Practicing urology takes physical toll

Richard R. Kerr / Content Channel Director

Urologists face a significant risk of on-the-job pain and injury, an exclusive Urology Times survey has found. Ninety percent report experiencing work-related musculoskeletal pain or other discomfort, most commonly in the neck or back, over the course of their career. In what one leading urologist called a “shocking” finding, nearly two-thirds of practicing urologists say they have been threatened by a patient, and about a fourth have suffered a physical attack or abuse at the hands of a patient.

The findings raise questions both about the safety of urologic practice but also effective preventive measures, as just over half of survey respondents say they have “adequate” (44%) or “extensive” (9%) knowledge of surgical ergonomics.

The survey was conducted in late June and July 2019 via email to readers of Urology Times with email addresses on file. It was designed to examine the prevalence and type of physical and psychological harm encountered by U.S. urologists, possible causes, preventive measures, and the perceived need for training in ergonomics.

Half of respondents are employed by a hospital/health system (27%) or a private practice with seven or fewer physicians (23%). The majority fall in the 30- to 44-year age range (34%) or 45- to 59-year range (33%). (Also see, “How the survey was conducted,” page 29.)

The concept for the survey was initiated by Stacy Loeb, MD, MSc, a member of the Urology Times Editorial Council who is assistant professor of urology and population health, New York University Langone and the Manhattan VA, New York.

“There is increasing recognition about physician burnout,” said Dr. Loeb, noting the topic was discussed in a 2019 AUA annual meeting plenary session and featured in the 2018 AUA Update Series. “Less attention has been paid to some of the physical consequences of being a physician.

“Having personally suffered a back injury from lifting a patient, I have spoken to many other urologists about job-related physical issues.

See TOLL, on page 28

Source: Graphics based on Urology Times survey, June/July 2019

Also See: Addressing dangers in the OR starts with education, page 30

PET use in prostate cancer widens, but questions remain

Mark Frydenberg, MD, of Australia’s Monash University, explains the evolution of PET scanning in prostate cancer, particularly for identifying metastases. He also discusses PET’s clinical indications, its advantages and drawbacks, and key questions that remain about its use.

For the full article, please turn to page 32
Guest Editorial

Class effect is good news for men with nonmetastatic CRPC

MICHAEL COOKSON, MD, AND TONY RODRIGUEZ, MD

Dr. Cookson is professor and chairman of urology and Dr. Rodriguez is a urologic oncology fellow at the University of Oklahoma, Oklahoma City. Disclosure: Dr. Cookson is a consultant to Astellas Pharma US, Inc. and serves on the advisory board of Bayer Healthcare Pharmaceuticals, Inc. and Ferring Pharmaceuticals, Inc.

The landscape for management of men with advanced prostate cancer continues to evolve. This is true for patients with newly diagnosed metastatic prostate cancer and those who have progressed to castration resistance. Recently, Fazzi et al reported the results of the ARAMIS trial (N Engl J Med 2019; 380:1235–46). This study adds additional level 1 evidence for improved outcomes in men with nonmetastatic (M0) castrate-resistant prostate cancer (CRPC) using darolutamide (Nubeqa), a new antiandrogen (see page 8).

Importantly, in this study, men with M0 CRPC at high risk for development of metastases were continued on their traditional castration and then randomized to either darolutamide or placebo. Similar to the earlier PROSPER and SPARTAN studies of enzalutamide (XTANDI) and apalutamide (Erleada), respectively, the primary endpoint of ARAMIS was metastasis-free survival (MFS) (N Engl J Med 2018; 378:M1408-18; N Engl J Med 2018; 378:2465–74). In all three trials, all M0 CRPC patients were at high risk for the development of metastases due to the eligibility requirement of a PSA doubling time of 10 months or less.

Additionally, assessment of metastatic disease was based on conventional CT or MRI imaging and bone scan. In ARAMIS, the study met this primary endpoint with MFS increasing by 22 months, corresponding to a significant relative risk reduction of 59% (95% CI: 0.66 to 0.50; p<0.001). This is consistent with the magnitude of the benefit observed in the PROSPER and SPARTAN trials.

Darolutamide is a nonsteroidal antiandrogen with novel chemical structure limiting blood-brain barrier penetration (J Clin Oncol 2019; 37 [suppl]:156). Accordingly, there were no differences in CNS-related adverse events, including seizures, dizziness, falls, fractures, or cognitive impairment compared to placebo. More patients in the study arm experienced mild fatigue, and quality of life was no different between both groups; this is an important consideration in the mostly asymptomatic patient population with M0 CRPC.

The ARAMIS authors note that darolutamide was associated with “fewer adverse events than those reported in the respective phase III trials.” While there is biologic plausibility for a real difference in side effects among these agents, we would caution against making conclusions about comparative safety without head-to-head studies. At press time, darolutamide was approved by the FDA and became a third option for the treatment of M0 CRPC. This follows the established pattern of expanding indications for therapies by instituting treatment at earlier disease states.

How indications might change with the redefining of disease states being ushered in by advanced radiotracers is a coming challenge. A recent study of prostate-specific membrane antigen-targeted imaging in patients with recurrent prostate cancer found metastases in >85% of patients with PSA >2.0 ng/mL, which was a minimum inclusion value for ARAMIS (JAMA Oncol 2019; 5:856–63). This further complicates the problem of appropriate sequencing of all available antiandrogens.

In addition, we are learning that incorporation of germline and somatic genetic information may better inform treatment decisions.

While much work is still to be done, we have excellent evidence that there is a beneficial class-like effect for the androgen inhibitors enzalutamide, apalutamide, and darolutamide used within the current definition of men with M0 CPRPC.
Novel nonsteroidal AR antagonist shows benefit in treating nmCRPC

Cheryl Guttman Krader
UT Contributing Editor

Chicago—Results of a phase III trial show the benefit of darolutamide (Nubeqa) in reducing the risk of metastases or death compared with placebo in men with nonmetastatic castration-resistant prostate cancer (nmCRPC). At press time, the FDA announced approval of the novel nonsteroidal androgen receptor (AR) antagonist for the treatment of this patient population.

Study data presented at the American Society of Clinical Oncology annual meeting in Chicago show that men treated with darolutamide maintain quality of life and benefit with delays in worsening of pain and time to symptomatic skeletal events.

The research was presented by Karim Fizazi, MD, PhD, head of cancer medicine, Institut Gustave Roussy, and professor of oncology, University of Paris-Sud, Villejuif, France.

“Recently, two AR antagonists, namely apalutamide [Erleada] and enzalutamide [XTANDI], demonstrated improvements in metastasis-free survival (MFS) in men with nmCRPC. However, they are associated with side effects, including fatigue, falls, and mental impairment, which may be related to their ability to cross the blood-brain barrier. Because most men with nmCRPC are asymptomatic, a major therapeutic objective is to prevent cancer progression while avoiding side effects and preserving quality of life,” Dr. Fizazi said.

“The [current] results show that darolutamide significantly improves MFS, has a very favorable safety profile with apparently no side effects associated with other AR antagonists, and delays worsening of pain and disease-related symptoms compared with placebo. This efficacy and safety profile could make darolutamide an attractive treatment option for men with nmCRPC.”

Known as ARAMIS, the phase III study investigating darolutamide included 1,509 men with nmCRPC who had a rapidly rising PSA, defined as a doubling time ≤10 months, and ECOG status 0 or 1. They were randomized 2:1 to treatment with darolutamide, 600 mg twice daily, or placebo. All patients continued on androgen deprivation therapy. The two study groups were well balanced in their baseline characteristics.

Metastasis-free survival was analyzed as the primary endpoint, and the results showed a 59% risk reduction (p<0.001). Median MFS was 18 months for the darolutamide group versus 14 months for the controls.

In an immature interim analysis, the 3-year overall survival rate was 83% for darolutamide and 73% for the control group (29% risk reduction; p=0.0452). Median time to PSA progression was also delayed by 15 months with darolutamide (median, 33.2 vs. 7.3 months; p<0.001).

“I would like to emphasize how rising PSA can be associated with patients’ anxiety,” Dr. Fizazi said.

Time to pain progression delayed by 15 months

Median time to pain progression, defined as an increase of ≥2 from baseline on the Brief Pain Inventory—Short Form or start of opioids, was delayed by 15 months with darolutamide (p<0.001). Analysis of the impact of darolutamide on symptomatic skeletal events was still immature due to a low number of events, but the available data showed a 57% reduction with darolutamide (p=0.011).

Data on quality of life collected with the FACT-P Prostate Cancer Subscale questionnaire showed mean scores were unchanged in both treatment groups throughout the available follow-up. Median time to deterioration, defined as a ≥3.0-point decline from baseline, was approximately 11 months in the darolutamide group and 8 months in the control group (p=0.005).

A post-hoc analysis of data from subscales of the EORTC Quality of Life-PR25 questionnaire showed darolutamide treatment was associated with significant delays in deterioration of bowel symptoms and urinary symptoms, and there was a trend for a benefit in delaying deterioration of sexual activity. There were no differences between study groups in time to deterioration of hormonal treatment-related symptoms or incontinence.

“Time to pain progression delayed by 15 months is an attractive option for patients with nmCRPC.”

NEAL D. SHORE, MD

Prior to Dr. Fizazi’s presentation, Neal D. Shore, MD, presented a separate paper also containing data from ARAMIS at the AUA annual meeting in Chicago. Among the findings Dr. Shore presented was that darolutamide delayed time to subsequent antineoplastic therapies compared with placebo.

“It would appear that [darolutamide] is a very attractive option for patients with nmCRPC,” said Dr. Shore, director of Carolina Urologic Research Center, Myrtle Beach, SC.

Dr. Fizazi is a consultant/adviser for Amgen, Astellas Pharma, AstraZeneca, Bayer, Clovis Oncology, Curevac, ESSA, Janssen Oncology, Orion Pharma GmbH, Roche/Genentech, and Sanoﬁ. For full disclosures from the study Dr. Fizazi presented, see bit.ly/aramisdisclosures. Dr. Shore is a consultant/adviser for Angen, AstraZeneca, Bayer, Dendreon, Ferring, Genentech/Roche, Janssen Scientific Affairs, Medivation/Astellas, Myovant Sciences, and Tolmar.

TABLE DAROLUTAMIDE VS. PLACEBO IN MEN WITH nmCRPC

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Darolutamide group (months)</th>
<th>Placebo group (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median metastasis-free survival</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>3-year overall survival rate</td>
<td>83%</td>
<td>73%</td>
</tr>
<tr>
<td>Median time to PSA progression</td>
<td>33.2</td>
<td>7.3</td>
</tr>
</tbody>
</table>

Source: Karim Fizazi, MD, PhD
Sipuleucel-T cost lower vs. oral drugs over time

Cost to achieve additional OS benefit increases for enza, abi

CHERYL GUTTMAN KRADER
UT Contributing Editor

Analyses based on number needed to treat benefit (NNTB) show that the overall survival (OS) benefit is similar when using abiraterone acetate (ZYTIGA), enzalutamide (XTANDI), or sipuleucel-T (Provenge) to treat men with chemotherapy-naive metastatic castration-resistant prostate cancer (mCRPC). The data, however, favor sipuleucel-T for having the lowest direct cost.

“There is no question that all three treatments for mCRPC are expensive and that sipuleucel-T carries the highest initial cost. However, the estimated total drug cost to achieve an additional patient OS benefit declines over time with sipuleucel-T whereas it increases for the oral drugs that are given as ongoing therapy,” said David Morris, MD, a urologist with Urology Associates, Nashville, TN, who presented the research at the AUA annual meeting in Chicago.

“NNTB represents the expected number of patients needed to be treated to prevent one additional death compared to placebo at a specified time point, and it is a useful and intuitive measure of OS that can be included in the shared decision-making process about initial treatment options for mCRPC,” Dr. Morris said. “Ultimately, treatment decisions should be individualized, taking into account side effect profiles, the physician’s experience, and the patient’s characteristics and preferences.”

The analyses were performed using data from placebo-controlled pivotal trials investigating each of the treatments in men with chemotherapy-naive mCRPC (COU-AA-302 for abiraterone, IMPACT for sipuleucel-T, and PREVAIL for enzalutamide). The NNTB values, which are calculated as the inverse of the absolute risk reduction, were derived from the studies’ Kaplan-Meier OS curves.

Costs for the oral drugs were taken from the 2019 Wholesale Acquisition Cost listed in the IBM Micromedex Red Book. The sipuleucel-T cost was based on the second quarter 2019 Medicare Part B payment and included both the leukopheresis and preparatory procedures needed for product manufacture.

For each of the oral drugs, the total drug cost at 24 months was calculated as the mathematical product of the monthly cost and its median treatment duration in the pivotal trial. For sipuleucel-T, the 24-month cost was based on the initial cost divided by 24 months. Cost per NNTB was calculated as the mathematical product of the drug cost, each NNTB value, and the duration of treatment.

The results showed that sipuleucel-T had the shortest median duration of treatment (1 month) followed by abiraterone (13.8 months) and enzalutamide (16.6 months). Cost of median duration of treatment for sipuleucel-T, abiraterone, and enzalutamide was approximately $133,000, $150,000, and $192,000, respectively.

The NNTB at 24 months was 10 for sipuleucel-T, 16 for abiraterone acetate, and 12 for enzalutamide, and the cost per NNTB for the three treatments was approximately $665,000.

See PCA DRUG COSTS page 10

**TABLE** COST COMPARISON: SIPULEUCEL-T, ABIRATERONE, ENZALUTAMIDE

<table>
<thead>
<tr>
<th></th>
<th>Sipuleucel-T</th>
<th>Abiraterone</th>
<th>Enzalutamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median duration of</td>
<td>1</td>
<td>13.8</td>
<td>16.6</td>
</tr>
<tr>
<td>treatment (months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of median</td>
<td>$133,000</td>
<td>$150,000</td>
<td>$192,000</td>
</tr>
<tr>
<td>duration of treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number needed to</td>
<td>10</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>treat benefit (NNTB)</td>
<td></td>
<td></td>
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<tr>
<td>at 24 months</td>
<td></td>
<td></td>
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<tr>
<td>Cost per NNTB</td>
<td>$665,000</td>
<td>$2.4 million</td>
<td>$2.3 million</td>
</tr>
</tbody>
</table>

Source: David Morris, MD

**“The estimated total drug cost to achieve an additional patient OS benefit declines over time with sipuleucel-T whereas it increases for the oral drugs that are given as ongoing therapy.”**

DAVID MORRIS, MD

Moreover, calipers are ineffective as a diagnostic tool in many cases of undescended testes. The Test-Size® Orchidometer affords more patient comfort and is easier to use…without compromising accuracy.

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Neoadjuvant chemohormonal therapy efficacious for high-risk prostate cancer

Outcomes significantly better with CHT compared with surgery alone

Cheryl Guttman Krader
UT Contributing Editor

CHICAGO—Neoadjuvant chemohormonal therapy (CHT) warrants consideration in the management of men undergoing radical prostatectomy for clinically localized high-risk prostate cancer, said James Eastham, MD, at the American Society of Clinical Oncology annual meeting in Chicago.

His statement was based on the results of a phase III randomized controlled trial (CALGB 90203) showing that pathologic features at surgery and biochemical progression-free survival (bPFS) were significantly better in men who received presurgical treatment with docetaxel (Taxotere) plus an LHRH agonist than in those who were managed with surgery alone.

After a median follow-up of 6 years (range, 0 to 12 years), overall survival (OS) was also better in men who received neoadjuvant CHT compared to those who underwent surgery alone, although the difference between groups only approached statistical significance ($p=.06$).

“Adding neoadjuvant ADT to RP has not improved outcomes for men with clinically localized high-risk prostate cancer compared to RP alone. The results of our study show that neoadjuvant CHT at least has a benefit for delaying bPFS, and we expect that it will be found to provide an overall survival benefit as follow-up continues,” said Dr. Eastham, CALGB 90203 study chair and chief of the urology service and Peter T. Scardino Chair in Oncology, Memorial Sloan Kettering Cancer Center, New York.

“We did not have any deaths related to the neoadjuvant CHT in our study, although docetaxel was associated with some grade 3/4 toxicities,” Dr. Eastham told Urology Times.

“Based on our findings, I believe that the potential benefits and risks of neoadjuvant CHT should be included in the discussion of management options with men who have clinically localized high-risk prostate cancer,” he added.

The study, which started in December 2006, enrolled men with clinical stage T1-3a prostate cancer, PSA ≤100 ng/mL, no radiographic evidence of metastasis, and a Kattan preoperative nomogram probability of <60% bPFS at 5 years after RP or biopsy Gleason score 8-10. Men were stratified prior to randomization based on nomogram prediction for bPFS and use of ADT.

A total of 788 men were randomized 1:1 to surgery alone or to receive six cycles of docetaxel, 75 g/m² IV every 21 days with 18 to 24 weeks of LHRH agonist treatment (leuprolide or goserelin) prior to surgical intervention (staging pelvic lymph node dissection and radical prostatectomy) or surgical intervention alone.

The two study groups were similar at baseline and suggest it is an effective therapy in African-American men,” said Dr. Morris.

Cost analysis did not account for subsequent therapies

Dr. Morris pointed out that as a limitation, the cost analysis did not account for subsequent therapies used to treat prostate cancer after men failed on their assigned treatment.

“About 50% to 80% of men in the three studies experienced disease progression and went on to other treatments, but the treatments received by men differed across the three studies. The sipuleucel-T study was performed earlier than the oral drug trials, and men in that study who failed sipuleucel-T went on to chemotherapy, whereas subsequent treatment for men in the oral drug studies could have included one of the oral drugs or sipuleucel-T because they were already approved,” Dr. Morris explained.

“There is no way to estimate exactly what the added cost would be to achieve the survival curves that represent treatment with initial and subsequent therapy.”

Dr. Morris also noted that the cost analysis does not include the indirect costs of treatment incurred because of monitoring visits or resulting from management of side effects.

“An ongoing analysis is trying to determine those additional costs using adverse event data from the pivotal trials,” Dr. Morris told Urology Times.

“We expect that the indirect costs will be lowest for sipuleucel-T because compared with either of the oral drugs, it tends to be associated with a lower rate of side effects that may require hospitalization or other intervention,” he added.

The research was sponsored by Dendreon. Dr. Morris is a consultant to Dendreon, Astellas/Pfizer, and Janssen.

**TABLE NEoadjuvant CHEMORHOMONAL THERAPY VS. SURGERY FOR PCA**

<table>
<thead>
<tr>
<th>Patients undergoing neoadjuvant CHT</th>
<th>Patients undergoing surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic T3/T4 disease rate</td>
<td>60%</td>
</tr>
<tr>
<td>Seminal vesicle invasion rate</td>
<td>32%</td>
</tr>
<tr>
<td>Positive lymph nodes</td>
<td>20%</td>
</tr>
<tr>
<td>Positive surgical margins</td>
<td>18%</td>
</tr>
</tbody>
</table>

Source: James Eastham, MD

**PCA DRUG COSTS**

continued from page 9

$2.4 million, and $2.3 million, respectively.

An NNTB calculation was also done for African-American men treated with sipuleucel-T with a result of 3 at 24 months.

**Sipuleucel-T efficacious in African-American men**

“Survival outcomes for the subgroup of African-American men were not reported in the abiraterone and enzalutamide clinical trials. The NNTB values for sipuleucel-T show that its OS benefit was greater in African-American men than in the overall IMPACT population and suggest it is an effective therapy in African-American men,” said Dr. Morris.
Pembro shows promising antitumor activity

**Clinical Updates**

**BLADDER CANCER / 41% CR in patients with high-risk, BCG-unresponsive disease**

Andrew D. Bowser  
UT Correspondent

CHICAGO—Pembrolizumab (Keytruda) is showing encouraging antitumor activity in an ongoing phase II study including patients with high-risk, nonmuscle-invasive bladder cancer that is unresponsive to bacillus Calmette-Guérin (BCG) treatment.

Treatment with the PD-1 monoclonal antibody as monotherapy produced a 41.2% complete response rate in an updated analysis including 102 patients with BCG-unresponsive carcinoma in situ who were ineligible for radical cystectomy or refused it, according to investigator Ronald de Wit, MD, PhD, professor of internal oncology at Erasmus University Medical Center, Rotterdam, the Netherlands.

The median duration of complete response was 13.5 months as of this update, though further follow-up is needed, Dr. de Wit told *Urology Times*. He presented the data at the American Society of Clinical Oncology annual meeting in Chicago.

“It’s a strong signal at this point,” he said in an interview. “What would matter for a patient is the likelihood that the cystectomy can ultimately be avoided, so I think it would be meaningful if it would be 3-plus years.”

Activation of the PD-1 pathway has been linked to BCG resistance, according to Dr. de Wit and his co-authors. Pembrolizumab, which blocks the interaction between PD-1 and its ligands PD-L1 and PD-L2, is active in metastatic urothelial carcinoma and has become a standard of care in that setting for certain patients.

The phase II study, known as KEYNOTE-057, enrolled patients with high-risk nonmuscle-invasive bladder cancer. The study included two cohorts, including one group of patients with carcinoma in situ with or without papillary disease, which was discussed by Dr. de Wit, and a second group of patients with papillary disease but no carcinoma in situ.

In the carcinoma in situ cohort, a total of 102 patients were treated with pembrolizumab, 200 mg every 3 weeks for up to 2 years. The median age of these patients was 73 years, about 83% were male, and the median number of prior BCG instillations was 12.

Complete responses were seen in 42 patients, or 41.2% (95% CI, 31.5-51.4). Dr. de Wit reported. As of this update, 52.4% had ongoing responses, and the median duration of complete response was 13.5 months (range, 0+ to 26.8+ months).

“The 95% confidence interval for OS was ≤.05) between group difference favoring the men who received neoadjuvant CHT.

Variables for which the neoadjuvant CHT and control groups were compared included: pathologic T3/T4 disease (60% vs. 77%, respectively), seminal vesicle invasion (32% vs. 41%, respectively), positive lymph nodes (20% vs. 34%, respectively), and positive surgical margins (18% vs. 45%, respectively). Gleason grade group distribution did not differ significantly between study groups.

Treatment-related adverse events occurred in about two-thirds of patients, and 13 (12.7%) were grade 3 or 4, according to the report. Discontinuations due to treatment-related adverse events were reported in nine patients, or 8.8%. Immune-related adverse events, characteristic of pembrolizumab and other checkpoint inhibitors, occurred in about 20% of patients, and of those, three (2.9%) reached grade 3 or 4.

May help patients avoid cystectomy

With further follow-up pending, these findings to date suggest pembrolizumab monotherapy could represent an option to avoid radical cystectomy, Dr. de Wit said.

“None of these patients who ultimately failed had progressed to muscle-invasive disease, so we didn’t waste an opportunity. Some failed, but then they underwent the cystectomy,” he added.

Ninety-five percent of the enrolled patients had no prior cystectomy because they had refused it, and only about 3% because they were ineligible for the procedure, according to reported data.

“If you are talking with patients about what to do, most of them want to keep the bladder in, and are keen to be on a study like this,” Dr. de Wit said.

Currently enrolling is KEYNOTE-676, a phase III study looking at the efficacy and safety of pembrolizumab plus BCG in high-risk nonmuscle-invasive bladder cancer that is persistent or recurrent after induction with BCG.

Dr. de Wit has received honoraria from Merck and Sanofi; is a consultant/adviser to Bayer, Clovis, Janssen, Merck, Roche/Genentech, and Sanofi; has received institutional funding from Bayer and Sanofi; and has received travel, accommodations, and expenses from Lilly. Several of his co-authors have disclosures related to one or more pharmaceutical companies; for full disclosures, see bit.ly/keynotedislosures.

Neoadjuvant CHT was associated with a 34% improvement in overall bPFS (p=0.02). There was also a suggestion of a survival benefit with neoadjuvant CHT.

“The 95% confidence interval for OS was 0.42 to 1.03, but there has been a steadily growing separation between groups over time, and the difference between groups is expected to achieve statistical significance in the next analysis,” Dr. Eastham told *Urology Times*.

Several of Dr. Eastham’s co-authors have one or more disclosures related to pharmaceutical companies; for full disclosures, go to bit.ly/CALGB90203.

The adverse event profile of pembrolizumab for these patients with nonmuscle-invasive bladder cancer in KEYNOTE-057 was consistent with what has been observed in studies of pembrolizumab as first- and second-line treatment of advanced urothelial carcinoma, according to Dr. de Wit.

“None of these patients who ultimately failed had progressed to muscle-invasive disease, so we didn’t waste an opportunity. Some failed, but then they underwent the cystectomy.”

RONALD DE WIT, MD, PhD

The following data were presented at the American Society of Clinical Oncology annual meeting in Chicago:

**Median duration of complete response was 13.5 months**

(range, 0+ to 26.8+ months).

Neoadjuvant CHT continued from page 10

in their median age, clinical stage and biopsy Gleason score distribution, median PSA distribution, nomogram risk group, and prior androgen deprivation therapy use.

**4/5 endpoints favor neoadjuvant CHT group**

The analysis of between-group differences in pathologic features was an exploratory analysis using reports from each treating center; results from central review are pending. In four out of five endpoints, there was a statistically significant (p=0.05) between-group difference favoring the men who received neoadjuvant CHT.

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(range, 0+ to 26.8+ months).
Urothelial cancer agent shows impressive response

Phase II data show 44% response rate in patients treated with antibody-drug conjugate

Lisette Hilton
UT Correspondent

The novel antibody-drug conjugate enfortumab vedotin produced an impressive 44% response rate in a phase II trial of urothelial cancer patients who had been treated with standard chemotherapy and a checkpoint inhibitor.

Researchers presented results of the study of 125 patients at the American Society of Clinical Oncology annual meeting in Chicago.

Twelve percent of bladder cancer patients studied had a complete response with no detectable sign of cancer. And 38% of patients whose cancer had metastasized to the liver responded to treatment, according to lead author Daniel P. Petrylak, MD, professor of medical oncology and urology at Yale Cancer Center, New Haven, CT.

This is the highest reported response rate in metastatic urothelial cancer to liver of any single agent or combination therapy to date, according to Dr. Petrylak.

“This is an area that we know does not respond well to the checkpoint inhibitor therapy. What we’re also seeing, which is very interesting, is that there is no difference in response in those patients who have had programmed-death ligand-1 (PD-L1) progression or PD-L1 response. So [enfortumab] seems to work with responders and non-responders,” he said.

While the average overall survival was 11.7 months in the phase II trial, it’s too early to tell whether enfortumab improves survival in bladder cancer patients. A current phase III study is looking at survival, according to Dr. Petrylak.

Enfortumab could help to fill a need in the treatment of bladder cancer because outcomes from standard chemotherapy and immune checkpoint inhibitors fall short.

“About three-quarters of patients will not benefit from immune checkpoint therapy. So there’s a need for third-line agents. In the past, we used single-agent chemotherapy for second line but really didn’t see great responses. At best, we saw a 20% response rate and no improvement in survival,” Dr. Petrylak said.

Dr. Petrylak calls enfortumab a “smart bomb” therapy because it targets Nectin-4, which is expressed in about 97% of bladder cancers. All the patients in the phase II trial expressed Nectin-4. The antibody to Nectin-4 is linked to a chemotherapy agent called monomethyl auristatin E (MMAE)—a similar agent to taxanes, according to Dr. Petrylak.

“Enfortumab vedotin will deliver MMAE directly to cancer cells as opposed to normal tissue, where there’s a much lower rate or no expression of Nectin-4,” he said.

12% discontinuation rate observed

Enfortumab was well tolerated, with 12% of patients in the trial discontinuing treatment because of adverse events. Side effects include neuropathy, neutropenia, and fatigue, according to Dr. Petrylak.

Dr. Petrylak, who conducted the phase I and II trials for the drug, says the phase II results were about the same as those in phase I. According to Dr. Petrylak, both the phase I and II results justify the application for accelerated approval for enfortumab in the treatment of bladder cancer. Researchers are conducting the international phase III trial comparing survival with enfortumab to standard chemotherapy in patients with metastatic urothelial cancer that has progressed after chemotherapy and checkpoint therapy.

A phase I trial is underway to examine the drug’s benefits for people who are newly diagnosed with advanced urothelial cancer but are ineligible for platinum chemotherapy. Another phase I trial is looking at treating advanced or metastatic disease by combining enfortumab with the checkpoint inhibitor pembrolizumab (Keytruda).

If enfortumab continues to show positive results in phase III trials, Dr. Petrylak said it will be integral in the armamentarium of bladder cancer treatment.

“I think back to 5 or 6 years ago when we really didn’t have anything for second-line patients. Now, we’re understanding more about the biology. We’re targeting different drugs to cancer cells. And again, I think patients who have metastases to the liver are a poor prognostic group, but now we’re starting to see ways of overcoming those challenges to treat these patients,” he said.

Seattle Genetics and Astellas Pharma, which are co-developing enfortumab, funded the study presented by Dr. Petrylak. Dr. Petrylak is a consultant/adviser for Astellas Pharma and has received research funding from Astellas Medication and Seattle Genetics. For full disclosures, go to bit.ly/EV201disclosures.

In Brief

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AMERICAN COLLEGE OF SURGEONS LAUNCHES SURGICAL QUALITY IMPROVEMENT PROGRAM FOR GERIATRIC PATIENTS

The American College of Surgeons recently launched its new Geriatric Surgery Verification (GSV) program at the ACS Quality and Safety Conference in Washington.

This new surgical quality improvement program introduces 30 new surgical standards designed to systematically improve surgical care and outcomes for the aging adult population.

The GSV Program provides hospitals with a validated list of 30 evidence-based and patient-centered standards for geriatric surgery that hospitals can implement to continuously optimize surgical care for this population. These standards define the resources and processes that hospitals need to have in place to perform operations effectively, efficiently, and safely in older adults, while also always prioritizing what matters most to individual patients with regard to their needs and treatment goals.

The standards include recommendations for improving communications between patients and their health care team; managing medications; screening for cognitive, nutrition, and mobility decline; and ensuring proper staffing is in place, among other concerns, according to an American College of Surgeons press release.
Surveillance safe for some mRCC patients

Andrew D. Bowser
UT Correspondent

CHICAGO—The largest analysis of active surveillance for metastatic renal cell carcinoma (RCC) presented to date shows that a proportion of patients can be safely observed without need to start systemic therapy right away.

The median time on active surveillance exceeded 14 months for patients starting systemic therapy at least 6 months after diagnosis in the study, based on patients with metastatic RCC in the Canadian Kidney Cancer information system (CKCis).

Overall survival was significantly longer in the 863-patient active surveillance cohort as compared to a group of 848 patients receiving immediate treatment, according to investigator Igal Kushnir, MD, a medical oncology fellow at Ottawa Hospital Cancer Centre in Ottawa, ON. The study was presented at the American Society of Clinical Oncology annual meeting in Chicago.

According to Dr. Kushnir, these new findings corroborate and strengthen the conclusions of a Lancet Oncology study (2016; 17:1317-24) and a presentation from the 2018 ASCO annual meeting that suggested the benefit and safety of selective active surveillance in smaller cohorts.

Surveillance now ‘supported with robust evidence’

“It’s something that is easier to endorse, because now it’s supported with robust evidence, and we can reassure the patient that it’s safe,” Dr. Kushnir said in an interview with Urology Times.

When exactly to utilize active surveillance still relies on the “art of oncology,” said Dr. Kushnir, who noted he and co-authors looked further and couldn’t find an obvious clinical marker—such as histology, International Metastatic RCC Database Consortium (IMDC) risk criteria, or metastatic burden—that predicted the benefit of the approach in the CKCis cohort.

Nevertheless, patients can probably be selected for active surveillance based on the rate of disease change seen in early serial imaging, according to Dr. Kushnir.

“Our guess is that if you have a patient that has no symptomatic disease, no pending visceral crisis, and the overall burden of disease is not high, it’s probably safe to defer treatment to at least the next serial imaging. If the growth kinetics on the next imaging are quite low, then probably this patient can be assigned to active surveillance,” said Dr. Kushnir, who worked on the study with M. Neil Reaume, MD, and co-authors.

To assess the outcomes and safety of active surveillance versus immediate systemic treatment, Dr. Kushnir and colleagues identified patients in the CKCis database diagnosed with metastatic RCC between 2011 and 2016.

They classified active surveillance as either starting systemic treatment at least 6 months after a diagnosis of metastatic RCC, which included 370 patients, or never starting systemic therapy at all, providing overall survival was greater than 1 year (to exclude patients likely not receiving treatment due to poor prognosis), which included 493 patients.

“We’re able to do that because we’re able to use serial imaging to reassure the patient that it’s safe,” Dr. Kushnir added.

Overall survival was significantly longer in the surveillance cohort as compared to the treatment cohort. Median time on active surveillance was 14.2 months, with a range of 6 to 71 months, Dr. Kushnir reported.

The 5-year probability of overall survival was 70.2% for the active surveillance cohort versus 32.1% for the immediate treatment group (p < .0001). After adjusting for age and IMDC risk criteria, both overall survival and time to treatment failure were significantly greater in the active surveillance patients who later started systemic treatment, as compared to those who had immediate treatment, according to his report.

Taked together, these findings suggest a significant number of patients can be safely observed for a long period of time, sparing both medical and financial toxicities associated with systemic therapy for a median of more than a year, Dr. Kushnir said.

“After a median follow-up of 41 months, still 57% of patients on active surveillance never received systemic therapy, which is quite significant,” he added.

Dr. Kushnir has stock or other ownership interests with Teva Pharmaceutical Industries Ltd. Several of his co-authors also reported disclosures; for a full list, go to bit.ly/CKCisdisclosures.

OVERACTIVE BLADDER Tx NOT LINKED TO CV EVENTS

The overactive bladder drug mirabegron (Myrbetriq) was not associated with an increased risk for cardiovascular (CV) events compared with other treatments, according to a recent study.

“Our findings are not meant to endorse preferential use of mirabegron but to support a growing body of evidence that mirabegron is not associated with an excess risk of CV events compared with other treatments in older patients,” the authors wrote in JAMA Internal Medicine (July 15, 2019 [Epub ahead of print]).

Mina Tadrous, PharmD, PhD, of the Women’s College Research Institute at Women’s College Hospital in Toronto, and colleagues, conducted a matched cohort study using administrative claims data from 38,818 patients aged 66 years or older using overactive bladder treatments.

The authors found that patients taking mirabegron did not have an increased risk of irregular heart rates, heart attacks, or stroke compared to patients taking other overactive bladder drugs.

“These findings offer a measure of reassurance for the decision-makers regarding the safety of mirabegron, a drug with growing utilization,” Dr. Tadrous told Urology Times sister brand FormularyWatch.
Spermatogenesis present in some transgender women pre-orchiectomy

Lisette Hilton
UT Correspondent

MORE THAN ONE-THIRD of transgender women on gender-affirming hormone therapy have some or intact spermatogenesis when they’re about to undergo bilateral simple orchietomy, according to research presented at the AUA annual meeting in Chicago.

It’s a finding that has important implications when urologists counsel these patients, many of whom want to preserve fertility.

Urologists play an important role in the care of transgender patients. One example: Urologists do gender-affirming bilateral simple orchietomy—a procedure they typically offer transgender women, according to lead author Tristan Nicholson, MD, PhD, a urology resident at the University of Washington, Seattle, working with Thomas J. Walsh, MD, MS, and colleagues.

One way individuals who are born with male sex characteristics but identify as female can better align their physical appearance with their gender identity is to take a combination of hormones, said Dr. Nicholson.

“These are known as feminizing hormones, and it’s typically a combination of estradiol and an antiandrogen. That’s one step toward a physical transition,” she said. “Another step is the surgical removal of both testicles. After their testicles are removed, patients can typically reduce their estradiol dosing and often stop antiandrogen therapy.”

Previous research suggests that up to half of transgender individuals are interested in future fertility, but historically these patients’ reproductive needs have been largely ignored, according to Dr. Nicholson.

Urologists and others caring for transgender patients should address fertility concerns and desires, and international guidelines recommend that providers and patients have the discussion, she said.

“One question that we had was how does hormone therapy affect the testicles and specifically fertility. We did a retrospective study of pathology reports at our institution for patients who had undergone this surgery,” Dr. Nicholson said.

She and colleagues examined 52 transgender women who had bilateral simple orchietomy and assessed the presence or absence of spermatogenesis in the testis tissue that was removed at the time of surgery. All patients were on feminizing hormones, and all are living as women.

The researchers found intact spermatogenesis in 13.5%, hypo-spermatogenesis in 23.1%, and no spermatogenesis in 51.9%. In 11.5% of testis specimens, spermatogenesis wasn’t reported, according to the study.

They found no difference in estimated testis volume among testes that did versus didn’t have spermatogenesis.

‘At least some fertility potential’

“Our finding that about a third of patients had some evidence of spermatogenesis in the testes at the time of bilateral simple orchietomy indicates that there is at least some fertility potential in these patients.”

Regardless of whether these patients have started feminizing hormone therapy or not, the potential for fertility exists and patients should know that, she said.

“We think this is a starting point for a prospective study. We’re interested in evaluating how different hormone regimens affect fertility potential and the biology of the testis. We’re specifically interested in how the feminizing hormones affect the supporting cells of the testis. We’re also very interested in how this particular surgery, bilateral simple orchietomy, may affect the quality of life of our patients, both before and after, as well as their perception of how well their physical appearance aligns with their gender identity,” Dr. Nicholson said.

Lisette Hilton
UT Correspondent

ER USE OF CT FOR SUSPECTED STONE DISEASE ON THE RISE

The relative use of CT of the abdomen and pelvis (CTAP) in emergency department patients presenting with suspected stone disease doubled between 2006 and 2014 and showed marked geographic variation, according to the authors of a new study published online in the Journal of the American College of Radiology (June 17, 2019).

“Overall, CT utilization rates in the ED continue to increase over time despite government and medical specialty organization initiatives to restrain the growth of advanced imaging services,” said first author Patricia Balthazar, MD, of Emory University in Atlanta. “Although the U.S. population grew by 6.9% from 2006 to 2014, the annual ED visits for suspected urolithiasis increased by 17.9%, and the number of visits for suspected urolithiasis involving advanced imaging increased by 100.8%.”

The study, performed in conjunction with the Harvey L. Neiman Health Policy Institute, showed CTAP was more frequent in patients from higher income ZIP codes, with private insurance, in the Northeast, and at urban and nonteaching hospitals.
Untreated MIBC has short natural course, significant morbidity

Patients deemed unfit for curative treatment still required 2-3 surgical interventions

Bladder cancer is a disease of the elderly, with an average age at diagnosis of 73 years. The advanced age and significant comorbidities, which are often noted in patients with muscle-invasive bladder cancer (MIBC), can render some patients ineligible for curative therapy. In a new study, Westergren et al report that patients with MIBC who are not treated with curative intent require multiple hospitalizations and procedures related to bladder cancer in their last year of life (J Urol, May 30, 2019 [Epub ahead of print]).

To study the natural history of patients with invasive bladder cancer whose initial management did not include any treatment with curative intent (eg, radical cystectomy or chemoradiation), the authors analyzed the data captured in several Swedish national databases and registries. Between 1997 and 2014, they identified 9,811 patients with MIBC. Of these, 5,592 patients (57%) were initially managed without curative intent; ie, they were not treated with radical cystectomy or radiation therapy. In this study cohort, 68% were men and 32% were women.

Charlson comorbidity index was 0 or 1 in 68% of patients. With a median age at diagnosis of 80 years, 55% of men and 62% of women with MIBC in this cohort did not receive initial treatment with curative intent. An average of 2.1 hospital admissions for 18.8 days per patient were recorded during the first year after diagnosis.

Bladder cancer-related morbidity was the primary reason for hospitalization in the vast majority of patients. These patients required multiple urologic procedures including transurethral resection of bladder tumor (32%), blood transfusions (18%), nephrostomy tubes (11%), palliative cystectomies (6%), and urinary diversion (7%).

Within 1 year of diagnosis, 63% of these patients with MIBC who did not receive curative treatment had died. The median overall survival was 8 months.

On multivariable analysis, tumor stage at diagnosis, older age, increased comorbidity, later year of diagnosis, and female gender increased the risk of death. The cancer-specific survival was 11 months (12 months for men; 9 months for women). Bladder cancer was recorded as the cause of death in 63% of cases.

**Median OS of 13 months reported**

In a subgroup analysis, 754 patients were identified with organ-confined cancer (T2-3, N0, M0) with a median age of 78 years. The median overall survival was only 13 months. Despite having initially organ-confined disease, they still required 2.3 hospitalizations/patient in the first year, mostly for genitourinary symptoms and procedures. The patients with organ-confined disease died of bladder cancer at the same rate as the entire cohort (including patients with N+ or M+).

**There appears to be a strikingly high likelihood of increased morbidity and poor outcomes in patients not receiving definitive therapy.**

Regardless, MIBC treated with less invasive therapies is associated with significant cancer-related morbidity and mortality within the first year. This report provides useful information about the short and complicated natural history of MIBC. Despite older age or other comorbidities, patients with untreated MIBC will typically die of progressive bladder cancer.

This information will allow us to properly counsel patients and their families to set realistic expectations during what may be their final year of life.
Waterjet ablation offers minimally invasive option for BPH

Treatment provides alternative to simple prostatectomy in men with large prostates

Over the past several years, urologists and men suffering from BPH have been introduced to a growing number of alternatives for managing this disease. In addition to the gold-standard transurethral resection of the prostate (TURP) and the simple prostatectomy (for larger prostates), urologists can now present men with symptomatic bladder outlet obstruction a variety of newer management options including UroLift and Rezum for prostate volumes 30-80 grams.

In clinical practice, some urologists are also performing these procedures in men with prostates >80 grams.

Other treatment options include photoablation of the prostate, holmium laser enucleation of the prostate (HoLEP), and variations of the more conventional treatments, such as the bipolar/button TURP and robot-assisted laparoscopic simple prostatectomy.

Each of these treatments has shared and individual risks and benefits that must be weighed and, of course, compared to the more conservative alternatives when considering “what to do next” in the personalized care of men with BPH requiring or desiring intervention. This article focuses on Aquablation, a newer approach to treatment involving the use of robotically controlled waterjet ablation for prostate tissue removal.

Deciding on surgery: Factors to weigh

BPH is a prevalent disease affecting approximately 50% of men age 60 years and older and up to 90% of men after the age of 85. Many factors must be weighed when considering the surgical management of BPH, including whether such treatment is necessary or whether more conservative options can be continued or initiated instead. If the decision to pursue surgery is made, the size and shape of the prostate play an important role in selecting the appropriate therapy to not only optimize efficacy but also minimize complications.

It’s important for patients to know that each individual’s prostate can have a different size and shape. The larger a man’s prostate, the longer it will take the surgeon to resect the obstructive tissue. In terms of shape, while every prostate has two lateral lobes, some men develop an additional median lobe that protrudes into the bladder and increases the complexity of the procedure. Although we know that appropriately removing the obstructive tissue provides patients with BPH effective symptom relief, prostates with increased size and complex shape can lead to suboptimal outcomes, longer operative times, and higher risks during surgery.

Additionally, more and more patients with BPH are asking for less invasive procedures expecting comparable outcomes to the more classic alternatives with less side effects and a more rapid return to their preoperative daily activities.

Over the course of my career, I have predominantly performed bipolar/button TURP, as my practice and referral patterns seemingly led themselves to the management of larger prostates (often with large and complex median lobes) in men with moderate to severe bladder outlet obstruction symptoms. In men with prostates <80 grams, I also perform and discuss the UroLift procedure as an option to consider.

How waterjet therapy works

More recently, I have started offering my patients PROCEPT AquaBeam Aquablation of the prostate, which combines robotic technology, multi-dimensional real-time imaging, and a heat-free waterjet to remove obstructive prostate tissue (figure 1). Aquablation therapy provides autonomous tissue removal to safely and effectively treat BPH. It offers predictable and reproducible outcomes independent of prostate anatomy, prostate size, or surgeon experience. The AquaBeam Robotic System is FDA approved.

The Aquablation system enables the urologic surgeon to combine the benefits of traditional cystoscopy (to visualize the anatomy of the prostatic urethra, bladder neck, and bladder) with intraoperative transrectal ultrasound (TRUS) imaging of the prostate. This allows for a multi-dimensional, real-time view of the entire prostate during all aspects of the procedure, enabling improved decision-making and treatment planning.

The procedure begins by developing a personalized treatment plan using multi-dimensional real-time imaging (figures 2a and 2b). The AquaBeam Robotic System then provides an accu-
rate, robotically controlled resection of prostate tissue using a heat-free waterjet (Aquablation), based on the surgeon’s personalized treatment plan for each patient (figure 3).

Data from multiple prospective studies (one of which was a randomized, double-blind study against the gold-standard TURP) have provided a body of clinical evidence demonstrating reproducible outcomes regardless of prostate size. Symptom relief is similar to that of other available resection techniques, while the procedural safety profile is minimized and markedly lower, especially for large, more complex prostates (J Urol 2018; 199:1252-61; Urology 2019; 125:169-73; BJU Int. Feb. 8, 2019 [Epub ahead of print]). For men concerned about the high risk of sexual side effects, namely postoperative anejaculation associated with the surgical management of BPH, Aquablation therapy has demonstrated strong efficacy outcomes comparable to TURP and a superior safety profile, including a reduction in sexual side effects by a ratio of four to one.

The typical patient is discharged in 1.5 days regardless of prostate size. This length of stay is seen as a benefit of Aquablation for patients with large prostates when compared to those who undergo an open simple prostatectomy, which typically requires a 4- to 5-day hospital stay.

The risk of transfusion across all prostate sizes has been observed to be similar to that of HoLEP and TURP. Following discharge, dysuria is typically less than that seen with traditional BPH surgical options due to the absence of heat for tissue removal.

Review of published data
The WATER (Waterjet Ablation Therapy for Endoscopic Resection of prostate tissue) study is a randomized, double-blind comparison of Aquablation therapy to TURP in 181 men with prostates between 30 and 80 grams. The study demonstrated similar efficacy between the two treatment groups and a shorter mean resection time (4 vs. 27 minutes, p<0.001), a lower complication rate, and sustained and improved preservation of ejaculation favoring Aquablation (J Urol 2018; 199:1252-61).

At a follow-up of 2 years, International Prostate Symptom Score (IPSS) improved by 14.7 points in the Aquablation group and 14.9 points in the TURP group (p<0.001, 95% CI for difference: –2.1 to 2.6 points) (Adv Tiber 2019; 36:1326-36). Two-year improvements in maximum flow rate (Qmax) were large in both the Aquablation and TURP groups at 11.2 and 8.6 cc/sec, respectively (p<0.001, 95% CI for difference: –1.3 to 6.4). Sexual function as assessed by the Male Sexual Health Questionnaire was stable in the Aquablation group and decreased in the TURP group.

Further analysis of the data from the WATER study revealed that Clavien-Dindo grade 1 persistent or grade 2 or higher events occurred in the first 3 months in 20% of Aquablation subjects and 46% of TURP subjects (p<0.02). At 180 days, men with a prostate volume >50 mL experienced a statistically significant decrease in IPSS of 17.4 points with Aquablation versus 13.3 points in men who underwent TURP (p<0.02). Compared with TURP, the WATER study also demonstrated a greater reduction in IPSS with Aquablation in men with a low baseline flow rate <9 mL/s (17.9 vs. 14.3, respectively, p<0.03), greater reduction in IPSS in men with median lobe (19.9 vs. 11, respectively, p<0.005), and a seven-point greater reduction in Please see WATERJET, page 18.
continued from page 17

IPSS in men with both larger prostate and lower baseline flow rate, <9 mL/s (p<0.0001).

From the surgeon’s perspective, a major advantage of this procedure in my opinion is the short learning curve and reproducibility of technique from one case to another. During each procedure, the urologic surgeon follows the same planning steps. Once satisfied with the individualized treatment plan, the robot will execute the precise Aquablation in approximately 3 minutes or less regardless of prostate size or shape. Patients’ concerns regarding an autonomous robot can be easily calmed, as the urologic surgeon monitors every aspect of the procedure and is able to instantly stop the procedure at any time by simply lifting his or her foot off the activation pedal.

Another advantage of Aquablation is the ability to perform this technique on any prostate regardless of size, thus allowing an option for men with larger prostates for whom the only alternative is often the more invasive simple prostatectomy. The single-arm WATER II study looked at 12-month safety and efficacy outcomes of the Aquablation procedure for the treatment of men with symptomatic BPH and large-volume prostates (mean prostate volume, 107 cc; range, 80-150 cc) (Urology 2019; 129:1-7). Mean operative time was 37 minutes, and mean Aquablation resection time was 8 minutes. Average length of hospital stay following the procedure was 1.6 days.

Mean IPSS improved from 23.2 at baseline to 6.2 at 12 months (p<0.0001). Mean IPSS quality of life improved from 4.6 at baseline to 1.3 at 12-month follow-up (p<0.0001). Significant improvements were seen in Qmax (12-month improvement of 12.5 cc/sec) and post-void residual (decrease of 171 cc in those with PVR >100 at baseline). Antegrade ejaculation was maintained in 81% of sexually active men. No patient underwent a repeat procedure for BPH symptoms. WATER II demonstrated that Aquablation is a safe and effective surgical alternative for men with large prostate glands, with durable outcomes at 1 year, fast operative times, short hospitalizations, maintenance of antegrade ejaculatory function, and no significant increase in procedure or resection time compared to smaller sized glands.

To date, our team has performed 40 Aquablation procedures with maximum prostate size of 201 cc (32 to 201 cc). Of the 40 patients who underwent Aquablation, 29 had prostates larger than 80 cc, 15 greater than 100 cc, and three greater than 150 cc. Thirty-three of the 40 men had prostates with a median lobe, 37 had severe obstruction on urodynamic evaluation, and 19 men suffered from urinary retention, 13 of whom required catheterization. Average change in IPSS following Aquablation was 15.5 (range, 6-26) with average preoperative IPSS of 21.7 (range, 10-33) versus 6.6 postoperatively (range, 1-15).

Although we are still awaiting postoperative uroflow studies on all patients, several patients have registered postoperative flow rates greater than 40 mL/s. Additionally, all of the men with preoperative urinary retention are able to void spontaneously, completely, and without need for catheterization. Of those with catheter dependence preoperatively, all can void spontaneously, with bladder scan results demonstrating complete emptying.

**Conclusion**

Aquablation has a short learning curve, and the planning strategy and technique can be easily reproduced regardless of the prostate size or shape. Initial published data have demonstrated very strong efficacy outcomes comparable to TURP and simple prostatectomy with a superior safety profile, including a reduction in sexual side effects regardless of prostate size. One-year follow-up data confirmed a sustained reduced rate of sexual side effects, durability in symptom reduction, improved flow rates, and a very low rate of re-treatment.

In prostates larger than 50 cc, the Centers for Medicare & Medicaid Services found Aquablation therapy to represent “a substantial clinical improvement” to both TURP and simple prostatectomy. The AUA recently joined the Canadian Urological Association in adding Aquablation therapy to treatment guidelines for men suffering from LUTS due to BPH. The benefit of Aquablation’s minimal invasiveness is especially true for men with very large prostates for whom the simple prostatectomy had previously been among the few options to consider.


FIGURE 2 / Angle planning in transverse view (A). Contour planning in sagittal view (B).

FIGURE 3 / Prostate sagittal view with AquaBeam handpiece in position. (Photos and illustration courtesy of PROCEPT BioRobotics)
A great challenge in the management of high-grade nonmuscle-invasive bladder cancer (NMIBC) is the detection of disease recurrence and progression following induction bacillus Calmette-Guerin (BCG) therapy. Moreover, predicting disease responsiveness to BCG has remained elusive. Current gold standard follow-up involves regular cystoscopic evaluation with visual inspection for disease recurrence. Although cystoscopy is associated with minimal morbidity, it remains invasive, and detection of recurrence is surgeon dependent.

Given the limitations of cystoscopy, a multitude of complementary tests (urine cytology, fluorescence in situ hybridization, cytokine and genetic profiling) have been investigated as potential biomarkers to predict NMIBC responsiveness, recurrence, and progression. Unfortunately, a sensitive and specific biomarker for NMIBC has not been discovered.

Our understanding of NMIBC biomarkers and BCG therapy has relied on the historical dogma that urine is sterile. However, recent advances in microbial detection have greatly expanded our knowledge of bacterial communities within the human body. Using enhanced culture techniques and DNA sequencing technology, live bacteria and bacterial DNA have been identified in urine samples deemed “culture negative” using standard clinical microbiology techniques (J Clin Microbiol 2012; 50:1376-83). Initial investigations in female patients supported the hypothesis that certain bacterial communities provide protection and that disruption of these communities may cause lower urinary tract symptoms (MBio 2014; 5:e01283-14). Subsequent investigation led to similar findings in men, with increased bacterial detection in more symptomat ic patients (Eur Urol Focus Aug 21, 2018 [Epub ahead of print]).

The role of microorganisms as carcinogens is widely understood in the gastrointestinal tract. Infection and chronic gastric inflammation associated with Helicobacter pylori is a strong risk factor for gastric malignancy and esophageal adenocarcinoma. Moreover, dysbiosis of the colonic microbiome has been implicated in development of colorectal cancers.

In the genitourinary system, schistosomiasis and recurrent urinary tract infection are known factors in the development of squamous cell carcinoma of the bladder. However, interactions between microbes and the development of urothelial cell carcinoma (UCC) have not been characterized. It is feasible that urinary tract dysbiosis may influence the development of malignancy, and recent urinary microbiome investigations have paved the way for an exciting new area of bladder cancer research (Urology 2019; 126:10-5).

While investigation into the association of the urinary microbiome and NMIBC is in its infancy, initial studies have associated patients at high risk for UCC pathogenesis and progression with enrichment of certain bacterial communities (Front Cell Infect Microbiol 2018; 8:167). Unfortunately, the studies to date on this topic have been limited by their design, with all being case control studies with heterogeneous patient populations and small sample sizes.

Despite the limitations of these studies, their findings have exciting implications. There is a significant need for noninvasive biomarkers to predict the clinical course of UCC, and the possibility of using the urinary microbiome for risk stratification is highly intriguing. Further investigation of the relationship between the urinary microbiome and UCC may also shed light on pathophysiologic mechanisms and assessing response to therapy (figure).

Implications for treatment

In a more direct sense, urologists have been manipulating the urinary microbiome to treat UCC for decades. Since the 1990s, instillation of BCG, an attenuated form of the bacterium Mycobacterium bovis, has been the gold standard for intravesical therapy of nonmuscle-invasive UCC. BCG presumably relies on an immune interaction between the BCG bacterium and the urothelium. The variability of responsiveness to therapy as well as the current national BCG shortage raise the question, “Can we harness the urinary microbiome to better treat UCC?”

In the past, urologists have made numerous efforts to utilize the bladder environment to predict and potentiate the effects of BCG. Various molecular biomarkers, immune cell response characteristics, and cytokine profiles have been investigated to predict BCG responsiveness. To date, no biomarker has shown high enough predictive value to warrant...
widespread clinical use (Eur Urol 2018; 73:738-48). With regard to potentiating BCG effects, adding interferon to BCG treatments attempts to modulate the bladder’s immune response. Modifying the bladder microbiome before or during BCG therapy may be a means to the same end.

The implications of the urinary microbiome on BCG therapy are unknown. It is plausible that certain bacteria may interact with the bladder to make the urothelium more or less susceptible to BCG binding. Furthermore, certain microbes may directly inactivate instilled BCG in the bladder, thereby reducing immunoinflammatory response.

Lastly, persistence of BCG in the bladder following therapy may serve as a biomarker for treatment success. If any of these theoretical mechanisms are true, it is feasible that the urinary microbiome might be harnessed to enhance BCG response or to facilitate an immune response using a novel treatment modality (BJU Int 2019; 124:7-8).

Conclusion

Our growing understanding of the urinary microbiome necessitates a complete reevaluation of the management of urologic disease, NMIBC included. With countless patients undergoing treatment for UCC every day and with BCG shortages at our door, it is of utmost importance that methods for enhancing UCC management be investigated. Noninvasive analysis of the urinary microbiome may further expand our knowledge of NMIBC pathogenesis and diagnosis, offering a potentially modifiable environment to enhance treatment for our patients.

FIGURE / Proposed relationships between the urinary microbiome and urothelial cell carcinoma (UCC). The bladder may promote or inhibit UCC pathogenesis, progression, or recurrence (A). Differences in microbiota may lead to different tumor types or grades (B). Local microbiota may interact with bacillus Calmette-Guerin (BCG) to inactivate BCG or modulate urothelial sensitivity to BCG response (C). (Source: Reprinted from Urology 2019; 126:11 with permission from Elsevier)

Adding interferon to BCG treatments attempts to modulate the bladder’s immune response. Modifying the bladder microbiome before or during BCG therapy may be a means to the same end.

POSTMENOPAUSAL WOMEN WHO QUIT SMOKING GREATLY REDUCE BLADDER CANCER RISK

By Lisette Hilton

A new study shows that quitting smoking can greatly reduce risk of bladder cancer among menopausal women.

Researchers analyzed data on 143,279 postmenopausal women and found former smokers who quit within the last 10 years were 25% less likely to be diagnosed with bladder cancer compared to current smokers. Women’s bladder cancer risk continued to fall with greater years since quitting but remained higher than the risk among never smokers even 30 or more years after quitting, according to the data, which were published in Cancer Prevention Research (2019; 12:305-14).

“Patients should be advised to not smoke, because in addition to all of the other health problems that smoking causes, bladder cancer is also a risk. And... if patients are smoking, they can be advised to quit to reduce bladder cancer risk even if they are older—all women in this study were postmenopausal at baseline. It is not too late for older people to benefit from quitting smoking,” study author Michael Hendryx, PhD, of the Indiana University School of Public Health-Bloomington, wrote in an email to Urology Times.

The authors found that when they adjusted for age only, former smokers were at 2.01 times higher risk and current smokers at 3.39 times the risk of bladder cancer compared to never smokers. They didn’t find a significant risk difference between never smokers and former smokers who had quit more than three decades prior. However, when they adjusted for number of cigarettes a day or pack-years of smoking, former smokers were at significantly higher risk of bladder cancer than never smokers, even if they had quit more than three decades prior.
Chart reviews: Make these changes to prevent payer mistakes

Detailed consent statements recommended, even for repeated treatments

We have performed many audits/chart reviews throughout the years. Many of these reviews have been educational. However, a number of the chart reviews have been undertaken to review payer takeback requests, educational reviews performed by others, Medicare integrity actions, and legal actions. In this article, we discuss a few of the items we have discovered in reviewing medical charts as a response to reviews conducted by payers.

Mistakes by reviewers

In all the cases we have been involved with, we have yet to find a review that does not contain a significant number of mistakes. These mistakes can range from simple oversight of information included in the record to a complete misunderstanding of a payer’s own payment rules. Here is a list of common mistakes we have seen and have been able to overturn on follow-up appeal, some suggestions as to how change your documentation to prevent future payer mistakes, and a few examples of each one:

Incorrect understanding of service provided. Example 1: Chart includes findings from automated urinalysis plus red blood cell count, leukocyte count, and epithelial cell count. The chart review by payer changes code from UA automated with microscopy to UA automated without microscopy. It was clear the person reviewing the chart did not understand that the cell counts can only be obtained using microscopy. In order to prevent this misunderstanding, chart documentation can be changed to include “microscopy findings – RBCs 0-3, WBCs 5-10, etc.”

Example 2: The chart indicates “cath residual 5 mLs.” The chart is reviewed by the payer, who denies 51701 but allows 51798 (ultrasound post-void residual). To prevent misunderstanding in the future, include catheter type and size of inserted catheter in addition to “residual 5 mL.”

Evaluation and management code denied as included in services provided even with modifier –25 applied. Example 1: Chart indicates patient presents for surveillance cystoscopy. Cystoscopy findings are included and indicate new growth in bladder dome. A further indications discussion with the patient over treatment options and full course treatment ensued, lasting 20 minutes. E/M code is denied by payer as included because of a lack of a second diagnosis.

Example 2: The chart indicates “cath residual 5 mLs.” The chart is reviewed by the payer, who denies 51701 but allows 51798 (ultrasound post-void residual). To prevent misunderstanding in the future, include catheter type and size of inserted catheter in addition to “residual 5 mL.”

E/M code lowered. Many methodologies and score cards have been used by payers to judge the appropriate level of evaluation and management. Our approach in dealing with these reviews has been to first provide the payer with our scoring methodology and pocket card/wall chart system. Some payers have accepted the system, including most Medicare payers and the Office of the Inspector General. Other payers push back with scoring systems developed internally and used by their auditors.

For the payers with different scoring methodologies, we will review the chart again using the payer’s methodology, often finding the support required for the original level of service under their rules by pointing out the information included in the chart, based on a better understanding of urologic medical care.

As one would expect, the payer does get it right sometimes. For those cases, it is important to agree with the payer’s findings.

Example 2: Chart indicates patient is present for bacillus Calmette-Guérin instillation. Chart also includes physician review of patient history, computed tomography scan and cytology, and review with patient of alternative treatments due to BCG shortage. Payer denies E/M code as included with BCG instillation.

This denial was similar to the example above. The physician spent time evaluating and recommending treatment for the disease process, clearly a separately identifiable and significant E/M service. As we have previously discussed, clear separation of a procedure note and E/M note is the best defense against denial; however, most auditors do not have a clear understanding of all medical specialties.

It is difficult to prevent some of these misunderstandings, even with a clear separation of procedure notes and patient discussion. However, this denial could potentially have been avoided by using the diagnosis “bladder neoplasm of unspecified behavior” for the cystoscopy instead of “Hx of bladder cancer.”

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CHART REVIEWS
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We encourage each practice to contact their medical malpractice carrier for both advice and [informed consent form] templates that may be used for the office and hospital specific to your practice and location(s).

In looking for further legal guidelines for informed consent, we found a few general rules that are applied but found that these requirements are, like many rules in medicine, variable and geographic in nature. Hospitals and other entities overseen by the Joint Commission have rules that require a signed consent form (by physician and patient) that clearly indicates that the patient understands the service being provided and the risks associated with procedure to be provided that is specific for the encounter.

For the office-based setting, we did not find the same clarity or application. Specifically, we did not find any legal language or contract language that mandated that a consent form had to be in writing. We think we have a good argument with legal backing that documenting the consent statement in your record is adequate without a signed consent form. However, the audit is pending, and we do not have a clear answer for you.

Therefore, we offer the following advice for your own protection.

• First, check your state for any specific requirements for both general and informed consent. We encourage each practice to contact their medical malpractice carrier for both advice and templates that may be used for the office and hospital specific to your practice and location(s).

• From our review of records for many offices, General Consent to Treat remains a part of the new patient or “welcome to the practice” paperwork. This is a good start and should be continued.

• Based on American Medical Association guidance and review of legal firms’ opinion, you should include clear and specific informed consent in the medical record. For smaller, low-risk procedures, no separate form is required; however, it is in your best interest to have signed consent forms for any procedure in the office setting that has a moderate to high risk level.

• All consent forms and information included in the medical record should include not only a discussion of the risks, benefits, and options for treatment but a statement that indicates that the patient has acknowledged and understands these issues as it relates to the service to be provided and agrees to proceed.

Returning to our informal review of several records from few offices, we have found many groups include some standard language that will reflect a discussion of risks, benefits, and options without specific information for the procedure or drug to be provided. Additionally, we have seen a number of groups that include phrases that indicate that “all patient questions have been answered.”

The problem we see with these types of general statements is that they do not include specifics for any given procedure or drug. Many of you have secondary language that is added to the record for specific drugs and services, but these are not included in all cases. Take care to add the specifics. Also, indicating that all patients’ questions have been answered or similar phrasing does not necessarily communicate that the patient understands and agrees to proceed with the specific treatment/service/drug prescribed.

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Conclusion
Medical record review is inevitable in today’s world. Take care to include all relevant data when sending in record requests. It is far easier to pass a record review if the record is complete and the information is clear and easy to follow.

If you do run into issues where a payer disagrees with what you have billed based on record review, always review the records, find any additional documentation that may be needed, and finally, use data-based arguments to refute any incorrect findings. Document well, and good luck.

ARE YOU PAYING ATTENTION TO ONLINE REVIEWS?
A majority of physicians and health care providers are concerned with maintaining a quality patient connection, yet nearly one-third of practices do not spend the time or resources to achieve this, according to a recent survey. Urology Times sister brand Medical Economics recently reported on the survey results.

The survey of 233 health care providers conducted by the online management vendor PatientPop found that nine out of 10 providers have seen reviews of their practice online, but they don’t always respond to them. Fifty-two percent of providers who don’t respond believe it won’t make a difference.

This is true especially if they are negative—nearly one in five practices don’t respond to negative patient feedback at all, the survey says.

To read the complete article, go to bit.ly/online-docreviews.
The average industry payment to a urologist saw a decline in 2018 compared with the previous year.

That’s according to the Centers for Medicare & Medicaid Services’ (CMS) annual update of Open Payments Financial Data (calendar year 2018) ([https://openpaymentsdata.cms.gov/](https://openpaymentsdata.cms.gov/)). Section 6002 of the Affordable Care Act, also known as the Physician Payments Sunshine Act, requires that manufacturers of “covered drugs, devices, biologicals, and medical supplies” report payments and other transfers of value to physicians to CMS. It also requires that manufacturers and group purchasing organizations report physician (or their family) ownership and investment interests. In this article, I review some summary information and analysis about urology as it pertains to Open Payments data.

In 2018, $9.35 billion in payments or investment value was reported by 1,582 unique companies to physicians, teaching hospitals, and other entities; this is an increase of 3.7% in payments compared to the 2017 total. The total amount of general payments to individual physician recipients was $2.17 billion. According to the data, 9,405 urologists received a total of $35,444,486.60 in general payments to physicians, or 1.63% of the total general payments.

The largest single payment to a urologist was $1,964,352 for a royalty/license, and the average payment to a urologist in 2018 was $162.10 (down from 2017). In addition, 58 urologists each received more than $100,000 and collectively represented more than 45% of all payments to urologists (table, figure). As in past years, most of these payments are from device manufacturers, and payments are concentrated in a handful of individual companies, drugs, devices, recipients, and disease states. Prostate cancer (drugs), BPH (devices), and overactive bladder (drugs) continue to represent most of the collective spending in the specialty. Although the vast majority of urologists appear in the data, but payments are generally so insignificant that most need not worry about the appearance of impropriety.

### Drug/biologic-related payments increase
CMS requires manufacturers to associate a payment with a drug, biologic, device, or medical supply where appropriate. General payments to urologists associated with devices comprised the largest collective payments, totaling $18,430,482, or more than half of all general payments. Payments associated with drugs and biologicals totaled almost $13.7 million, significantly more than in 2017; three drug manufacturers accounted for almost 50% of total payments in this category.

The database also associates payments with a product category or therapeutic area; payments to urologists came largely from manufacturers who classified their product as urology, oncology, or male health related. Eight single products (one device and seven drugs) accounted for more than 50% of payments in 2018.

Bottom line: General payments from manufacturers to urologists in 2018 reported to and by CMS under the Sunshine Act represent a tiny fraction of general payments to physicians and average less than $200.

### TABLE SUMMARY OF PAYMENTS TO UROLOGISTS, 2015-'18

<table>
<thead>
<tr>
<th>Year</th>
<th>Providers (unique)</th>
<th>Manufacturers (unique)</th>
<th>Count of unique payments</th>
<th>Average payment</th>
<th>Max. individual payment</th>
<th>Max. individual recipient</th>
<th>Sum of payments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>9,285</td>
<td>331</td>
<td>205,151</td>
<td>$153.91</td>
<td>$566,857</td>
<td>$1,365,311.69</td>
<td>$31,575,262.38</td>
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<tr>
<td>2016</td>
<td>9,366</td>
<td>359</td>
<td>207,247</td>
<td>$149.39</td>
<td>$449,963</td>
<td>$1,623,328.95</td>
<td>$30,775,803.22</td>
</tr>
<tr>
<td>2017</td>
<td>9,343</td>
<td>379</td>
<td>203,836</td>
<td>$176.42</td>
<td>$3,000,000</td>
<td>$3,000,187.97</td>
<td>$35,961,655.09</td>
</tr>
<tr>
<td>2018</td>
<td>9,405</td>
<td>405</td>
<td>218,656</td>
<td>$162.10</td>
<td>$1,964,352</td>
<td>$1,964,508.08</td>
<td>$35,444,486.60</td>
</tr>
</tbody>
</table>

Source: Adapted from Centers for Medicare & Medicaid Services data ([https://openpaymentsdata.cms.gov](https://openpaymentsdata.cms.gov)) by Robert A. Dowling, MD
When getting married, don’t forget financial planning

Work out decisions on combined accounts, long-term goals before big day

Q: I’m getting married soon. What financial items should I consider when tying the knot?
A: The marriage process, regardless of age, requires careful thought about a number of financial situations a couple will likely face. With financial disagreements being a leading cause of marital problems, why not tackle them ahead of time? This may include reaching out to your financial planner and other legal and tax advisers well in advance of the nuptials.

The starting point is to have a candid discussion with your fiancé about your overall finances. For example, how much debt is each of you bringing to the marriage? What about savings? The older you are, the more (good and bad) financial baggage you’re likely to bring to the partnership.

Next, from a savings standpoint, you’ll need to decide if you will be combining accounts or keeping them separate. Your financial adviser can walk you through what will be needed to combine checking, savings, and money market accounts. He or she can also advise you about adding or changing beneficiaries on your individual retirement accounts and other retirement plans.

Even if you decide to maintain separate accounts, it may be helpful to have at least one joint account to pay for shared expenses, such as mortgage or car payments, rent, household expenses, and insurance premiums. This account is meant strictly for household needs, and it allows you both to keep track of how you are spending money.

A joint account can also help avoid complications in the event one spouse dies. When a spouse or common law partner dies and there are separate accounts, the survivor will be excluded from the other separate account if the estate goes into probate. That could take months and add additional expenses due to court and attorney fees.

If you are both employed, you must take time to review and coordinate your employee benefits. You might save money by eliminating duplicate health care, for example. This process also allows you to determine and then make any changes to the beneficiary designations on retirement plans and insurance policies held through your employers.

Next, sit down and identify financial goals as a couple. Start by creating an annual budget, as well as a contingency plan in case a spouse gets laid off or becomes disabled. Make sure you have an emergency cash reserve. Designate who will be responsible for paying the bills and keeping you on budget. Also look beyond your current financial situation. For example, discuss what you envision your retirement will look like and whether current retirement account contributions are sufficient to achieve your long-term goals.

People who have been previously married may bring additional financial issues to the table, especially if they have children or are required to pay alimony, child support, or insurance premiums under the terms of a divorce settlement agreement.

Q: What estate planning items should be considered when getting married?
A: Marriage is a good time to meet with an estate planning attorney and get a plan in place. Estate planning is often pushed aside because it deals with a conversation most couples don’t like having—“What happens if one of us dies?” However, it is important to have a plan in place.

A will may be a good first step, but may not be necessary depending on the assets that are owned. An estate planning attorney will be able to provide specific guidance. Having health care and durable power of attorneys in place is always smart in the event you are incapacitated. Depending on your assets, certain trusts may also play an important role in accomplishing your estate planning goals.
How benchmarking helps manage your time, identify problem areas

Analytics tool provides LUGPA members insights to improve performance

KEITH LORIA
Mr. Loria is an Oakton, VA freelance writer.

Benchmarking involves collecting information from various sources and comparing processes and performance metrics to determine how other businesses achieve their high levels of performance. It’s data collection that urologists can utilize to discover ways to improve their practices. LUGPA recently teamed with IntrinsIQ Specialty Solutions (IQSS), part of AmerisourceBergen, to support a new benchmarking program powered by InfoDive, IQSS’s business analytics solution. This collaboration, LUGPA says, will allow LUGPA member practices to compare independent group practice performance metrics against that of other member practices.

Cass Schaedig, vice president of provider analytics, ION Solutions for AmerisourceBergen, says this benchmarking tool will ultimately enable hundreds of urology practices to manage their time, lower administrative costs, and spend more time with patients while implementing the latest treatments into their practices.

Schaedig spoke with Urology Times about the value of benchmarking in patient care, practice management, and health policy.

Urology Times: Characterize how benchmarking data is changing practices in 2019.

Schaedig: By giving practices the ability to quantify the value of their care, particularly in comparison to similar-sized or focused peers, benchmarking helps practices demonstrate their eligibility for appropriate reimbursement to public or private payers. Benchmarking also helps control for a practice’s possible overutilization, and it allows providers to identify areas of strength or opportunity, where they can continue investing, or where they may eliminate a service or develop an action plan to address any underperformance.

Urology Times: What do urologists need to know to utilize InfoDive properly? Is there a significant learning curve?

Schaedig: There is no learning curve for InfoDive; we’ve worked hard to make it an intuitive tool. We help practices understand how the variables reported in InfoDive relate to one another, so they know what underlying or complementary factors may be contributing a particular result.

Urology Times: What sets InfoDive apart from other similar platforms?

Schaedig: We are the only source of benchmarking that can provide more detail around relative value units, a measure of value and productivity used in the Medicare reimbursement formula for physician services. We calculate metrics from the raw billing data and apply the exact same cleansing rule and logic to create statistics from the filed claims.

Urology Times: What will the program inform education programs and advocacy priorities?

Schaedig: LUGPA and its member groups can use the insights drawn from the benchmarking program to better inform legislators and other stakeholders on how policies impact both practices and patients. Just as individual practices can use the data available through this partnership to demonstrate their value to payers, LUGPA can leverage membership-wide insights to demonstrate the value and needs of urology practices across the country.

For example, when a new government rule is proposed that could affect practices, we can apply the proposed changes in InfoDive, so LUGPA groups are able to see the potential impact. Practices can then use that information to shape their responses to legislators’ calls for public comment.

Urology Times: Who can participate? Is the program available only to LUGPA member practices?

Schaedig: In order to establish critical practice benchmarks, LUGPA established a task force of informed professionals from member practices to provide oversight for the benchmarking program, establish key metrics, and determine the reporting structure and cadence to members. IQSS will provide consultative support to the task force and, using InfoDive, data analysis for ongoing reporting. The relationship we have with LUGPA offers discounted licensing of InfoDive as well as access to LUGPA-specific benchmarking reports.

Urology Times: How can it improve performance and patient outcomes?

Schaedig: Having access to InfoDive gives practices insights into the full patient care journey, making it easier for practices to identify pain points and where there is room for improvement. The platform provides a view of a practice’s performance and operations that’s not often visible through its existing billing and EMR systems and can inform how to restructure services to a patient’s benefit.

For example, “Physician A” may only do a few procedures of a certain type a year, while “Physician B” may perform a high volume and have a high patient success rate. A group practice may be able to use InfoDive to analyze whether it makes more sense for Physician A to refer his or her patients requiring the procedure to Physician B and focus on other patient needs. Ultimately, InfoDive helps practices to determine the more efficient route that will also protect and promote patient health.

UT
and wondered why this topic has not received more attention. One recent multinational survey of urologists reported a 45% incidence of spinal pain," she said, citing a July 17, 2019 paper in the *Journal of Endourology* (Epub ahead of print).

In the *Urology Times* survey, most urologists continued to work despite minor/moderate discomfort (56%) or significant discomfort (29%). Another 5% were able to continue working, but their ability to perform surgery was affected. Two respondents said their pain or discomfort led to early retirement or ended their career.

“Most shocking and concerning of all, 62% of urologist respondents have been threatened and 23% were physically attacked or abused by a patient. Among respondents, 21% were threatened and 8% were physically attacked or abused by another provider,” Dr. Loeb said.

“Many urologists experienced other issues such as needle sticks (75%), dry/cracked skin (58%), and eyestrain (39%) as a result of work activities.”

Twenty percent have been diagnosed with degenerative lumbar spine disease, 17% with degenerative cervical spine disease, 15% with arthritis, and 13% with rotator cuff pathology.

The survey was not designed to determine whether the high prevalence of physical pain/injury is a new phenomenon among urologists, but such occurrences have been common over the last year. When asked how frequently they have experienced work-related musculoskeletal pain or other discomfort in the past 12 months, 32% of respondents said it occurred more than once per week, 21% said it occurred weekly, and 18% said it occurred monthly.

In terms of possible causes of their work-related pain or discomfort, urologists most often cited awkward positioning in the operating room (33%), repetitive movements during surgery (30%), extended periods of standing (15%), and equipment such as a lead apron or loupes (8%).

More than two-thirds (68%) said they took non-steroidal anti-inflammatory drugs to reduce musculoskeletal strain/injury while performing surgery. Forty-three percent have altered the manner in which they hold instruments, 19% have used mechanical aids to move patients, and 19% have minimized the use of lead aprons.

Only 17% of urologists report receiving training on surgical ergonomics, and 70% would like to receive such training. (Also see, “Addressing dangers in the OR starts with education,” page 30.)

The issues surrounding both the physical and emotional/psychological issues affecting urologists “urgently need to be addressed,” Dr. Loeb said. “To take the best possible care of our patients, we must first take care of ourselves.”

**Where has pain/discomfort been experienced?**

- Neck: 70%
- Shoulders: 48%
- Back: 66%
- Elbows: 10%
- Wrists/hands: 39%

**Which condition(s) have you been diagnosed with?**

- Degenerative lumbar spine disease: 20%
- Degenerative cervical spine disease: 17%
- Arthritis: 15%
- Rotator cuff pathology: 13%
- Carpal tunnel syndrome: 8%
- Acute spinal injury: 4%

**To what do you attribute your pain/discomfort?**

- Awkward position in OR: 33%
- Extended periods of standing: 15%
- Equipment (eg, lead apron, loupes): 8%
- Lifting/moving a patient: 6%
- Assault/physical abuse by a patient: 1%
- Assault/physical abuse by a provider: 1%
Urology Times conducted a survey of readers via email in June and July of 2019 to determine the frequency and type of work-related pain/injury they have experienced. Special thanks to Stacy Loeb, MD, MSc, of the Urology Times Editorial Council, who reviewed and critiqued survey questions developed by the editorial staff. All survey recipients were subscribers to Urology Times, and all were required to report being a urologist or urology resident before responding. A total of 165 responses were received.
Addressing dangers in the OR starts with education

Injury stemming from awkward maneuvers, equipment can and should be prevented

It started as a tightening of my lower back, sort of a twinge. I had been helping move a patient from the transport bed to the operating room bed. It was something I’ve done countless times. I reached over the operating room table to pull the patient over that incredibly firm and uncomfortable roller board we use when it happened. I didn’t think much of it at the time, finished the case, and went about my normal day.

By that night, my back hurt and by the following day (thankfully a Saturday), I couldn’t even stand up straight. I tried anti-inflammatories and even borrowed my wife’s TENS unit. By Monday, while I was in no shape to do anything terribly physical, I was on the mend.

I was lucky. According to the World Health Organization, the lifetime prevalence of significant back pain is 70% with a 5% per year incidence. The incidence of this injury peaks between the ages of 35 and 55. Further, low back pain is the number one cause of activity limitation and work absence, according to WHO. Back injuries are real and not easy to fix.

Consider all of the maneuvers we do in the operating room: awkward positions, lifting objects above the waist, standing in one position for long periods of time, rotating the torso while bearing weight, wearing heavy lead, adding weight to our neck in the form of loupes or operating lights, pulling patients up in a bed, or as in my case, repositioning a patient.

Last year, an article in *JAMA Surgery* (2018; 153[2]:e174947) looked at the prevalence of work-related musculoskeletal disorders and found that the incidence of these injuries was much higher in surgeons than in other physicians. The authors found that among surgeons, the risk of degenerative cervical disease and degenerative lumbar disease was 17% and 19%, respectively. Rotator cuff pathology and carpal tunnel syndrome were also abnormally high at 18% and 9%, respectively.

These injuries resulted in 12% of surgeons requiring a leave of absence or a practice modification. These are incredibly high numbers.

**What can urologists do?**

What can you do? Protect yourself. All surgeons need to be educated on the dangers associated with what we do. Proper technique when moving patients, including the use of mechanical aids, is vital. Minimizing the use of lead gowns with judicial use of radiation cannot be understated. Exercising to strengthen your core and maximize internal support has been shown to decrease the risk of low back disease.

This education needs to happen before the injury and should likely start at the resident or even medical school level. If you wait until your back hurts, you’ve waited too long.

**Steps are available to minimize these risks, and education regarding the dangers we face on a daily basis is the first step to preventing the problem.**

But it’s worse than you think. As surgeons, not only do we expose ourselves to musculoskeletal disorders, we face additional personal risks we need to monitor and mitigate. Take needle sticks, for example. While most surgeons are vaccinated against hepatitis B, as we know, there are no vaccines available for numerous other pathogens such as hepatitis C and HIV. It has also been shown that surgeons tend to have poor compliance with universal precaution procedures (*Ann R Coll Surg Engl* 2009; 91:430-2).

Worse, we tend to be poorly complaint with reporting our injuries. Simple maneuvers such as double gloving can significantly reduce the risk of disease transmission from exposure, an *Infection Control Today* article explains. As we all know, the problem with double gloving is the change in tactile sensation. However, studies have shown that this change, while real, can be overcome with time and training (*J Hosp Infect* 1995; 30:305-8). Again, education is key and while it may be challenging to convince the current cohort of surgeons to change their gloves, there is no reason why all residents shouldn’t be trained to use double gloves.

**Protect your skin**

There is more to skin protection than simply wearing gloves. Frequent scrubbing and other hand hygiene tends to dry out skin, and that problem is made worse by prolonged periods of occlusion from gloves. Why is that a problem? It can lead to dry, cracked skin, which increases the risk of pathogen transmission. Routine use of a moisturizer should be considered; if your operating room doesn’t offer access to one, ask. When you consider moisturizer use as a way to protect yourself against bloodborne pathogens, even the toughest of surgeons may start using it.

But wait, there’s more. Intraoperative imaging is key to safely performing many of the procedures we do. Unfortunately, as Marie Curie learned many years ago, uncontrolled exposure to radiation can have detrimental effects. We all know common techniques to reduce exposure such as distance, shielding, and dose reduction, but how much risk is there? A recent study that prospectively measured radiation exposure during more than 100 common urologic procedures found that surgeons’ exposure during any one case was less than 1/100th of the maximum permissible dose (*J Urol* 2014; 191:e109, abs. MP12-10). While that is good news, for those of us who tend to do a lot of fluoroscopy-intense procedures, individual doses can add up over years.

No one is advocating that we stop operating, and some of the risks discussed here cannot be modified. But steps are available to minimize these risks, and education regarding the dangers we face on a daily basis is the first step to preventing the problem.
RISK ASSESSMENT IN MODERN UPPER TRACT UROTHELIAL CARCINOMA (UTUC) TREATMENT

How multivariable models and emerging diagnostic imaging may help better identify candidates for kidney-sparing treatment

Patients with UTUC may present with a wide range of disease characteristics, in addition to clinical risk factors such as advanced age, tobacco use, environmental exposure, and comorbid conditions. A comprehensive risk stratification approach is imperative when determining optimal treatment in this patient population, as kidney function is often significantly compromised, and radical nephroureterectomy (RNU) introduces risk of complications and further renal impairment.

**UTILIZING A MULTIVARIABLE MODEL TO ASSESS RISK**

In addition to histopathology, a full complement of diagnostic procedures may be employed to assess the variables associated with UTUC risk, including high-quality axial imaging, cystoscopy, urinary cytology, retrograde pyelography, and ureteroscopy. Other key factors should be considered to provide a complete patient picture, including renal function, pre-existing comorbid conditions, and prior health history.

The viability of multivariable models has been steadily increasing, supported by multiple studies in past years, and now includes an April 2019 retrospective study (N=699) of preoperative nomograms for prediction of high-risk nonorgan-confined (NOC)-UTUC. Some multivariable models are more extensively validated than others, but regardless of the nature of the nomogram, the fact remains: When it comes to identifying candidates for kidney-sparing treatment, more information is better.

**EMERGING IMAGE ENHANCEMENT TECHNIQUES AND OPTICAL DIAGNOSTIC TOOLS**

Better visualization of suspect lesions that can provide real-time optical biopsies could allow higher diagnostic precision and optimal, individualized treatment of patients with UTUC. Although exploratory and evaluated only in small populations, a number of emerging imaging techniques may enhance UTUC risk assessment, including narrow-band imaging, photodynamic diagnosis (PDD), optical coherence tomography (OCT), and confocal laser endomicroscopy. In particular, preliminary data for PDD is encouraging. In a 2016 study in UTUC (N=106) in which 48 tumors were identified, 95.8% were visualized with PDD vs only 47.9% with white light (P<0.0001). Additionally, PDD was shown to provide greater sensitivity for UTUC (96% versus 54%) with no difference in specificity (96% vs 95%).

In a recent follow-up to an initial pilot study, OCT demonstrated higher correlation with surgical pathology vs biopsy in regard to both stage (83% vs 49%) and grade (88% vs 79%). OCT staging also showed extremely high sensitivity (100%), specificity (92%), positive predictive value (92%), and negative predictive value (100%).

Although they have not achieved the level of evidence necessary to justify incorporation into daily practice, these emerging imaging modalities offer exciting potential and should be considered in cases where kidney-sparing treatment may be appropriate.

**Preoperative nomograms for prediction of NOC-UTUC**

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<th>Accuracy</th>
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Some multivariable models are more extensively validated than others, but regardless of the nature of the nomogram, the fact remains: When it comes to identifying candidates for kidney-sparing treatment, more information is better.

**References:**

PET use in prostate cancer widens, but questions remain

Imaging with positron emission tomography (PET) in prostate cancer represents an important clinical advance, especially for identifying metastases. Its use has expanded significantly, especially outside of the United States. In this interview, Mark Frydenberg, MD, discusses the evolution of PET scanning, its clinical indications, its advantages and drawbacks, and key questions that remain about its use.

Q: To start, tell me what you consider positron emission tomography (PET) scanning today and how it has evolved.
A: PET scanning today has moved on from where it was previously with vastly improved tracers. We’re really looking for an imaging tool that better identifies metastatic spread of any malignancy, in this case, prostate cancer. Urologists have been well aware of PET scans in the past and had used PET choline scans, but they never became popular because they weren’t particularly sensitive and specific. Choline is also quite difficult and expensive to produce; it requires a cyclotron on site.

Since then, other PET tracers have been studied, including sodium fluoride, which is very good at detecting bone metastases. More recently, people have looked at floricholine F18 (Axumin), and in Australia where I practice, the most common one is a Gallium 68 PET PSMA scan, which is prostate-specific membrane antigen.

Q: The dissemination of PET scanning now in Australia is well ahead of the United States. How is it being used in Australia?
A: Its use has really exploded in Australia over the last 5 years or so. The reason is that most of the nuclear medicine departments actually have their own gallium generators. As such, it is relatively quick, easy, and inexpensive to manufacture and deliver, so the dissemination has been very rapid in both public and private sectors.

The main use for PET initially was in biochemical recurrence following definitive treatment for prostate cancer, predominantly radical prostatectomy, but also primary radiotherapy. It’s also been used to monitor metastatic disease, especially in the setting of castrate-resistant disease, and more recently it’s been used in primary staging, in particular in patients with high-risk prostate cancer, to look for oligometastatic spread.

Our group did a study years ago showing that the CT scan in high-risk disease doesn’t offer much past the bone scan, and this has been confirmed by others.

Could you see PET replacing CT?

J. BRANTLEY THRASHER, MD

Very much so. In fact, in Australia that largely has already happened with high-risk disease.

MARK FRYDENBERG, MD

Q: There’s worry always in the U.S. about cost. What would be a similar cost for a PET scan in U.S. dollars, and how are you able to justify the cost in certain patient groups?
A: The cost in Australia would be approximately $500 U.S., so it has become quite affordable. It is not something that the government pays for the patient right now. Government approvals for payment of new technologies often take 2 to 3 years so it may be some time before it is covered for the general public by a government rebate. However, it is readily available in virtually all of the university public hospitals in Australia. Many of the private providers also have access to PET PSMA, with most patients being reasonably comfortable paying for it privately if it’s not covered through the university hospital.

It obviously is important to use it wisely because there is a direct patient cost associated with it, especially in the U.S. As such, it’s important to try to choose the patients who are most likely to have a positive scan. In the primary staging setting, there’s no doubt we really need to look at the high-risk cases only. For the intermediate- and low-risk cases, less than 5% of patients will have a positive PET scan, and it will probably not be a cost-effective strategy for them. However, most of the studies looking at high-risk prostate cancer have shown 30% to 50% of patients do show oligometastatic sites on a PET PSMA scan, so it’s definitely worthwhile to consider it in that population.

The other group where it should be considered is obviously those with biochemical recurrence, and we’ve learned there is probably little point in doing a PET PSMA scan when PSA is below 0.2 ng/mL. The likelihood of a positive result is very low in that group, but it starts increasing from 0.2 ng/mL onwards. Most of the data show that about 30% of patients with PSA between 0.2 and 0.5 ng/mL will have a positive PET PSMA scan. That will increase to about 60% when PSA is between 0.5 and 1.0 ng/mL and will increase to about 80% when it’s above 1.0 ng/mL.

Q: Does it display the prostate only, or do other organs light up?
A: With PET PSMA, there are numerous other organs that will demonstrate uptake in addition to the prostate. Probably the most troublesome are the kidneys and the associated urinary excretion because it will actually show up in the ureter and bladder. One of the tricky aspects of PET PSMA is that a peristaltic wave of urine across the pelvic brim can be mistaken as a pelvic lymph node quite easily, so you need to be careful of that. It shows up in the bladder, which can obscure the detection of local recurrences, and is also taken up by the bowel and salivary glands.

Interestingly, it’s been shown that PET PSMA can be a useful tool for kidney cancers as well, but a lot of further work needs to be done in that area before it can be used clinically for that indication.
Last year, the AUA updated its guidelines for benign prostatic hyperplasia (BPH). The update includes a recommendation for urologists to consider prostatic urethral lift (PUL) for the treatment of some patients with BPH.

Six experienced providers of PUL joined a panel to examine the AUA’s new guidelines, the current status of the UroLift System® within the standard of care for BPH, and how to improve the care pathway for BPH.

read this supplement at urologytimes.com/bphcare
Q: Do you put in a Foley catheter to decrease the possibility of hydrenephrosis or something similar that would throw off the sensitivity of the scan?

A: Usually we don’t put in a catheter, but we do virtually always give Lasix to get some urinary clearance, then do the scan soon after that.

Q: Our group did a study years ago showing that the CT scan in high-risk disease doesn’t offer much past the bone scan, and this has been confirmed by others. Could you see PET replacing CT?

A: Very much so. In fact, in Australia that largely has already happened with high-risk disease. We’re waiting with interest the results of a trial being done in Australia, in which I was a co-investigator, called the ProPSMA study, which is looking at conventional imaging versus PET PSMA for staging high-risk prostate cancer. It’s examining the utility of PET PSMA for identifying metastases but also for determining the likelihood of altering treatment. The main question that still arises is whether it makes any difference to long-term patient survival, but there’s no doubt the more information and the more accurate information you have, the better choices you can make for the patient.

Q: One of the big criticisms with PET scanning is that we don’t have histologic confirmation when something lights up. In the ProPSMA study, will we have histologic confirmation?

A: Patients on trial who have gone on to have a radical prostatectomy and extended node dissection will have histologic confirmation of the positive nodes and how they correlated with the histopathology at the surgery. Hopefully we will get some more information because we’ve made the decision that all the patients in the trial will receive extended node dissections since they’re considered high risk. Even if they’re PET negative, we hope to also identify those patients who are missed because we know that the sensitivity is not perfect with PET PSMA scans.

However, if you look historically at the data when there has been correlation with histopathology, the specificity is excellent—often 95%-plus. Even with the data we have to date, we can be fairly comfortable that if something is positive on a PET PSMA scan, it will be histologically malignant.

For me, the bigger issue is the negative PET PSMA scan in a high-risk patient because we know that 30% to 40% of patients will not have a positive PET PSMA signal even though there might be disease present, which largely has to do with tumor volume. If the patient has lymph node metastases that’s less than 2 to 3 mm in size, for example, that isn’t going to get picked up on the scan. But if you wait for it to get over 5 mm or so, there’s a much greater chance it will show up. So the problem is that we will end up missing small malignant nodes with a negative PET PSMA scan.

Q: When do you think we will see the data from the ProPSMA trial?

A: We’re currently in the follow-up phase, so all the recruiting is finished. We’re basically looking at the 6- and 12-month reviews since patients have gone on to treatment, and we would expect that data around the time of both the European and American urology meetings in 2020. It’s very likely that data will be presented as an abstract at both the EAU and AUA annual meetings next year.

Q: Let’s talk about PET’s use in oligometastatic disease or biochemical recurrence. First, when do you generally use it? Is there a PSA threshold that practicing urologists might take home if they have access to the scan? Second, what are you doing when you find oligometastatic disease or biochemical recurrence—surgery, radiation therapy, or continuing hormonal therapy?

A: It’s a very challenging area. The whole problem with the PET PSMA scan is it improves our ability to stage the disease or to restage the disease, but we have no idea whether the interventions we’re studying now have actually changed long-term survival. That remains a challenge for us moving forward.

A number of studies have shown that the PET PSMA results change management. If we look at biochemical-recurrent patients, about 30% to 80% have their management changed as a result of the PSMA scan. Typically what will happen is that instead of there being a presumed local recurrence, we find a pelvic node, an extrapelvic node, a bony metastasis, or sometimes a combination. As such, instead of radiation to the prostate bed, which would normally be standard of care for PSA rise post prostatectomy, we are then faced with the decision whether this should be done, combined with stereotactic ablative radiotherapy to involved nodes, or consider a salvage lymph node dissection, androgen deprivation therapy, or combination of therapies.

I don’t think there’s a belief that we’re going to cure the disease with ablative radiotherapy or salvage node dissections alone because usually the PET PSMA scan underestimates the degree of metastatic spread. However, we have data that we hope to publish soon that will suggest that it at least delays androgen deprivation therapy in about 50% of patients by at least a couple of years. That may at the very least provide the patient some quality of life benefits.

Q: For a young, healthy patient with 20 years life expectancy, do you see a role for surgical removal in a patient with a positive PET scan? Let’s say it’s right at the bifurcation of the aorta and you’ve got one nodal spot that lights up on PET.

A: It’s clearly another strategy, as is stereotactic ablative radiotherapy, and it certainly been done in the U.S. but especially in Europe. Again, the results haven’t been that spectacularly successful because PET PSMA underestimates the amount of metastatic disease that’s present, and the small additional lymph nodes that are present just don’t demonstrate uptake. So you can do an extended node dissection and even a retroperitoneal node dissection, but there may well still be micrometastases in nodes further upstream that you haven’t visualized and hence haven’t been able to tackle.

I think this is an area we have to look at. The role of either radiation or aggressive surgery is very ripe now for clinical trials. But I think the take-home message is, what you see on the PET is probably just the tip of the iceberg, and there’s probably more microscopic disease beyond what is seen. Also, I certainly would not recommend a node pluck to take out the lymph node. You must do a proper node clearance in that area if you’re going to make any impact at all.

Q: Let’s talk about the future. Do you see new radionuclides or new tracers coming out for PET scanning or imaging in general?

A: There are two aspects of the future: therapeutic and further imaging. With regard to further imaging, I think there will definitely be a swing toward using a fluoridated PSMA tracer rather than gallium. Fluoridated PSMA is a little more difficult to manufacture because it requires a cyclotron, but it has a very long half-life, which means it can sit on the shelf for quite a long time and can be made in large batches.
Thus, a lot of nuclear medicine departments can store it on site. The advantage for me is that there is no urinary excretion, and the ureteric peristalsis mimicking a pelvic node won’t occur. It should be much better at picking up the local recurrences at the bladder neck after radical prostatectomy.

Interestingly, we’ve found in Australia that a multiparametric MRI of the pelvis probably actually identifies local recurrences often a lot better than a PET PSMA scan, purely because of the problem with urinary excretion. You can still pick them up on the PET scan, but an MRI is often better.

The other future direction relates to theranostics or treatment of advanced disease. We’ve been running some trials in Australia using lutetium as the agent, which is bound onto the PSMA and has effectively been used to treat castrate-resistant prostate cancer when all therapeutic options have been exhausted. There have been some very impressive results; we’ve had at least 50% PSA drops in well over 50% of patients and about 10% to 20% have extraordinary drops where the disease virtually melts away with a couple of treatments with lutetium. It’s generally relatively well tolerated. This is another very ripe area of research.

Q: What you’re talking about is what some say is “calling in the fire department after the house has burned down.” Do you see a future where we take a nuclear tracer and attach a therapeutic molecule of some type at an earlier stage—perhaps biochemical recurrence with nothing showing up beside a small area?

A: I would agree with you. I think there’s a real chance of bringing these in much earlier in the treatment paradigm compared to where we are. In the current trials, we are using lutetium to look at toxicities and make sure it’s safe, and it appears to be very well tolerated. Once we confirm that it’s safe, it would make sense to be using it earlier.

Also, in patients with widespread metastatic disease, we often have to do a PET 18F-fluorodeoxyglucose (FDG) scan with glucose as well as the PET PSMA scan. In fact, we’re finding that some patients will have completely separate sites of disease and the PSMA and the FDG sometimes don’t match, and if this is the case the effectiveness of lutetium theranostics is reduced.

Q: That’s interesting because we’ve always thought that it’s not glucose avid.

A: I think as it dedifferentiates, it actually becomes glucose avid. So when you’re using lutetium PSMA as a therapeutic target, it will track to the PSMA-positive sites, but if there is non-concordant FDG-avid disease those areas will not be well treated. Those patients actually don’t do well with lutetium PSMA because you’re not actively treating all of their disease, but you only see that in very end-stage disease.

Q: Is there anything you’d like to add regarding imaging in prostate cancer?

A: I think it’s an exciting time. Both the advent of MRI and these new PET tracers like PSMA have altered the way we stage and restage prostate cancer. It does create a number of questions that we have to answer, including whether or not it ultimately leads to improved survival. Hopefully further trials will help answer the questions that have arisen.
Avelumab/axitinib combo is first-line treatment for advanced RCC
Merck and Pfizer recently announced FDA approval of avelumab (BAVENCIO) in combination with axitinib (INLYTA) for the first-line treatment of patients with advanced renal cell carcinoma. The companies say this is the first such approval for an anti-PD-L1 therapy as part of a combination regimen for patients with advanced RCC. The approval was based on positive results from the phase III JAVELIN Renal 101 study (NCT02684006), in which the combination significantly improved median progression-free survival compared with sunitinib (Sutent) by more than 5 months in the intent-to-treat patient population (HR: 0.69 [95% CI: 0.56–0.84]; 2-sided p-value=0.002; median progression-free survival for BAVENCIO/INLYTA combination: 13.8 months [95% CI: 11.1–NE]; sunitinib: 8.4 months [95% CI: 6.9–11.1]). The intent-to-treat population included patients regardless of PD-L1 expression and across International Metastatic Renal Cell Carcinoma Database prognostic risk groups.
For more information, visit www.pfizer.com and www.merck.com.

NCCN publishes patient-focused bladder cancer guidelines
The National Comprehensive Cancer Network announced the publication of “NCCN Guidelines for Patients: Bladder Cancer.” Created with funding through the NCCN Foundation, the guidelines have been endorsed by the Bladder Cancer Advocacy Network, the American Bladder Cancer Society, and the Urology Care Foundation. The document is based on the evidence and expert consensus from the NCCN Guidelines. The recommendations are determined by a multidisciplinary panel of bladder cancer experts from across the 28 NCCN member institutions. Treatment options are presented in user-friendly terms in the patient guidelines, complete with glossary, illustrations, suggested questions for the provider, and a space to take notes.
For more information, visit www.nccn.org.

FDA approves bevacizumab biosimilar; mRCC among indications
The FDA has approved bevacizumab-bvzr (ZIRABEV), a biosimilar to bevacizumab (Avastin), for the treatment of five types of cancer, including metastatic renal cell carcinoma. The approval was based on review of a comprehensive data package that demonstrated biosimilarity of bevacizumab-bvzr to the reference product.
For more information, visit www.pfizer.com.

New combination antibacterial indicated for complicated UTIs
The FDA has approved Merck’s imipenem, cilastatin, and relebactam for injection, 1.25 grams (RECARBRIO), a new combination antibacterial. The treatment is indicated in patients 18 years of age and older who have limited or no alternative treatment options for the treatment of complicated urinary tract infections, including pyelonephritis, caused by the following susceptible Gram-negative microorganisms: Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae, and Pseudomonas aeruginosa. Merck said it anticipates making the treatment available later this year.
For more information, go to www.merck.com.

New vaginal ring pessary for pelvic organ prolapse available
The FDA has granted approval for ConTIPI Medical Ltd. to market its new product, ProVate, which is designed to treat pelvic organ prolapse in women. The ProVate Device is a vaginal ring pessary that comes ready for use in small dimensions (compacted mode) within a disposable applicator. The applicator allows for a smooth insertion into the vagina. When the plunger of the applicator is depressed, the device becomes fully deployed, restoring its predefined size (deployed mode), and separates from the applicator, which is then removed from the vagina for disposal. Once deployed within the vagina, as with other ring pessaries, the ProVate support distends lateral vaginal walls aside, mechanically prevents cervical/vault descent, and with its central piece, blocks further descent of the anterior/posterior walls within the hollow of the ring, ConTIPI Medical says. The device is provided in six sizes.
For more information, visit www.contipi.com.

PatientPoint, Us TOO to partner on prostate Ca patient information
PatientPoint and prostate cancer nonprofit Us TOO International have announced a new partnership to bring a custom blend of actionable prostate cancer education, treatment, and support information to urology exam rooms nationwide. The partnership pairs PatientPoint education with information about Us TOO resources via a newly updated PatientPoint prostate cancer brochure designed exclusively for the exam room. The PatientPoint prostate cancer brochure in which Us TOO resources are featured addresses all phases of the prostate cancer journey, including diagnosis, treatment, side effects, coping, and ongoing care.
For more information, go to www.patientpoint.com.

Melanocortin agonist treats hypoactive sexual desire disorder
The FDA has approved bremelanotide injection (Vyleesi), a melanocortin receptor agonist, to treat acquired, generalized hypoactive sexual desire disorder in premenopausal women. The Vyleesi autoinjector is the first treatment for this patient population that can be self-administered as needed in anticipation of sexual activity, according to manufacturer AMAG Pharmaceuticals, Inc. The FDA approval is based on data from approximately 1,200 women in two pivotal, double-blind placebo controlled phase III trials (RECONNECT). In both clinical trials, bremelanotide injection met the pre-specified co-primary efficacy endpoints of improvement in desire and reductions in distress as measured by validated patient-reported outcome instruments. Upon completion of the trial, women had the option to continue in a voluntary open-label safety extension study for an additional 12 months. Nearly 80% of patients who completed the phase III trials elected to remain in the open-label portion of the study.
For more information, visit www.amagpharma.com.
**What are you doing to safeguard patient information?**

The security of patient information is a difficult balance because you’re using 21st-century technology to deliver information to the patient, but it comes at a risk or cost. We start by having a discussion with patients and letting them know about available resources, but that they have to accept some responsibility themselves. They need to use the portals appropriately, not only protecting their login information, but following the steps for two-factor identification. Some patients are very up to date with technology and are comfortable accepting responsibility.

Secondly, in urology we tend to have an office-based practice and a hospital-based practice. We partner with a tertiary-care hospital here and discuss the information, the security, and the encryption we can use to protect both of us from malware or hacking. We also talk about protecting ourselves financially—as the consumer and the provider—from the medical/legal risks by having appropriate insurance from our malpractice insurance carriers to protect ourselves if there is a breach and know what the financial consequence of that is.

I try to look at it from every angle, of everything that could possibly happen if there’s a data breach, if their information gets out. We also have the ability to deal with the generation of patients who aren’t as computer savvy, who rely on a follow-up visit or telephone call to get that information, and that’s completely fine. As for our internal EMR, we have gone to a cloud-based system from a server-based system. When we had a server-based system, patient confidentiality and information breaches were quite new. As we moved to the cloud-based system, we relied more on our EMR vendor to help protect patient information.”

**J. Paul Yurkanin, MD**

**“We start by having a discussion with patients and letting them know about available resources, but that they have to accept some responsibility themselves.”**

**J. Paul Yurkanin, MD**

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Urologist – General and Reconstructive Surgeon

The University at Buffalo, in association with Western New York Urology Associates and the Erie County Medical Center (ECMC), is seeking candidates for a full-time position specializing in reconstructive surgery. Eligible candidates should be board-certified or board-eligible in urology, fellowship-trained in Reconstructive Surgery, and be eligible for a New York medical license. Additional information is available online on the Modern Medicine Career Board.

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The Division of Urology at the University of Vermont Larner College of Medicine in alliance with the University of Vermont Medical Center, is seeking Clinical Practice Physicians who are board eligible/board certified Urologists to join the Urology service at our affiliate community medical center, Champlain Valley Physicians Hospital (CVPH) in Plattsburgh, New York. CVPH is a progressive medical center with nine state-of-the-art OR’s and Ambulatory Surgery Center. This position offers the unique opportunity to work in a community setting while having an active affiliation with Vermont’s only Academic Medical Center; the only ACS verified Level 1 trauma center in the state providing tertiary care to patients from Vermont and Northern NY. Serving the patients from Upstate New York for decades, the local urologic surgery practice recently joined the faculty at the University of Vermont and are now seeking additional colleagues to join the dynamic Urology faculty that span the network hospitals. Specifically, the Division seeks applications from individuals seeking a community Urology employment opportunity with a collegial and collaborative setting with University support. Plattsburgh is located on the shores of Lake Champlain with easy access to the Adirondack Mountains, Olympic-Lake Placid region, Montreal and Burlington, VT.

Applicants must be board certified or board eligible and eligible for medical licensure in the state of New York. This is a full-time, 12 month, salaried position.

Interested individuals should apply online at https://www.uvmjobs.com/postings/31529 (position number 00024781). Inquiries may be directed to Mark Plante, MD, FRCS(C), FACS, Chief of Urology via Kristin Allard at Kristin.Allard@uvmhealth.org

The University is especially interested in candidates who can contribute to the diversity and excellence of the academic community through their research, teaching, and/or service. Applicants are requested to include in their cover letter information about how they will further this goal.

The University of Vermont is an Equal Opportunity/Affirmative Action Employer. All qualified applicants will receive consideration for employment without regard to race, color, religion, sex, sexual orientation, gender identity, national origin, disability, protected veteran status, or any other category legally protected by federal or state law. The University encourages applications from all individuals who will contribute to the diversity and excellence of the institution.
The Department of Surgery at the University of Vermont College of Medicine is seeking a board certified/board eligible Urologist in The Division of Urology. The successful candidate will receive an appointment at the Assistant/Associate Professor level in the clinical scholar pathway and must have completed a board approved urology residency, be eligible for medical licensure in the State of Vermont and eligible to work in the United States. Advanced training in female urology, neuro-urology and reconstructive urology is preferred. Duties will include general urologic patient care opportunities aligned with the teaching of medical students and urology residents.

All applicants must be board certified/board eligible in all aspects of Urology. He or she must be eligible for licensure in the State of Vermont, eligible to work in the United States, and have experience in the administrative, teaching, clinical, and research activities of an academic division. This is a full-time, 12-month, salaried position with attending staff privileges at the University of Vermont Medical Center.

Located in Burlington, the University of Vermont and the University of Vermont Medical Center serve as Vermont’s only academic medical center. It is the only ACS verified Level 1 trauma center in the state and provides tertiary care to patients from Vermont and Northern NY. Burlington is a vibrant community located on the shores of Lake Champlain, between the Adirondack and Green Mountains. With year-round recreational opportunities, safe communities and excellent schools, this progressive community has been frequently cited as one of the most livable cities in the U.S.

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Interested individuals should apply online at https://www.uvmjobs.com/postings/36230 (position number 014007). Inquiries may be directed to Mark Plante, MD, FRCS(C), FACS, Chief of Urology, via Kristin Allard at Kristin.Allard@uvmhealth.org.
Medicare for All has become the battle cry for many of the multitude of candidates for the Democratic presidential nomination as they declare that every American should have easy access to affordable health care and should not have to choose between going to the doctor and putting food on the table.

“Health care should be a right, not a privilege,” they say.

But what about a huge segment of the population that would be dramatically affected by such a massive revamping of our health care system: the nation’s doctors? What do they think about the idea? How about urologists?

Traditionally, organized medicine has opposed any sort of single-payer system. However, in June, the American Medical Association’s House of Delegates nearly voted to overturn that position. When the votes were counted, 47% favored eliminating the AMAs official opposition to single-payer, while 53% voted to maintain it.

Within urology, there is continuing debate about the implications of Medicare for All, recognizing, of course, that while the main focus is on legislation sponsored by Sen. Bernie Sanders (D-VT) and endorsed by Sens. Elizabeth Warren (D-MA) and Kamala Harris (D-CA), among other Democratic presidential candidates, many iterations are likely to take place before they would ever actually be considered by Congress.

Asked for the views of LUGPA, Mara Holton, MD, LUGPA health policy committee vice chair, replied with caution.

“LUGPA, as an organization, has been stalwart in its role as an advocate for the preservation of patient access to high-quality, cost-efficient, and integrated genitourinary care in the independent practice setting,” she said.

While, in general, LUGPA would support any initiative that would improve or expand access to these resources, the organization has not evaluated any proposal in enough detail to determine its effectiveness at achieving that goal or its potential impact on physician practices, she added.

Dr. Holton stressed that “LUGPA remains committed to working with regulatory agencies and policymakers to enhance the quality and access to care for patients impacted by genitourinary disease and will carefully analyze any proposal put forth from that precept.”

MARA HOLTON, MD
LUGPA HEALTH POLICY COMMITTEE VICE CHAIR

“Nobody talks about the cost of that,” he added. “It would be exorbitant.”

Advocates contend that doctors’ administrative overhead and headaches resulting from onerous paperwork and preauthorization requirements, limited formularies, narrow networks, and high-deductible insurance plans of many patients would be reduced or eliminated under Medicare for All, providing incentives for physician support.

Paper: Single-payer would depress income

In a March 15, 2019 commentary published by the conservative think tank The Heritage Foundation, Senior Fellow Robert E. Moffit, PhD, contended that enacting such a plan would worsen the growing physician shortage largely because it would depress physicians’ income.

He pointed out that American general physicians earn an average annual salary of $218,173 compared to $146,286 for their counterparts in Canada, with its government-run health care system. Combining a mammoth pay cut with the abolition of private-sector alternatives would hurt morale and accelerate the shrinkage of the medical work force, Moffit said.

That has been a major concern for urology, as the AUA warns that as practicing urologists continue to age and retire, and with inadequate financial support for graduate medical education, the pipeline of urologists continues to thin.

According to the 2018 AUA Census, the number of urologists per capita has declined by more than 10% over the past 20 years. The median age of a urologist is 56 years, so many are approaching retirement. Complicating that situation is that training for urologists following medical school graduation is a minimum of 5 years and often longer.

Thus, if physician compensation is sharply reduced as a result of implementation of Medicare for All, it stands to reason that the already low number of urologists in the nation would be further reduced.

When contacted for this article, an AUA spokesperson said the organization does not have a position on Medicare for All.
WHO’S TO BLAME FOR MAN’S LOSS OF KIDNEY FUNCTION?

Lawsuit brought against urologist, nephrologist

A 43-year-old male presented to a urologist to whom he had been referred by his primary care physician. The patient had made an ER visit to a New York hospital due to severe flank pain while traveling from Massachusetts to Rochester, NY.

Doctors at that hospital advised the patient of a probable kidney stone. When the patient met with the urologist, the urologist reviewed the results of a computed tomography scan of the patient’s kidneys that had been ordered by the primary care physician. The CT scan reportedly revealed a possible ureteropelvic junction obstruction. The urologist also took a measurement of the patient’s creatine levels and decided to monitor the patient’s condition. Further, the urologist recommended that the patient consult with a nephrologist.

One month later, the patient returned to the urologist’s office for a follow-up appointment. The second evaluation revealed that the patient’s creatine levels had improved but were still at abnormal levels and indicative of a kidney ailment. Thus, the urologist instructed the patient to undergo a vasectomy and also instructed him to schedule a follow-up appointment in 1 year.

The following month, the patient visited a nephrologist, who tested the patient’s creatine levels, the results of which were abnormal. The nephrologist provided the patient a requisition order for another lab test.

Two months later, when the patient did not hear back from the nephrologist with the lab test results, the patient brought the unused lab requisition order to a laboratory, underwent tests, and submitted the results to his nephrologist’s office. After 3 weeks had passed, the nephrologist left a message for the patient and indicated it was urgent that he present to the hospital for further tests.

The patient alleged that the urologist failed to diagnose the obstruction and failed to meet the medical standard of care. The plaintiff’s medical expert, a urologist, opined that the patient’s left kidney demonstrated probable impairment at the time of first and second exam by the defendant urologist.

Both the urologist and nephrologist denied any violations in the standard of care. They argued that the patient, during his second appointment with the urologist, told the urologist that he was going to visit a Massachusetts hospital for further evaluation of his kidney function and never instructed him to forward any medical records to the hospital. Further, the defense maintained that the urologist was not informed of the patient’s care following the second appointment, and that the urologist was absolved of responsibility to monitor the patient’s kidney issues.

Additionally, the defense contended that the patient presented to a non-party internist, who performed the CT scan. The defense asserted that the internist detected the blockage and told the patient to follow up with his urologist. The defense claimed that the patient’s kidney function was intact at the time of the CT scan and that the patient failed to follow up with his urologist. The defense additionally argued that the patient’s kidney function could have been restored had he followed up with his urologist at the time of his CT scan and results.

The defense’s nephrology expert opined that the patient would be compelled to enter dialysis treatment should his right kidney cease to function. The defense expert opined that the plaintiff could live a normal, healthy life with his functioning right kidney.

JURY AWARDS PLAINTIFF $172K

After 6 hours’ deliberation, the jury returned a verdict in the plaintiff’s favor. The jury determined that the defendants were negligent but determined that only the urologist’s negligence was the proximate cause of the plaintiff’s loss of kidney function. The jury awarded the plaintiff $150,000, plus statutory interest of $22,044. Thus, the plaintiff’s total award amounted to $172,044 against defendant urologist. The nephrologist received a defense verdict.

LEGAL PERSPECTIVE: In medical malpractice actions, the rules require that the plaintiff prove that the standard of care was breached and that the breach proximately caused the plaintiff’s injuries. Both must be shown by expert testimony. And, each element must be proven against each defendant.

Here, the jury determined that the plaintiff proved his case against the urologist, but not the nephrologist. The fact that the first and second exams with the urologist revealed a possible ureteropelvic junction obstruction and abnormal creatine levels, coupled with plaintiff’s expert testimony regarding probable impairment at the time of those exams, likely tipped the scales against the urologist and in favor of the patient in this case. [11]
The UroLift System procedure is FDA-cleared for the treatment of symptoms due to urinary outflow obstruction secondary to BPH, including lateral and median lobe hyperplasia, in men 45 years of age or older. Results and patient experience may vary. Most common adverse events reported include hematuria, dysuria, micturition urgency, pelvic pain, and urge incontinence. Most symptoms were mild to moderate in severity and resolved within 2 to 4 weeks after the procedure. Consult the Instructions for Use (IFU) for more information.

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