance at 3 months with at least 3 out of 5 dietary recommendations  
• Low dropout rates both at 12 months (11.8%) and at longer than 12 months follow-up periods (12.4%)  
• Majority of patients (80%) underwent repeat 24-hour urine analysis at 12 month follow-up |
| Hughes2/2021 | Prospective | Applicability and cost-effectiveness of telephone follow-up with stone-nurse, for asymptomatic patients with renal stones and high risk stone formers | • At 12 months only 2/290 patients chose to return to face to face clinic and another 8 (2.8%) did not attend appointments  
• Cost reduction of 93% (£26 per appointment) considering only direct costs (salaries) |
| Johnston4/2005 | Prospective | Agreement between initial CT scan diagnosis and urolgist evaluation of images sent by email | 100% agreement for hydronephrosis and 80% agreement for perinephric fat stranding |
| Ong9/2021 | Prospective | Avoidance of clinic consultation in patients with uncomplicated ureteric colic (no fever/infection, intense pain or hydronephrosis) with a telephone consultation | • 93.1% of patients were satisfied with the services provided  
• 71.1% reduction for direct meeting due to normal CT scan (46.2%) or nonattendance for performing CT scan (24.9%) |

Impact of Irrigation on Endoscopic Stone Surgery

There is a fine balance between being able to see and elevated intrapelvic pressures and sepsis risks in endoscopic stone surgery. Increase in intrapelvic pressures can lead to pyelovenous backflow which, especially in the setting of bacterial load, can increase risk of bacteremia and in turn sepsis. Lee-Brown and Laidley reported in 1927 that pyelovenous backflow occurred at sustained pressures over 30 mmHg. Thomsen et al in 1984 showed that the threshold for pyelovenous backflow was 30–45 mmHg. As such, ensuring stable pressures in the collecting system during endoscopic stone surgery is essential. Moreover, stones may harbor bacteria that do not show up on a preoperative urine culture and despite best efforts to sterilize the urine prior to an operation, risks of infectious complications are not fully mitigated simply by giving antibiotics. Omar et al showed that 35% more patients had systemic inflammatory response syndrome (SIRS) if they underwent percutaneous nephrolithotomy at 200 mmHg than 80 mmHg. Thus, it is prudent that irrigation pressure be minimized as much as reasonably possible to minimize infectious related complications. Similar to radiation, one might consider the ALARA (as low as reasonably achievable) principle to apply to intrapelvic pressures.

What are some ways this has been accomplished?

In a benchtop cadaveric study, Landman et al in 2002 showed that with both a 10/12F and 12/14F ureteral access sheaths, intrapelvic pressures were reduced with concomitant increase in irrigant flow. In a similar study for a ureteroscopy model, even in the presence of increased irrigation pressures renal pelvic pressures remained low (<20 mmHg). However, moving to smaller ureteral access sheaths (<10F) has been shown to negatively impact irrigation flow and lead to increased intrapelvic pressures (>40 mmHg). In clinical retrospective studies, smaller ureteral access sheaths and increased irrigation pressures have been shown to be associated with increased rates of SIRS. In a prospective study of 5 patients undergoing flexible ureteroscopy, measurements of renal pelvic pressures were measured through a nephrostomy tube. It was shown uniformly that pressures in the absence of ureteral access sheaths were higher in all locations including renal pelvis, proximal ureter and mid ureter.

Besides ureteral access sheaths, are there any other mechanisms to safeguard against increased intrapelvic pressures and resultant pyelovenous backflow?

Running irrigation fluid solely by gravity may mitigate concerns about increased intrapelvic pressures and pyelovenous backflow. Manual pump irrigation to improve visualization invariably leads to increased pressures within the collecting system. One potential solution is to combine gravity drainage and the use of a single action hand pump only at times where increased visualization is needed during ureteroscopy. In an in vitro study, multiple irrigation systems were evaluated and, besides gravity irrigation, the single action irrigation pump exerted the least amount of maximal force during use. The benefit of using a single action irrigation pump can be twofold in that stone migration can be minimized compared to continuous pressurized irrigation.

Effects of irrigation and as a consequence intrapelvic pressures can be magnified in the case of percutaneous nephrolithotomy (PCNL), as some of these patients are at higher baseline risks of sepsis prior to the operation. With the recent addition of mini-PCNL to the endourologist’s armamentarium, the question becomes, “is it safe?” In porcine models, mini-PCNL was associated with higher intrapelvic pressures and higher bacterial seeding compared to standard PCNL. Clinical studies are limited in terms of evaluation of intrapelvic pressures and sepsis risks for mini versus standard PCNL. Investigators from China reported an inverse relationship to percutaneous renal sheath diameter and intrarenal pressure, with higher pressures (>20 mmHg) associated with a higher risk of postoperative fever. Head-to-head prospective trials are underway to try to answer this very question regarding both safety and efficacy to each technique. While concerns about sepsis with PCNL exist, irrigation by gravity and adjunct measures to limit pressure increases (i.e. ureteral access sheaths) can be utilized to lower sepsis risks.

Until pressures can be obtained from the collecting system during endoscopic stone surgery, the recommendation would be to limit operating room time, utilize as much gravity irrigation as possible and maintain optimal outlets for drainage during the case to balance inflow of irrigation with outflow.


Vaginal Remnants after Transmasculine Gender Affirmation Surgery

University of Belgrade and Belgrade Center for Genitourinary Reconstructive Surgery

Marta R. Bizic, MD, PhD
Miroslav L. Djordjevic, MD, PhD

There has been an increased number of requests for gender affirmation treatment (GAT) worldwide in the last decade. Gender affirming treatment has a multidisciplinary approach and involves mental health support, hormonal treatment and surgical treatment, which together lower the level of dysphoria and distress for these individuals.

Transmasculine gender affirmation surgeries (TGAS) are still challenging, as the creation of the neophallus with functional urethra is the most demanding step in surgical treatment. There are 2 main surgical approaches in TGAS available today: metoidioplasty and phalloplasty. Metoidioplasty denotes the creation of the neophallus out of the hypertrophied clitoris, while phalloplasty presents the surgical creation of a larger neophallus using extragenital tissue in various forms of local pedicled or distant

Continued on page 9
Vaginal Remnants after Gender Affirmation Surgery

Continued from page 8

A review of the available literature suggests that patients undergoing TGAS with urethral reconstruction have a higher chance of developing some form of postoperative complications related to the neourethra because of the different anatomy and histology of this “man-made” urethra when compared to cisgender. The most common complications after urethral reconstruction in TGAS are urethral fistula and urethral stricture, and complication rate varies from 10% to 78%. Diagnosis of a vaginal remnant can be made using retrograde urethrogram and voiding cystourethrogram with the definition of vaginal remnant size (fig. 1). The treatment of choice is complete excision of rejuvenated vaginal mucosa with subsequent urethroplasty by closing any fistulous tracts. Furthermore, there is no consensus on the best surgical technique for vaginal remnant management. The use of the perineal approach in combination with flexible endoscopy provides good visibility for the vaginal remnant to be completely excised and closed with final reconstruction of the perineum (figs. 2 and 3).

Different methods include the robotic transabdominal approach for performing the dissection between the bladder and rectum, with vaginal mucosa excision and closure. Recurrence of the repaired vaginal remnant is very rare—and has not been reported in the literature data so far—but may require repeated surgical repair.

There are a lack of literature data regarding vaginal remnant rates in transmen after colpectomy and TGAS. Causes may be different, from asymptomatic cases long after primary genital reconstructive surgery to cases presented to reconstructive urologists not primarily involved in these patients’ TGAS. Despite the increased need for TGAS worldwide, patients should also be provided with information regarding the possibility of local followup and possible treatment of urological complications as the most common in TGAS.

Virtual Resident Education in the Era of COVID

Nora G. Kern, MD
University of Virginia

When the COVID-19 pandemic emerged in March 2020, the majority of in-person activities, including clinical care and educational conferences, came to a screeching halt. With hospitals required to stop all elective surgeries and clinic visits, telemedicine was quickly assimilated into clinical practice and was widely utilized. Similarly, training programs struggled to provide adequate education to residents who were predominantly furloughed to reduce person-to-person contact. The primary challenge was faculty at each institution were unable to provide enough new educational content to residents to make up for the lost time previously spent on both in-person conferences and clinical care experiences. Thankfully, through great innovation and collaboration, institutions started to realize the importance of pulling resources together to form educational consortium groups.

Following otolaryngology’s collaboration starting at the University of California-San Francisco (UCSF), the collaborative online video didactics (COVID) lecture series was created for urology. The group was composed of program directors and faculty members at UCSF, the University of Washington, the University of California-Davis, Stanford University, the University of Minnesota, the University of Michigan, Northwestern University, and the University of Virginia. An initial outreach email was sent on March 22, 2020 and the first COVID lecture was delivered to residents nationwide on March 30, 2020. Two lectures were available every weekday from March to September 2020, after which lectures were held on a weekly basis. These lectures were available via live Zoom sessions and then made publicly available on YouTube for later viewing.

Shortly after creation of the COVID lecture series, the New York Section of the American Urological Association (AUA) created the Educational Multi-institutional Program for Instructing Residents (EMPIRE) lecture series. This coalition differed from the COVID lecture series in that it was a trainee-led initiative, and the lectures were preceded by a brief mentoring session with the session’s speaker. The intent was to promote networking and provide opportunities to the viewers to encourage camaraderie and interaction. Other sections of the AUA and sub-specialty groups began their own initiatives for online virtual learning. The Mid-Atlantic section of the AUA started UroBrief, a series of short videos on high yield topics, many that focus on in-service preparation. Pediatric urologists formed PedsUroFLO (Pediatric Urology Fellowship Lectures Online) as a spin-off from the COVID series, also housed at UCSF. Endourologists created EDGE (Endourology Disease Group for Excellence) talks, andrologists created SMILES (SSMR Male Infertility Lecture Education Series), and reconstruction specialists at Case Western created Genitourinary Reconstruction Online Learning Series. Virtual learning became a huge phenomenon as a result of the COVID shutdown.

But what happens now as the pandemic slowly subsides? Practices have been picking up their volumes again, some exceeding their normal volumes to make up for lost time. Are these virtual learning programs valuable enough to continue running at full steam? Or like the COVID-19 virus, will online lectures also fade away? Certainly the cost to organize these endeavors is not trivial. These lecture series require immense organization and time from the consortium group to select speakers, schedule lectures, advertise the event, coordinate the production of the lecture, post the recording for later viewing etc. Furthermore, the lecturers devote time to preparing and delivering the lecture, and the learners devote time to watching the lectures. This is made even more difficult with schedules normalizing after the initial shutdown. However, the bright side is that residents do seem to value the new wave of learning.

Viewers of the COVID lecture series overwhelmingly felt the sessions were useful to their learning and education (fig. 1), and in a different survey to residents, the majority felt the lecture series had a large or very large impact on their education (fig. 2). Additionally, learners do appear to benefit from online learning. Multiple studies prior to the pandemic have cited equal effectiveness of video lectures compared to in-person learning. In unpublished data, urology residents scored higher on a knowledge-based test after watching COVID lectures, and a greater improvement in test scores was seen with the more lectures that were watched. This may support the continuation of virtual learning and the value it may have for resident education.

Despite the devastation that COVID-19 has caused on the world, the silver lining for urology residents has been the accessibility to online lectures provided by experts in the field and outside their own training programs. While unable to travel to national and regional conferences, residents, students, and faculty were able to gain educational content through these lectures right in their homes. The future of these novel programs is unknown, but one can hope for a hybrid model of in-person learning along with these online lectures to continue to provide residents with this valuable resource. At the very least, a large collection of these archived lectures is available for years to come, and perhaps residents will continue to think of these lectures...
## AUA TAKE 5 — THE TOP 5 AUA HAPPENINGS THIS MONTH!

1. **Join the AUA for Summer School!** Each week from June through August 2021, the AUA will release two live instructional course webinars on topics that span the spectrum of urology. It’s a perfect way for urology health care professionals who find themselves with unpredictable schedules and travel restrictions to find opportunities for continuing education. Register today!  
   [AUA2021.org/SummerSchool](http://AUA2021.org/SummerSchool)

2. **Calling all APP and Allied Health Professional members — AUA’s new APP & Allied Network online community is for you!** Connect with peers about clinical questions, career advice and everything in between in this new, members-only and private online forum sponsored by the APP Membership Committee. Learn more!  
   [AUAnet.org/APPAlliedNetwork](http://AUAnet.org/APPAlliedNetwork)

3. **The Journal of Urology® and Urology Practice** now offer a full suite of author services! Once your paper is accepted, you will have the option to purchase video and visual abstracts, cover posters featuring your article’s artwork and more. Learn more!  
   [authorservices.auajournals.org/](http://authorservices.auajournals.org/)

4. **Put your advocacy in action!** Join the AUA on July 20 and 21 for the popular AUA Annual Urology Summit! There has never been a more critical time to engage in the legislative process. You don’t need to travel to Washington to participate in our Virtual Hill Day. Register for free today!  
   [AUASummit.org](http://AUASummit.org)

5. **Purchase the 2021 Update Series and improve your practice and patient care with 40 lessons on the most up-to-date urological advances!** Take advantage of this convenient, easy-to-access educational product that fits your individual learning style. Learn more!  
   [AUAnet.org/Update](http://AUAnet.org/Update)
As the therapeutic options for patients with nonmuscle invasive bladder cancer (NMIBC) expand,1 choosing the right treatment at the right time for the right patient becomes increasingly challenging. Providers must consider NMIBC risk stratification, the reported efficacy of potential treatments, side-effect profiles, costs, and logistical concerns such as the burden of scheduling, as well as patient goals. Frequent bacillus Calmette-Guérin (BCG) supply shortages and the lack of clinical trials directly comparing novel therapies further complicate decision making.

Cost-effectiveness analyses (CEA) represent a relatively underutilized yet powerful technique that has the potential to improve care for NMIBC patients. While commonly used to comment on the pricing of interventions, cost-effectiveness analyses can more importantly integrate the spectrum of clinically relevant information to inform guideline recommendations and treatment decisions for NMIBC.

Cost-effectiveness analyses—or, more appropriately, cost-utility analyses—assimilate information on the quality and quantity of life as well as cost for each treatment option. The Appendix outlines basic definitions of CEA terminology.2 A common CEA format utilizes Markov models with relevant “health states” downstream of each treatment option. The figure is a schematic of sample NMIBC health states such as recurrence, progression, and toxicity. Each health state is ascribed unique costs and a utility value, which reflects the quality of life for the given state. The probability of transitioning between health states for each time cycle in the Markov Model is derived from oncologic and toxicity data from the literature. The utility values for all health states downstream of a treatment are then summed in a probability-weighted manner for every time cycle to calculate the quality-adjusted life-years (QALYs) for the given treatment. A similar summation is performed for costs. The “expected” QALYs and costs for treatments can then be compared using the Incremental Cost-Effectiveness Ratio (ICER), which is the difference in cost divided by the difference in QALYs between 2 treatments. Treatments with an ICER of less than $100,000 per additional QALY (the conventional willingness to pay threshold) are considered cost-effective.

Although this approach may seem abstract, the resulting models are particularly useful in NMIBC decision making. For example, given frequent BCG shortages, and the resulting emphasis on conservation and appropriate allocation of supply,3 we conducted a CEA evaluating maintenance BCG for intermediate and high risk NMIBC.4 We found that maintenance BCG only became cost-effective if it reduced 5-year progression by at least 2.1%. Given the modest effect size of maintenance BCG on progression, we reasoned that maintenance BCG is likely only cost-effective for subsets of high risk NMIBC with a significant risk of 5-year progression and can likely be foregone for intermediate risk NMIBC, especially during times of BCG shortage. In fact, further probabilistic sensitivity analysis demonstrated that maintenance BCG was only cost-effective in ~17% of intermediate and high risk NMIBC simulations. In this way, the CEA not only identified which patients would benefit most from maintenance BCG treatments, but also aligned with American Urological Association policy statements on the matter.3

Moreover, determining treatment for patients with BCG-unresponsive NMIBC represents another significant opportunity for CEA utilization. Here, the decision making remains challenging as the U.S. Food and Drug Administration has permitted single-arm trials to be used for agent approval,4 causing the number of agents being tested in this disease space to increase rapidly. CEAs thereby offer the opportunity to contextualize the results of the existing and emerging single-arm trials to standards of care, such as radical cystectomy or salvage intravesical chemotherapy. As a proof of concept, we recently evaluated the cost-effectiveness of pembrolizumab relative to radical cystectomy and intravesical gemcitabine-docetaxel for patients with BCG-unresponsive carcinoma in situ.2 We found that pembrolizumab was not cost-effective relative to radical cystectomy (ICER $1,403,008) or intravesical gemcitabine-docetaxel (ICER $2,011,923), regardless of cystectomy eligibility status. Its marginal benefit (0.10 QALYs) over radical cystectomy was not justified by its high cost and high risk of adverse events. In fact, a greater than 90% price reduction would be required to render pembrolizumab cost-effective for this indication. However, we did find that intravesical gemcitabine-docetaxel, based on retrospective multi-institutional data,4 was cost-effective in about 46% of simulations vs radical cystectomy and warrants further study as a treatment option. Thus, by quantifying the balance of side-effects, oncologic benefit, and cost relative to existing standards of care, CEAs can help interpret single-arm trial data for BCG-unresponsive NMIBC patients.1

Cost-effectiveness analysis (CEA) represents a relatively underutilized yet powerful technique that has the potential to improve care for NMIBC patients. While commonly used to comment on the pricing of interventions, cost-effectiveness analyses can more importantly integrate the spectrum of clinically relevant information to inform guideline recommendations and treatment decisions for NMIBC.

Figure. Hierarchy illustrating several of common health states typically experienced by patients with NMIBC. Note: this representation is not intended to be a Markov Diagram demonstrating transitions possible from one health state to another.
Cost-Effectiveness Analyses in NMIBC

NMIBC and guide future treatment selection. Other potential uses for CEAs in BCG-unresponsive NMIBC include testing the relative importance of various oncologic endpoints over complete response thresholds, which may improve trial design.6 In addition, CEAs may be incorporated into shared decision making tools (akin to WiserCare© in prostate cancer) that weigh treatment risks and benefits according to an individual patient’s preferences to help patients decide between treatment options. CEAs may also provide rough estimates of expected costs for patients, thereby assisting in patient counseling. Considering that NMIBC is one of the most expensive cancers on a per-patient level, CEAs can as well inform personalized surveillance schedules for NMIBC patients. Importantly, CEAs are limited by the quality of data used for the modeling, including the oncologic and cost data sources. A particularly critical limitation is the utility value data, which can vary widely depending on the method used to derive the utility values9 and thus alter expected QALY calculations.10 Nevertheless, this limitation may be addressed by encouraging the collection of utility value assessments along with patient-reported outcome questionnaires in clinical trials. In addition, sensitivity analyses varying utility values over broad ranges can be conducted to determine how susceptible the model is to small changes in utility values (see table).

In summary, cost-effectiveness analyses offer the opportunity to quantify the costs, toxicity and oncologic benefit of NMIBC treatments, facilitating both an understanding of treatment tradeoffs and the comparison of novel agents to existing standards of care. Sensitivity analyses may further identify subsets of patients for whom a given treatment may be preferred, thereby enabling more personalized treatment recommendations. In this manner, CEA represents a tool to assist clinicians as well as guideline panels in interpreting data and individualizing options for NMIBC patients.

Appendix. Review of CEA terminology.

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition/Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health State/Markov Node</td>
<td>A clinical state/scenario that can be found after the given treatment. Generally, the more granular and comprehensive the list of health states modeled, the higher the quality of the CEA. The figure displays common health states in NMIBC. Although it is easier to think of health states as mutually exclusive, compound health states are also possible, for instance patients with both recurrence and treatment toxicity.</td>
</tr>
<tr>
<td>Time Cycle/Markov Cycle</td>
<td>Corresponds to the number of iterations that participants are allowed to transition between health states. The amount of time per cycle varies based on the clinical question ranging from days to years. For NMIBC, we have chosen to use 3-month time cycles to correspond with common cystoscopic surveillance and therapy schedules.</td>
</tr>
<tr>
<td>Time Horizon</td>
<td>The number of time cycles of the model that are completed before calculating the model outputs. Often this corresponds to clinically meaningful time points specific to the given cancer. When possible, a lifetime horizon is also useful to characterize the impact of an intervention over the remaining life of a patient. Such structures allow assessment of delayed impacts of interventions but also require adding more assumptions into the model.</td>
</tr>
<tr>
<td>Transition Probability</td>
<td>The chance of moving from one health state to another between successive time cycles. Probabilities reported in the literature (such as 5-year risks recurrence/progression) are first converted to rates and those rates are then used to calculate per-cycle transition probabilities.</td>
</tr>
<tr>
<td>Cost</td>
<td>Usually represents the monetary cost of a given treatment and a given health state. A CEA from a payer/insurer perspective generally only considers the direct costs borne by the entity. But CEAs from a societal perspective also account for other sources of financial strain, such as patient out-of-pocket costs and indirect costs such as lost wages, caregiver productivity loss and travel time.</td>
</tr>
<tr>
<td>Utility Value</td>
<td>A value between 0 and 1 that represents the quality of life of a patient in a given health state, with 1 being perfect quality of life. This can be assessed with several methods, such as a rating scale, visual analog scale, formulaic conversion from quality of life questionnaires, time tradeoff, and standard gamble – each with its own set of pros and cons.9</td>
</tr>
<tr>
<td>QALY</td>
<td>The Quality Adjusted Life Year is a summation of product of the utility value and the time spent in a given health state across all health states downstream of a treatment option. Expected QALYs, also referred to as the “effectiveness” in CEAs, are then reported for each option at the final time horizon.</td>
</tr>
<tr>
<td>ICER</td>
<td>The Incremental Cost Effectiveness Ratio is a summary measure comparing two options within a CEA. It is calculated by dividing the difference in costs by the difference in QALYs for two options (eg A or B): ICER_{AB} = (C_A − C_B)/(QALY_A − QALY_B).</td>
</tr>
<tr>
<td>WTP Threshold</td>
<td>The Willingness-to-Pay Threshold represents a monetary cost a particular society is willing to pay for one additional QALY. For the US, this is frequently $100,000 per QALY but can range from $50,000 to $150,000 per QALY. If the ICER of a treatment is less than the WTP, then that treatment is considered cost-effective.</td>
</tr>
<tr>
<td>One-Way Sensitivity Analysis</td>
<td>Individual model inputs (usually costs, utility values, and transition probabilities) are varied over large but biologically plausible ranges to determine the threshold at which model conclusions change. Frequently depicted as Tornado Diagrams.</td>
</tr>
<tr>
<td>Probabilistic Sensitivity Analysis</td>
<td>Monte-Carlo simulations in which input values are simultaneously varied within pre-specified distributions bounded by ranges used for one-way sensitivity analyses. The number of simulations are usually between 1,000 and 100,000, and entire CEA is re-run for each simulation to produce estimates of the percent of simulations in which a given treatment was cost-effective.</td>
</tr>
</tbody>
</table>

Virtual Resident Education

fondly as they eradicate the memory of COVID-19 forevermore.◆

Upper tract urothelial carcinoma (UTUC) comprises 5% to 10% of urothelial malignancies but demonstrates unique clinical and molecular characteristics compared to urothelial carcinoma of the bladder (UCB). While histologically similar, UTUC and UCB are now considered “disparate twins” based on our increasing knowledge of their biological differences. The advent of next-generation sequencing (NGS) has enabled further molecular characterization of urothelial tumors, with initial efforts focused on bladder tumors and then extrapolated to UTUC. Urologists must be aware of the clinical implications of UTUC genomics. 

Prior work by our group and others used bulk sequencing of tumor tissue to identify the most common somatic DNA alterations present in UTUC, demonstrating a high incidence of potentially actionable genomic alterations including FGFR3 (48%), KDM6A (38%), KMT2D (26%), TERT (26%), TP53 (25%), ARID1A (20%), PIK3CA (16%), TSC1 (14%), HRAS (12%), and ERBB (9%; fig. 1). Higher stage (pT2) UTUC was associated with more frequent activating alterations in TP53 and MDM2, while lower stage disease was characterized by more frequent FGFR3 and HRAS alterations. Whole transcriptome RNA expression analysis of a subset of these tumors demonstrated that 82.5% possessed a luminal-papillary molecular phenotype based on the consensus classifier developed by the Bladder Cancer Molecular Taxonomy Group. When compared to UCB, the overall spectrum of somatic alterations is similar, but there are notable differences with significantly more frequent alterations in FGFR3 and HRAS in UTUC, vs TP53, RB1 and ERBB2 in UCB (fig. 2). Intravesical recurrence is relatively common in UTUC, with 22% to 47% of patients developing a bladder tumor. Our group investigated this relationship further in 29 matched pairs of UTUC and UCB tumors, finding that alterations in FGFR3, KDM6A, CCND1 and TP53 were associated with an increased risk of recurrence and that all pairs were deemed to have a shared clonal origin, suggesting drop-down intravesical seeding. This finding emphasizes the importance of limiting the risk of lower tract seeding with such steps as early clipping of the ureter during nephroureterectomy, evidence-based use of intravesical chemotherapy, and judicious use of ureteroscopy and postoperative stenting.

While sporadic UTUC is much more common, UTUC is known to be associated with Lynch syndrome, a hereditary cancer syndrome characterized by germline mutations in mismatch-repair (MMR) associated genes which results in tumors with microsatellite instability (MSI) and hypermutation. Lynch-associated UTUC tumors may account for up to approximately 20% of all newly diagnosed UTUC and, without targeted testing, many tumors may be misclassified as sporadic. UTUC tumors in Lynch patients demonstrate a higher tumor mutational burden (TMB) compared to sporadic UTUC, even those with MMR alterations. This can have profound treatment implications as MSI tumors with high TMB demonstrate better response to immunotherapy. National Comprehensive Cancer Network® guidelines currently recommend germline testing...
Urothelial Carcinoma Genomics

DNA testing be considered for all UTUC patients younger than 60 at presentation or with a family history of colon/endometrial cancer. However, given the implications and published age ranges of newly diagnosed cases, our institution and others advocate for broader testing of all UTUC patients to promote increased detection of occult Lynch syndrome prompting appropriate counseling, screening and testing. While sequencing of tumor tissue provides clinically relevant information, characterization of the tumor immune microenvironment provides additional insight into tumor biology and behavior. Using bulk RNA sequencing, Robinson et al demonstrated that 28 of 32 UTUC tumors analyzed had a T-cell depleted phenotype. Notably, this immune phenotype was associated with upregulated FGFR3 signaling, suggesting a central role of this pathway in shaping the UTUC immune contexture and a potential therapeutic target with targeted agents such as erdafitinib.

However, bulk genomic characterization of UTUC has some limitations due to intratumoral and temporal heterogeneity. Sequencing 1 area of the tumor may not adequately represent the remainder of the disease burden. Similarly, biomarker data may be influenced by sampling techniques and prior therapy. To overcome these limitations, there is increasing interest in single-cell and spatial multi-omics paired with computational methods to more comprehensively characterize these tumors and their immune microenvironment with the goal of better characterizing tumor immune biology and identifying reliable and predictive biomarkers.

Our understanding of the genomics of UTUC will continue to grow with widespread molecular profiling and collaborative research. Increasing clinical utilization of genomic profiling for UTUC will facilitate better screening for hereditary disease, identifying candidates for systemic therapies, and hopefully increasing the ability to provide kidney-sparing treatments to a select group of patients. As urologists, understanding these clinical implications is paramount as we strive to provide the best care for these complex patients.
Management of Primary Carcinoma of the Urethra

Epidemiology and Risk Factors

Primary urethral carcinoma (PUC) is a rare malignancy with potentially devastating consequences for patients for both treatment and mortality. The incidence is approximately 4.3 per million and 1.5 per million for men and women, respectively. Risk factors, histopathology, and treatment have gender based differences due to the anatomical and embryological distinctions between the male and female urethra. However, in both genders, advanced age (>60 years) is a significant risk factor.

Male PUC is more common in African Americans than Caucasians. The most common risk factor is chronic urethral irritation with urethral stricture, which can be found in up to 50% of men with PUC. The male urethra can be divided into the anterior urethra, which consists of the fossa navicularis, pendulous urethra, and bulbar urethra, and the posterior urethra, which consists of the membranous urethra and prostatic urethra. The anterior urethra is lined by stratified squamous epithelium, which transitions to stratified and pseudostratified columnar epithelium. The posterior urethra is lined by urothelium. As such, tumor histology varies by location of primary carcinoma, with urothelial carcinoma accounting for the majority of cases, followed by squamous cell and adenocarcinoma.

Female PUC is exceedingly rare and, as such, relatively little is known about underlying causes. However, a urethral diverticulum may predispose women to PUC. The female urethra is approximately 4 cm long, with the distal 2/3 lined by nonkeratinizing stratified squamous epithelium and the proximal third lined by urothelium. There is approximately equal prevalence of urothelial, squamous cell, and adenocarcinoma, with adenocarcinoma more likely to be found in women than men and serving as the predominant histology found within urethral diverticulum.

Clinical Presentation, Diagnostic Evaluation and Staging

The majority of patients present symptomatically with obstructive voiding uropathy, hematuria, or a penile/vaginal or perineal mass. All patients with suspected urethral cancer should undergo an examination under anesthesia with bimanual examination, a thorough examination of the external genitalia, including urethra, rectum, perineum, and inguinal nodes to assess for lymphadenopathy. Cystoscopy should be performed in all patients and a tissue diagnosis is necessary. Transurethral, transvaginal, or percutaneous needle biopsies are all acceptable methods of tissue sampling. Patients should undergo cross-sectional imaging of the abdomen and pelvis with a computerized tomography scan or magnetic resonance imaging (MRI). Though either imaging modality is acceptable, MRI provides superior soft tissue resolution and can allow for more accurate local staging (fig. 2). The American Joint Committee on Cancer (AJCC) urethral tumor, node, metastases (TNM) staging is based on the depth of invasion, presence or absence and number of nodes, and distant metastasis (see Appendix).

Management of Primary Urethral Carcinoma

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Disease Management

Male Anterior Urethra

Distal PUC (ie within the fossa navicularis or penile urethra) is often curable with aggressive local control, and because of this, penile preservation therapy has been explored. Tumor excision with a distal urethrectomy with or without a partial glansectomy is acceptable for localized cancers ≤T2N0M0.1 While historically a 1-cm negative margin has been required, a 5-mm negative margin is sufficient for cancer control.4 Care must be taken to ensure the proximal margin is negative if performing a partial urectomy. Patients with positive surgical margins may have a repeat resection, or undergo chemotherapy or radiation (XRT). Further, patients who refuse surgery may be treated with primary XRT. These patients should undergo prophylactic XRT to the inguinal lymph nodes as well. In contrast, patients with clinically node negative disease undergoing surgical excision are not required to have prophylactic inguinal lymph node dissection.3

Patients with advanced disease of the distal urethra (≥T3) should be considered for chemoradiation with or without surgical resection. Patients treated with 45–55 Gy of external beam radiation and systemic 5-FU and mitomycin C can have a 5-year disease specific survival of up to 68%.2 Patients with node positive disease should also undergo either inguinal lymph node dissection on the side of clinically positive disease, or be treated with both modalities.

Tumors arising from the proximal (bulbar) anterior urethra are not only more common than distal urethral tumors, but also have a much higher mortality, with survival rates as low as 20%–30%.5 Because these tumors typically present at a later stage, they often require aggressive surgical management with a urethrectomy with or without a cystoprostatectomy, pelvic lymphadenectomy, and total penectomy. In patients with advanced disease, surgical monotherapy has a poor overall 5-year survival of 26%. As the surgery itself is extremely debilitating, patients with advanced disease may consider chemoradiation as a primary modality of treatment (fig. 3).

Male Posterior Urethra

Men with posterior (prostatic) PUC should be evaluated for synchronous urothelial cancer of the bladder and upper tracts. Patients with T1-T3-T1 disease can be managed with complete transurethral resection of the prostate followed by induction BCG. Patients with stromal invasion (pT2) or more advanced disease should undergo neo-adjuvant cisplatin based chemotherapy followed by radical cystoprostatectomy with urethrectomy and pelvic lymphadenectomy (fig. 3).3

Female Urethra

Given the rarity of female PUC, the ideal treatment does not have robust supporting data. Tumors of the anterior urethra are typically low stage and can be cured with endoscopic resection or laser fulguration +/- bacillus Calmette-Guérin. Small, exophytic anterior tumors may be excised transvaginally with a portion of anterior vaginal wall. Because of the short female urethra, partial urethrectomy does carry a significant risk of incontinence. For more aggressive tumors of the anterior urethra, a radical urethrectomy with bladder neck closure and creation of a stoma may be employed.6 Radiation monotherapy is also an option for low stage anterior tumors.7 A prophylactic lymph node dissection is not generally performed. In the case of lymph node metastasis, aggressive multi-modal therapy with radiation, chemotherapy, and surgical excision should be employed.3

Posterior female PUC is typically advanced stage and aggressive. Surgical therapy involves an anterior pelvic exenteration. Surgery and radiation alone have similarly low rates of control and survival outcomes. As such, these patients should be treated with multimodal therapy including radiation, chemotherapy, and consolidative surgery (fig. 3).8

Followup

Given the rarity of PUC, ideal followup has not been critically studied. Generally, patients with urethra sparing surgery should undergo periodic urinary cytology.

Table. Median survival by histological subtype and sex.

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urothelial carcinoma</td>
<td>55 (mos)</td>
<td>48 (mos)</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>55 (mos)</td>
<td>48 (mos)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>53 (mos)</td>
<td>38 (mos)</td>
</tr>
<tr>
<td>Overall 5-yr survival</td>
<td>48%</td>
<td>32%</td>
</tr>
<tr>
<td>Overall 10-yr survival</td>
<td>43%</td>
<td>29%</td>
</tr>
</tbody>
</table>

Figure 2. MRI of posterior urethral tumors of male (a) and female (b).

Figure 3. Management algorithm adapted from European Association of Urology (EAU) guidelines on primary urethral carcinoma, 2020, with permission. TUR, transurethral resection. CT, computerized tomography. BCG, bacillus Calmette-Guérin.
Color Duplex Doppler Ultrasonography in the Current Management of Erectile Dysfunction: What/When/How

Ultrasonography has gained significant importance in the evaluation of organ systems, and often leads to the diagnosis of diseases and conditions without exposure to ionizing radiation. The use of ultrasonography in the management of erectile dysfunction (ED) is well established and dates back to the early 1990s. Advances in this technology now allow for submillimeter evaluation of anatomical structures and real-time evaluation of blood flow in small vessels. While ultrasonography is now the primary imaging modality used for evaluating anatomical and functional changes of the penis in the setting of ED, its utility and popularity have changed over the last 30 years.

ED is defined as the inability to attain and/or maintain an erection sufficient for sexual satisfaction. ED is generally divided into organic and psychogenic types, and within the organic category ED can be caused by abnormalities in blood flow. Vasculogenic ED is the most common cause of organic ED and accounts for approximately 30%–50% of cases. Penile arterial insufficiency, venous leak, or a combination of the two define vasculogenic ED and can be diagnosed using imaging modalities. Prior to ultrasound, arteriography and dynamic infusion cavernosometry/cavernosography were the gold standard in diagnosing arterial insufficiency and veno-occlusive disease. The advent of color duplex Doppler ultrasonography (CDDU) consolidated both studies into 1 and made diagnosing vasculogenic ED a much simpler and conventional process without venous contrast or radiation exposure.

Penile ultrasonography for the evaluation of ED is done with the patient in the supine position and with the assistance of erectogenic medications injected directly into the corpora cavernosa. In our practice we inject approximately 10 mcg of alprostadil and rarely redose in order to minimize the risk for priapism, hematoma, pain, and hypotension. The patient is then given privacy and encouraged to self-stimulate prior to starting the examination. A 12 MHz linear transducer is then used to evaluate penile anatomy and hemodynamics in both the longitudinal and transverse views. Cavernosal artery blood flow is evaluated by placing the probe at the most proximal area of the penis, typically at the penoscrotal junction, in order to minimize the effect intracavernosal pressure has on peak systolic and end diastolic velocities. We ensure the probe is tilted at an angle of under 60 degrees with respect to the penis in order to capture accurate hemodynamic readings. A peak systolic velocity (PSV) of >35 cm/s is considered normal, <25 cm/s is suggestive of arterial insufficiency, and a value between 25 and 35 is considered a gray zone and should be interpreted with caution. In younger men, sympathetic overtone from psychological stress can affect the PSV and appear to be within the indeterminate or even low range. The end diastolic velocity of the cavernosal artery is also measured and a value of >5 cm/s suggests a venous leak. Additional values such as the resistive index, systolic rise time, and acceleration time of blood flow within the cavernosal arteries can help paint a more defined picture of flow variations that may be present. While CDDU provides a detailed assessment of fluid dynamics and anatomical evaluation of the penis, its utility has come into question when evaluating patients with ED.

The 2018 AUA Guideline for ED outlines the conditions in which CDDU can be used to help guide treatment. The recommendation, based on expert opinion, states that patients who are young, have a strong family history of cardiac illness, history of pelvic trauma, failed prior ED therapies, a strong likelihood of primary psychogenic ED, concomitant Peyronie’s Disease (PD), or have had lifelong ED can benefit from CDDU. In our practice, we most commonly employ CDDU to guide treatment for patients who have failed prior ED therapy and wish to explore alternative treatments. This is especially true for those who are under 40 years of age, have suffered prior pelvic trauma, have undergone prior prostate, bladder, or rectal surgery, or have penile deformities suggestive of PD or have confirmed PD. Penile ultrasonography may also have the added benefit of identifying men at a higher risk for cardiovascular disease, findings that include cavernosal artery calcifications or intimal thickening (see figure). While the frequency in which CDDU is performed has decreased since the widespread adoption of phosphodiesterase type 5 inhibitors, it continues to serve a purpose, but under more defined criteria. Ultimately, it is important to ask whether the examination results will guide subsequent medical or surgical treatments, or elucidate early or silent cardiovascular disease.


Management of Primary Urethral Carcinoma

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urethrocystoscopy, and cross-sectional imaging. Patients generally have a poor prognosis with less than 50% 5-year survival (see table).1,2

Predicting the Need for CIC and Its Effect on Renal Replacement Therapy in Posterior Urethral Valves

Posterior urethral valves (PUVs) are a leading cause of pediatric end-stage kidney disease (ESKD) and renal transplantation in children. The eventual fate of the kidneys is a cumulative result of a multitude of factors, which include decreased nephron mass at birth, lower urinary tract dysfunction (LUTD) and recurrent infection. A proposed serum surrogate of nephron mass at birth, lower urinary tract dysfunction (LUTD) and recurrent infection. A proposed serum surrogate of nephron mass for young PUV patients is the serum nadir creatinine in the first year of life (SNC1). In a multicenter cohort of early diagnosis and treatment of PUV, all boys with a SNC1 ≥1 mg/dl required renal replacement therapy (RRT) by 8 years of age, while no child with a SNC1 <0.4 mg/dl progressed to RRT with median age at followup of 6 years. This was in sharp contrast to the variable course of kidney disease progression in those children with SNC1 0.4–0.99 mg/dl. Accordingly, in patients with PUV in the SNC1 range of 0.4–0.99 mg/dl, there may exist greater potential to modify disease course and prevent or delay a tenuous kidney homeostasis from progressing.

LUTD is prevalent in PUV. Typical bladder patterns in pediatric PUV patients range from a high capacity and poorly emptying bladder in adolescence. This phenomenon has been described as the valve bladder. Multiple strategies to combat this LUTD in PUV patients have been utilized ranging from timed and double voiding to pharmacotherapies such as antimuscarinics and/or alpha blockers. Implementation of clean intermittent catheterization (CIC) with or without nighttime bladder emptying (NBE) is also often initiated due to concerns for significant LUTD and/or polyuria, with the goal of preserving bladder and kidney function. Furthermore, introduction of CIC may provide urinary continence in these children, which can have psychosocial benefit. Evidence suggests that both CIC and NBE are feasible and have potential benefit in patients with PUV. Introduction of catheterization of any type in patients with PUV, especially in older children, can be challenging given their senesce urethra. CIC introduced early can circumvent this issue, as can a surgically created abdominal catheterizable channel (ie Mitrofanoff).

The ESKD observed in PUV patients is due to a combination of unmodifiable factors such as renal hypoplasia/dysplasia and potentially modifiable factors such as urinary tract infection and LUTD. While numerous retrospective studies have shown that CIC can ameliorate LUTD, there exists conflicting evidence demonstrating that CIC unequivocally delays chronic kidney disease (CKD) progression or ESKD incidence. These mixed results may in part be due to patient selection where CIC is preferentially implemented in children with more severe disease who are less likely to show kidney benefit from the intervention. This highlights the importance of individualized treatment plans based on risk stratification.

Determining which child would ultimately benefit from initiation of CIC or NBE as a method to impede progression of CKD is a particularly challenging aspect of PUV management. Holmdahl proposed, and we agree, the easiest age to start CIC is during year 1 when there is less expectation of pain or fear of catheterization. However, variability exists between providers across the management spectrum of PUV, including indications to initiate CIC or NBE. On an internal audit of provider practice patterns within our Pediatric Urology Midwest Alliance we found initiation of bladder drainage ranged from 5% to 54% depending on institution. This

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Is Routine Postoperative Urethrography Following Urethroplasty Necessary?

Andrew J. Cohen, MD
The Brady Urological Institute
The Johns Hopkins School of Medicine

X-ray urethrography characterizes urethral strictures for those patients with urethral stricture disease. As strictures are often impassable by cystoscopy, such studies are necessary to understand stricture length for operative planning. X-ray urethrography can be performed in a retrograde (RUG) fashion or matched with a voiding cystourethrogram (VCUG), which can be particularly informative for visualizing the posterior urethra. While sonography and magnetic resonance imaging are increasingly used, urethrography remains the undisputed preoperative test of choice.

In contrast, the role of urethrography in the postoperative period is evolving. Urethrography after urethroplasty has traditionally been used to confirm a well-healed anastomosis. The presence of extravasation often results in a clinical decision to increase the duration of catheterization. Of late, there is growing evidence that extravasation may reveal extravasation. Furthermore, patients with longer strictures and complex repairs including grafts were more likely to have extravasation detected. Extravasation on postoperative urethrography was strongly correlated with anatomical recurrence at 1 year. Of course, the relationship between anatomical recurrence identified on cystoscopy and functional recurrence requiring repeat procedure is yet another controversy. Indeed, another recent retrospective single center series noted extravasation was not predictive for stricture relapse accounting for stricture etiology, location, length and type of surgery in multivariate analysis among 630 patients (HR: 1.57, 95% CI: 0.8–3, p=0.173).

One criticism of available studies is a question of heterogeneous techniques: pull-back RUG, peri-catheter RUG, or VCUG are all options after catheter removal. Over pressurization may reveal extravasation that would not otherwise be present with physiological voiding pressures. Under pressurization may lead to false-negative results. The inter-observer agreement for performing and interpreting these studies is unknown. There also is likely a difference between a wisp of extravasation and a completely failed anastomosis in terms of management and pathophysiology.

One could hypothesize these complications are actually signs of ongoing urine extravasation or poor healing. Such clinical signs may help to identify patients in whom postoperative urethrography may reveal extravasation. Furthermore, patients with longer strictures and complex repairs including grafts were more likely to have extravasation detected. Extravasation on postoperative urethrography was strongly correlated with anatomical recurrence at 1 year. Of course, the relationship between anatomical recurrence identified on cystoscopy and functional recurrence requiring repeat procedure is yet another controversy. Indeed, another recent retrospective single center series noted extravasation was not predictive for stricture relapse accounting for stricture etiology, location, length and type of surgery in multivariate analysis among 630 patients (HR: 1.57, 95% CI: 0.8–3, p=0.173).

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There are additional arguments that favor continued postoperative urethrography. The available literature summarizes surgical results among expert surgeons. The steep learning curve for urethral stricture treatment is well characterized. One may hypothesize increased extravasation rates for surgeons with less experience. Such information provides tangible feedback for the surgeon. Consistent followup after urethroplasty remains a challenge. In the turns protocol, for instance, less than 50% of patients return for cystoscopy. Therefore, the RUG/VCUG potentially represents an opportunity for a surgeon to collect objective feedback. Moreover, there is psychological benefit for nervous patients (and surgeons) knowing the repair has healed in a water tight fashion that in some cases supersedes anxieties about the test itself.

Like most things in life, the best approach may require nuance. For more complex surgery, in particular long urethral repairs employing grafts, postoperative urethrography may help drive postoperative decision making. Early career surgeons should likely rely more heavily on postoperative urethrograph to guide catheter management as well as serve as a quality control check. On the other hand, for straightforward cases postoperative imaging may be omitted at the discretion of an experienced surgeon. If extravasation is noted, given the potential increased risk of anatomical recurrence, more stringent surveillance should be encouraged.


CIC for Renal Replacement in PUVs

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variation in provider practice, even among academic pediatric urologists within a similar geographic region highlights a significant barrier in retrospective outcomes data. This exemplifies the importance of standardized management and prospective data collection so that care and subsequently outcomes can be optimized.

Unfortunately, with reviewing current retrospective data, it is difficult to definitively comment on the potential impact on kidney outcomes from starting CIC in the pediatric patient with PUV. Acknowledging the high risk of progression to ESKD in the PUV population, all avenues of potential disease mitigation must continue to be explored. Optimization of LUTD in these high risk children is worthwhile as any ability to delay, or perhaps prevent altogether, the need for RRT can be of immeasurable clinical benefit.

Alternatives to Opioids for Postoperative Pain Control More Important Than Ever during Pandemic Surge

Surgical opioid prescribing has been linked to increased lengths of stay, emergency department visits, hospitalizations, encounter costs, and new persistent opioid use. Two studies have found that the rate of new persistent opioid use after urological surgery is 6%,2,3 establishing persistent opioid use as one of the most prevalent iatrogenic complications of surgery. Given the now well-established harms of opioids, and the lack of evidence regarding their ideal use, there has been vigorous interest in opioid dose reduction and multi-modal treatment pathways for surgical pain which incorporate nonopioid medications to reduce opioid use. Increasingly there is evidence that the lowest effective dose of opioids may often be zero, as nonopioid based protocols have been shown to achieve equivalent pain outcomes across a wide spectrum of surgical procedures.

Setting realistic pain expectations preoperatively is a crucial first step to reducing postoperative opioid use. Establishing that the goal after surgery is not zero pain but, rather, pain that is managed well enough to allow for functional movement and recovery has been shown to reduce the amount of postoperative opioid consumption. The impact is largest when also educating patients about the harms of opioids and the rationale for limiting their use.4 Many institutions have now shown that significantly reducing the amount of opioids prescribed after surgery is safe and effective, without any impact to patient satisfaction, number of phone calls to the office, or increased emergency department visits. A recent study from a large statewide collaborative, the Michigan Opioid Prescribing and Engagement Network, found that patients who were counseled preoperatively about nonopioid pain options and given low-dose or no opioids postoperatively had, in fact, improved pain scores compared to patients given usual care.5 Patients prescribed more tend to use more, without an improvement in outcomes. Regardless of what was prescribed, most patients did not use all of their pills, a consistent finding across studies with significant implications for the community as diversion of unused opioids for illicit use is a common issue. From this vantage, opioid stewardship can serve the purposes of both primary and secondary prevention, as the excess supply of opioids from historical prescribing patterns puts not only the intended recipient at risk, but also other members of their household and community.

Successful urological opioid dose reduction protocols for minimally invasive and open surgery have been published from the University of Pittsburgh, Johns Hopkins University and our own institutions, amongst others.1,5 These studies consistently show equivalent outcomes from low/no opioid protocols across a wide variety of urological procedures: pediatrics, uroscopy with stent placement, reconstructive pelvic surgery, penile implantation, and oncologic procedures such as radical prostatectomy, partial and radical nephrectomy, and open cystectomy. For example, while prescriptions of 30 or more oxycodone pills following laparoscopic/robotic surgery were previously standard, several of these protocols have shown that 0–7 pills often work just as well. In addition to reducing the number of pills prescribed, the opioid strength can be adjusted—hydrocodone is half the morphine equivalent of oxycodeone.6

Tramadol is a weak partial opioid agonist but has highly variable metabolism based on variants of the CYP2D6 gene—in the United States an estimated 40% of people are either poor metabolizers who will have poor pain control with tramadol, or ultra-rapid metabolizers who are at risk for potentially lethal respiratory depression. Along with its potentially morbid serotonergic interactions, prescribing tramadol requires caution but can be considered in patients with a prior good response. Of note, benzodiazepines are never recommended for pain control and patients on benzodiazepines require nonopioid alternatives given U.S. Food and Drug Administration “black box” warnings of a 10x higher risk of overdose in patients taking both medications.

Nonopioid multi-modal analgesia is thus an important adjunct to opioid dose reduction protocols, especially if the goal is to get to zero opioid use. Multi-modal analgesia involves using multiple agents which target pain via different pathways with potentially synergistic effects. The best studied is the combination of acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), which has been shown to have synergistic effects which are equally effective to opioids for a variety of acute pain conditions.

Specifically, NSAIDs have been shown to be safe and efficacious following endourological, minimally invasive prostate and kidney, and open oncologic surgeries. Many surgeon concerns about NSAIDs are addressed in the literature. Notably, NSAIDs have not been shown to increase postoperative bleeding in multiple meta-analyses and large studies, even after high risk procedures like partial nephrectomy. Cardiovascular risk is not increased with short-term use. NSAIDs are safe for patients with healthy kidneys but do have a risk of acute kidney injury in patients with chronic kidney disease, significant dehydration, or those on angiotensin-converting enzyme (ACE) inhibitors.

Other common medications used in multi-modal analgesia pathways are gabapentinoids and muscle relaxants (such as Flexeril®). Neither has been shown, thus far, to have significant addictive potential but both carry risks of respiratory depression when mixed with other potentially sedating drugs such as opioids so they may be best suited for nonopioid protocols. Of note, there are several nonopioid adjuncts which have been shown to be quite effective for stent-related pain specifically. These include tamsulosin and anticholinergic medications, such as Ditropan or belladonna/opium suppositories. In combination with acetaminophen/NSAIDs, several large institutions have been able to prescribe zero opioids for the majority of their patients after stent placement.

In summary, despite some initial progress in reducing opioid-related morbidity and mortality in the past 5 years, the past year unfortunately saw record-breaking levels of these devastating complications. It is increasingly recognized that long-held
Ischemia Time during Partial Nephrectomy: Can We Stop Counting the Minutes?

Jared Schober, MD       Kevin Ginsburg, MD, MS       Alexander Rutikov, MD, FACS
Fox Chase Cancer Center

Partial nephrectomy (PN) is a critical clinical tool in the kidney surgeon’s armamentarium. Although “off clamp” partial nephrectomy is performed at times, clamping of the renal artery not only prevents significant blood loss, but also affords clear visualization of the tumor resection bed (see figure). Yet, during arterial clamping, the kidney is in an ischemic state and may be harmed.

The magnitude and clinical significance of various ischemia types and lengths have been a point of intense discussion both in the peer-reviewed literature and at academic meetings.1 The tenet “Every Minute Counts” was canonized into urological dogma and supported by some early reports.2 With this principle in mind, innovative surgical strategies such as unplanned tumor enucleation, super-selective arterial clamping and others were developed with the goal to drive down ischemia time in an effort to optimize functional outcomes.3 However, surgical complexity of these approaches was often high, resulted in extended operative times and required expertise that may not have been generalizable to the urological community at large. As a result, the clinical traction garnered by these techniques is currently unclear.

In recent years, the relentless pursuit of shortening ischemia time has come under question. The realization that “Every Minute” may actually “Not Matter Much” stems from better understanding of 3 factors: 1) functional residual parenchymal volume, not ischemia, appears to drive long-term renal function outcomes after PN; 2) the human kidney is extremely resilient to warm ischemia; and 3) in the presence of a normal contralateral kidney harms of even radical nephrectomy (RN) are difficult to prove.

**Functional Residual Parenchymal Volume, Not Ischemia, Is the Main Predictor of Long-Term Renal Function**

While warm ischemia time (WIT) received significant attention in the early development of partial nephrectomy, several studies have indicated parenchymal preservation is the main driver for long-term postoperative functional outcomes. In a seminal report, Simmons et al demonstrated that both percent of the functional renal volume preserved and ischemia time predicted early postPN estimated glomerular filtration rate (eGFR), while volume preservation alone affected long-term renal function with ischemia falling out as a significant factor in a multivariable model.4 Ginzburg et al confirmed that although WIT was associated with decline in eGFR after partial nephrectomy in their univariable models, only preoperative eGFR and functional parenchymal volume were determinants of eGFR at 6 months.5 Consistent with the findings by Simmons et al, WIT was not significantly associated with postoperative eGFR after appropriate adjustment.

**Human Kidney Tolerates Ischemia Extremely Well**

Early animal studies and limited clinical reports were contradictory but suggested ischemia time of >30 minutes was detrimental to both short-term and long-term kidney function recovery. Yet a prospectively designed study by Parekh et al challenges this assertion. In their study, the effect of ischemia was studied in real-time using tissue biopsies taken before, during and after renal clamping in 40 patients undergoing partial nephrectomy with a healthy contralateral kidney (ischemia duration >30 minutes in 82.5% of patients).6 Their findings crystallized for many in the kidney cancer community the fact that the human kidney is highly resilient to WIT. Patients experienced only mild transient elevations in creatinine, renal functional studies did not correlate with ischemia time and histologic structural changes after prolonged ischemia were...
Ischemia Time during Partial Nephrectomy

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significantly less severe than previously shown in animal models with prompt recovery after reinstitution of arterial flow.

This prospectively designed, real-time analysis study represents arguably the highest quality tissue-based evidence to date with findings suggesting that ischemia time up to 60 minutes should result in prompt recovery and lack of long-term renal deficits. The main limitations of this work are heterogeneous use of cold and warm ischemia, lack of followup beyond the hospital stay and absence of data detailing parenchymal volume preservation.

Furthermore, patients with chronic kidney disease (CKD) appearing from surgery (CKD-S) appear to be largely indistinguishable from patients without CKD and thus face a much more favorable destiny than those with CKD stemming from intrinsic renal disease (CKD-Medical). Therefore, the role of PN vs RN in patients for whom additional risks of complex surgery may not be justified or for whom oncologic compromise may result from renal preservation is currently being debated. In the context of this larger debate, arguments regarding whether several additional minutes of ischemia during PN are clinically relevant become rather moot.

In conclusion, the guiding principles of partial nephrectomy should be oncologic integrity, renal preservation, and surgical safety. The data of yesteryear has now been clarified by work that shows ischemia to have limited impact on long term functional outcomes. As such, without an entirely cavalier disregard for ischemia time, the urological community should no longer fixate on “counting the minutes.”

ORGOVYX achieved sustained testosterone suppression

- 97% of men achieved and maintained testosterone suppression to <50 ng/dL from Day 29 through Week 48 with ORGOVYX

MAJOR EFFICACY OUTCOME MEASURE: SUSTAINED TESTOSTERONE SUPPRESSION RATE (TESTOSTERONE LEVELS <50 ng/dL FROM DAY 29 THROUGH WEEK 48)

Results from the HERO study, a multinational, randomized, open-label, phase 3 trial in 934 men with advanced prostate cancer. Patients were randomized 2:1 to receive ORGOVYX (360 mg on the first day followed by daily doses of 120 mg orally \(n=634\)) or leuprolide acetate (22.5 mg injection \(n=308\) in Japan and Taiwan per local guidelines) subcutaneously every 3 months \(n=300\) for 48 weeks.\(^1,2\)

CI = confidence interval.

\(^1\)Kaplan-Meier estimates within each group.

\(^2\)11.25 mg is a dosage regimen that is not approved for use in the United States.\(^3\)The subgroup of patients receiving 22.5 mg leuprolide \(n=264\) was 88.0% (95% CI: 83.4%, 91.4%).

\(^3\)Two patients in each arm did not receive the study treatment and were not included.

INDICATION

ORGOVYX is a gonadotropin-releasing hormone (GnRH) receptor antagonist indicated for the treatment of adult patients with advanced prostate cancer.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

QT/QTc Interval Prolongation: Androgen deprivation therapy, such as ORGOVYX may prolong the QT/QTc interval. Providers should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, or frequent electrolyte abnormalities and in patients taking drugs known to prolong the QT interval. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolytes.

Embryo-Fetal Toxicity: The safety and efficacy of ORGOVYX have not been established in females. Based on findings in animals and mechanism of action, ORGOVYX 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 2 weeks after the last dose of ORGOVYX.

Laboratory Testing: Therapy with ORGOVYX results in suppression of the pituitary gonadal system. Results of diagnostic tests of the pituitary gonadotropic and gonadal functions conducted during and after ORGOVYX may be affected. The therapeutic effect of ORGOVYX should be monitored by measuring serum concentrations of prostate-specific antigen (PSA) periodically. If PSA increases, serum concentrations of testosterone should be measured.

Adverse Reactions

Serious adverse reactions occurred in 12% of patients receiving ORGOVYX. Serious adverse reactions in ≥0.5% of patients included myocardial infarction (0.8%), acute kidney injury (0.6%), arrhythmia (0.6%), hemorrhage (0.6%), and urinary tract infection (0.5%). Fatal adverse reactions occurred in 0.8% of patients receiving ORGOVYX including metastatic lung cancer (0.3%), myocardial infarction (0.3%), and acute kidney injury (0.2%). Fatal and non-fatal myocardial infarction and stroke were reported in 2.7% of patients receiving ORGOVYX.
IMPORTANT SAFETY INFORMATION

Most common adverse reactions (≥10%) and laboratory abnormalities (≥15%) in patients receiving ORGOVYX were hot flush (54%), glucose increased (44%), triglycerides increased (35%), musculoskeletal pain (30%), hemoglobin decreased (28%), alanine aminotransferase increased (27%), fatigue (26%), aspartate aminotransferase increased (18%), constipation (12%), and diarrhea (12%).

Drug Interactions

Co-administration of ORGOVYX with a P-gp inhibitor increases the area under the curve (AUC) and maximum concentration (C_{max}) of ORGOVYX, which may increase the risk of adverse reactions associated with ORGOVYX. Avoid co-administration of ORGOVYX with oral P-gp inhibitors. If co-administration is unavoidable, take ORGOVYX first, separate dosing by at least 6 hours, and monitor patients more frequently for adverse reactions. Treatment with ORGOVYX may be interrupted for up to 2 weeks for a short course of treatment with certain P-gp inhibitors. If treatment with ORGOVYX is interrupted for more than 7 days, resume administration of ORGOVYX with a 360 mg loading dose on the first day, followed by 120 mg once daily.

Co-administration of ORGOVYX with a combined P-gp and strong CYP3A inducer decreases the AUC and C_{max} of ORGOVYX, which may reduce the effects of ORGOVYX. Avoid co-administration of ORGOVYX with combined P-gp and strong CYP3A inducers. If co-administration is unavoidable, increase the ORGOVYX dose to 240 mg once daily. After discontinuation of the combined P-gp and strong CYP3A inducer, resume the recommended ORGOVYX dose of 120 mg once daily.

Please see Brief Summary of Prescribing Information for ORGOVYX on adjacent pages.

References:

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BRIEF SUMMARY

ORGOVYX™ (relugolix) tablets, for oral use

The following is a brief summary of the full prescribing information for ORGOVYX™ (relugolix). Please see the full prescribing information for complete product information.

1 INDICATIONS AND USAGE

ORGOVYX is indicated for the treatment of adult patients with advanced prostate cancer.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 QT/QTc Interval Prolongation

Androgen deprivation therapy, such as ORGOVYX may prolong the QT/QTc interval. Providers should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, or frequent electrolyte abnormalities and in patients taking drugs known to prolong the QT interval. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolytes.

5.2 Embryo-Fetal Toxicity

The safety and efficacy of ORGOVYX have not been established in females. Based on findings in animals and mechanism of action, ORGOVYX can cause fetal harm and loss of pregnancy when administered to a pregnant female. In an animal reproduction study, oral administration of relugolix to pregnant rabbits during the period of organogenesis caused embryo-fetal lethality at maternal exposures that were 0.3 times the human exposure at the recommended dose of 120 mg daily based on area under the curve (AUC). Advise males with female partners of reproductive potential to use effective contraception during treatment and for 2 weeks after the last dose of ORGOVYX.

5.3 Laboratory Testing

Therapy with ORGOVYX results in suppression of the pituitary gonadal system. Results of diagnostic tests of the pituitary gonadotropic and gonadal functions conducted during and after ORGOVYX may be affected. The therapeutic effect of ORGOVYX should be monitored by measuring serum concentrations of prostate specific antigen (PSA) periodically. If PSA increases, serum concentrations of testosterone should be measured.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

• QT/QTc Interval Prolongation.

6.1 Clinical Trials 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 safety of ORGOVYX was evaluated in HERO, a randomized (2:1), open-label, clinical study in patients with advanced prostate cancer. Patients received orally administered ORGOVYX as a loading dose of 360 mg on the first day followed by 120 mg taken orally once daily (n = 622) or received leuprolide acetate administered by depot injection at doses of 22.5 mg (n = 264) or 11.25 mg (n = 44) per local guidelines every 12 weeks (n = 308). Leuprolide acetate 11.25 mg is a dosage regimen that is not recommended for this indication in the US. Among patients who received ORGOVYX, 91% were exposed for at least 48 weeks. Ninety-nine (16%) patients received concomitant radiotherapy and 17 (3%) patients received concomitant enzalutamide with ORGOVYX.

Serious adverse reactions occurred in 12% of patients receiving ORGOVYX. Serious adverse reactions in ≥ 0.5% of patients included myocardial infarction (0.8%), acute kidney injury (0.6%), arrhythmia (0.8%), hemorrhage (0.6%), and urinary tract infection (0.5%). Fatal adverse reactions occurred in 0.8% of patients receiving ORGOVYX including metastatic lung cancer (0.3%), myocardial infarction (0.3%), and acute kidney injury (0.2%). Fatal and non-fatal myocardial infarction and stroke were reported in 2.7% of patients receiving ORGOVYX.

Permanent discontinuation of ORGOVYX due to an adverse reaction occurred in 3.5% of patients. Adverse reactions which resulted in permanent discontinuation of ORGOVYX in ≥ 0.3% of patients included atrioventricular block (0.3%), cardiac failure (0.3%), hemorrhage (0.3%), increased transaminases (0.3%), abdominal pain (0.3%), and pneumonia (0.3%).

Dosage interruptions of ORGOVYX due to an adverse reaction occurred in 2.7% of patients. Adverse reactions which required dosage interruption in ≥ 0.3% of patients included fracture (0.3%).

The most common adverse reactions (> 10%) and laboratory abnormalities (> 15%), were hot flush (54%), glucose increased (44%), triglycerides increased (35%), musculoskeletal pain (30%), hemoglobin decreased (28%), alanine aminotransferase increased (ALT) (27%), fatigue (26%), aspartate aminotransferase increased (AST) (18%), constipation (12%), and diarrhea (12%).

Table 1 summarizes the adverse reactions in HERO.

Table 1: Adverse Reactions (> 10%) of Patients with Advanced Prostate Cancer Who Received ORGOVYX in HERO

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ORGOVYX N = 622</th>
<th>Leuprolide Acetate N = 308</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot flush</td>
<td>54</td>
<td>0</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td>General</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Constipation</td>
<td>12</td>
<td>10</td>
</tr>
</tbody>
</table>

* Includes arthralgia, back pain, pain in extremities, musculoskeletal pain, myalgia, bone pain, neck pain, arthritis, musculoskeletal atrophy, non-cardiac chest pain, musculoskeletal chest pain, spinal pain, and musculoskeletal discomfort.

Clinically relevant adverse reactions in < 10% of patients who received ORGOVYX included increased weight, insomnia, gynecomastia, hyperhidrosis, depression, and decreased libido.

Table 2 summarizes the laboratory abnormalities in HERO.

Table 2: Select Laboratory Abnormalities (> 15%) That Worsened from Baseline in Patients with Advanced Prostate Cancer Who Received ORGOVYX in HERO

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>ORGOVYX</th>
<th>Leuprolide Acetate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemistry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose increased</td>
<td>44</td>
<td>54</td>
</tr>
<tr>
<td>Triglycerides increased</td>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>ALT increased</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>AST increased</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Hemoglobin decreased</td>
<td>28</td>
<td>29</td>
</tr>
</tbody>
</table>

* The denominator used to calculate the rate varied from 611 to 619 in the ORGOVYX arm and from 301 to 306 in the leuprolide arm based on the number of patients with a baseline value and at least one post-treatment value.

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on ORGOVYX

P-gp Inhibitors

Co-administration of ORGOVYX with a P-gp inhibitor increases the AUC and the maximum concentration (C_max) of relugolix, which may increase the risk of adverse reactions associated with ORGOVYX. Avoid co-administration of ORGOVYX with oral P-gp inhibitors.

If co-administration is unavoidable, take ORGOVYX first, separate dosing by at least 6 hours, and monitor patients more frequently for adverse reactions.

Treatment with ORGOVYX may be interrupted for up to 2 weeks for a short course of treatment with certain P-gp inhibitors.

If treatment with ORGOVYX is interrupted for more than 7 days, resume administration of ORGOVYX with a 360 mg loading dose on the first day, followed by 120 mg once daily.

Combined P-gp and Strong CYP3A Inducers

Co-administration of ORGOVYX with a combined P-gp and a strong CYP3A inducer decreases the AUC and C_max of relugolix, which may reduce the effects of ORGOVYX. Avoid co-administration of ORGOVYX with combined P-gp and strong CYP3A inducers.

If co-administration is unavoidable, increase the ORGOVYX dose. After discontinuation of the combined P-gp and strong CYP3A inducer, resume the recommended dose of ORGOVYX once daily.
8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

The safety and efficacy of ORGOVYX have not been established in females.

Based on findings in animals and mechanism of action, ORGOVYX can cause fetal harm and loss of pregnancy when administered to a pregnant female. There are no human data on the use of ORGOVYX in pregnant females to inform the drug-associated risk. In an animal reproduction study, oral administration of relugolix to pregnant rabbits during organogenesis caused embryo-fetal lethality at maternal exposures that were 0.3 times the human exposure at the recommended dose of 120 mg daily based on AUC (see Data). Advise patients of the potential risk to the fetus.

Data

Animal Data

In an embryo-fetal development study, oral administration of relugolix to pregnant rabbits during the period of organogenesis resulted in abortion, total litter loss, or decreased number of live fetuses at a dose of 9 mg/kg/day (approximately 0.3 times the human exposure at the recommended dose of 120 mg daily based on AUC).

8.2 Lactation

Risk Summary

The safety and efficacy of ORGOVYX at the recommended dose of 120 mg daily have not been established in females. There are no data on the presence of relugolix in human milk, the effects on the breastfed child, or the effects on milk production. Relugolix and/or its metabolites were present in milk of lactating rats (see Data).

Data

Animal Data

In lactating rats administered a single oral dose of 30 mg/kg radiolabeled relugolix on post-partum day 14, relugolix and/or its metabolites were present in milk at concentrations up to 10-fold higher than in plasma at 2 hours post-dose.

8.3 Females and Males of Reproductive Potential

Contraception

Males

Based on findings in animals and mechanism of action, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 2 weeks after the last dose of ORGOVYX.

Infertility

Males

Based on findings in animals and mechanism of action, ORGOVYX may impair fertility in males of reproductive potential.

8.4 Pediatric Use

The safety and efficacy of ORGOVYX in pediatric patients have not been established.

8.5 Geriatric Use

Of the 622 patients who received ORGOVYX in the HERO study, 81% were 65 years of age or older, while 35% were 75 years of age or older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. There was no clinically relevant impact of age on the pharmacokinetics of ORGOVYX or testosterone response based on population pharmacokinetic and pharmacokinetic/pharmacodynamic analyses in men 45 to 91 years of age.

12.3 Pharmacokinetics

Specific Populations

No clinically meaningful differences in the pharmacokinetics of relugolix were observed based on age (45 to 91 years), race/ethnicity (Asian [19%], White [71%], Black/African American [8%]), body weight (41 to 193 kg), mild to severe renal impairment (creatinine clearance [CLcr] 15 to 89 mL/min, as estimated by the Cockcroft-Gault equation), or mild to moderate hepatic impairment (Child-Pugh A or B). The effect of end-stage renal disease with or without hemodialysis or severe hepatic impairment (Child-Pugh C) on the pharmacokinetics of relugolix has not been evaluated.

Drug Interactions Studies

Clinical Studies

Combined P-gp and Moderate CYP3A Inhibitor: Co-administration with erythromycin (P-gp and moderate CYP3A inhibitor) increased the AUC and Cmax of relugolix by 6.2-fold.

Combined P-gp and Strong CYP3A Inhibitor: Co-administration with ritonavir (P-gp and strong CYP3A inhibitor) decreased the AUC and Cmax of relugolix by 55% and 23%, respectively.

Other Drugs: No clinically significant differences in the pharmacokinetics of relugolix were observed when co-administered with voriconazole (strong CYP3A inhibitor), atorvastatin, enalapril, or acid-reducing agents. No clinically significant differences in the pharmacokinetics of midazolam (sensitive CYP3A substrate) or rosuvastatin (BCRP substrate) were observed upon co-administration with relugolix.

In Vitro Studies

Cytochrome P450 (CYP) Enzymes: Relugolix is a substrate of CYP3A and CYP2C8. Relugolix is not an inhibitor of CYP1A2, CYP2B6, CYP2C8, CYP2D6, CYP2C9, CYP3A4, or CYP3A5. The in vitro chromosomal aberration assay in Chinese hamster lung cells demonstrated evidence of reversibility after cessation of treatment. The significance of this finding in humans is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Two-year carcinogenicity studies were conducted in mice at oral relugolix doses up to 100 mg/kg/day and in rats at doses up to 600 mg/kg/day. Relugolix was not carcinogenic in mice or rats at exposures up to approximately 75 or 224 times, respectively, the human exposure at the recommended dose of 120 mg daily based on AUC.

Relugolix was not mutagenic in the in vitro bacterial reverse mutation (Ames) assay or clastogenic in the in vitro chromosomal aberration assay in Chinese hamster lung cells or the in vivo rat bone marrow micronucleus assay.

In human GHRH-receptor knock-in male mice, oral administration of relugolix decreased prostate and seminal vesicle weights at doses ≥ 3 mg/kg twice daily for 28 days. The effects of relugolix were reversible, except for testis weight, which did not fully recover within 28 days after drug withdrawal. In a 26-week toxicity study in monkeys, there were no significant effects on male reproductive organs at oral relugolix doses up to 50 mg/kg/day (approximately 53 times the human exposure at the recommended dose of 120 mg daily based on AUC).

13.2 Animal Toxicology and/or Pharmacology

Phospholipidosis (intracellular phospholipid accumulation) was observed in multiple organs and tissues (e.g., liver, pancreas, spleen, kidney, lymph nodes, lung, bone marrow, gastrointestinal tract or testes) after repeated oral administration of relugolix in rats and monkeys. In a rat 26-week toxicity study, phospholipidosis was observed at doses ≥ 100 mg/kg (approximately 18 times the human exposure at the recommended dose based on AUC). In a monkey 39-week toxicity study, this effect was observed at doses ≥ 1.5 mg/kg (approximately 0.6 times the human exposure at the recommended dose based on AUC) and demonstrated evidence of reversibility after cessation of treatment. The significance of this finding in humans is unknown.

17 PATIENT COUNSELING INFORMATION

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

QT/QTc Interval Prolongation

• Advise patients that androgen deprivation therapy treatment with ORGOVYX may prolong the QT interval. Inform patients of the signs and symptoms of QT prolongation. Advise patients to contact their healthcare provider immediately for signs or symptoms of QT prolongation.

Androgen Deprivation

• Inform patients about adverse reactions related to androgen deprivation therapy with ORGOVYX, including hot flashes, flushing of the skin, increased weight, decreased sex drive, and difficulties with erectile function.

Embryo-Fetal Toxicity

• Inform patients that ORGOVYX can be harmful to a developing fetus and can cause loss of pregnancy.

• Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 2 weeks after the last dose of ORGOVYX.

Infertility

• Inform patients that ORGOVYX may cause infertility.

Manufactured by Bushu Pharmaceuticals, Ltd, Kawagoe, Saitama, Japan
Manufactured for Myovant Sciences, Inc., Brisbane, CA 94005

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The Emerging Role of Social Media in Pelvic Floor Disorders

Women presenting with pelvic floor disorders like urinary incontinence and pelvic organ prolapse (POP) are highly motivated to use Internet and social media (SoMe) platforms to learn about their diseases. Approximately 59% of patients less than 65 years old and 40% of patients greater than 65 years old reported using SoMe to learn more about their pelvic floor complaints. SoMe studies have been conducted using keywords like “urinary incontinence” and/or “pelvic organ prolapse,” and findings emphasize the widely varying content available to patients. The following is a review of patient-centric studies assessing the role of SoMe in pelvic floor disorders (see figure).

YouTube

In a review of 100 YouTube videos on POP with a total of 6,307,202 views, researchers found 77% of videos contained poor quality content (ie videos omitting other treatment options, failing to discuss benefits/risks of treatment, and/or shared decision-making with health care professionals). Despite YouTube being the most commonly used SoMe platform in the United States, over 50% of the POP videos had low levels of understandability (ie were difficult to understand), and 31% of videos contained misinformative or biased content. Surgery was the most common treatment option discussed across all videos. Also, Sajadi and Goldman assessed the first 30 YouTube videos on urinary incontinence and reported over 50% of videos had misinformative content. Ultimately, patients may unknowingly encounter information that is low quality and hard to comprehend.

Instagram

A review of 105 Instagram posts with nearly 9,000 likes was conducted using the term “POP.” Researchers found more than 75% of POP posts had moderate to poor quality information and 25% of posts had commercial bias. Thirty-six percent of posts were not easy to understand (ie did not use common language or simple terminology), and 69% of posts left consumers unable to identify at least 1 action they could take to address their POP. Instagram is an easily accessible SoMe interface, yet only 8% of posts were uploaded by physicians, with the majority of posts published by health and wellness groups (44%). Furthermore, posts published by physicians did not contain misinformation or commercial bias. Pelvic floor muscle training was the most frequently mentioned treatment modality. Overall, POP posts on Instagram lack complete information, which may contribute to the preexisting lack of fundamental knowledge present for many consumers on the topic of POP.

Pinterest

Pace et al analyzed 100 pins with >5 million followers on Pinterest using the search term “POP.” POP pins had moderate to poor quality information (69%); however, the pins were understandable and provided consumers with the ability to take action after viewing. Misinformation and commercial bias were present in 27% and 36% of pins, respectively. Health and wellness groups were the foremost publishers (33%). The most discussed treatment option was pelvic floor muscle training. This study concluded POP content on Pinterest contained pins that were easy to understand with poor quality information.

Podcasts

The podcast, Stitcher, has a female driven audience with over 12 million downloads. Using Stitcher, a review of 100 podcasts was conducted using the search term “stress urinary incontinence.” Many podcasts were low quality (67%) and difficult to understand (69%). The primary publishers of the podcasts were health and wellness groups (64%). The most discussed treatment was pelvic floor muscle training, followed by surgical management. Over 60% of podcasts mentioning treatment options failed to address shared medical decision-making. As patients with intimate medical conditions seek additional knowledge on SoMe, providers should be aware of the quality and difficulty of these supplementary resources.

Figure. Patient-centric studies assessing SoMe role in pelvic floor disorders.
Emerging Role of Social Media in Pelvic Floor Disorders

Among physicians, SoMe is an emerging medical educational outlet used to discuss topics like urinary incontinence and POP. In urology, SoMe has been used to: spread information from prominent medical journals, facilitate discussions with diverse audiences, identify improvements in patient educational materials, and improve access to online surveys.

Many Female Pelvic Medicine and Reconstructive Surgery (FPMRS) specialists use Twitter to spread medical information and to disseminate recently published articles. This serves as a vehicle to have real-time discussions and expand medical knowledge across specialties and to lay users. Similarly, medical journals are harnessing the force of SoMe to promote articles and to interact with users on the Internet. On Twitter medical journals can start a chain of tweets, called a “thread,” to garner attention from readers. This can work to increase readership while providing a secondary medium to spread medical information. When used correctly SoMe is a great tool to provide medical information on pelvic floor disorders outside the office.

There is a growing number of urologists and patients embracing SoMe. As urologists continue to use SoMe, they should remember that patients are searching for health information online and would benefit from recommendations of online search criteria, links to comprehensive videos, and/or SoMe presence of urologists.

Real-Time Evaluation and Feedback of Medical Students and Urology Residents—A Role for Tech Innovation?

Kate H. Kraft MD, FAAP, FACS
University of Michigan

Over the past decade, there has been rising concern that some surgical residents are not competent to enter independent practice by the time they complete their residency training.1 Recent graduates of U.S. urology residency training programs express a lack of confidence in performing procedures commonly encountered in general urological practice. For example, 61% of young urologists report they do not feel prepared to perform a robotic radical prostatectomy, an index procedure per the Accreditation Council for Graduate Medical Education case log requirements for urology.2 The majority of recent surgical graduates also seek fellowships, which may reflect the need for further training after residency.3 Additionally, decreasing autonomy in surgical residency can contribute to the lack of readiness for independent practice.4 Multiple forces are at play for meaningful learning in the operating room: work hour restrictions, expanding residency program requirements, regulations surrounding supervision, and pressure to improve clinical throughput, all within a fixed length of training.

Dr. William Halsted’s century-old principles of surgical training remain relevant today, including acquisition of technical skills through graded enhanced responsibility and independence. How trainees achieve that responsibility has shifted from pure discovery learning (learning by doing) to a need for guided discovery learning, in which an expert provides the novice with preparatory information before the experience, offers verbal and perhaps even manual guidance during the experience, and delivers feedback afterward. Learners using guided discovery learn more quickly, more accurately and are more likely to remember what they learned when compared to those who use pure discovery learning.5 Guided discovery learning partners well with deliberate practice to improve performance, and core to this partnership is the concept of feedback. Learners who receive regular feedback about their performance perform significantly better, develop better judgment, and learn faster.6 Feedback not only fuels but accelerates learning. More importantly, the quality of feedback is essential to propel skill development. At the very least, feedback should be specific and encouraging. Effective feedback should additionally be corrective, rectifying undesirable or even harmful habits; speak to entrustment, defining learners’ independence with respect to expected level of performance; and design a learning plan for skill development, providing a recommendation on how to address a particular learning goal.7

The recent development of workplace-based assessments provides opportunities for delivering more formative feedback. Workplace-based assessment (WBA) comprises evaluation methods involving direct observation of routine clinical practice and has become a central component of competency-based medical education. Compared to more traditional assessment methods such as simulation and end of rotation evaluations, WBAs can better capture real-world clinical skill performance in real time, all while drawing views of multiple diverse raters. These assessments have been particularly effective in surgical specialties in which direct observation of procedures can be recorded instantaneously.

Communicating feedback in a timely, high-volume manner using WBAs has posed some challenges, not the least of which are time constraints and cumbersome delivery systems. The most cost-effective model of assessment is to ask faculty already working with trainees to assess their performance, but they must do so without significant disruption of their normal work flow to guarantee completion of the assessment. Technology in the form of web-based instruments and smartphone apps addresses the logistical barriers to implementing WBAs in surgical training.

The Minute Feedback System (MFS) is a web-based feedback tool developed to deliver more frequent, timely and meaningful feedback to medical students on their surgical clerkship. Medical students and faculty alike have found that the MFS is easy to use, encourages same-day assessment, and increases the quantity of documented feedback. Over 80% of students believe the MFS facilitates their receiving more formative feedback, and over 70% find the feedback useful for improving their surgical performance.8 One disadvantage of this system, however, is that it relies on logging into a computer to complete, which can be inefficient and burdensome.

Apps such as SIMPL (System for Improving and Measuring Procedural Learning) now afford educators and learners alike a mechanism for delivering and receiving dictated feedback literally in their back pocket. Smartphones make it possible to collect and use ratings of observed performances while adhering to evidence-based best practices, such as recording an assessment close in time to an observed performance. These

![Autonomy](image1)

![Performance](image2)

Figure. SIMPL data demonstrate development of operative autonomy and performance in urology residency training.

Continued on page 31
Tech Innovation in Real-Time Evaluation and Feedback

Impact of Shift to Pass/Fail System
Since the announcement of the scoring change to pass/fail, numerous studies have emerged examining the potential impact. Although there are limited studies quantifying the medical student perspective, proposals prior to the announcement suggest medical students are in favor of the scoring change whereas program directors are not. Only 15.3% of program directors among all specialties agree with this change in scoring, and only 19% of urology program directors agree. Many reservations regarding this change center around the impact on residency program selection. Nevertheless, among program directors, medical school administrators, and medical students, there is agreement regarding the potential positive and negative impacts of a pass/fail scoring system [see figure].

What does a pass/fail Step 1 examination mean for the urology residency application cycle? Undoubtedly, this will change application requirements. Historically, despite the availability of multiple USMLE scores, programs often only consider the USMLE Step 1 score. Programs may now mandate a Step 2 Clinical Knowledge (CK) score, which remains on a numerical scale, a change nearly a quarter of urology program directors supported. In the context of the early match, the requirement of Step 2 CK scores will likely impose on the already tight timeline for applicants managing away rotations and residency interviews.

Alternatively, programs may migrate from USMLE altogether and develop a urological subspecialty examination. While USMLE may

Positive Impacts of Pass/Fail
- Improves recruitment of diverse candidates
- Encourages holistic evaluation of residency candidates

Negative Impacts of Pass/Fail
- Eliminates an easy screening tool and makes residency application review more burdensome
- Increases potential for bias with less objective data available
- Makes it more challenging to distinguish applicants with otherwise similar applications
- Removes predictor for passing specialty board exams

Figure. Comparison of potential positive and negative impacts of pass/fail Step 1 scoring system.
Urology Application Process

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not prove urological knowledge, some program directors believe the USMLE score is a marker of dedication, self-drive and stamina, which are attractive qualities in a resident. Development of a urology-focused test may allow applicants to demonstrate these qualities while better assessing their knowledge of the field. However, the development of such a test may again emphasize medical student knowledge and standardized test taking skills as a basis for residency selection, disadvantage students without home urology programs or access to preparatory resources and contribute to already observed testing related disparities.

Lastly, urology has historically lacked in diversity and the elimination of numeric Step 1 scoring has the potential to expand applicant recruitment. The removal of score thresholds may capture qualified applicants who defer applying due to a “noncompetitive” test score, while also ensuring qualified applicants with lower test scores undergo review by programs, therefore expanding diversity in the applicant pool and in turn within the field of urology. However, with a steadily increasing number of urology applicants, there is concern regarding the increased burden on program leadership.

Adapting to USMLE Scoring Change

We have recently seen various adaptations to the interview process with the COVID-19 pandemic and with the scoreless application season approaching, residency programs must again undergo process transformation. There is a call to transition to a holistic review of applications. Although an all-inclusive evaluation is time consuming, it would be the best way for programs to assess an applicant’s fit. However, there remains concern for bias due to the lack of objective data to compare applicants. Program directors already express frustration regarding applicant similarity secondary to lack of medical school grades or distinctive letters of recommendation, and the elimination of test scoring further complicates this issue. In order to truly assess candidates’ alignment with their program, faculty will be tasked with creating other metrics for evaluation, such as secondary applications, additional essays, or video interviews, aimed at capturing attributes prioritized by programs.

Still, a barrier to holistic review or additional application components is the urology match timeline constraint. Programs are tasked with developing strategies to effectively and efficiently evaluate candidates without overwhelming program directors and selection committees. To offset this burden, urology could consider delaying the match or joining the regular match to extend the timeline for reviewing applications or contemplate transitioning to a tiered approach with multiple stages within the cycle. There is also discussion around limiting program applications per student.

Regardless of the adaptations made, urology as a field will undoubtedly continue selecting top-notch candidates as future trainees. With the imminent changes to the residency match process, we must innovate and refine—abilities honed by urologists—our practices to strengthen the capability to attract and choose capable, committed, and diverse candidates.


New York Section EMPIRE Virtual Lecture Series: Updates and Next Steps

At the onset of the COVID-19 pandemic in early 2020, the New York Section of the AUA created the “Educational Multi-Institutional Program for Instructing RESidents” (EMPIRE) series in an effort to virtually supplement trainee education during those difficult early months. Members of the New York Section and colleagues around the country rose to the occasion and delivered dozens of high quality seminars on wide-ranging topics, attracting thousands of viewers.

After the conclusion of the first series, we received feedback requesting subsequent sessions focused on preparation for the AUA In-Service Exam (ISE). A list of topics was generated based on the AUA Core Curriculum to target high-yield information for the ISE. Eighteen lectures were delivered via Zoom over 9 weeks by New York Section faculty. These sessions combined topic review and discussion of practice ISE questions. All lectures were streamed live and recordings were archived on the EMPIRE YouTube channel.

The EMPIRE YouTube channel drew a large audience with 1,800 subscribers, 11,638 total views and a total watch time of 2,592 hours leading up to the examination on November 21, 2020. The figure highlights the total views and watch times for each session, with Dr. Steven Brandes’ “Comprehensive Review of Genitourinary Anatomy” lecture being the most popular in the series. These lectures have subsequently garnered a total of 29,024 views with a watch time rising to 6,183 hours since the examination, suggesting these topic reviews provide continuing educational value outside of ISE test preparation.

We found that viewers of the series were between 25 and 34 (74%) and 35 and 44 (24%) years old, consistent with the mean age of active urology residents (31±4 years old) published in the 2019 AUA resident census (AUAnet.org/Census). Mobile devices were often used (45%) to access recorded content, suggesting that ease of accessibility and portability of information are important factors for the current generation of learners. On a post-series survey (n=46), 92% of respondents felt increased confidence for the ISE as a result of these seminars.
EMPIRE Virtual Lecture Series

Continued from page 32

The next phase of the EMPIRE lecture series aims to address aspects of urological education that are nonclinical and are not explicitly taught. In a survey of the New York Section young urologists in 2020, respondents expressed interest in learning more “skills” such as billing and coding, academic promotion, financial planning, and wellness and burnout.

With this information in mind, the EMPIRE “Hidden Curriculum” series was created in conjunction with New York Section support and leadership.

The EMPIRE “Hidden Curriculum” series aims to address gaps in training to create an everlasting resource for early-career urologists as they transition to the world of independent practice. Lectures will include the aforementioned topics in addition to principles of malpractice, pathways for political advocacy, surgeon-scientist career advice, private practice employment models, and contract negotiation.

Those interested can tune in to these free CME-accredited lectures through July 1. The full schedule and more information will be posted on the New York Section AUA website (nyaua.com) as well as Twitter @ NYSAUA @EMPIREurology.

The EMPIRE urology YouTube channel (tinyurl.com/empireuro) will also house all sessions, in addition to the original COVID-era lectures and the ISE review.


ATOMS: An Emerging and Versatile Treatment for Post-Prostatectomy Incontinence

Keith Rourke, MD, FRCS
University of Alberta

Despite advances in prostatectomy technique, incontinence remains an impactful complication following prostate cancer treatment. The incidence of urinary incontinence following radical prostatectomy varies widely from 1%–40% depending on the length of followup and definition of incontinence. While the artificial urinary sphincter (AUS) remains the gold standard for treatment of post-prostatectomy incontinence (PPI), since its introduction by American Medical System Holdings, Inc. in 1973, there remain several drawbacks to this procedure including a continence rate of 75%–80% (incurring a 20%–25% incontinence rate), a revision rate of 15%–60% at 7–10 years, requirement of an

![Incontinence and Prostate](image1)

![Prostate](image2)

![Urology](image3)

![Neurology](image4)

![Surgery](image5)

![Pathways](image6)

![Management](image7)

![Hydration](image8)

![Urethral](image9)

![Bowel](image10)

![Cancer](image11)

![Surgery](image12)

![Prostate](image13)

![Urology](image14)

![Neurology](image15)

![Surgery](image16)

![Pathways](image17)

![Management](image18)

![Hydration](image19)

![Urethral](image20)

![Bowel](image21)

![Cancer](image22)

![Surgery](image23)

![Prostate](image24)

![Urology](image25)

![Neurology](image26)

![Surgery](image27)

![Pathways](image28)

![Management](image29)

![Hydration](image30)

![Urethral](image31)

![Bowel](image32)

![Cancer](image33)
ATOMS Treatment for Post-Prostatectomy Incontinence

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is filled with 10 ml saline solution and then allowed to equilibrate until reaching ambient pressure. At this point of equilibrium typically a further 2 ml is added, but this may depend on the patient’s degree of incontinence and detrusor contractility. Adjustments are typically performed (if required) beginning 4 weeks after placement and up to 26 ml in total. ATOMS is not currently available in the United States but has been available in Canada since 2014.

There is currently no randomized study comparing ATOMS to other devices, but based on multi-center reports and meta-analysis the continence rates of ATOMS is typically 70%–75% even in patient populations typically deemed less than ideal candidates for slings, including concurrent radiotherapy and prior incontinence surgeries.8,9 Likewise, improvement rates typically approach 90% after postoperative adjustments.8,9 On balance, overall efficacy seems to fall just below the AUS but is typically superior to the majority of nonadjustable male slings. However, in common with all slings, prior radiotherapy and severe incontinence (>5–6 pads) are factors associated with failure to achieve continence, but may not diminish efficacy as dramatically as seen in nonadjustable slings.8,9 Complications of any grade occur in approximately 15% of patients with a 3% rate of major complications.8,9 The majority of complications include scrotal pain or parenthesis, wound infection, hematoma or transient urinary retention. Device explantation occurs in ~6% of patients, which falls within the range of other male slings but lower than the explantation rate associated with an artificial urinary sphincter.

Overall, ATOMS has emerged as an acceptably safe and effective treatment for varying degrees of post-prostatectomy incontinence even in patient populations not typically deemed ideal candidates for a male sling procedure.1


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Erythropoietin and Erectile Function after Radical Prostatectomy

Hiten D. Patel, MD, MPH

Arthur L. Burnett, MD, MBA

Mohamad E. Aliaf, MD

Loyola University Medical Center

Brady Urological Institute

The Johns Hopkins University School of Medicine


While survival outcomes are generally excellent for patients diagnosed with clinically localized prostate cancer, functional outcomes are more variable. Optimization of the bilateral nerve-sparing approach has enabled erectile function recovery for patients undergoing radical prostatectomy, and urologists have several management options for post-surgical erectile dysfunction to help patients after definitive cancer treatment. However, the goal of further impacting the natural history of erectile dysfunction after radical prostatectomy has remained elusive.

Even with bilateral nerve-sparing radical prostatectomy, some degree of crush, stretch, or thermal injury may occur to the neurovascular bundles with known variation in outcomes between providers.1 Several groups have recently turned to evaluating agents or strategies that could have neuroprotective effects on the periprostatic structures. Preclinical studies on erythropoietin found the glycosylated cytokine hormone to have receptor expression in both human penile tissue as well as the neurovascular bundles.2 Followup evaluations showed promise in a rat cavernous nerve injury model and on retrospective evaluation for use in humans.3,4 Based on these findings, we designed and pursued ERECT (NCT00737893) as a phase 2, double blinded, placebo-controlled randomized clinical trial to evaluate the efficacy and safety of perioperative erythropoietin to enhance erectile function recovery after radical prostatectomy.5,6

A total of 56 patients without baseline erectile dysfunction scheduled to undergo radical prostatectomy were randomized to arms receiving erythropoietin (29) or placebo (27). Subcutaneous injections of 20,000 units of erythropoietin or a saline placebo were given the day before, day of, and day after radical prostatectomy, of which most patients received a robotic approach.5,6 The primary outcome of interest was International Index of Erectile Function (IIEF)-erectile function (EF) domain score at 6 months after surgery, with secondary outcomes evaluated by several other validated survey instruments for up to 12 months after surgery.

Notably, median IIEF-EF scores nearly doubled from 12.5 at 3 months after surgery to 24.5 at 12 months, and there was an increase in 2-week serum hemoglobin values in the erythropoietin arm compared to the placebo arm, as would be expected. However, there were no statistically significant differences

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Figure. Anatomical placement and configuration of current (third generation) ATOMS device.
in IIEF-EF scores at any time point evaluated (see figure). Other patient-reported outcomes were also similar during followup, including urinary function, mental health component scores, and physical health component scores.

The primary factor associated with better IIEF-EF scores was excellent nerve-sparing rating (a rating of 10/10 in 24 patients [43%]), which was associated with a 5.2-point improvement. This is notable as nerve-sparing was still subjectively quite good in the remaining patients (12 [21.4%] had 9/10, 17 [30.4%] had 8/10, and 3 [5.4%] had 6-7/10). Additionally, no safety or oncologic concerns were identified among patients studied, and use of erectile dysfunction therapies did not differ between arms.

While ERECT was a negative trial, it does raise the question of whether alternative dosing regimens or combination with local adjuncts could provide improved efficacy. For example cryopreserved placental membrane is a candidate for local placement during surgery, which may carry tissue, growth, and cellular factors. One retrospective study reported that use of dehydrated human amnion/chorion membrane was associated with improvement in IIEF-5 after radical prostatectomy.

At the same time, our experience indicates that retrospective results in this area should be interpreted with caution. Careful evaluation in a controlled trial setting is necessary prior to routine clinical use to confirm efficacy of sometimes expensive therapies and to inform patients of potential adverse events. Other therapies with promise which did not hold up in randomized trials for recovery of erectile function after radical prostatectomy include sural nerve grafting and hyperbaric oxygen.

Future clinical studies of neurotrophic agents or targeted agents regulating neural and muscular function, which have been evaluated in preclinical nerve crush injury models, are needed.

We were in heavy chop in the Mindoro Strait at 3 a.m. in the South China Sea off the coast of the Philippines when the first victim was spotted. Barely visible in the dark, clinging to a small board, we maneuvered to fish the woman out of roiling seas. Her tale was chilling: Their overloaded vessel had sunk 8 hours earlier with over a hundred passengers, and we were 5 miles from shore with the current headed out to sea. No sharks had arrived yet. As a newly minted medical school graduate and the only doctor on board, medical responsibilities were mine, but despite extensive ambulance experience and Eagle Scout training, I was immediately struck by the lack of resources in this remote area. Our rescue of 87 people, including many children, really sparked my lifelong interest in remote medical care and expedition medicine.

It has been said that a medical degree is a passport to travel and that certainly has held true for me. Since that maritime disaster, expedition medicine has been a major interest alongside my academic medical career, allowing me to contribute to many exciting adventures. Whether barely avoiding a coup while traveling to the most remote jungles in Africa, descending over two miles in the ocean where the Titanic rests, riding camels deep in the Mongolian Gobi desert observing the newly described highly endangered wild camel, rescuing a trapped ship on an icebreaker in Antarctica, exploring the Amazon rainforest, or traversing the deepest canyon in the world, each destination has had its unique problems for preparation and safety, yet many share common elements.

My background and avid interest in field exploration and expedition medicine has led to a fascinating array of experiences. I remain a consultant to National Geographic® for medical issues and served on the NASA Aerospace Medicine and Occupational Health Advisory Committee, responsible for the care of our astronauts. Shortly after leaving academic medicine at George Washington University where I was professor of urology, engineering, microbiology and tropical medicine, I became chief medical officer for a high threat security company. We had 7,000 special forces contractors deployed in Iraq and Afghanistan, and I had 62 medical personnel reporting to me from battle zones. We dealt with mundane occurrences like a broken ankle while playing touch football, but we also managed medical evacuation and management of men injured by mortar attacks or exposed to active tuberculosis.

Other exploration activities have included diving the famous Spanish treasure galleon Nuestra Señora de Atocha in search of artifacts, digging million-year-old early human fossils with the Smithsonian Institution’s Human Origins Program in Kenya, and evaluating a new spectacular finding of early human footprints in rural Tanzania that is now a world heritage site. The common thread of all these activities is medicine, because I oversaw or provided medical care for the expeditions in these remote sites.

Continued on page 37
Social Media Utilization and Applicant Perception in the SARS-CoV-2 Match Era

The effects of the novel coronavirus SARS-CoV-2 on the urology match were numerous and widespread. Beginning in March of 2020, administrative bodies, including the American Association of Medical Colleges and the Society of Academic Urologists (SAU), released changes to the standard residency application process including cancellation of away subinternships, delay of Electronic Residency Application System submission and release to programs, and cancellation of in-person interviews. Programs explored a number of unique approaches to facilitate applicant exposure and fill the void, including virtual open houses, virtual subinternships, developing social media presence, updating websites, or some combination thereof. Given the novelty of these approaches, it was imperative to assess the efficacy of these contemporary offerings for applicants to guide future program efforts.

We created a 19-question survey utilizing Likert, dichotomous yes/no, and free text questions to inquire about applicant attitudes regarding social media, open houses and meet and greets, virtual subinternships, and other assorted application behaviors during the SARS-CoV-2 match era. The survey was provided to attendees registering for the American Urological Association (AUA) Medical Student Education Committee webinar entitled “Optimizing Medical Student Exposure and Interaction with Urology Remotely,” which took place on June 24, 2020, the recording of which is available on the AUA University YouTube channel. A total of 105 registrants completed the survey, representing roughly 20% of the ultimate applicant pool (see table).

Overall, applicants found virtual offerings by programs helpful in guiding their applications. For learning remotely, the AUA Medical Student Education Curriculum and Core Curriculum continued to prove valuable resources for urological education. The creation of virtual subinternships, a herculean effort by the SAU, was also appreciated by applicants as the majority of them planned to complete at least 1. The most preferred platform for interacting with programs was Twitter. A previous study completed in 2015 found that only 30% of urology residency programs had Twitter accounts, but cursory review in 2020 revealed at least 75% of urology residency programs or departments now have a Twitter account. Accordingly, many applicants have pursued the creation of social media accounts specifically for interacting with programs. The so-called “Urology Twistersphere” provides a unique opportunity for self-promotion of applicant or program strengths while also allowing a modality of interaction and direct communication not previously available. Zoom was rated second to Twitter for preferred technology with regard to interacting with programs. The number of Zoom networking opportunities, often in the form of open houses or meet and greets, was significant, averaging 2 to 1/2-hour-long events from different programs per week over the month of July 2020.

Although online outreach was perceived as a valuable tool for the urology match, applicants had reservations with regard to online assessment of their qualifications, ability to evaluate programs, and ability to build relationships with faculty, residents, and staff. The latter point is of particular importance given prior studies which identified interaction with current residents and perceived relationship between faculty and residents as 2 of the top 3 criteria in evaluating a residency program. Perhaps a degree of this trepidation was from a lack of experience with these previously underutilized modalities, as well as a lack of available guidance on how to maximize the potential of these opportunities. The variable structure of online offerings and the robust number of online events may also have contributed. Future iterations of online modality utilization in the match should consider these perceived limitations and incorporate feedback from applicants to optimize outreach efforts. These important efforts are already underway with survey studies from multiple organizations, including the SAU, being collected and analyzed to assess applicants’ experiences during the SARS-CoV-2 match era. This data will be informative.

As programs move towards a post-SARS-CoV-2 match era, we would suggest continuing the trend of increasing program visibility through the creation of curated social media accounts, updating program websites regularly, and offering online experiences for applicants to learn about programs including use of testimonials of current residents and faculty, such as those currently being collected and hosted on UroResidency.com. Despite many residency websites undergoing overhaul in this match cycle, there remains a dearth of objective information for applicant evaluation of programs. A prior study found that applicants’ number 1 criterion in program evaluation is operative experience, yet only 1% of programs listed information regarding operative experience or case logs on their website. Ready available online
Applicant Perception of Social Media Match Use

Continued from page 37

rankings such as Doximity and US News and World Report, which have variable methodology and are of questionable utility to applicants, continue to be easily accessible.

The 2021 Urology Residency Match was significantly altered due to SARS-CoV-2 necessitating novel virtual and social media-based solutions. In these initial data, just preceding the 2021 urology application cycle in late June 2020, online offerings and social media were highly utilized and felt to be valuable for guiding residency applications. As the next application cycle approaches, we hope programs continue to enhance this online and social media presence.

The authors would like to acknowledge the Medical Student Education Committee within the Office of Education of the American Urological Association for access to the survey data in this report, as well as collaborators Phillip G. Key, BS (Kalamazoo, Michigan), Jinping Jiang, BA (Omaha, Nebraska), Gina M. Badalato, MD (New York, New York), and Chad R. Tracy, MD (Iowa City, Iowa) who assisted with these efforts.

<table>
<thead>
<tr>
<th>Has the increased virtual presence of programs (updated websites, open houses, meet and greets, social media presence) been helpful in guiding your upcoming applications?</th>
<th>Are you currently planning to pursue a virtual subinternship?</th>
</tr>
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<tbody>
<tr>
<td>Yes</td>
<td>87%</td>
</tr>
<tr>
<td>If yes, which technology platform has assisted you the most?</td>
<td>If yes, how many?</td>
</tr>
<tr>
<td>Twitter</td>
<td>50%</td>
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<tr>
<td>Twitter and Zoom</td>
<td>23%</td>
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<tr>
<td>Zoom</td>
<td>19%</td>
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<tr>
<td>No</td>
<td>13%</td>
</tr>
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<tr>
<th>Have you created social media accounts specifically to interact with programs during this application cycle?</th>
<th>How well have you been able to evaluate programs with virtual open houses and meet/meets at date? (Scale, 1 = not well at all to 5 = very well)</th>
</tr>
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<tbody>
<tr>
<td>Yes</td>
<td>70%</td>
</tr>
<tr>
<td>No</td>
<td>30%</td>
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<tr>
<th>How well do you think programs have been able to evaluate you as a candidate through current online offerings? (Scale, 1 = not at all to 5 = very well)</th>
<th>Do you feel you have been able to form relationships with faculty and residents at open houses and meet and greets?</th>
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<tr>
<td>Not Well (1-2)</td>
<td>82%</td>
</tr>
<tr>
<td>Neutral</td>
<td>17%</td>
</tr>
<tr>
<td>Well (4-5)</td>
<td>1%</td>
</tr>
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</table>

Which top 2 sources have you used to date for your remote urological learning (ie COVID lecture series, EMPIRE lecture series, Tweetorials, AUA Medical Student Core Curriculum, Pocket Guide to Urology, a textbook, podcasts)?

| AUA Medical Student Curriculum or Core Curriculum | 75% |
| Pocket Guide | 48% |
| COVID Lecture Series | 22% |

Lessons from a Teenage Dishwasher

Neil H. Baum, MD
Tulane Medical School

In the summer of 1960, I had my first job as a dishwasher at a local college during summer school. I was paid an hourly minimum wage. My assignment was scrubbing and cleaning pots and pans. Since this was my first paid job, I was eager to demonstrate my energy and enthusiasm. I was able to complete my dishwashing assignment in 2 hours and sat down and looked at a magazine. (There were no cell phones at that time!) The kitchen manager asked, “What are you doing?” I told him I finished my job. The manager then told me to polish the silverware. I completed that task very quickly and he then sent me home. I was only able to be paid for working 3 hours. I did not need to be a time-and-motion expert to understand that I had to work slower to increase the hours worked and increase my income.

So, what does this have to do with the practice of medicine?

The working hours in my practice were 8 a.m. to 5 p.m., and the staff always stayed until 5 p.m. even if they were done with their workload before QT (ie quitting time). One of the problems we had was controlling the 3 to 5 no-shows that might occur each day. We had the receptionist call patients at home 24 hours before their appointment to remind them of their appointment. We also took the names of patients who wanted earlier appointments if slots became available. These were patients who were willing to come in on short notice.

On several occasions, there were open slots in the schedule, and I asked if patients who were willing to come in on short notice were contacted. The answer was almost always that the waiting list was not used and yet the staff was doing unproductive work waiting for 5 o’clock. Reflecting back on my days as a dishwasher, I told the staff if they were able to fill the no-show slots making use of the waiting list, and the work was completed, they would be permitted to leave before 5 p.m. Voila, all the holes in the schedule were filled and the no-show problem was solved.

Another practice was having issues putting patients in the rooms at 9:00 a.m. to start the clinic schedule. The doctors blamed the staff for not moving the patients into the rooms at 9:00 a.m., and the staff blamed the doctor for arriving after 9:00. The office manager, the nurses and the doctors had a meeting, and they all agreed that patients would be advised to arrive at 8:30–8:45 a.m., and the doctor would also arrive at 8:45 a.m., and now the schedule commenced at 9:00 a.m. and was kept on track for most of the day.

Recently, several companies are offering 4-day work weeks because they noted a decrease in productivity on Fridays, especially Friday afternoons. Microsoft in China offered a 4-day work week and noted that productivity increased by 40%. Perhaps this could apply to medical practices. How? The staff could work 10-hour days for 4 days a week. Friday would be used for surgery—especially Friday morning—and if the urologist finished early, he or she could also go home early and spend time with the family and be home for dinner.

Bottom Line: We should reward staff for being efficient. Making the staff stay when all the patients have been seen and all the tasks have been completed is going to motivate the staff to behave like the teenage dishwasher and work slower to increase the hours worked.

With the proliferation of choices to treat benign prostatic hyperplasia, patient choice should be driven by transparency of all outcomes. A choice dependent on type of anesthesia, convenience, chance of retrograde ejaculation, symptom improvement and time-dependent risk of recurrence all require good data for those variables. In this study the authors looked at reintervention outcomes for the surgical options available.

A total of 43,041 male patients with lower urinary tract symptoms who underwent transurethral resection (34,526), photoselective vaporization (3,050), laser enucleation (1,814) or open simple prostatectomy (3,651) between 2011 and 2013 were identified in the German local health care funds and followed for 5 years. Surgical reinterventions for lower urinary tract symptoms, urethral stricture or bladder neck contracture were evaluated. A total of 5,050 first reinterventions were performed within 5 years of primary surgery. Photoselective vaporization carried an increased hazard of reintervention (HR 1.31, 95% CI 1.17–1.46, p <0.001) relative to transurethral resection, open simple prostatectomy carried a lower hazard (HR 0.43, 95% CI 0.37–0.50, p <0.001) and laser enucleation of the prostate did not differ significantly (HR 0.84, 95% CI 0.66–1.08, p=0.2). This pattern was more pronounced regarding reintervention for lower urinary tract symptom recurrence.

The authors conclude that 5-year reintervention rates of transurethral resection and laser enucleation did not differ significantly, while photoselective vaporization had a substantially higher rate. Open simple prostatectomy remains superior to transurethral resection with respect to long-term efficacy.


Hitchen’s razor states: “What can be asserted without evidence can also be dismissed without evidence.” Sadly, this cannot apply to overlapping surgery restrictions which have been implemented without demonstration of patient harm. In this study the authors wished to evaluate whether the practice of procedure-time overlapping surgery (OS) is associated with inferior outcomes compared to nonoverlapping surgery (NOS) in urology. They reviewed all urological surgeries at a single tertiary-level academic center from July 2016 to July 2018. Patients who received OS were matched 1:2 to patients who had NOS. The primary outcomes were perioperative and postoperative complications and mortality. Of 8535 urological surgeries in-room time overlap was seen in 50.5% of cases and procedure-time overlap in 74.4%. Eleven out of the 13 attending urologists performed OS. The average time in the operating room was greater for OS by an average of 14 minutes. The average operative time was greater for OS than NOS by 11 minutes, but this did not reach statistical significance. There was no significant difference between the cohorts for rate of blood transfusions, ICU stay, need for postoperative invasive procedures, length of postoperative hospital stay, discharge location, emergency room visits, hospital readmission rate, 30-day and 90-day rates of postoperative complications, and mortality.

The authors conclude that procedure-time overlapping surgeries constituted a minority of urological cases. OS were associated with greater in-room time. They found no increased risk of perioperative or postoperative adverse outcomes in OS compared to matched NOS.


A lot of weight is placed on symptoms and signs compiled during an office visit, but is what we see in a snapshot of time really representative of the patient’s at-home behaviors? Certainly the advantage of 24-hour Holter monitor over an in-office EKG are well known. In this study, the authors used a home uroflow device to assess individual voiding variability, temporal distribution of voiding parameters and the impact of age on voiding. A total of 19,824 unique voiding profiles were captured using the Stream Dx Uroflowmeter and retrospectively analyzed. A total of 637 patients were identified with 625 meeting inclusion criteria, producing 19,824 voids. Mean age was 67 years old, and each patient provided on average 5 (±3.3) voids a day through 7 days. Average intrapatient voiding parameters showed notable variability, where the coefficient of variation for maximum flow was 27.6% (95% CI 26.6–28.6). Early morning voids were associated with higher volume and lower number of voids. As age progressed, voiding profiles worsened in a linear fashion. Afternoon and evening voids were associated with reduced intra-patient variability relative to early morning voids.

The authors conclude that an individual’s voiding parameters vary greatly from day to day, throughout the day, and worsen with age. Multiple measurements performed at home provide a more realistic assessment of true voiding behavior by capturing individual voiding variability.
**FROM THE AUA Secretary**

*An Update on the Impact of COVID-19*

John D. Denstedt, MD, FRSC, FACS, FCAMS
Editor, AUA News

After more than a year of living in the global COVID-19 pandemic, we have started to settle into a new normal. While most urologists and medical professionals are back to practice, performing elective surgeries and having adapted to virtual learning, the specialty of urology will forever be impacted by the pandemic.

Virtual programming has become the go-to for education. The pandemic gave us the opportunity to find new ways to utilize technology to connect and educate our global community, advance our specialty and improve the care of the patients we serve. While we look forward to returning to in-person education, we remain proud of our swift adaptation over the last year to digital education.

Last year, the AUA leveraged the latest technologies to bring the best science from the AUA Annual Meeting to its members through various virtual programs. The success of this online education format provided the AUA with new opportunities to deliver urological education right to your computer. The AUA adapted to digital formats for its educational courses, Annual Urology Advocacy Summit and other programs that were traditionally in-person events. We’re hopeful to reunite the world of urology in Las Vegas this September and are pleased with the response to last month’s virtual kick-off weekend. With our AUA Summer School courses starting, we have a lot of great science and information to share with you leading up to the in-person Annual Meeting in September.

As providers around the globe work to diagnose, treat and understand COVID-19, a growing body of clinical insights are becoming available, and the AUA has curated the latest clinical information of interest to the urology community. *The Journal of Urology™* and Urology Practice have published COVID-19-related articles that are open access for all readers. The AUA also has a COVID-19 Info Center full of information about the pandemic’s impact on urology clinical insights, telehealth, advocacy and more. The AUA COVID-19 Info Center can be accessed at www.AUAnet.org/COVID19.

This unprecedented public health emergency has showcased the resilience of the global urology community. While we are still feeling the impact of this pandemic, we are thankful for the new opportunities it has created, the lessons it has taught us and how it has brought people, communities and nations together. As we continue to navigate our new normal, the AUA will continue to support the urology community and the patients they serve.◆

**FROM THE Chief Executive Officer**

*Value of Continuing Education, Developing Teams (The AUA Gives You the Tools to Fully Arm Your Staff!)*

Mike Sheppard, CPA, CFE
CEO, American Urological Association

The AUA is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. As a leader in providing quality, evidence-based urological education, the AUA takes great pride in this honor. We work diligently, year-round to provide courses that will best develop personal and professional growth.

The AUA2021 Annual Meeting Kick-off Weekend was held May 21–23 and launched the beginning of the educational opportunities provided during the 116th meeting. The 3-day program provided instructional courses and additional programs that spanned the full spectrum of urology. Specialty courses were provided for researchers, young urologists, residents and advanced practice providers. The AUA Practice Management Program was held May 22–23. This virtual education experience, designed for practice managers, featured relevant and timely topics such as patient-centered care, strategic business planning, best practices in practice operations professional development and leadership topics, financial management, and coding and reimbursement, as well as federal law, regulations and advocacy.

AUA2021 education will continue with the Summer School series. This virtual series is perfect for urology health care professionals who find themselves with unpredictable schedules to take advantage of opportunities for continuing education. Each week from June through August, 2 instructional course webcasts will be released covering a vast area of urology topics including women’s health, cancer treatments and sexual function.

All educational content will cumulate at AUA2021 in Las Vegas September 10–13. Attendees will have access to Plenary programming, featuring the very latest from leaders in urological medicine. Popular not-to-be-missed activities include Hands-On Skills Training, Instructional Courses, Scientific Abstracts, and Cross-Fire Debates. Attendees will also be able to enjoy 2 exciting new programs: “When Disaster Strikes: Preventing and Managing Nightmares in Urology” and “Game Changers: Newsmakers in Urology.”

We make it our mission to offer our members a vast catalog of continuing education programs. We meet you where you are—at home, in the office, on a weekend or at a conference—because your individual growth increases the strength of the entire urological community and improves patient outcomes for years to come.

Learn more about all of the educational opportunities provided at the 2021 AUA Annual Meeting at AUA2021.org. ◆

**FROM THE Urology Care Foundation**

*The Urology Care Foundation LEADS the Way in Diversity and Inclusion through Research*

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

The Urology Care Foundation is a driving force in the discovery of new treatments and is committed to ensuring the future of urological health by supporting and improving the prevention, detection and treatment of urological disease through research and education.

Each year, the Foundation invests in the brightest minds and the best urology research—research that leads to better treatments and improved quality of life.

The Foundation offers a portfolio of mentored research training awards intended to recruit outstanding young investigators into urology research and foster their career success. In 2020, we awarded nearly $1.5 million in funding through such programs.◆

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programs as the Research Scholar Awards, Residency Research Awards, Rising Stars in Urology Research Awards and our Summer Medical Student Fellowships.

We continue to focus on developing resources to make urologic research training more compelling to all young scientists, especially the physician-scientists in underrepresented communities. Our goal is to ensure urologic research is strengthened through diversity and inclusion by providing opportunities to ALL.

We recognize the critical need to create and maintain opportunities for all investigators and especially those of underrepresented minorities and understand that the path to developing a strong and sustainable research career is faced with many challenges. Therefore, the Foundation and the AUA took a comprehensive approach to providing research support and announced earlier this year, a new urology research program aimed at fostering diversity and inclusion within urology research, supported by a generous $2 million donation from Urovant Sciences (Urovant).

A comprehensive award program, the Leadership Education, Achievement and Diversity (LEAD) program will support 3 urology residents, per year, from racial and ethnic backgrounds underrepresented in urological research, to conduct mentored research, engage in research education and be championed through networking, as they develop successful research careers and better serve the urology patient community.

The LEAD program will leverage both the Urology Care Foundation Residency Research Award and the AUA's existing Urology Scientific Mentoring and Research Training (USMART) Academy to engage each young surgeon-scientist in additional mentoring and career development with established urology investigators who are leaders in their field.

In addition to research training and mentoring opportunities, the LEAD program will:

• Support the participation of its urology residents for 2 years in the AUA Research Honors Program.

• Support the participation of its urology residents in 2 scientific meetings during their funding year, including the AUA Annual Meeting and another meeting of their choice, based on scientific relevance.

• Support the participation of its urology residents in 2 AUA Early Career Investigator Workshops, one during their residency and one during the research year of their clinical fellowship.

Applications for the LEAD program will be accepted starting in October and Award recipients will be announced in March 2022, before being recognized at the AUA Annual Meeting in May 2022. We encourage you to learn more about the LEAD program and all the Award support programs the Foundation has to offer by visiting: UrologyHealth.org/Research.

We are excited by this new initiative and look forward to receiving applications from the many qualified applicants we would like to support.

FROM THE Education Council

Forever Forward during Ever-Changing Times

Jay D. Raman, MD, FACS
Chair, AUA Office of Education

“Knowledge is an unending adventure at the edge of uncertainty.” – Jacob Bronowski

I was delighted in November of 2019 to be selected as the next Chair of the Office of Education (OE) by the search committee and the AUA Board of Directors. I readily anticipated a year-plus in the Chair-Elect role learning how to keep the well-oiled machine on track while expanding on the work done by Dr. Vic Nitti and the OE staff. And then (as we all know) COVID-19 hit, thereby impacting best laid plans. While there were many challenges that arose, it also presented an opportunity to adapt and refine our programming, harnessing lessons learned over the past year.

I am, therefore, excited to begin my 4-year term in June 2021 leading the AUA’s Office of Education hoping to bring the best educational content in the most engaging way possible to our AUA members.

From a content perspective, the AUA’s New Technologies and Imaging Committee is doing exciting work mapping out adoption cycles of technologies across various domains (BPH, Endourology, Imaging, and Robotics) to better drive the AUA’s surgical skills training education. This work is reflected in the strong lineup of hands-on courses offered at the annual meeting in Las Vegas, including Introduction to Office-Based Transperineal Prostate Interventions, Prostate MR Imaging, Interventional Ultrasonography, Practical PCNL, Introduction to Prostate Tissue Ablation and Single-Port Robotic Surgery. These courses will be offered foremost with your safety in mind adhering to approved guidelines. Make sure to sign up before these important courses sell out!

If you have not registered for AUA2021—don’t wait! The AUA2021 May Kick-off Weekend will be held virtually from May 21 through 23 and will provide over 35 hours of live educational content. Thereafter, the 2021 Summer School courses (aka AUA2021 Instructional Courses) will run on Tuesdays and Thursdays from June 3 through August. Each of these 24 courses will be offered as a live, virtual, 1.5-hour event and afterwards will be available on-demand if you miss the live activity. Please make sure to sign up for one of our registration packages to access some or all of this great content.

In June, the AUA’s Annual Review (June 4–6) and Fundamentals Courses (June 11–13)—2 long-standing educational programs for residents—will be offered virtually after feedback from training programs. This method of delivery has received very high evaluation results from our learners. In fact, the 2020 Annual Review Course was done virtually in December, and 97% of participants rated it excellent or very good in overall quality, and 99% would recommend the course to others.

In addition to these great live courses, the brand-new SASP app is now available. Since its launch in October 2020, more than 230,000 questions have been answered within the app. Based on type of purchase, you can also sort your questions by year or by topic and create personalized question decks to focus on your areas of improvement. New features will continue to be added to the app including flash card animated decks and a Question of the Day. For the smartphone savvy, the new AUAUniversity mobile app is also in development and will be available later this year.

To access all of these great educational opportunities, go to AUAUniversity at https://aua.auanet.org/. And if you need any assistance, OE staff is always available to help (education@auanet.org), and I am always interested in your feedback.

AUA RESIDENTS & FELLOWS Committee News

Inspiration from Innovation—Is It Worth It?

Daniel Joyce, MD
Vanderbilt University Medical Center

On July 20, 1969, all eyes watched as Neil Armstrong set foot on the moon. Thirteen years later (and 4 months before my birth) the country was consumed once again by what many believed to be the medical moon landing equivalent. On that day in 1982, my father was listening to Ravel’s Boléro as he and Dr. William DeVries implanted the first total artificial heart (TAH) for destination therapy into...
AUA Residents & Fellows Committee News

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a human being. I recall looking at old photos of my pregnant mother standing next to Barney Clark, the recipient of that heart, as he lived an extra 112 days thanks to the aluminum and polyurethane technological marvel powered by a 400-pound air compressor (see figure).

In a country reckoning with social inequality, Apollo 11’s $28 billion price tag was not overlooked. Similarly, just 2 years after Clark’s death, Colorado Governor Richard Lamm joined the increasing swell of TAH critics proclaiming, “High-tech medicine is really the Faustian bargain, where for a few extra days of life, we have to pay the price that could bankrupt the country.” The cover of Time magazine read, “Medical Miracles, But How to Pay the Bill?” with a picture of DeVries standing next to Barney Clark, the recipient of that heart, as he lived an extra 112 days thanks to the Jarvik-7 total artificial heart.

Figure. My 3 siblings sitting with Barney Clark following implantation of the Jarvik-7 total artificial heart.

Five years ago, I began my residency at Vanderbilt, a program that grew its reputation under the guidance of Dr. Joseph A. Smith. In Dr. Smith I saw many of the qualities I admired in my father: compassion, surgical expertise, a passion for teaching, a dedication to family, and a desire to explore the limits of medical technology. The example of his pioneering in laser and robotic surgery was a continual reminder to question the status quo and confront the fear of abandoning what’s comfortable in order to push the limits of what’s possible.

And yet again I saw critics push back against innovative initiative, pointing out that, despite providing no difference in long-term outcomes, more than 90% of radical prostatectomies are performed robotically today, contributing to a global market for surgical robotics that is projected to reach $17 billion by 2025.

Like any trainee about to enter the workforce, I felt the dissonance between the desire to innovate and the desire to reduce healthcare’s financial toxicity. Not long ago, as he performed his 7,000+ robotic prostatectomy, I listened as Dr. Smith shared with me the impact that Apollo 11 had on him. He explained how it guided and informed his circuitous path from astronaut training to making now legendary contributions to the field of urology.

The value of the ripple effect of inspiration cannot be quantified. Perhaps these (and future) costly achievements will inspire others to innovatively reduce health care costs. Or perhaps they will “simply” recruit more physicians who emulate the admirable qualities of the mentors I’ve been so fortunate to learn from. As Gene Cernan, the last man to walk on the moon, said, “As I take these last steps from [the moon]… I’d just like to record that America’s challenge of today has forged man’s destiny of tomorrow.”

FROM THE AUA Research Council

Passing the Gavel

Aria F. Olumi, MD
Past Chair, Research Council

Steven A. Kaplan, MD
Chair, Research Council

The greatest honor of serving as the AUA Research Council Chair for the past 6 years has been the opportunity to work with the best and brightest in our field and having a collective mission to advance urological research. To reach this ever-evolving goal, our mission statement focused on educating our community so that our scientists have the proper knowledge and tools to focus on impactful research to improve the health of our patients. By creating the new Physician Science Residency Training program, an alternate path for urology residency training that was approved by the AUA Board of Directors, American Board of Urology and Accreditation Council for Graduate Medical Education, we developed a path to educate our young physician-scientists to obtain the necessary knowledge and lead independent research programs. Our online courses on “Big Data and ‘Omics’ Analysis in Urologic Research” and “The Researcher’s Toolkit” created innovative interactive learning modules. Recognizing that mentorship is a necessary component for advancement in one’s career, the USMART (Urology Scientific Mentoring and Research Training) Academy was created to enhance mentorship for our young scientists. We advocated to the federal government to maintain the U.S. Department of Defense’s disease-focused research support and played a key role in bringing to the fore bladder cancer as a funding opportunity that has benefited many of our scientists. And perhaps, most importantly, even before the recent changes in political climate, we raised awareness about diversity, equity and inclusion in our research community for proper representation in our committees and research award portfolios.
None of the above-mentioned examples, and many more that the Office of Research has tackled, would have been possible without Dr. Carolyn Best, AUA Director of Research, and her dedicated Office of Research team whose commitment and focus to advance urological research was unwavering.

As leadership of the AUA Research mission is passed on to Dr. Steven Kaplan, challenging headwinds will need to be navigated. Yet there is tremendous optimism, energy and enthusiasm, and opportunity to build on the foundations noted above. Too often, research is viewed as a loss leader at the local and institutional level as well as nationally. We have not valued and are therefore inadequately populated by state-of-the-art urology-themed researchers. Moreover, urology has not fully recognized the deleterious effects of health care disparities in our cities and country, and has not supported underrepresented minorities in helping to foster their early clinical and research careers. This will be a major emphasis moving forward with measurable milestones. In addition, we intend to create initiatives and pathways to coalesce the various groups who are needed to create a renaissance in urological research. This will incorporate scientists, urologists, legislators, leaders at both the sectional and national AUA levels, and other engaged partners in being the leaders in understanding both benign and malignant diseases.

FROM THE Public Policy Council

AUA Members Invited to Put Advocacy into Action in July

Eugene Rhee, MD, MBA
Chair, AUA Public Policy Council

July Is Advocacy Action Month for AUA Members!

This past year has been transformative on many levels. We have been forced to pivot in this pandemic, adeptly changing the way we do things—from the way we see patients to the way we manage our staffs, to the way we educate ourselves and conduct research. More than ever before, we must continue our vigilance, advocating and protecting the interests of urology. There has never been a more critical time to engage in the legislative process! July is Advocacy Action Month at the AUA, and members are invited—and encouraged—to take part in the array of free, virtual programs that will culminate with our keynote speaker and the 4th Annual Urology Advocacy (AUA) Summit on July 21.

How Do I Place Advocacy in Action This July?

EDUCATE: Educate yourself on the issues and policies affecting urology! Learn about the most pressing issues facing our specialty, from expanded access to telehealth services and medical liability reform, to workforce shortages and funding for urological research. The AUA Summit and other advocacy events in July will help educate you on the latest laws and regulations impacting you and your practice. You will also hear from the keynote speaker, Dr. Ashish Jha, Dean of the Brown University School of Public Health and a world authority on the COVID-19 pandemic. A featured guest on MSNBC and CNN, Dr. Jha will bring his unique perspective in public health with the pandemic and how it is shaping public policy.

ENGAGE: Engage with the urology community, lawmakers and agencies on the issues affecting urology! On July 20, the Summit will feature a special virtual session to explore and examine this year’s Congressional “asks” (6 to 8 p.m. EDT), followed by a virtual Hill Day on July 21 where attendees will have an exclusive opportunity to share their voices and personal stories with those shaping laws and regulations.

EMPOWER: Empower yourself to make a difference! Urology is best served—and most powerful—with our voices united. Join in these virtual events to learn how you can put advocacy in action. Here are unique and powerful ways to get involved before the AUA Summit.

• Sign Up for AUA Grassroots Alerts. Phone2Action is a grassroots advocacy platform to connect you with your elected officials at the federal and state level through email, social media and phone—all with a single click! Visit www.AUAnet.org/ActNow to sign up and urge your colleagues to do the same.

• Spread the Word. Sharing news about AUA advocacy is one of the most important things you can do, whether you’re telling your friends about the AUA’s Political Action Committee, AUAPAC (www.myauapac.org), sharing grassroots alerts with colleagues or urging residents and fellows to sign up for free fireside chat webinars sponsored by the Policy & Advocacy Resident Workgroup.

IMPACT: Finally, use your voice and resources to make an impact! It works. Whether it’s meeting with legislators and key federal agencies on Hill Day, or supporting AUAPAC, your voice and support as physicians absolutely has a profound impact on the laws and regulations that impact you, your practice and your patients.

Legislative and regulatory advocacy has always been a priority of the AUA, but this past year has especially shown us that there is power in numbers, and advocacy for urology should be a priority as an AUA member.

I hope to see you join us in July throughout the month and experience advocacy in action, assuring the voice of urology is heard! 😊
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