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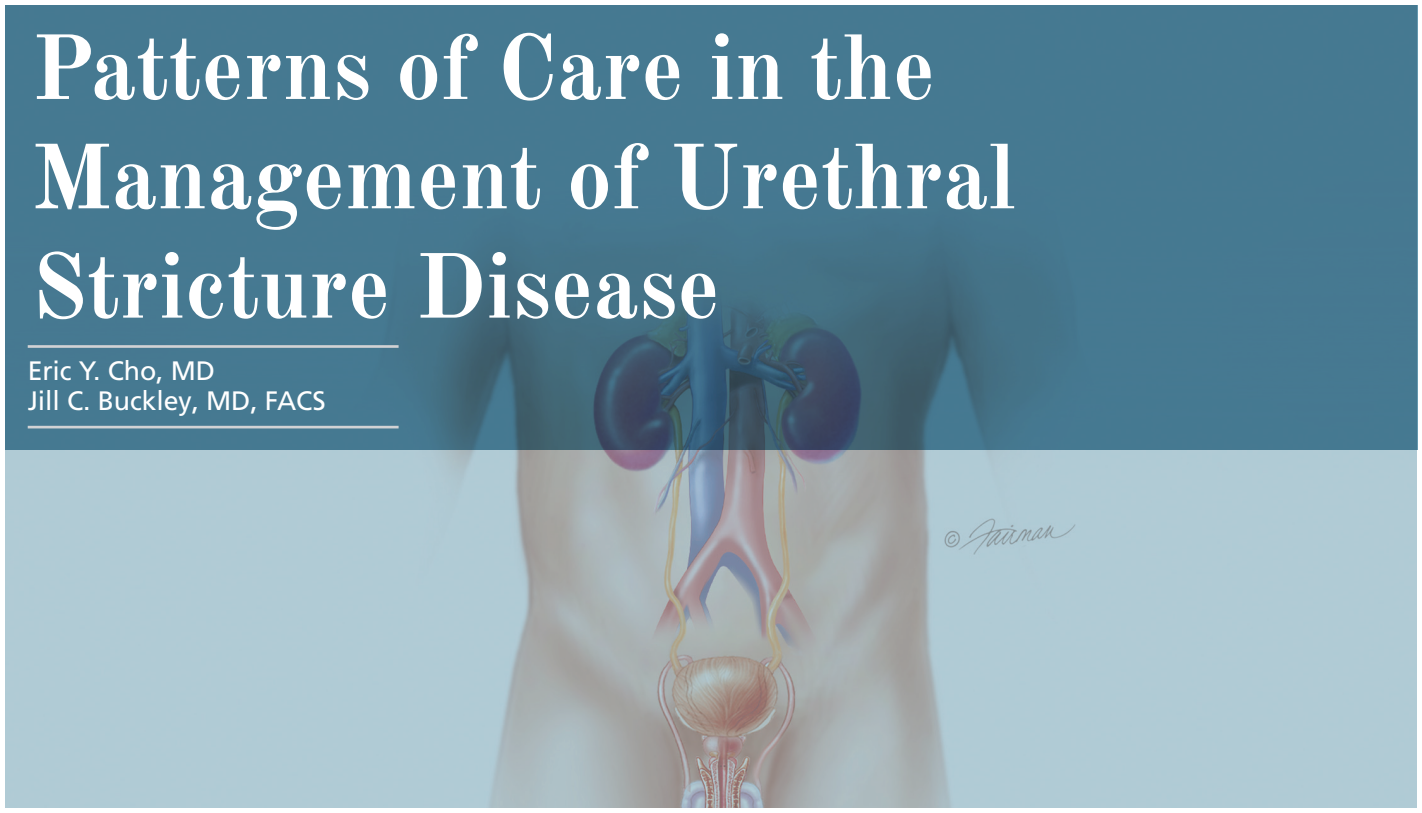
Jill C. Buckley, MD, FACS



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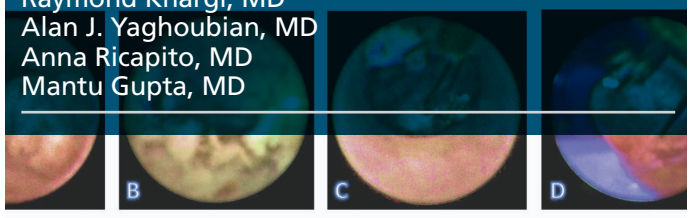

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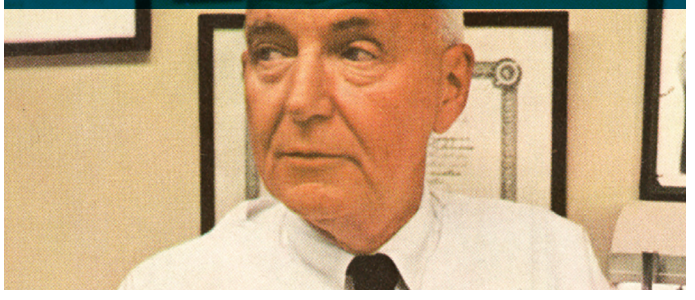

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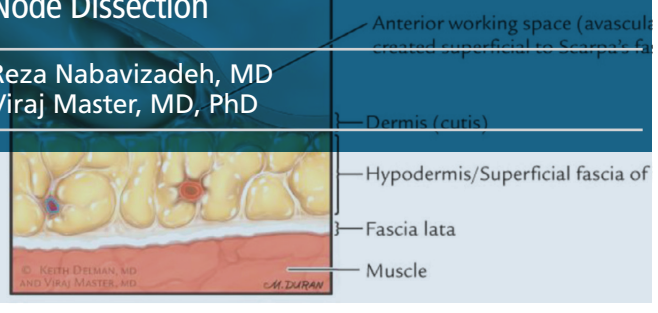

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Monica H. Xing, BA
Max J. Hyman, BA
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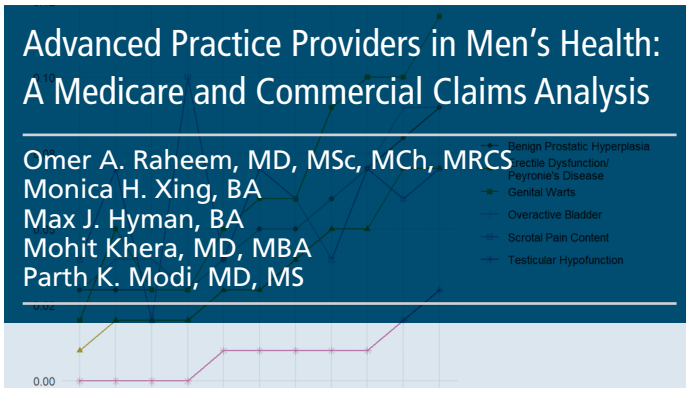

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NEWS FROM THE AUA

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INDICATION

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.5% of patients exposed to LYNPARZA monotherapy, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was 2 years (range: <6 months to >10 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

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

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

Pneumonitis: Occurred in 0.8% of patients exposed to LYNPARZA monotherapy, and some cases were fatal. If patients present with new or worsening respiratory symptoms such as dyspnea, cough, and fever, or a radiological abnormality occurs, interrupt LYNPARZA treatment and initiate prompt investigation. Discontinue LYNPARZA if pneumonitis is confirmed and treat patient appropriately.

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

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

Females

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

Males

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

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

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

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

DRUG INTERACTIONS

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

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

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

USE IN SPECIFIC POPULATIONS

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

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

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

PROfound: A phase 3 trial of LYNPARZA in mCRPC[1,3]

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

Although patients with *PPP2R2A* gene mutations were enrolled in the trial, LYNPARZA is not indicated for the treatment of patients with this gene mutation due to unfavorable risk-benefit ratio.

*HRR gene mutations (*BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D,* and/or *RAD54L*) were identified by tissue-based testing using the Foundation Medicine FoundationOne® clinical trial HRR assay performed at a central laboratory. No patients were enrolled who had mutations in 2 of the 15 prespecified HRR genes: *FANCL* and *RAD51C*.

†Patients with co-mutations (*BRCA1, BRCA2,* or *ATM* plus a Cohort B gene) were assigned to Cohort A.

‡All patients received a GnRH analog or had prior bilateral orchiectomy.

§*BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D,* or *RAD54L*.

‖Upon radiological progression confirmed by BICR, patients randomized to enzalutamide or abiraterone were given the option to switch to LYNPARZA.

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

LYNPARZA more than doubled median rPFS vs investigator's choice of enzalutamide or abiraterone **in Cohort A**

LYNPARZA median rPFS (n=162)

7.4 MONTHS (95% CI: 6.2–9.3)

Investigator's choice of enzalutamide or abiraterone median rPFS (n=83)

3.6 MONTHS (95% CI: 1.9–3.7)

>2x median rPFS

66% relative risk reduction of disease progression or death
HR=0.34, 95% CI: 0.25–0.47, *P*<0.0001

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

SELECT SECONDARY ENDPOINT: OVERALL SURVIVAL (OS)[1,3]

LYNPARZA demonstrated an OS benefit and reduced risk of death by 31% vs investigator's choice of enzalutamide or abiraterone **in Cohort A**

LYNPARZA median OS (n=162)

19.1 MONTHS (95% CI: 17.4–23.4)

Investigator's choice of enzalutamide or abiraterone median OS (n=83)

14.7 MONTHS (95% CI: 11.9–18.8)

31% reduced risk of death
HR=0.69, 95% CI: 0.50–0.97, *P*=0.0175

PROfound was powered to evaluate several secondary endpoints within a hierarchical statistical analysis, including: ORR in Cohort A, rPFS in Cohorts A+B, OS in Cohort A

ADDITIONAL SECONDARY ENDPOINTS[1,3]

- **ORR in Cohort A:** LYNPARZA significantly improved confirmed ORR as assessed by BICR vs investigator's choice of enzalutamide or abiraterone for patients with measurable disease at baseline: 33% (n=28) with LYNPARZA (95% CI: 23–45, *P*<0.0001; n=84) vs 2% (n=1) with investigator's choice of enzalutamide or abiraterone (95% CI: 0–12, *P*<0.0001; n=43)
- **rPFS in Cohorts A+B:** LYNPARZA improved median rPFS as assessed by BICR vs investigator's choice of enzalutamide or abiraterone: 5.8 months median rPFS with LYNPARZA (95% CI: 5.5–7.4; n=256) vs 3.5 months median rPFS with investigator's choice of enzalutamide or abiraterone (95% CI: 2.2–3.7; n=131)

IMPORTANT SAFETY INFORMATION (CONT'D)
USE IN SPECIFIC POPULATIONS (CONT'D)

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

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

Please see Brief Summary of Prescribing Information on the following page.

BICR=blinded independent central review; CI=confidence interval; CRPC=castration-resistant prostate cancer; FDA=US Food and Drug Administration; GnRH=gonadotropin-releasing hormone; HR=hazard ratio; HRR=homologous recombination repair; HRRm=homologous recombination repair gene–mutated; mCRPC=metastatic castration-resistant prostate cancer; ORR=objective response rate; OS=overall survival; PARPi=poly (ADP-ribose) polymerase inhibitor; PCWG3=Prostate Cancer Working Group 3; RECIST=Response Evaluation Criteria in Solid Tumors; rPFS=radiological progression-free survival.

References: 1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022. **2.** Teo MY, Rathkopf DE, Kantoff P. Treatment of advanced prostate cancer. *Annu Rev Med.* 2019;70:479-499. **3.** de Bono J, Mateo J, Fizazi K, et al. Olaparib for metastatic castration resistant prostate cancer. *N Engl J Med*. 2020;382(22):2091-2102.

MERCK AstraZeneca

LYNPARZA® (olaparib) tablets, for oral use

Initial U.S. Approval: 2014

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

INDICATIONS AND USAGE

HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

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

DOSAGE AND ADMINISTRATION

Patient Selection

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

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

Table 1 Biomarker Testing for Patient Selection*

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

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

Recommended Dosage

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

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

HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

Continue treatment until disease progression or unacceptable toxicity for:

- HRR gene-mutated metastatic castration-resistant prostate cancer

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

Dosage Modifications for Adverse Reactions

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

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

Dosage Modifications for Concomitant Use with Strong or Moderate CYP3A Inhibitors

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

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

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

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

Dosage Modifications for Renal Impairment

Moderate Renal Impairment

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

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia

Myelodysplastic syndrome (MDS)/Acute Myeloid Leukemia (AML) has occurred in patients treated with Lynparza and some cases were fatal.

In clinical studies enrolling 2901 patients with various cancers who received Lynparza as a single agent *[see Adverse Reactions (6.1) in the full Prescribing Information]*, the cumulative incidence of MDS/AML was approximately 1.5% (43/2901). Of these, 51% (22/43) had a fatal outcome. The median duration of therapy with Lynparza in patients who developed MDS/AML was 2 years (range: < 6 months to > 10 years). All of these patients had received previous chemotherapy with platinum agents and/or other DNA damaging agents including radiotherapy.

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

Pneumonitis

In clinical studies enrolling 2901 patients with various cancers who received Lynparza as a single agent *[see Adverse Reactions (6.1) in the full Prescribing Information]*, the incidence of pneumonitis, including fatal cases, was 0.8% (24/2901). If patients present with new or worsening respiratory symptoms such as dyspnea, cough and fever, or a radiological abnormality occurs, interrupt Lynparza treatment and promptly assess the source of the symptoms. If pneumonitis is confirmed, discontinue Lynparza treatment and treat the patient appropriately.

Venous Thromboembolic Events

Venous thromboembolic events (VTE), including severe or fatal pulmonary embolism (PE), occurred in patients treated with Lynparza *[see Adverse Reactions (6.1) in the full Prescribing Information]*. VTE occurred in 7% of patients with metastatic castration resistant prostate cancer who received Lynparza plus androgen deprivation therapy (ADT) compared to 3.1% of patients receiving enzalutamide or abiraterone plus ADT in the PROfound study. Patients receiving Lynparza and ADT had a 6% incidence of pulmonary embolism compared to 0.8% of patients treated with ADT plus either enzalutamide or abiraterone. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate, which may include long-term anticoagulation as clinically indicated.

Embryo-Fetal Toxicity

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

ADVERSE REACTIONS

The following adverse reactions are discussed elsewhere in the labeling:

- Myelodysplastic Syndrome/Acute Myeloid Leukemia *[see Warnings and Precautions (5.1) in the full Prescribing Information]*
- Pneumonitis *[see Warnings and Precautions (5.2) in the full Prescribing Information]*
- Venous Thromboembolic Events *[see Warnings and Precautions (5.3) in the full Prescribing Information]*

Clinical Trial Experience

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

The data described in the WARNINGS AND PRECAUTIONS reflect exposure to Lynparza as a single agent in 2901 patients; 2135 patients with exposure to 300 mg twice daily tablet dose including five controlled, randomized, trials (SOLO-1, SOLO-2, OlympiAD, POLO, and PROfound) and to 400 mg twice daily capsule dose in 766 patients in other trials that were pooled to conduct safety analyses. In these trials, 56% of patients were exposed for 6 months or longer and 28% were exposed for greater than one year in the Lynparza group.

In this pooled safety population, the most common adverse reactions in ≥10% of patients were nausea (60%), fatigue (55%), anemia (36%), vomiting (32%), diarrhea (24%), decreased appetite (22%), headache (16%), dysgeusia (15%), cough (15%), neutropenia (14%), dyspnea (14%), dizziness (12%), dyspepsia (12%), leukopenia (11%), and thrombocytopenia (10%).

HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

PROfound

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

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

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

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

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

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

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

* Graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03
† Includes anemia and hemoglobin decreased
‡ Includes platelet count decreased and thrombocytopenia

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

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

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

* Patients were allowed to enter clinical studies with laboratory values of CTCAE Grade 1.
† This number represents the safety population. The derived values in the table are based on the total number of evaluable patients for each laboratory parameter.

Postmarketing Experience

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

Immune System Disorders: Hypersensitivity including angioedema.
Skin and subcutaneous tissue disorders: Erythema nodosum, rash, dermatitis.

DRUG INTERACTIONS

Use with Anticancer Agents

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

Effect of Other Drugs on Lynparza

Strong and Moderate CYP3A Inhibitors

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

Strong and Moderate CYP3A Inducers

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

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

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

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

Data

Animal Data

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

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

Lactation

Risk Summary

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

Females and Males of Reproductive Potential

Pregnancy Testing

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

Contraception

Females

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

Males

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

Pediatric Use

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

Geriatric Use

Of the 2901 patients with advanced solid tumors who received Lynparza as a single agent, 680 (23%) patients were aged ≥65 years, and this included 206 (7%) patients who were aged ≥75 years. Thirteen (0.4%) patients were aged ≥85 years.

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

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

Renal Impairment

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

Hepatic Impairment

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

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Patterns of Care in the Management of Urethral Stricture Disease

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Introduction

Urethral stricture disease (USD) is a narrowing of the lumen of the urethra secondary to spongiofibrosis of the surrounding corpus spongiosum.[1] USD most commonly involves the bulbar urethral segment of the urethra. Etiologies of bulbar urethral strictures vary (traumatic, iatrogenic, idiopathic or inflammatory/infectious) as does management: endoscopic vs surgical repair. We have seen a shift away from the palliative repeat maneuvers of dilation and incision to more definitive reconstructive techniques. Herein, we aim to outline the current patterns of management in USD of the bulbar urethra (see Figure).

Dilation, Direct Vision Internal Urethrotomy vs Urethroplasty

Procedures such as dilations and direct vision internal urethrotomy (DVIU) have been shown to have similar efficacy for primary short bulbar USD.[2,3] The EAU (European Association of Urology) and AUA guidelines include dilation or DVIU for the initial management of short (<2 cm or grade L1S1a), singular bulbar strictures or in the emergent setting of acute urinary retention from USD.[4] Although less efficacious than the gold standard urethroplasty, dilation or incisions are included as a primary treatment option.[5,6]

In consideration of a recurrent bulbar urethral stricture, a randomized controlled trial of urethroplasty vs endoscopic urethrotomy for recurrent stricture disease was performed (known as the OPEN trial). This was the first high-level evidence that favored urethroplasty over endoscopic management with a 48% lower risk of re-intervention (at 4 years follow-up time) when patients underwent urethroplasty.[7]

"Procedures such as dilations and direct vision internal urethrotomy (DVIU) have been shown to have similar efficacy for primary short bulbar USD."

From a cost-effectiveness standpoint, urethroplasty has furthermore been demonstrated to be safe for outpatient surgery with 70.4% of reconstructive urologists doing so according to a 2019 survey conducted by Hoare et al.[8]

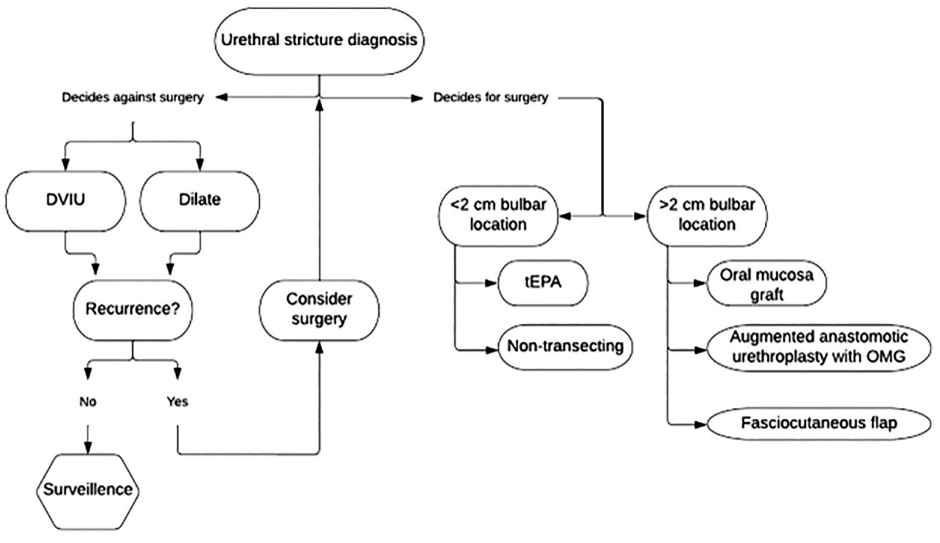

Figure. Decision tree for management of urethral stricture disease. DVIU indicates direct vision internal urethrotomy; OMG, oral mucosa graft; tEPA, transecting excision and primary anastomosis.

Urethroplasty: Short Bulbar

For short bulbar urethral strictures (<2 cm), anastomotic urethroplasty has been the most commonly employed technique for repair with oral mucosa graft (OMG) reserved for longer strictures. This has traditionally been done in a transecting excision and primary anastomosis, which has been reported to have a success rate of up to 94%-96%.[9] Recently, there has been debate regarding whether transection of the urethral blood supply would decrease sexual side effects (ie, erectile function, glans sensitivity, penile length, and ejaculatory dysfunction) following urethroplasty. In response to this, a non-transecting anastomotic urethroplasty technique for short bulbar urethral strictures was first introduced by Andrich and Mundy in 2011 with such blood preservation in mind.[10] Although there have been no randomized controlled trials to definitively conclude that vessel-sparing OMG is beneficial for patients, many studies have supported its benefits.[11-13] A randomized clinical trial comparing transecting excision and primary anastomosis vs the vessel-sparing technique is currently underway, known as the VeSpAr trial, to answer this very question.[14]

Urethroplasty: Long Bulbar

The standard of care for long bulbar urethral strictures (>2 cm) is a urethroplasty with an OMG. Although fasciocutaneous flaps have been described as substitution tissue coverage for longer stricture segments, these are not commonly used in isolated bulbar urethral structures. When strictures are both long and obliterated, an augmented anastomotic urethroplasty with OMG has been described, which is a transection technique combined with grafting. Although this technique is used when necessary, it was found to be associated with higher stricture recurrence (HR 4.8) over a 78.9-month follow-up period based on a 2020 review by Redmond et al.[15]

With OMG urethroplasty being the standard protocol, there has been controversy regarding optimal graft placement: dorsal vs ventral.[16,17] Both are reported to be highly successful. In an attempt to answer this question, a randomized controlled trial of dorsal vs ventral onlay OMG urethroplasty is currently underway (the "DoVe trial").[18] When oral mucosa is not available, the use of rectal mucosa has shown some promising results as an alternative graft.[19] As our field continues to advance, we will look to tissue engineering and improved matrix for future reconstructive use.

Future Trends

Trends in management of USD are favoring more minimally invasive techniques. Investigational animal studies utilizing liquid mucosa grafts following DVIU are showing some promise, as well as endoscopic suturing techniques.[20,21]

"When strictures are both long and obliterated, an augmented anastomotic urethroplasty with OMG has been described, which is a transection technique combined with grafting."

Furthermore, in December 2021, the Food and Drug Administration approved a paclitaxel-coated balloon for anterior urethral strictures based on a randomized controlled trial comparing the drug-coated balloon vs conventional dilation

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AUA TAKE 5

THE TOP 5 AUA HAPPENINGS THIS MONTH!

1. The new *AUANews* site is live! Read the best clinical, business, and personal content written for urologists, by urologists, in one easy-to-access spot!

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2. Don't miss the most groundbreaking science and education in urology at the 2023 AUA Annual Meeting in Chicago, from April 28 to May 1! Explore the Scientific Program and register today!

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3. The AUA is now accepting application for the 2023 Holtgrewe Legislative Fellowship. This program provides a unique opportunity for a young urologist to engage on policy issues and legislation that affect the practice of urology. Learn more and apply!

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PATTERNS OF CARE IN THE MANAGEMENT OF URETHRAL STRICTURE DISEASE

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for anterior urethral strictures ≤3 cm in length.[22] Six months following intervention, those treated with the drug-coated balloon had an anatomical success rate of 75% vs the control arm at 27%. This intervention appears to remain robust through a 3-year follow-up period from a prior interventional nonrandomized study.[23] There is still much to be learned regarding the changes in cellular makeup of urethral scar tissue and how we can attempt to affect the pathogenesis of scar formation/recurrence. ■

1. Latini JM, McAninch JW, Brandes SB, Chung JY, Rosenstein D. SIU/ICUD Consultation On Urethral Strictures: epidemiology, etiology, anatomy, and nomenclature of urethral stenoses, strictures, and pelvic fracture urethral disruption injuries. *Urology*. 2014;83(3 Suppl):S1-S7.
2. Lumen N, Campos-Juanatey F, Greenwell T, et al. European Association of Urology guidelines on urethral stricture disease (part 1): management of male urethral stricture disease. *Eur Urol*. 2021;80(2):190-200.
3. Buckley JC, Heyns C, Gilling P, Carney J. SIU/ICUD Consultation on Urethral Strictures: dilation, internal urethrotomy, and stenting of male anterior urethral strictures. *Urology*. 2014;83(3 Suppl):S18-22.
4. Erickson BA, Flynn KJ, Hahn AE, et al. Development and validation of a male anterior urethral stricture classification system. *Urology*. 2020;143:241-247.
5. Wessells H, Angermeier KW, Elliott S, et al. Male urethral stricture: American Urological Association guideline. *J Urol*. 2017;197(1):182-190.
6. Campos-Juanatey F, Osman NI, Greenwell T, et al. European Association of Urology guidelines on urethral stricture disease (part 2): diagnosis, perioperative management, and follow-up in males. *Eur Urol*. 2021;80(2):201-212.
7. Goulao B, Carnell S, Shen J, et al. Surgical treatment for recurrent bulbar urethral stricture: a randomised open-label superiority trial of open urethroplasty versus endoscopic urethrotomy (the OPEN trial). *Eur Urol*. 2020;78(4):572-580.
8. Hoare DT, Doiron RC, Rourke KF. Determining perioperative practice patterns in urethroplasty: a survey of genitourinary reconstructive surgeons. *Urology*. 2021;156:263-270.
9. Morey AF, Watkin N, Shenfeld O, Eltahawy E, Giudice C. SIU/ICUD Consultation on Urethral Strictures: anterior urethra–primary anastomosis. *Urology*. 2014;83(3 Suppl):S23-S26.
10. Andrich DE, Mundy AR. Non-transecting anastomotic bulbar urethroplasty: a preliminary report. *BJU Int*. 2012;109(7):1090-1094.
11. Virasoro R, DeLong JM. Non-transecting bulbar urethroplasty is favored over transecting techniques. *World J Urol*. 2020;38(12):3013-3018.
12. Anderson KM, Blakely SA, O'Donnell CI, Nikolavsky D, Flynn BJ. Primary non-transecting bulbar urethroplasty long-term success rates are similar to transecting urethroplasty. *Int Urol Nephrol*. 2017;49(1):83-88.
13. Chapman DW, Cotter K, Johnsen NV, et al. Nontransecting techniques reduce sexual dysfunction after anastomotic bulbar urethroplasty: results of a multi-institutional comparative analysis. *J Urol*. 2019;201(2):364-370.
14. Verla W, Waterloos M, Waterschoot M, Van Parys B, Spinoit AF, Lumen N. VeSpAR trial: a randomized controlled trial comparing vessel-sparing anastomotic repair and transecting anastomotic repair in isolated short bulbar urethral strictures. *Trials*. 2020;21(1):782.
15. Redmond EJ, Hoare DT, Rourke KF. Augmented anastomotic urethroplasty is independently associated with failure after reconstruction for long bulbar urethral strictures. *J Urol*. 2020;204(5):989-995.
16. Hosseini J, Kaviani A, Hosseini M, Mazloomfard MM, Razi A. Dorsal versus ventral oral mucosal graft urethroplasty. *Urol J*. 2011;8(1):48-53.
17. Wang K, Miao X, Wang L, Li H. Dorsal onlay versus ventral onlay urethroplasty for anterior urethral stricture: a meta-analysis. *Urol Int*. 2009;83(3):342-348.
18. ClinicalTrials.gov. *Dorsal Onlay Versus Ventral Onlay in Isolated Bulbar Urethral Strictures (DoVe). ClinicalTrials.gov Identifier: NCT04551417*. Updated January 24, 2022; Accessed December 15, 2022. https://clinicaltrials.gov/ct2/show/NCT04551417.
19. Palmer DA, Marcello PW, Zinman LN, Vanni AJ. Urethral reconstruction with rectal mucosa graft onlay: a novel, minimally invasive technique. *J Urol*. 2016;196(3):782-786.
20. Scott KA, Li G, Manwaring J, et al. Liquid buccal mucosa graft endoscopic urethroplasty: a validation animal study. *World J Urol*. 2020;38(9):2139-2145.
21. Abramowitz DJ, Balzano FL, Ruel NH, Chan KG, Warner JN. Transurethral incision with transverse mucosal realignment for the management of bladder neck contracture and vesicourethral anastomotic stenosis. *Urology*. 2021;152:102-108.
22. Elliott SP, Coutinho K, Robertson KJ, et al. One-year results for the ROBUST III randomised controlled trial evaluating the Optilume® drug-coated balloon for anterior urethral strictures. *J Urol*. 2022;207(4):866-875.
23. Virasoro R, DeLong JM, Estrella RE, et al. A drug-coated balloon treatment for urethral stricture disease: three-year results from the ROBUST I study. *Res Rep Urol*. 2022;14:177-183.

Endoscopic Management of Upper Tract Urothelial Carcinoma: New Lasers and Techniques

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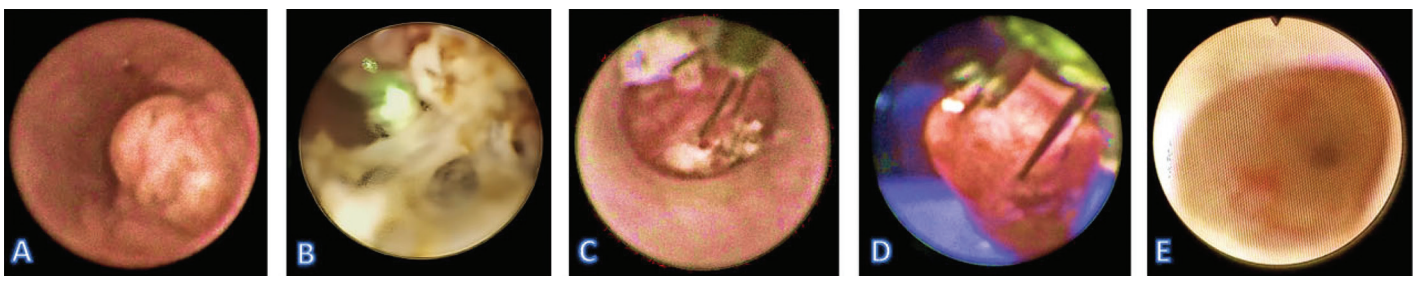

Figure. A, Papillary tumor. B, En bloc laser enucleation with thulium fiber laser. C and D, En bloc specimen retrieved with tipless nitinol basket. E, 3-month surveillance ureteroscopy showing no recurrence or residual disease.

Upper tract urothelial carcinoma (UTUC) is a heterogeneous group of malignancies that accounts for 5%-10% of all urothelial carcinomas. Approximately 30% of UTUCs are diagnosed as low grade upon clinical presentation.[1,2] In past years, due to the anatomical intricacy of the upper tracts and the potential of recurrence and progression, low-grade UTUCs were frequently treated in the same manner as high-grade UTUCs, for which radical nephroureterectomy and bladder cuff excision is the current gold standard. However, recent advances in ureteroscopic and laser technologies have made endoscopic kidney-sparing surgery a viable treatment option for low-risk UTUC. According to the European Association of Urology guidelines, favorable clinical and pathological criteria for endoscopic management of UTUC are as follows: low-grade histology based on cytology and biopsy; papillary architecture; tumor size less than 2 cm; unifocality; and cross-sectional imaging demonstrating no invasive disease.[1] In addition, it may be carefully considered for a subset of high-risk patients with severe renal insufficiency or a solitary kidney.

Current endoscopic therapy options for UTUC consist of a retrograde procedure involving ureteroscopy, tumor biopsy, and ablation, and an antegrade percutaneous method involving excision and fulguration. Antegrade techniques have been reserved for large, bulky tumors and otherwise difficult-to-reach parts of the collecting system in which ureteroscopy has failed. As such, retrograde ablation is the most popular method employed by the urological community and can be dated back to the era of small electrocautery probes placed through ureteroscopes. Electrocautery had the drawbacks of being unable to ablate larger tumors due to the inability to remove treated tissue, causing charring requiring frequent cleaning of the probe and lack of precise control with resultant thermal effects on surrounding healthy tissue. Lasers provided a tremendous advance in terms of precision, but early lasers such as the neodymium:yttrium-aluminum-garnet (Nd:YAG), with its 1,064 nm continuous wavelength, while providing excellent hemostasis and ablation, lacked the ability to remove ablated tissue, preventing visualization of deeper

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ENDOSCOPIC MANAGEMENT OF UPPER TRACT UROTHELIAL CARCINOMA

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layers of tumor and preventing the treatment of larger tumors. Newer laser technologies are available, but unfortunately, surgeons have been left to their own devices when deciding which laser technology is best for UTUC management, as there is currently no clear guidance on the subject.

"Newer laser technologies are available, but unfortunately, surgeons have been left to their own devices when deciding which laser technology is best for UTUC management, as there is currently no clear guidance on the subject."

Holmium:YAG (Ho:YAG) lasers became the default laser for the endoscopic treatment of upper tract tumors for the last 3 decades due to their widespread availability and dependability in the field of stone management, as opposed to their specific efficacy in tumor ablation. The ability to deliver energy through smaller fiber sizes compared to electrocautery electrodes allows better irrigation flow and visualization, whether using flexible or semirigid ureteroscopes. It is a solid-state laser with a wavelength of 2,100 nm and a 0.5 mm penetration depth. It operates in a pulsatile mode and is better absorbed by water, which is the main constituent of body tissues.[3] Unlike the Nd:YAG laser, it can "vaporize" tissue via a photothermal effect, not just ablate it, allowing treatment of deeper layers of tumor and, therefore, larger tumors. Due to its fundamental nature, in which energy is transmitted in pulses, the laser tip must be in contact or near contact with the tissue for effective ablation. Treatment can be hampered by undesired tissue adherence to the laser fiber, which ultimately reduces efficiency. In addition, hemostasis is not as good as with the Nd:YAG laser. In order to overcome some of these negatives, a combination of Ho:YAG and Nd:YAG laser was developed in the early 2000s, with both laser energies housed in 1 machine with a dual foot pedal and a single silica fiber capable of transmitting both energies, allowing for switching from one source of energy to the other for ablation and hemostasis, respectively.

Recent developments in holmium laser technology include high-powered lasers capable of 150 watts of energy and pulse modulation. High-powered holmium lasers permit pulse energies as high as 5 J and frequencies as high as 120 Hz. The potential benefit is a smoother ablation, but in reality, high frequencies are not critical for effective tissue ablation. Pulse modulation can also be used to selectively modify tumor treatment. In the authors' experience, a short pulse mode can permit faster ablation of large volumes of relatively avascular tumors, with the downside of more bubble production and more bleeding. Switching to long pulse mode, however, in which the same energy per pulse is delivered over a longer duration, can be used for "spot coagulation" of specific bleeding vessels and can also aid in the treatment of more vascular tumors, albeit at the expense of decreased vaporization and more charring of tissue. More advanced pulse modulation techniques, in particular, "double bubble" technology, in which an initial pulse generates a vapor bubble and a second pulse is delivered through the vapor bubble, allow for more effective energy delivery to the targeted tissue with less retropulsion, which is very useful for treating kidney stones. In the authors' experience, it also has a salutary effect on the treatment of tumors, allowing for faster tissue ablation while promoting better hemostasis compared to single pulse technology. Some examples of double bubble technology include the Moses from Lumenis Inc and the Virtual Basket from Quanta Inc. Despite all their benefits, high-power holmium lasers have some drawbacks, such as noise production, size, higher voltage requirements, and the need for large, water-based fans for cooling.

Thulium-based laser systems have gained prominence as a promising option for safer and more efficient tumor ablation. Proietti et al demonstrated in their ex vivo porcine model that, when compared to Ho:YAG, thulium:YAG (Tm:YAG) lasers, with their 2,010 nm of continuous wave energy delivery, create a shallower (0.2–0.4 mm) and smoother incision, with a larger coagulative area.[4] These characteristics make it an ideal alternative for soft tissue ablation, especially in the context of limited anatomical space. However, one drawback observed in the literature is the relative degree of tissue carbonization and the generated layer of coagulative necrosis at the tumor base that may prevent complete tumor ablation and could potentially lead to increased cicatricial effects such as strictures.[5] One recent advance in Tm:YAG laser technology is the ability to switch from continuous mode to pulsed mode, with the former being better for hemostasis and ablation and the latter for tissue separation and incision. In the pulsed mode, there is high peak power, allowing for tissue separation or "blast" effect, but with less heat generation due to the energy profile of Tm:YAG crystals compared to the heat generated by a thulium fiber laser (TFL). Examples of this type of laser are the Thulio laser from Dornier Inc and the Revolix laser from Lisa Lasers Inc.

"High-powered holmium lasers permit pulse energies as high as 5 J and frequencies as high as 120 Hz. The potential benefit is a smoother ablation, but in reality, high frequencies are not critical for effective tissue ablation."

In contradistinction to Tm:YAG, the new superpulsed TFLs have a pulsed diode energy source delivered through silica fibers doped with thulium ions, producing a laser beam with a wavelength of 1,940 nm. This wavelength is almost precisely at the peak absorption coefficient of water, allowing for enhanced tissue effects. Despite being in its infancy, based on initial experience, TFL demonstrates the positive characteristics of both Ho:YAG and Tm:YAG laser devices, namely effective and efficient tumor ablation, preserved hemostatic potential, limited tissue carbonization, and limited depth of penetration. Although the literature is currently limited, one recent retrospective study showed that TFL is a safe and effective laser technology for treating upper tract tumors in the short-term follow-up period without any significant complications.[6] Other advantages of TFL systems are their smaller profile, lower voltage requirements, quiet performance, and smaller, lighter, air-based cooling fans. In our experience, the smaller 150 µm laser fibers of TFL systems allow for better irrigation and increased flexibility, permitting access to lower pole tumors without sacrificing ablation ability (possibly due to the better coherence of TFL laser beams compared to holmium). The TFL lasers also have a wider range of pulse energy and frequency, but in practical terms this does not provide a benefit for the purposes of tumor ablation. Two major advantages, however, are better hemostasis and tissue separation effects. This has permitted our center to perform en bloc enucleation of ureteral and renal pelvis tumors, similar to what is becoming popular for bladder tumors (see Figure). Although this is also possible with holmium laser systems, the hemostasis and, therefore, visualization is not as good.

Despite the advancements in laser technology and ureteroscopic equipment, there remains no substitute for surgeon expertise and meticulous technique. In our practice,

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a no-touch method is employed in which a flexible ureteroscope is advanced under direct visualization in a retrograde fashion without any guidewires or access sheaths into the ureteral orifice. The flexible scope is advanced slowly and meticulously up the ureter with minimal irrigation. This is particularly important when trying to lateralize hematuria. The culprit could be a very tiny carcinoma in situ lesion that would otherwise become obscured and impossible to find if a guidewire were placed prior to advancing the scope. Adjuvant visualization technologies such as Clara and Chroma (Storz Medical Inc) or Narrow Band Imaging (Olympus Medical Inc) can be invaluable for discovering these subtle lesions. A thorough mapping of the entire collecting system is performed. This is done even if a lesion in the ureter is discovered because missing a lesion in the kidney could affect management, especially when kidney-sparing treatment is being contemplated (whether local resection, segmental ureterectomy, or distal ureterectomy with reimplant). In addition, multifocality is a negative prognostic indicator, especially in endoscopic management. Finally, a saline barbotage for cytology in the vicinity of the lesion can be critical to finding high-grade disease, especially when biopsies come back nondiagnostic. Grading is paramount; therefore, every attempt should be made to obtain adequate biopsy samples. In this respect, the authors favor the use of the Piranha 3F biopsy forceps (Boston Scientific Inc) for flat lesions, nitinol or stainless-steel baskets for sessile lesions, forward opening graspers such as the Dakota (Boston Scientific Inc) or the N-Gage (Cook Medical Inc) for papillary lesions, and the BIGopsy backloaded trans-access sheath device (Cook Urological Inc) for nontangential intrarenal lesions. However, these ancillary devices tend to deform the urothelial architecture and cause unintended bleeding, leading to poor visibility and inadequate diagnostic assessment despite best efforts. If feasible, en bloc laser enucleation is the preferred approach when an endoscopic cure is being attempted. The primary benefits include a sufficient and representative pathological specimen, a reduction in tissue artifacts, and superior hemostasis.

Regarding laser choice, the authors favor the TFL for en bloc enucleation for most lesions, although we have used all 3 technologies for enucleation. In the authors' experience, the Tm:YAG laser is a hybrid in terms of effect when compared to TFLs and Ho:YAG lasers, with better vaporization and less charring than TFL but less vaporization and more charring than Ho:YAG. These laser technologies are perfectly acceptable and reasonable for endoscopic management. Ultimately, the choice of laser boils down to availability, surgeon experience, and preference. ■

1. Rouprêt M, Babjuk M, Burger M, et al. European Association of Urology guidelines on upper urinary tract urothelial carcinoma: 2020 update. *Eur Urol.* 2021;79(1):62-79.
2. Browne BM, Stensland KD, Moynihan MJ, Canes D. An analysis of staging and treatment trends for upper tract urothelial carcinoma in the National Cancer Database. *Clin Genitourin Cancer.* 2018;16(4):e743-e750.
3. Petros FG, Li R, Matin SF. Endoscopic approaches to upper tract urothelial carcinoma. *Urol Clin North Am.* 2018;45(2):267-286.
4. Proietti S, Rodríguez-Socarrás ME, Eisner BH, et al. Thulium:AG versus holmium:YAG laser effect on upper urinary tract soft tissue: evidence from an ex vivo experimental study. *J Endourol.* 2021;35(4):544-551.
5. Defidio L, Antonucci M, De Dominicis M, Fuchs G, Patel A. Thulium-holmium:YAG duo laser in conservative upper tract urothelial cancer treatment: 13 years experience from a tertiary national referral center. *J Endourol.* 2019;33(11):902-908.
6. Proietti S, Johnston T, Pupulin M, et al. Effectiveness and safety of thulium fiber laser in the conservative management of patients with upper tract urothelial carcinoma. *Eur Urol Open Sci.* 2022;46:99-104.

Advancements in Androgen Deprivation Therapy

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Androgen deprivation therapy (ADT) has served as the backbone of treatment for advanced prostate cancer (APC) since Charles Huggins' discovery of its inhibitory effect on prostate cancer in 1941. With recent FDA (Food and Drug Administration) approvals of novel hormonal therapies (NHTs) for androgen blockade and newly published data supporting combination therapies, treating APC is now more complex. In this rapidly evolving landscape, urologists must stay apprised of advances in ADT to appropriately manage APC patients.

Advancements in ADT for APC have been made across the disease spectrum. Multiple randomized trials have demonstrated superior efficacy of combination ADT compared with monotherapy in different disease states, and the field continues to move toward treatment intensification (see Table). In patients with biochemical recurrence, the recent 2020 AUA/American Society for Radiation Oncology/Society of Urologic Oncology APC guidelines recommend against routine initiation of ADT. In metastatic hormone-sensitive prostate cancer (mHSPC), recently published data from the PEACE-1[1] and ARASENS[2] have paved the way for triplet therapy in select patients. Among patients with nonmetastatic castration-resistant prostate cancer and metastatic castration resistant

Table. Summary of Key Randomized Trials Involving Androgen Deprivation Therapy Published Since 2020

Trial Name (Year)	Population	Intervention	Key findings
PEACE-1[1] (2022)	1,173 patients with de novo mHSPC	2×2 factorial randomization to SOC (ADT±docetaxel), SOC+radiotherapy, or SOC+abiraterone. 177 assigned ADT+abiraterone+docetaxel and 115 assigned ADT+abiraterone without docetaxel	Triplet therapy (ADT+abiraterone+docetaxel) → 2.5 y rPFS benefit (HR 0.54, 95% CI 0.46-0.64, *P* < .0001) and improved OS (HR 0.75, 95% CI 0.59-0.95, *P* = .017) Mild increase in toxicity, mainly increased hypertension (22% ADT+docetaxel+Abi vs 13% ADT+docetaxel)
ARASENS[2] (2022)	1,306 patients with mHSPC	All patients received ADT+docetaxel 1:1 randomization to receive darolutamide (n = 651) or placebo (n = 655)	Triplet therapy (ADT+darolutamide+docetaxel) → 32.5% decreased mortality (HR 0.68; 95% CI 0.57-0.80; *P* < .001) with similar adverse events vs placebo
HERO[3] (2020)	934 patients with APC (BCR, mHSPC, or locally advanced disease)	2:1 randomization to receive novel oral GnRH antagonist relugolix or leuprolide for 48 wk	– Relugolix superior to leuprolide for maintenance of castrate T through 48 wk (96.7% vs 88.8%, *P* < .001) – 56% had castrate T by d 4 – 54% had testosterone recovery to normal levels by 90 d vs 3% in leuprolide group (*P* = .002) – Lower risk of major adverse cardiovascular events in relugolix group vs leuprolide (HR 0.46; 95% CI, 0.24-0.88)

Abbreviations: Abi, abiraterone; ADT, androgen deprivation therapy; APC, advanced prostate cancer; BCR, biochemical recurrence; CI, confidence interval; GnRH, gonadotropin releasing hormone; HR, hazard ratio; mHSPC, metastatic hormone-sensitive prostate cancer; SOC, standard of care; T, testosterone.

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ADVANCEMENTS IN ANDROGEN DEPRIVATION THERAPY

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prostate cancer, use of combination NHT and gonadotropin releasing hormone (GnRH) agonist/antagonists remains critical, but novel treatment options such as PARP (poly [ADP-ribose] polymerase) inhibitors and radioligand-based therapies along with the shift toward use of NHT in earlier disease states leaves numerous unanswered questions about which agents to use and when.

PEACE-1 was an international multicenter, phase 3 trial of 1,173 men with de novo mHSPC who were randomized to standard of care (SOC) with ADT alone or with docetaxel, SOC plus radiotherapy, SOC plus abiraterone, or SOC plus radiotherapy plus abiraterone. Patients receiving triplet therapy (ADT+abiraterone+docetaxel) had a 2.5-year radiographic progression-free survival benefit (HR 0.54, 95% CI 0.46-0.64, $P < .0001$) and improved overall survival (HR 0.75, 95% CI 0.59-0.95, $P = .017$) compared to ADT+docetaxel alone.

Similarly, ARASENS was an international multicenter, phase 3 trial of 1,306 men with mHSPC treated with ADT and docetaxel who were randomized to receive darolutamide or placebo. Compared to placebo, those who received darolutamide had 32.5% lower risk of death (HR 0.68; 95% CI 0.57-0.80; $P < .001$). Darolutamide was also associated with longer time to castration-resistant prostate cancer, longer time to progression, longer symptomatic skeletal event–free survival, and longer time to initiation of subsequent therapy (all $P \leq .01$) with a similar adverse event profile to the placebo group.

PEACE-1 and ARASENS both provide strong evidence for treatment intensification in select men with mHSPC. The new AUA APC guidelines and these recent trials have virtually eliminated the routine role for ADT monotherapy. Which agents, and in what combination and sequence, provide optimal outcomes remains unknown at present but we anticipate more answers as additional data are published.

While most urologists are familiar with injectable GnRH agonists (eg, leuprolide) and antagonists (eg, degarelix), the introduction of relugolix, the first oral GnRH antagonist, provides a new treatment option. Relugolix was FDA approved for use in APC in December 2020 based on the results of the HERO trial,[3] a phase 3 randomized, controlled trial that compared relugolix and leuprolide in APC patients. Relugolix was superior to leuprolide in several key endpoints including sustained testosterone (T) suppression through 48 weeks (96.7% relugolix vs 88.8% leuprolide, $P < .001$), probability of castrate T on day 4 (56% relugolix vs 0% leuprolide, $P < .001$), and >50% reduction in PSA at day 15 (79.4% relugolix vs 19.8% leuprolide, $P < .001$). Notably, although cardiovascular events were low overall, the incidence of major adverse cardiovascular events (MACE) was significantly lower in the relugolix group compared to leuprolide (2.9% vs 6.2%, HR 0.46, 95% CI 0.24-0.88).

> "The potential benefits of an oral GnRH antagonist include improved patient acceptance due to avoidance of injection site reactions (40% incidence with degarelix), patient preference for oral formulations, and flexible administration schedule facilitating intermittent ADT due to its once-daily administration and rapid T suppression and recovery."

The potential benefits of an oral GnRH antagonist include improved patient acceptance due to avoidance of injection site reactions (40% incidence with degarelix[4]), patient preference for oral formulations, and flexible administration schedule facilitating intermittent ADT due to its once-daily administration and rapid T suppression and recovery. While adherence to relugolix in the HERO study was excellent (99%), whether this level of adherence can be maintained in a real-world setting is unknown. Cost remains a significant concern with annual out-of-pocket costs for U.S. Medicare beneficiaries estimated to be $3,731 for relugolix and $745 for leuprolide.[5] Despite these concerns, relugolix represents an exciting new option for some patients with APC.

Aside from the introduction of novel agents and expanding indications for existing ADT, there has been significant recent progress in the recognition and study of the adverse effects of ADT including changes in cardiovascular, bone, endocrine MACE, and cognitive health. While a link between ADT and risk of MACE has been drawn for decades, how significant this risk is, which agents have the lowest risk, and how to manage this risk remains controversial.[6] Observational data have shown that ADT is associated with increased risk for MACE[7] and randomized trial data pooled post hoc have suggested lower risk of MACE for GnRH antagonists compared to agonists.[8]

The PRONOUNCE trial was a recently active international multicenter randomized trial designed to evaluate the relative cardiovascular safety of GnRH antagonists compared with agonists.[9] Although the study was terminated prematurely due to poor recruitment and low event rate, no difference was observed in MACE at 1 year between degarelix and leuprolide (5.5% degarelix vs 4.1% leuprolide; HR 1.28, 95% CI 0.59-2.79). Given a lack of power and early termination of the study, the differential impact of GnRH agonists and antagonists on cardiovascular risk remains unknown. While some aspects of the cardiovascular impact of ADT remain controversial, there is broad consensus that rigorous cardiovascular risk factor control is imperative and a collaborative multidisciplinary approach is critical for patients on long-term ADT to mitigate risk.

APC remains a rapidly changing field with multiple recent advancements. Urologists should be aware of new agents available for ADT and the varying potential clinical scenarios for their use. It is increasingly important for urologists to work in collaboration with a multidisciplinary team including primary care physicians, cardiologists, medical oncologists, and radiation oncologists for optimal management of patients with APC. ■

1. Fizazi K, Foulon S, Carles J, et al. Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design. *Lancet*. 2022;399(10336):1695-1707.
2. Smith MR, Hussain M, Saad F, et al. Darolutamide and survival in metastatic, hormone-sensitive prostate cancer. *N Engl J Med*. 2022;386(12):1132-1142.
3. Shore ND, Saad F, Cookson MS, et al. Oral relugolix for androgen-deprivation therapy in advanced prostate cancer. *N Engl J Med*. 2020;382(23):2187-2196.
4. Klotz L, Boccon-Gibod L, Shore ND, et al. The efficacy and safety of degarelix: a 12-month, comparative, randomized, open-label, parallel-group phase III study in patients with prostate cancer. *BJU Int*. 2008;102(11):1531-1538.
5. Borrelli E, McGladrigan CG. PCN80 Estimating the difference in annual out-of-pocket costs for relugolix and leuprolide for Medicare patients with metastatic prostate cancer. *Value Heal*. 2021;24:S34.
6. Omland T, Heck SL, Gulati G. The role of cardioprotection in cancer therapy cardiotoxicity: *JACC: CardioOncology* state-of-the-art review. *JACC CardioOncol*. 2022;4(1):19-37.
7. Zhao J, Zhu S, Sun L, et al. Androgen deprivation therapy for prostate cancer is associated with cardiovascular morbidity and mortality: a meta-analysis of population-based observational studies. *PLoS One*. 2014;9(9):e107516.
8. Albertsen PC, Klotz L, Tombal B, Grady J, Olesen TK, Nilsson J. Cardiovascular morbidity associated with gonadotropin releasing hormone agonists and an antagonist. *Eur Urol*. 2014;65(3):565-573.
9. Lopes RD, Higano CS, Slovin SF, et al. Cardiovascular safety of degarelix versus leuprolide in patients with prostate cancer: the primary results of the PRONOUNCE randomized trial. *Circulation*. 2021;144(16):1295-1307.

Minimizing Complications of Inguinal Lymph Node Dissection

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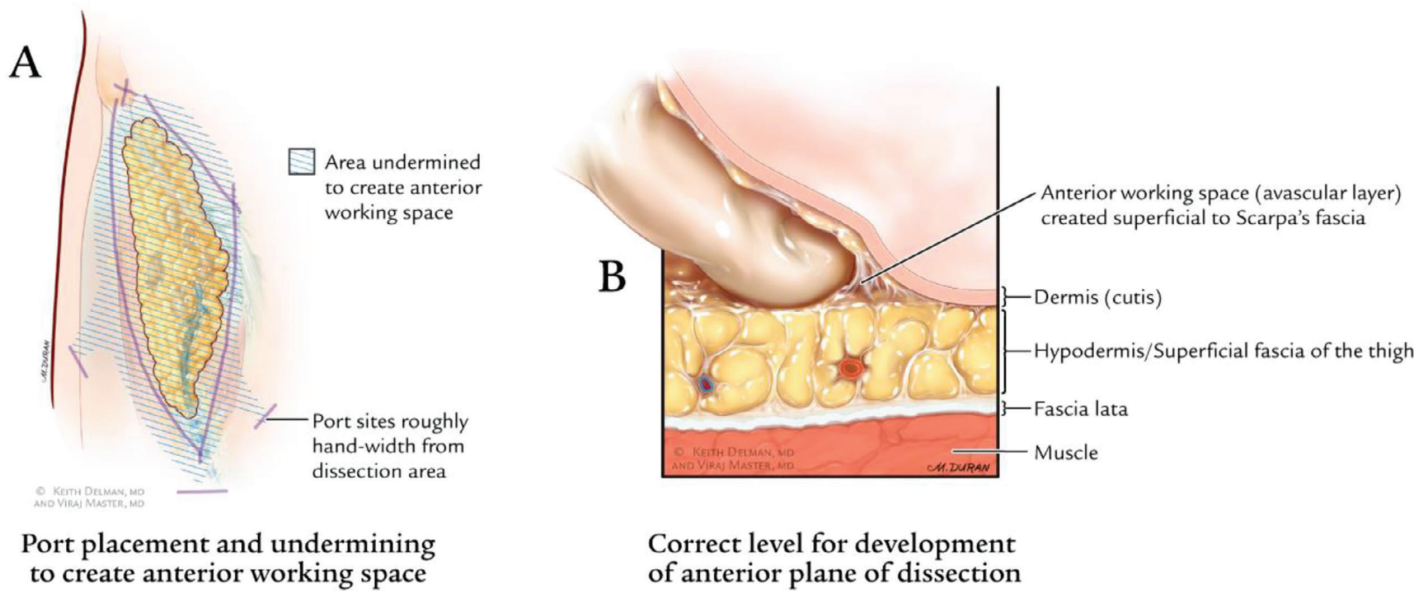

Figure 1. A, Boundaries of dissection as well as area undermined to create anterior working space. B, Correct level for development of anterior plane dissection.

Inguinal lymph node dissection (ILND) is an important component both in staging and also in treatment of different malignancies including penile and vulvar cancers according to National Comprehensive Cancer Network guidelines.[1,2]

Traditionally, a full template ILND was performed using a large open incision. The perioperative morbidities of this surgery include skin edge necrosis, wound dehiscence, infection, lymphocele, lymphorrhea, deep vein thrombosis, and chronic extremity lymphedema. The complication rates with open full template were historically high, and as a result it can dissuade patients and even physicians from prescribing this necessary surgery.[3,4] Adherence to guideline recommendations for ILND is unfortunately very low with only 1 out of every 4 patients who meet criteria eventually undergoing ILND.[5] This low guideline adherence is concerning considering the oncologic and survival benefits of ILND in indicated cases. Therefore, there is a need to discuss approaches that surgeons can use to reduce the morbidities and complications of ILND and to inform the urologic oncology community about the improved outcomes using these approaches so that more patients can safely receive this operation.

Dynamic sentinel node biopsy (DSNB) is perhaps the least morbid method for excisional biopsy of clinically nonpalpable groin lymph nodes. While negative DSNB avoids the morbidity of a full ILND, a positive DSNB mandates proceeding with formal ILND. Additionally, this approach should be avoided in the setting of palpable inguinal nodes.

Another approach to decrease morbidity of ILND is to modify the dissection template and reduce the field of dissection. Standard open ILND template involves removal of the lymphatic tissue from the inguinal ligament superiorly to the apex of the femoral triangle inferiorly, and from the adductor longus muscle medially to the sartorius muscle laterally with mobilization of the sartorius muscle for coverage of the femoral vessels. The dissection involves ligation and excision of the proximal greater saphenous vein and complete dissection of the femoral vessels. There are different modified templates proposed to date. Catalona first described a modified ILND template preserving the greater saphenous vein and limiting the dissection to the lateral edge of the femoral artery and superficial to the fossa ovalis, and reported a diminished incidence of lymphedema and wound complications.[6] Avoiding mobilization of the sartorius muscle has also been shown to reduce wound healing complications.[7] Spiess et al report their own contemporary series of modified template with a minor and major complication rate of 19% and 27%, respectively, with superficial diagnostic ILND.[3] While superficial and modified templates reduce the morbidity of ILND, they theoretically increase the risk of undersampling, and advantage is lost when histopathological examination reveals a positive node as radical dissection often becomes mandatory at that point.

Another approach to decrease the morbidity of ILND is to use minimally invasive surgical techniques such as videoscopic inguinal lymphadenectomy (VEIL) and robotic videoscopic inguinal lymphadenectomy (RVEIL).[8-10] Minimally invasive techniques have primarily been described in penile cancer patients with nonpalpable or small palpable lymphadenopathy. However, the use of these techniques in patients with significant palpable inguinal lymphadenopathy as well as following systemic treatment is also reported. In experienced hands VEIL and RVEIL have shown promising results.

Figure 1 shows the area of dissection and the correct level for development of anterior plane of dissection prior to port placement for VEIL or RVEIL. This plane is usually bluntly developed prior to placing the trocars and/or docking the robot. Surgeons are advised to take caution to not develop this plane too close to the epidermis so as not to compromise the vascular supply to the skin flap above the working field, which will often result to skin necrosis postoperatively. In most patients, skin flap should be about 5 mm in thickness. A well-dissected anterior plane should demonstrate arterial blood supply to the above skin with transillumination from the endoscopic camera (Figure 2). Figure 3 shows steps of the case as well as the surgical field after a complete dissection. The groin wounds below the inguinal ligament that are used for open incision are notorious for skin necrosis, wound breakdown, and infection. A major advantage of minimally invasive approaches, whether robotic-assisted or pure laparoscopic, is the transition of the wound (port sites and extraction site) from the groin area to distal to the apex of the femoral triangle (Figure 4). Although minimally invasive techniques use a smaller incision, the most benefit in this case perhaps comes from transitioning of the wound location, and

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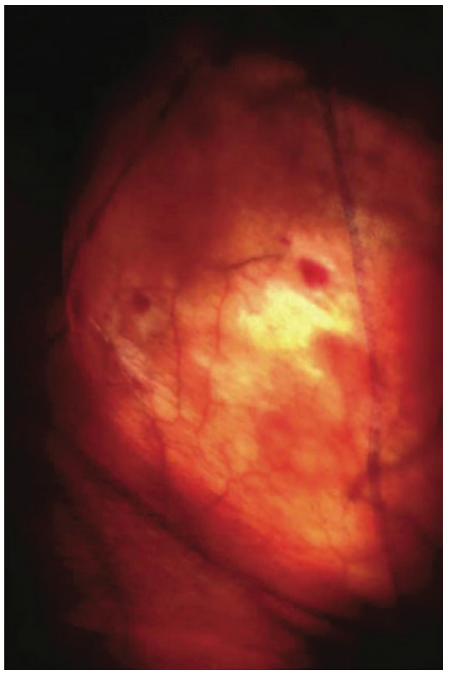

Figure 2. Transillumination of skin flap delineates arterial supply.

MINIMIZING COMPLICATIONS OF INGUINAL LYMPH NODE DISSECTION

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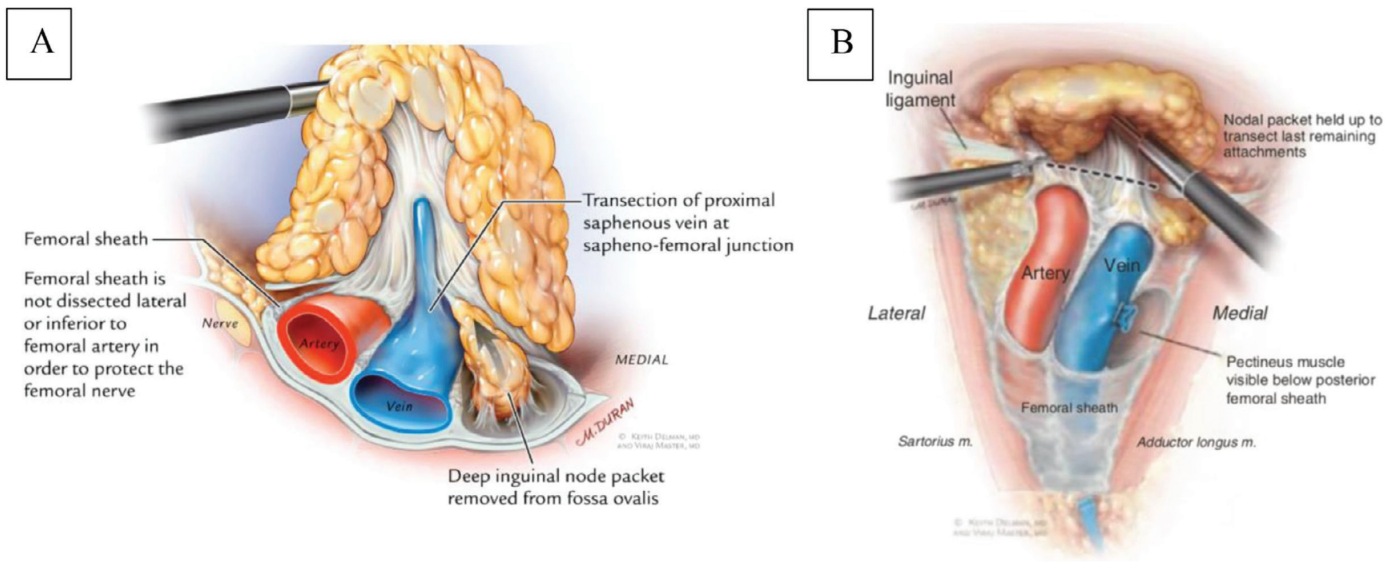

Figure 3. A, Dissection is carried in caudal to cephalad direction. Assistant can lift the nodal packet and allow the surgeon to carry dissection above the vessels. B, All remaining attachments are freed in preparation for nodal retrieving.

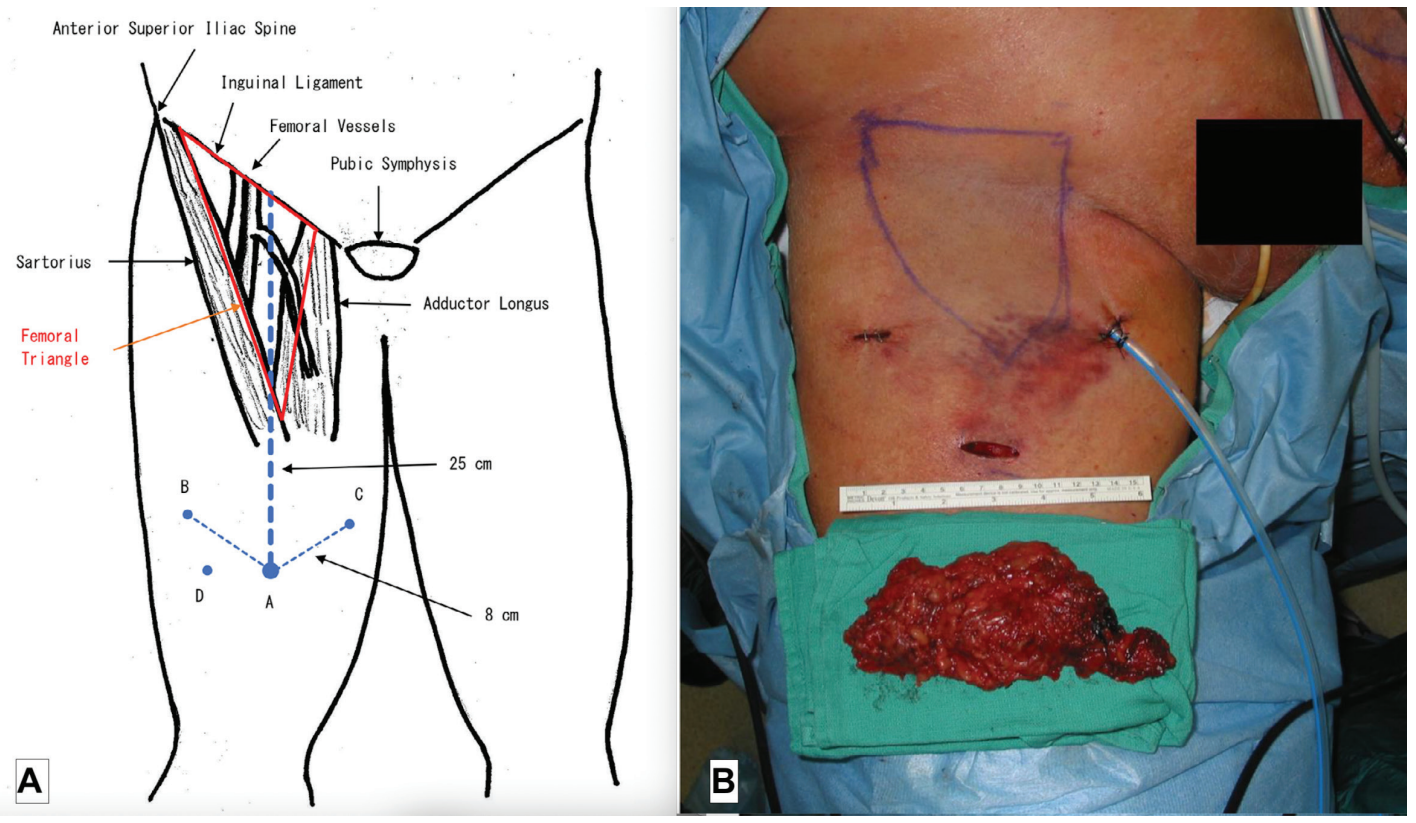

Figure 4. A, Robotic port sites. Camera port (12 mm for da Vinci Si and 8 mm for da Vinci Xi; A). Eight mm robotic arm ports (B and C). Assistant port (D). B, Lymph node packet is retrieved usually through one of the port sites, and a closed-suction drain is placed through another one.

not necessarily the cumulative relative size of the wound.

We previously analyzed the outcomes and complications of reported retrospective case series comparing VEIL and RVEIL to open ILND.[8-10] In brief, estimated blood loss is low regardless of the approach. RVEIL and VEIL appear to be safe with rarely required conversion to open approach. They have a longer operative time but a shorter hospital stay and reduced perioperative complication rate. The nodal yield and rate of recurrence, a surrogate for oncologic adequacy, indicate that RVEIL and VEIL techniques perform comparable to open ILND. However, potential selection bias should be considered when it comes to interpreting outcomes and complications since most of the current data on minimally invasive approaches come from nonrandomized retrospective series. Currently, data indicate patients and surgeons may shy away from ILND, with only 25% of appropriate indication patients getting ILND.[5] With these modifications showing significantly reduced morbidities and complications, hopefully more patients who meet criteria will get this important operation. ■

> "RVEIL and VEIL appear to be safe with rarely required conversion to open approach. They have a longer operative time but a shorter hospital stay and reduced perioperative complication rate."

1. Clark PE, Spiess PE, Agarwal N, et al. Penile cancer: clinical practice guidelines in oncology. *J Natl Compr Canc Netw.* 2013;11(5):594-615.
2. Koh WJ, Greer BE, Abu-Rustum NR, et al. Vulvar cancer, version 1.2017. NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw.* 2017;15(1):92-120.
3. Spiess PE, Hernandez MS, Pettaway CA. Contemporary inguinal lymph node dissection: minimizing complications. *World J Urol.* 2009;27(2):205-212.
4. Marilin N, Master VA, Pettaway CA, Spiess PE. Current practice patterns of society of urologic oncology members in performing inguinal lymph node staging/therapy for penile cancer: survey study. *Urol Oncol.* 2021;39(7):439.e9-439.e15.
5. Mistretta FA, Mazzone E, Palumbo C, et al. Adherence to guideline recommendations for lymph node dissection in squamous cell carcinoma of the penis: effect on survival and complication rates. *Urol Oncol.* 2019;37(9):578.e11-578.e19.
6. Catalona WJ. Modified inguinal lymphadenectomy for carcinoma of the penis with preservation of saphenous veins: technique and preliminary results. *J Urol.* 1988;140(2):306-310.
7. Gopman JM, Djajadiningrat RS, Baumgarten AS, et al. Predicting postoperative complications of inguinal lymph node dissection for penile cancer in an international multicentre cohort. *BJU Int.* 2015;116(2):196-201.
8. Nabavizadeh R, Master V. Minimally invasive approaches to the inguinal nodes in cN0 patients. *Curr Opin Urol.* 2019;29(2):165-172.
9. Nabavizadeh R, Petrinec B, Nabavizadeh B, Singh A, Rawal S, Master V. Inguinal lymph node dissection in the era of minimally invasive surgical technology. *Urol Oncol.* 2023;41(1):1-14.
10. Nabavizadeh R, Petrinec B, Necchi A, Tsaur I, Albersen M, Master V. Utility of minimally invasive technology for inguinal lymph node dissection in penile cancer. *J Clin Med.* 2020;9(8):2501.

Advanced Practice Providers in Men's Health: A Medicare and Commercial Claims Analysis

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The number of practicing urologists in the U.S. has steadily increased between 2015 and 2021, yet approximately 60% of U.S. counties are without a practicing urologist.[1] In an effort to offset the increasing demand placed on the urologist workforce, the AUA formally endorsed partnerships in 2014 between physicians and advanced practice providers (APPs), including physician assistants and nurse practitioners.[1] As of 2020, the average urologist-to-APP ratio was 2:1 within a medical care team.[1]

The compositional changes to the urological care team are important to consider in the context of men's health because the increasing involvement of APPs may be a unique mechanism to further bridge men's urology to their general health. The global average life expectancy for men is approximately 5 years less than for women, with men engaging in more risky lifestyle choices and lower health care seeking behavior.[2,3] As male urological health conditions frequently intersect with other underlying issues, including those related to endocrine, sexual, and reproductive health, the growing roles of APPs in urology may be utilized to further expand men's health.[2,4]

To better understand the roles of APPs in male-specific disease conditions and how urological care delivery in the U.S. continues to evolve to meet patient needs within both publicly and privately insured patient groups, Medicare and commercial insurance claims from the Physician/Supplier Procedure Summary and the IBM MarketScan Commercial Database were queried for procedures submitted by APPs between 2010 and 2020. Common urological conditions were identified using Current Procedural Terminology codes and grouped into 6 categories: overactive bladder, testicular hypofunction, erectile dysfunction and Peyronie's disease, benign prostatic hyperplasia, genital warts, and scrotal pain. The proportion of procedures submitted by APPs was calculated for each year and category.

Our analysis demonstrates that between 2010 and 2020 the role of APPs in men's urological health has increased in each condition within both the MarketScan and

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ADVANCED PRACTICE PROVIDERS IN MEN'S HEALTH

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Medicare groups–particularly in the treatment of genital warts (6-fold growth) and erectile dysfunction/Peyronie's disease (13-fold growth; Figures 1 and 2). This is consistent with the trends of urology APP growth reported in the existing literature. Hyman and Modi demonstrated the growing proportion of urological procedural claims submitted by APPs between 2010 and 2020, with the greatest proportion of APP claims in procedures such as percutaneous tibial nerve stimulation (24% and 10%) and bladder instillations (16% and 8%) in both privately and publicly insured populations in 2020.[5] We are currently unable to determine if our data are reflecting the effects of a growing scope of practice for APPs, an increase in the total number of practicing APPs, or a combination of the two.

To our knowledge, previous studies have only studied the growth of specific procedures performed by APPs.[6-8] In addition, most studies have not examined recent growth trends past 2017.[5] We examined the growth of APP roles in various men's health conditions through 2020, allowing a unique perspective on the care provided to a subset of the urological patient population.

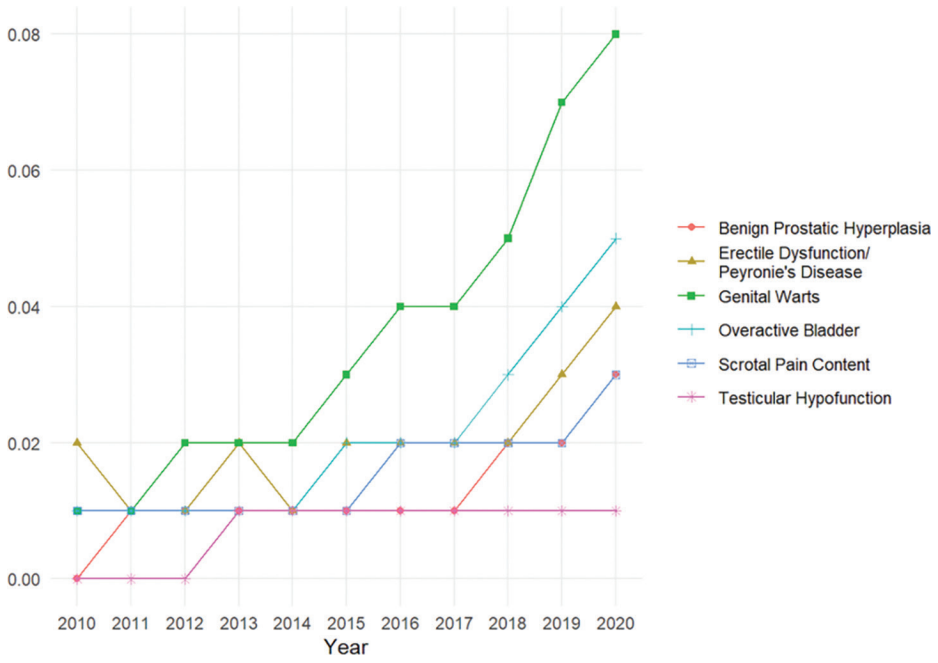

Figure 1. The proportion of urological procedural claims submitted by advanced practice providers to MarketScan (2010-2020).

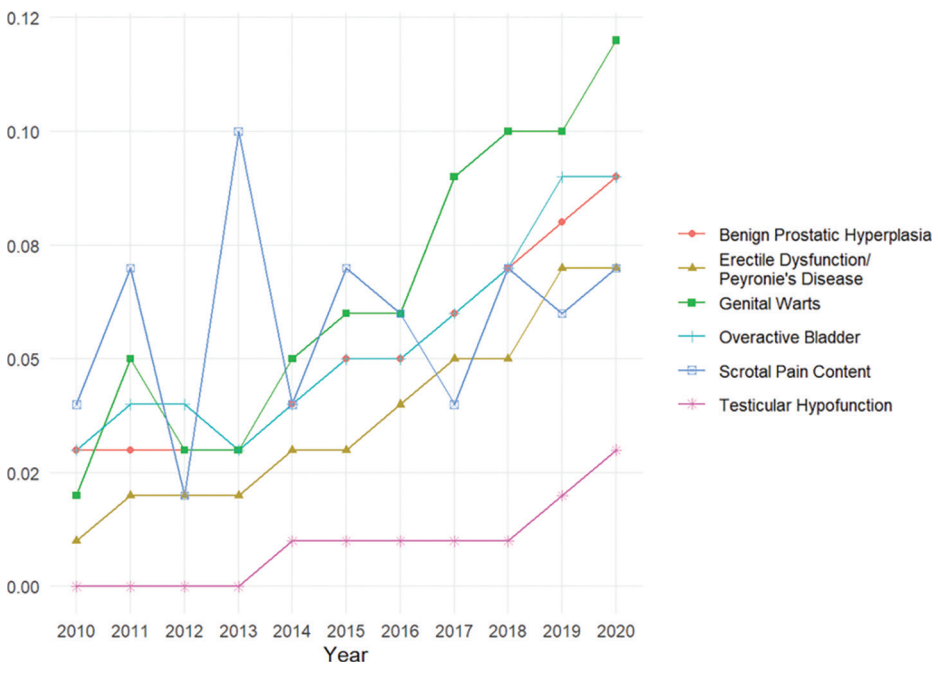

Figure 2. The proportion of urological procedural claims submitted by advanced practice providers to Medicare (2010-2020).

We believe that our observed rates of growth may underestimate the roles of APPs in men's health. "Incident to," "split/shared," and "direct" billing are the methods by which an APP may bill for rendered services. However, billing requirements vary by site of service and insurance company.[9] In particular, "incident to" billing involves independent evaluation and treatment of a patient, but bill submission by the supervising physician.[10] This billing practice is a challenge in quantifying the extent of APP care within the medical field.[10] The insurance claims in our data were billed by APPs, which does not capture the count of shared cases that may ultimately have been billed by the physician, thereby underestimating the APPs' true caseload and clinical involvement.

The increasing role of APPs in urological practice can help relieve the growing burden of the urology workforce shortage. While our data do not provide an assessment of patient outcomes and satisfaction, Hollenbeck et al assessed the effects of adding APPs to single specialty surgical practices and found that 1 year after adding the first APP to a practice, the odds of post-procedure complications, length of stay, and episode spending were reduced.[11] Further, general surgical, orthopedic, and urological practices had increases of 49 to 205 in-office visits per surgeon, demonstrating increased access to care. Similarly, Lai et al found that multispecialty group practices with higher rates of APP integration had lower rates of patient mortality, major complications, and readmission following major surgery.[12] Within urology specifically, studies have found that scheduling an initial visit with an APP could reduce wait time by 10-15 days.[13,14]

> "Within urology specifically, studies have found that scheduling an initial visit with an APP could reduce wait time by 10-15 days.[13,14]"

Understanding the growing role of APPs can be utilized to guide the development of targeted training curricula and certification criteria, potentially improve clinical care and costs for patients, and relieve the worsening physician workforce shortage in urology. Further research on implementation of APPs in men's health clinics, as well as the health outcomes of these workforce modifications, is warranted. ■

1. American Urological Association. *The State of Urology Workforce and Practice in the United States, 2020.* 2021. https://www.AUAnet.org/common/pdf/research/census/State-Urology-Workforce-Practice-US.pdf.
2. Tharakan T, Salonia A, Minhas S. Male life expectancy is still inferior to that of women: urologists must refine and develop the concept of men's health. *Eur Urol.* 2019;76(6):712-713.
3. Weiner PR, Salib A. Developing a men's health program. *Can J Urol.* 2020;27(S3):51-53.
4. Houman JJ, Eleswarapu SV, Mills JN. Current and future trends in men's health clinics. *Transl Androl Urol.* 2020;9(Suppl 2):S116-S122.
5. Hyman MJ, Modi PK. The growth of advanced practice providers in urology procedural care: evidence from public and private health insurers. *Urology.* 2022;168:110-115.
6. Langston JP, Duszak R, Orcutt VL, et al. The expanding role of advanced practice providers in urologic procedural care. *Urology.* 2017;106:70-75.
7. Erickson BA, Han Y, Meeks W, et al. Increasing use of advanced practice providers for urological office procedural care in the United States. *Urol Pract.* 2017;4(2):169-175.
8. Brand TC, Mitchell K, Quallich S, et al. Current state of advanced practice providers in urological practice. *Urol Pract.* 2022;9(1):1-7.
9. Kapoor DA. The role of advanced practice providers in urology. *Urol Clin North Am.* 2021;48(2):203-213.
10. Patel RA, Torabi SJ, Kasle DA, Pivirotto A, Manes RP. Role and growth of independent Medicare-billing otolaryngologic advanced practice providers. *Otolaryngol Head Neck Surg.* 2021;165(6):809-815.
11. Hollenbeck BK, Kaufman SR, Oerline M, et al. Effects of advanced practice providers on single specialty surgical practice. *Ann Surg.* 2023;277(1):e40-e45.
12. Lai LY, Kaufman SR, Modi PK, et al. Impact of advanced practice provider integration into multispecialty group practices on outcomes following major surgery. *Surg Innov.* 2022;29(1):111-117.
13. Chen M, Kiechle J, Maher Z, Gonzalez C. Use of advanced practice providers to improve patient access in urology. *Urol Pract.* 2019;6(3):151-154.
14. Singh A, Lassner JW, Sleiman MG, Diaz A, Quallich S, Modi PK. Advanced practice providers and wait times in urology offices: a secret shopper study. *Urol Pract.* 2022;9(5):389-395.

Update on Sexual and Reproductive Function in Bladder Exstrophy

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Bladder exstrophy is a congenital anomaly that exists on a spectrum between epispadias to cloacal exstrophy.[1] Children affected by this condition are born with an open bladder plate, a hemiclitoris or epispadias, low umbilicus, pubic diastasis, and anteriorly displaced anus. The incidence of bladder exstrophy has been reported as 2.15 in 100,000 live births in the United States and affects 2.3 males for every female.[2] Common immediate postnatal care includes keeping the bladder plate moist with saline irrigation and covered with plastic wrap as well as avoiding mucosal irritation from foreign bodies like clamps controlling the umbilical stump.

Surgical management for these individuals can vary considerably. Typically, primary closure of the bladder with bilateral osteotomy is performed. This can be done shortly after birth if the bladder is an appropriate size or can be delayed 6-12 months to allow further growth. Historically, primary urinary diversion was more commonly performed, though it is still done for children not suitable for closure or who have failed bladder closure in the past. Beyond bladder closure these children also typically undergo epispadias repair, possible bladder neck repair or reconstruction, and bilateral ureteral reimplantation. These can be completed in multiple stages or in 1 procedure. These repairs are technically challenging and complications that arise can include bladder dehiscence, urethral stricture, glans necrosis, vesicocutaneous fistula, bladder prolapse, and more.

As these patients transition into adolescence and adulthood, sexual function and fertility become an important aspect for many. The anatomical impact of exstrophy can affect their reproductive organs, leading to a shortened vagina in women and male penis with an anterior corporal length about half of that compared to controls, even after bladder closure. Individuals with a history of bladder exstrophy can struggle with low satisfaction with their genital appearance. Suomen et al surveyed 21 men with a history of bladder exstrophy treated between 1956 and 1992 compared with age matched controls.[3] They reported similar erectile function, desire, and sexual satisfaction between groups, however only 12/21 men were satisfied with the appearance of their genitals. Rubenwolf et al surveyed 39 males with a history of bladder exstrophy, all of whom underwent urinary diversion rather than bladder closure.[4] They found relatively high rates of erectile and orgasmic dysfunction (50%) and reduced sexual desire (86%) with similar low rates of satisfaction with cosmesis (30%). However, greater than 90% of the men surveyed were sexually active and satisfied with intercourse. On average these men had 10.4 surgeries, 3.4 of which were for genital reconstruction specifically.

Exstrophy male genital reconstructive procedures can include skin grafting, tissue expansion, and radial forearm free flap phalloplasty. Harris et all reported outcomes for 28 males on the exstrophy epispadias spectrum who underwent one of these 3 reconstructive procedures.[5] Of the 25 men who completed answers pertaining to penile length, 23 were preoperatively dissatisfied with their penile length, with 18 noting improvement postoperatively. Ultimately, the importance of preoperative counseling should be emphasized as only 61% of patients were satisfied with their reconstruction.

> "As these patients transition into adolescence and adulthood, sexual function and fertility become an important aspect for many."

Unassisted male fertility rates have been reported at 10% or lower. Fertility rates are impacted by antegrade ejaculate volume, which is at least somewhat dependent on number and character of prior surgical procedures but may simply be a result of an incompetent bladder neck. These patients do have an increased risk of low sperm counts: Ebert et all reported only 3 of 16 men with a history of bladder exstrophy had antegrade ejaculation with normal sperm counts.[6] Use of assisted reproductive technology (ART) has had good success. One series reported 11 out of 39 males with classic bladder exstrophy who fathered children. Ten of the 16 children were conceived using ART in the form of homologous insemination or testicular sperm extraction with intracytoplasmic sperm injection.[4]

Female exstrophy patients have been reported as having comparable sexual pleasure when compared with age matched controls in one series of 11 patients.[3] Of these 11 women, 4 underwent procedures for vaginal stenosis. In another series of 29 women with continent urinary diversion, 90% regularly had intercourse.[7] However, only 44% were satisfied with the cosmetic appearance of their genitals and repeat vaginoplasty was required in 33% due to dyspareunia. High rates of fertility are reported in this series with 12 women having 16 healthy children, all of whom were delivered via cesarean section. Yet, 12 of these pregnancies had some manner of complication. Pelvic organ prolapse is common, likely due to a widened diastasis and altered pelvic floor anatomy, with 11/29 developing this in this series. Surgical repair can be challenging for these individuals, however Everett et all described successful abdominal sacral colpopexy in 9 of 11 patients in their series.[8]

Adults with a history of bladder exstrophy can have satisfying sexual function and successfully conceive children. Considerations for males include low rates of genital appearance satisfaction. Many go through multiple genital reconstructive procedures but there are a variety

> "Adults with a history of bladder exstrophy can have satisfying sexual function and successfully conceive children."

of options to allow for not only cosmesis, but also function. Males can go on to father children, but with the majority requiring ART. Considerations for females include the importance for long-term urogynecologic follow-up given the high rates of vaginal reconstruction and prolapse. It is very feasible, however, for these patients to have a satisfying sexual life. Most females can become pregnant if they so desire, though they should be considered high risk and plan for cesarean section. Utilizing this information, we can not only provide surgical counseling for the initial procedures performed, but also help support these patients to achieve a high sexual quality of life and educate them on reproductive opportunities available. ■

1. Siffel C, Correa A, Amar E, et al. Bladder exstrophy: an epidemiologic study from the International Clearinghouse for Birth Defects Surveillance and Research, and an overview of the literature. *Am J Med Genet C Semin Med Genet.* 2011;157C(4):321-332.
2. Gearhart JP, Di Carlo HN. Exstrophy-epispadias complex. In: Partin AW, Wein AJ, Kavoussi LR, Peters CA, Dmochowski RR, eds. *Campbell-Walsh-Wein Urology.* E-Book. Elsevier Health Sciences; 2020:528-580.
3. Suominen JS, Santtila P, Taskinen S. Sexual function in patients operated on for bladder exstrophy and epispadias. *J Urol.* 2015;194(1):195-199.
4. Rubenwolf P, Thomas C, Thüroff JW, Stein R. Sexual function, social integration and paternity of males with classic bladder exstrophy following urinary diversion. *J Urol.* 2016;195(2):465-70.
5. Harris TGW, Khandge P, Wu WJ, et al. Sexual health outcomes after penile reconstruction in the exstrophy-epispadias complex. *J Pediatr Urol.* 2022;18(6):747-755.
6. Ebert AK, Schott G, Bals-Pratsch M, Seifert B, Rösch WH. Long-term follow-up of male patients after reconstruction of the bladder-exstrophy-epispadias complex: psychosocial status, continence, renal and genital function. *J Pediatr Urol.* 2010;6(1):6-10.
7. Rubenwolf P, Thomas C, Thüroff JW, Stein R. Sexual function and fertility of women with classic bladder exstrophy and continent urinary diversion. *J Urol.* 2016;196(1):140-145.
8. Everett RG, Lue KM, Reddy SS, et al. Patient-reported impact of pelvic organ prolapse on continence and sexual function in women with exstrophy-epispadias complex. *Female Pelvic Med Reconstr Surg.* 2017;23(6):377-381.

Shock Wave Therapy: Is It Ethical to Offer and Charge for Erectile Dysfunction or Other Sexual Dysfunctions?

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I first want to congratulate Dr Brock on his election and ascension to the presidency of the International Society for Sexual Medicine. *AUANews* has asked us to pen our positions on shock wave therapy for erectile dysfunction (ED) and other male sexual dysfunctions, and secondarily address the ethics of charging for shock wave therapy.

We debated this topic at the 22nd Annual Spring Meeting of the SMSNA (Sexual Medicine Society of North America) held in conjunction with the American Urological Association Meeting in New Orleans, May 2022. But that was not the beginning of this debate on shock wave therapy. In 2021, we were both authors on the SMSNA Position Statement on Restorative Therapies for Erectile Dysfunction. At that time, we both endorsed the recommendation that there was insufficient evidence to support stem cell therapies, platelet-rich plasma, and low-intensity shock wave therapy (LiSWT) in the routine management of ED.[1]

I am pleased to see that Dr Brock's review of the current literature has brought him around to supporting my argument: "as of today, it is unethical to charge for this therapy for all sexual dysfunctions. The 1 exception would be in patients with mild to moderate arteriogenic-induced erectile dysfunction…"

Why have we both modulated our positions on the role of LiSWT for the treatment of ED in clinical practice? Let's briefly review the physics, putative tissue effects, reported outcomes, and society guidelines. A shock wave is a transient pressure disturbance that propagates rapidly (5 µs duration); it is faster than the speed of sound in the given medium in which it is traveling (in air, 770 mph). A shock wave is associated with a rapid rise from ambient pressure to its maximum pressure, followed by a negative phase of wave propagation. A megapascal (MPa) is the basic unit of pressure or tension measurement used to describe shock waves (1 MPa = 145 psi). Energy is propagated in the medium through which the wave travels in a series of compressions and relaxations. Shock wave lithotripsy for nephrolithiasis was the first medical application of this technology; shock wave lithotripsy generators used for kidney stones create peak wave pressures from 30 MPa to 110 MPa. Energies used in orthopedics (plantar fasciitis, lateral epicondylitis, calcific tendinitis) range from 18-35 MPa. Energies used in the cardiology, diabetic foot ulcers and ED are much lower (5-9 MPa) and referred to as LiSWT. Therapeutic shock waves are characterized by short rise time from ambient pressure to high pressure. Urologists intuitively appreciate how high-energy shock waves can fracture kidney stones; less intuitive is the concept that LiSWT produces lower-energy waves with the same physical forces of compression and relaxation to exert biologic effects on tissues. LiSWT has been reported to induce angiogenesis and stimulate neovascularization in animal penile tissues. A note of warning to both potential patients and practitioners: radial shock wave devices produce dispersive pressure waves of much lower energy and tissue penetration than LiSWT. Radial pressure wave devices are classified by the Food and Drug Administration (FDA) as class I and are equivalent to vibrators. LiSWT devices are class II devices and should be operated under medical supervision.

> "A shock wave is a transient pressure disturbance that propagates rapidly (5 µs duration); it is faster than the speed of sound in the given medium in which it is traveling (in air, 770 mph)."

Studies have shown that LiSWT can improve erectile function assessed by the International Index of Erectile Function (IIEF) in prospective trials both single-armed and placebo-armed. The European Association of Urology and European Society of Sexual Medicine do address clinical applications for LiSWT and have included LiSWT in the management algorithm for vasculogenic ED.[2] European Association of Urology Guidelines conclude that LiSWT can ameliorate erection quality in patients with ED who are either nonresponders or inadequate responders to phosphodiesterase type 5 inhibitors and reduce the immediate need for more invasive treatments, like penile injections or penile prostheses. Similarly, the British Society for Sexual Medicine Guidelines on the Management of ED conclude LiSWT treatments are well tolerated and safe. LiSWT might be a preferred option for patients failing oral therapy but reluctant to advance to injection therapy.[3]

In 2017, the FDA approved an LiSWT machine in the management of diabetic foot ulcers. At this time, LiSWT is not FDA approved for ED. If a urologist wants to incorporate LiSWT into clinical practice of ED, there are several technical options which must be considered in the delivery of care. The various technical considerations are: which LiSWT generator (electrohydraulic, electromagnetic, piezoelectric); what types of shocks to deliver (focused, linear, semifocused, unfocused); what treatment parameters (energy flux density, number of shocks per session, number of sessions per week, total number of pulses delivered); and, lastly, which target sites (pendulous shaft vs pendulous shaft and crural bodies). Energy flux density (EFD) refers to the energy delivered per shock wave pulse (mJ/mm^2). Dr Harmut Porst has published a review of 6 LiSWT commercial generators using different sources of energy.[4] The paper serves as a primer for currently marketed SWT devices. The treatment protocols reviewed for vascular ED included EFDs ranging from 0.09 to 0.55 mJ/mm^2. A recent meta-analysis of 16 randomized, controlled trials of LiSWT found that when EFD of 0.09 mJ/mm^2 was applied the IIEF improvement was better than when EFD was between 0.1 and 0.2 mJ/mm^2, and that 1,500 or 2,000 pulses per treatment were similarly better for IIEF improvements than 600 or 3,000 pulses. Improvements after 6 months were better than at 1 or 3 months post-treatment. Only 1 of the 16 trials followed patients to 12 months. So, as Dr Brock points out, we do not have long-term efficacy data or know the impact of maintenance therapy.

Each of the guidelines cited provide consensus that LiSWT applied to the penis appears to be safe and well tolerated, with penile pain and bruising the most common complications. European and British Guidelines both advise that LiSWT appears to have some efficacy in men with mild-moderate vascular ED and may help nonresponders to phosphodiesterase type 5 inhibitor drugs. Any evidence that LiSWT may reduce penile pain in Peyronie's disease is confounded by the natural history of Peyronie's disease, which is associated with spontaneously ameliorating penile pain over 6-12 months. LiSWT efficacy on plaque size is confounded by lack of refinements on how to measure plaque length, width, and thickness. None of the guidelines cited has recommended LiSWT in the management of Prostatitis

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SHOCK WAVE THERAPY

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Category IIIb (NIH), which is genitourinary pain with or without voiding symptoms unaccompanied by bacteria. Nor have there been sufficient studies to suggest treatment protocols.

Dr Brock has cited 4 core beliefs as the foundation of medical ethics. I heartily agree with each, but my recollection of the classics calls for a different order, beginning with the admonition attributed to Hippocrates: "Primum non nocere." First, do no harm. Second would be "doing good." Third would be "giving the patient a voice in the choice of his care." The final would be "ensuring fairness." The clinical data on LiSWT for ED clearly support that it does no harm. Clinicians who apply the therapy are indeed attempting to do good, with a basis for that belief in the literature. Admittedly, LiSWT has not lived up to the promise of restoring normal erectile function, but neither do any of our homeopathic recommendations (lose weight, medically manage lipids/blood pressure/glucose, exercise). That does not stop us from attempts to do good by recommending lifestyle modification in the initial management of ED. Ensuring fairness in medical practice, I assume, means charging a fair price. That's a debate a U.S. physician could never win against a Canadian. One system ascribes to a fee-for-service model of health care and the other has opted for universal care. In the latter, there is greater financial fairness/equity, but government predominates in choice of options compared to the patient or the physician.

For any patients considering LiSWT for vascular ED management, I would advocate they ask their provider these questions:

- What does the procedure involve (how many treatments, how frequently) and what does it cost?
- What are the benefits and what are my chances of benefitting?
- Could the procedure make me worse?
- What are the alternatives?
- What are the risks?
- What will happen if I don't have the procedure? ■

"Ensuring fairness in medical practice, I assume, means charging a fair price."

1. Liu JL, Chu KY, Gabrielson AT, et al. Restorative therapies for erectile dysfunction: position statement from the Sexual Medicine Society of North America (SMSNA). *Sex Med.* 2021;9(3):100343.
2. Salonia A, Bettocchi C, Boeri L, et al. European Association of Urology Guidelines on Sexual and Reproductive Health-2021 update: male sexual dysfunction. *Eur Urol.* 2021;80(3):333-357.
3. Hackett G, Kirby M, Wylie K, et al. British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction in Men-2017. *J Sex Med.* 2018;15(4):430-457.
4. Porst H. Review of the current status of low intensity extracorporeal shockwave therapy (Li-ESWT) in erectile dysfunction (ED), Peyronie's disease (PD), and sexual rehabilitation after radical prostatectomy with special focus on technical aspects of the different marketed ESWT devices including personal experiences in 350 patients. *Sex Med Rev.* 2021;9(1):93-122.

The companion article, "Shock Wave Therapy: Is It Ethical to Offer and Charge for Erectile and Other Sexual Dysfunctions?" was published in the February 2023 issue of AUANews (Volume 28, Issue 2). This companion article can be accessed via the link: https://auanews.net/issues/articles/2023/february-2023/shock-wave-therapy-is-it-ethical-to-offer-and-charge-for-erectile-and-other-sexual-dysfunctions.

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Feasibility of Awake Intravesical Botulinum Toxin Injection in Pediatric Neurogenic Bladder

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Children's Hospital of Philadelphia, Pennsylvania

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Introduction

Intravesical botulinum neurotoxin (BoNT) injection is used to treat bladder dysfunction in both pediatric and adult patients.[1] The Food and Drug Administration approved intravesical BoNT injection in 2021 for patients ≥5 years old with inadequate response to or intolerance of anticholinergic medication. BoNT is also approved for treatment of muscular spasticity in patients as young as age 2.[2] While the demonstrated efficacy of BoNT injection for overactive bladder in spina bifida has been mixed,[3,4] it has been shown to improve both clinical symptoms and maximum cystometric capacity in the pediatric spina bifida population with neurogenic bladder and to reduce maximum detrusor pressures.[5,6]

BoNT injection must be repeated every 3-6 months to maintain its effects. In adults, injection is routinely performed with local analgesics in the office,[7] but awake invasive procedures in children are anathema to many urologists. Thus, pediatric BoNT injection is traditionally performed under general anesthetic, accumulating repeated anesthetic exposures and high costs. Most patients with neurogenic bladder who are candidates for BoNT injection already tolerate clean intermittent catheterization (CIC) with variable sensation. To incorporate BoNT into our standard arsenal without accumulating anesthetic exposures, we offer an awake injection trial. We present a retrospective review of our initial single-surgeon experience in a pediatric population with neurogenic bladder at the University of California, San Francisco.

> "Most patients with neurogenic bladder who are candidates for BoNT injection already tolerate clean intermittent catheterization (CIC) with variable sensation."

Methods

Procedural details. Injections were performed in the operating room (OR) with an anesthesia provider available. A parent or guardian accompanied the patient, as is our standard practice, and the patient was offered a movie to watch or video game to play. A 9.5F offset rigid cystoscope or 17F flexible cystoscope was used based upon urethral size and anatomy in supine, frogleg, or low lithotomy position, as appropriate for age and habitus. We injected weight-dosed

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Table 1. Summary Statistics of All Included Patients Undergoing Bladder Botulinum Neurotoxin Injection in the Operating Room Stratified by Anesthesia Utilization: No General Anesthesia (Awake) vs Under General Anesthesia

	Trial of awake BoNT (N = 18)	General anesthesia (N = 4)
Sex, No. (%)		
Male	10 (55.6)	1 (25.0)
Female	8 (44.4)	3 (75.0)
Age, y		
Mean (SD)	10.6 (4.49)	12.3 (3.77)
Median (min, max)	10.6 (4.80, 20.6)	11.7 (8.80, 17.2)
Diagnosis, No. (%)		
Sacral agenesis	1 (5.6)	0 (0)
Sacrococcygeal teratoma	0 (0)	1 (25.0)
Skeletal dysplasia	1 (5.6)	0 (0)
Spina bifida	16 (88.9)	2 (50.0)
Transverse myelitis	0 (0)	1 (25.0)
Intermittent catheterization, No. (%)	18 (100)	4 (100)
Sensation (S2 level), No. (%)		
Sensate	7 (38.9)	0 (0)
Insensate	10 (55.6)	4 (100)
Missing	1 (5.6)	0 (0)
Cognitive delay, No. (%)		
No	8 (44.4)	2 (50.0)
Yes	10 (55.6)	2 (50.0)
Behavioral/mental health issues, No. (%)		
No	4 (22.2)	1 (25.0)
Yes	14 (77.8)	3 (75.0)
Prior BoNT under anesthesia, No. (%)		
No	12 (66.7)	4 (100)
Yes	6 (33.3)	0 (0)

Abbreviations: BoNT, botulinum neurotoxin; SD, standard deviation.
Adapted with permission from Overland, *J Urol*. 2022;208(3):702-710.[9]

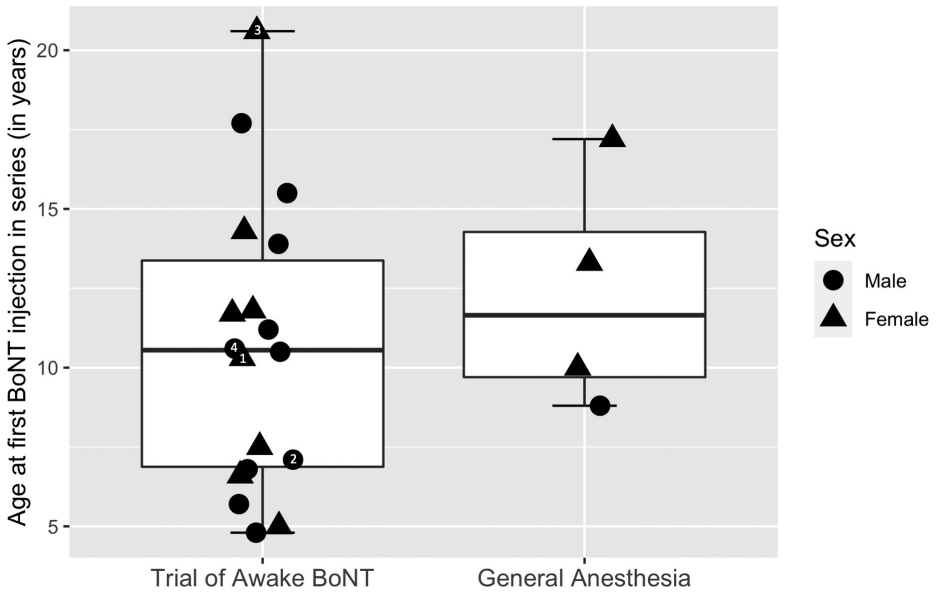

Figure 1. Age and sex distribution for each patient stratified by awake injection vs under general anesthesia. Within the awake injection group, only 3 of the 18 patients (17%) did not proceed with or plan for subsequent awake botulinum neurotoxin (BoNT) injection procedures. Of these, one 10-year-old female patient proceeded directly to bladder augment (1), 1 insensate 7-year-old male patient with anxiety, attention-deficit/hyperactivity disorder and a conduct disorder tolerated the initial awake attempt, but family requested subsequent injections be performed under general anesthesia due to progression of his conduct disorder (2), and a sensate 20-year-old female patient with severe anxiety required conversion to general anesthesia during the initial attempt but also did not have a sufficient response to BoNT injection to merit repeat injection (3). A fourth patient, an insensate 10-year-old male with hearing loss who had difficulty communicating with the operating room team, opted to convert to a general anesthetic prior to scope placement, but has since decided to proceed with awake BoNT injection in clinic with an American Sign Language interpreter present (4). Adapted with permission from Overland, *J Urol*. 2022;208(3):702-710.[9]

FEASIBILITY OF AWAKE INTRAVESICAL BOTULINUM TOXIN INJECTION

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onabutulinumtoxinA in 10 U/L mL saline increments into the detrusor muscle and submucosal layer of the bladder in trigone-sparing fashion. If the patient expressed discomfort or distress, we offered to convert to general anesthesia. A 2% preprocedural bladder lidocaine soak was added partway through the study period, and intraurethral lidocaine was administered on a case-by-case basis.

Chart review. Surgical records from 2018-2020 were searched to identify all pediatric patients under age 21 with neurogenic bladder who underwent isolated intravesical BoNT injection in the OR with H.L.C. as the primary provider. Procedure details were extracted from the operative report. Intraoperative procedure duration and use of general anesthesia were determined from anesthesia reports. Postoperative notes were reviewed to assess for subsequent planned or completed awake BoNT injection.

> "All patients catheterized at baseline. Eighteen families (82%) accepted a trial while 4 declined and proceeded under general anesthesia (Table 1)."

Results

A total of 43 BoNT injection encounters in the OR were identified for 22 pediatric patients meeting inclusion criteria, and awake injection was offered to all of them within the study period. All patients catheterized at baseline. Eighteen families (82%) accepted a trial while 4 declined and proceeded under general anesthesia (Table 1). Sixteen of the 18 patients (89%) tolerated awake injection (Figure 1) and no intraoperative complications occurred. Of the 18 patients who underwent a trial of awake injection, 8 were female and 10 were male, aged 4-20 years old. Sixteen patients (89%) had a diagnosis of spina

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Table 2. Summary Statistics and Procedural Details for All Patients Undergoing Trial of Awake Bladder Botulinum Neurotoxin Injection in the Operating Room Stratified by Patient Sex

	Male (N = 10)	Female (N = 8)
Age, y		
Mean (SD)	10.4 (4.34)	11.0 (4.96)
Median (min, max)	10.6 (4.80, 17.7)	11.0 (5.00, 20.6)
Diagnosis, No. (%)		
Sacral agenesis	0 (0)	1 (12.5)
Skeletal dysplasia	0 (0)	1 (12.5)
Spina bifida	10 (100)	6 (75.0)
Sensation (S2 level), No. (%)		
Sensate	2 (20.0)	5 (62.5)
Insensate	7 (70.0)	3 (37.5)
Missing	1 (10.0)	0 (0)
Cognitive delay, No. (%)		
No	5 (50.0)	3 (37.5)
Yes	5 (50.0)	5 (62.5)
Behavioral/mental health issues, No. (%)		
No	3 (30.0)	1 (12.5)
Yes	7 (70.0)	7 (87.5)
Prior BoNT under anesthesia, No. (%)		
No	5 (50.0)	7 (87.5)
Yes	5 (50.0)	1 (12.5)
Lidocaine bladder soak, No. (%)		
No	5 (50.0)	4 (50.0)
Yes	5 (50.0)	3 (37.5)
Missing	0 (0)	1 (12.5)
Urethral lidocaine gel, No. (%)		
No	5 (50.0)	7 (87.5)
Yes	5 (50.0)	0 (0)
Missing	0 (0)	1 (12.5)

	Male (N = 10)	Female (N = 8)
Cystoscope, No. (%)		
9.5F offset rigid	7 (70.0)	8 (100)
17F flexible	3 (30.0)	0 (0)
BoNT units injected		
Mean (SD)	255 (76.2)	258 (59.0)
Median (min, max)	300 (100, 300)	300 (180, 300)
Duration (min)		
Mean (SD)	29.7 (11.9)	17.4 (8.56)
Median (min, max)	29.5 (13.0, 47.0)	19.0 (6.00, 29.0)
Missing or censored, No. (%)	4 (40.0)	3 (37.5)
IV medications required, No. (%)		
No	9 (90.0)	7 (87.5)
Yes	1 (10.0)	1 (12.5)
General anesthesia required, No. (%)		
No	9 (90.0)	7 (87.5)
Yes	1 (10.0)	1 (12.5)
Subsequent awake planned, No. (%)		
No	1 (10.0)	2 (25.0)
Yes	9 (90.0)	6 (75.0)
Total awake injections in OR		
Mean (SD)	2.00 (1.56)	2.00 (1.41)
Median (min, max)	1.50 (0, 5.00)	2.00 (0, 4.00)
Total awake injections in clinic		
Mean (SD)	0.900 (1.29)	0.750 (0.707)
Median (min, max)	0.500 (0, 4.00)	1.00 (0, 2.00)
Follow-up, y		
Mean (SD)	2.16 (0.853)	2.00 (0.729)
Median (min, max)	2.14 (0.936, 3.88)	1.94 (1.12, 3.03)

Abbreviations: BoNT, botulinum neurotoxin; F, French; IV, intravenous; OR, operating room; SD, standard deviation.
Adapted with permission from Overland, *J Urol*. 2022;208(3):702-710.[9]

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> "Young age did not preclude successful awake injection, and we have since successfully performed awake injections in patients as young as 2 years old."

bifida. Fourteen patients (78%) had documented behavioral or mental health issues, 10 (56%) had a cognitive delay, and 7 (39%) had a sensory level below S2 on exam. Flexible cystoscopes were used for 3 male patients over the age of 14. Median follow-up was 2.0 years (Table 2).

Fifteen of 18 patients opted to proceed with subsequent awake injections, with a median of 1.5 awake procedures in the OR and 1.0 awake procedure in clinic per patient within the follow-up period. Procedure duration of the 43 BoNT injection events in the OR during the study period (24 awake, 17 under general anesthetic, and 2 awake attempts that required conversion) was not statistically different between the awake and general anesthesia groups (median duration 23 minutes vs 18 minutes, $P = .1$), though increased variability was seen in the awake group with a maximum procedure duration of 47 minutes. Average charges for awake BoNT injection episodes in the OR were lower than for BoNT injection under general anesthesia ($26,000±$3,260 vs $30,100±$4,960, $P < .01$; Figure 2).

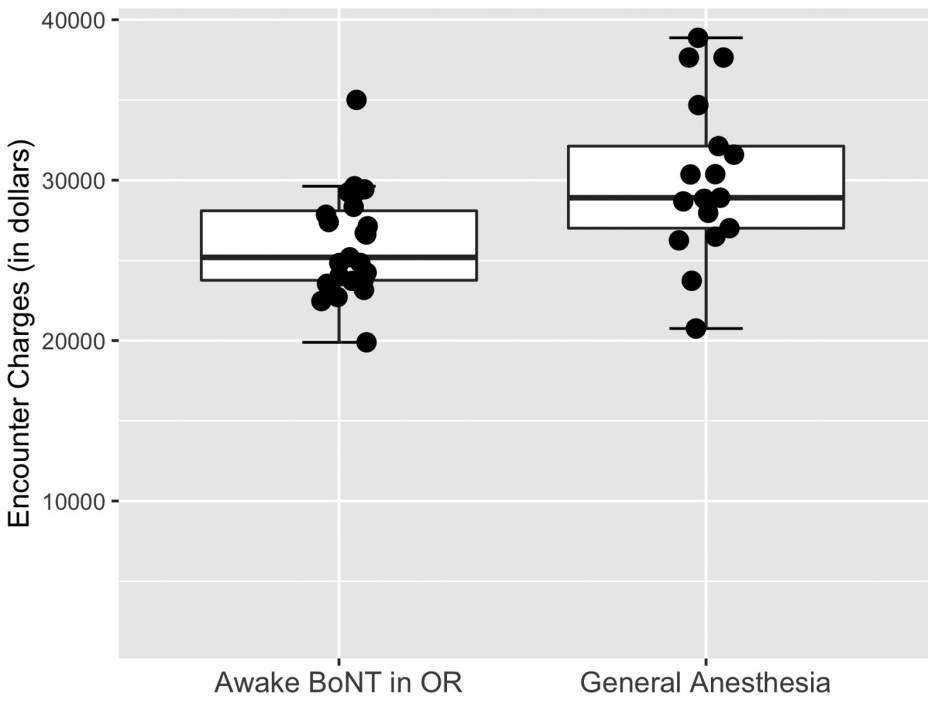

Figure 2. Operating room (OR) charge distribution per encounter stratified by awake injection vs under general anesthesia. Average charges for awake botulinum neurotoxin (BoNT) injection episodes in the OR were lower than for BoNT injection under general anesthesia ($26,000±$3,260 vs $30,700±$6,850, $P < .01$). Adapted with permission from Overland, *J Urol*. 2022;208(3):702-710.[9]

Discussion

Our experience supports awake BoNT injection as a feasible option for patients with neurogenic bladder managed with CIC as young as age 4, even in the setting of intact sensation, well-managed mental health issues, or cognitive delay. Thorough discussion of the risks, benefits, and procedure details (including possible conversion to general anesthesia if needed) with the family and patient was key in the shared decision-making to proceed with a trial of awake injection.

Although we predicted that sensation with catheterization and scope placement might influence the success of the procedure, 6 of our 7 patients with a sensory level below S2 (86%) tolerated awake injection.[8] We also were concerned that rigid cystoscopy might be poorly tolerated in awake male patients, but this was not the case. Young age did not preclude successful awake injection, and we have since successfully performed awake injections in patients as young as 2 years old. We now regularly perform awake BoNT injections in our pediatric clinic, allowing families to avoid the hassles of the perioperative experience. In our current preliminary experience, charges for clinic encounters are approximately 70% lower than for injection under anesthesia, providing further opportunity for significant cost and resource saving.

We have begun to prospectively study the experience of in-clinic injections for our patients and their families to further elucidate the intrinsic and modifiable factors that define a good pediatric candidate for awake BoNT injection, as well as to quantify the risk-benefit balance of interventions such as lidocaine soaks through controlled trials.

Conclusion

Awake BoNT injection in patients with neurogenic bladder managed with CIC is feasible in very young children, even in the setting of intact sensation, well-managed mental health issues, or cognitive delay. The ability to routinely offer this procedure without anesthesia for well-selected patients increases the viability of BoNT as an early tool in the armamentarium of the pediatric urologist managing a recalcitrant neurogenic bladder. ■

> "Awake BoNT injection in patients with neurogenic bladder managed with CIC is feasible in very young children, even in the setting of intact sensation, well-managed mental health issues, or cognitive delay."

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1. Schurch B, Stöhrer M, Kramer G, et al. Botulinum-A toxin for treating detrusor hyperreflexia in spinal cord injured patients: a new alternative to anticholinergic drugs? Preliminary results. *J Urol*. 2000;164(3 Part 1):692-697.
2. Botox–onabotulinumtoxina injection, powder, lyophilized, for solution. In: *US Food and Drug Administration (FDA) Approved Product Information*. US National Library of Medicine; 2021.
3. Hascoet J, Manunta A, Brochard C, et al. Outcomes of intra-detrusor injections of botulinum toxin in patients with spina bifida: a systematic review. *Neurourol Urodyn*. 2017;36(3):557-564.
4. Kaviani A, Khavari R. Disease-specific outcomes of botulinum toxin injections for neurogenic detrusor overactivity. *Urol Clin North Am*. 2017;44(3):463-474.
5. Hascoet J, Peyronnet B, Forin V, et al. Intradetrusor injections of botulinum toxin type A in children with spina bifida: a multicenter study. *Urology*. 2018;116:161-167.
6. Austin PF, Franco I, Dobremez E, et al. OnabotulinumtoxinA for the treatment of neurogenic detrusor overactivity in children. *Neurourol Urodyn*. 2021;40(1):493-501.
7. Cooley L. F, Kielb S. A review of botulinum toxin A for the treatment of neurogenic bladder. *PM R*. 2019;11(2):192-200.
8. Asato F, Kanai A. Sensory blockade of S3 dermatome prevents pain during bladder catheterization. *Can J Anaesth*. 2001;48(4):379-382.
9. Overland MR, Leva NV, DiSandro M, Copp HL. Feasibility of awake intravesical botulinum toxin injection in pediatric neurogenic bladder. *J Urol*. 2022;208(3):702-710.

Do We Agree on Hematuria? Evaluating the Drinks Rating System

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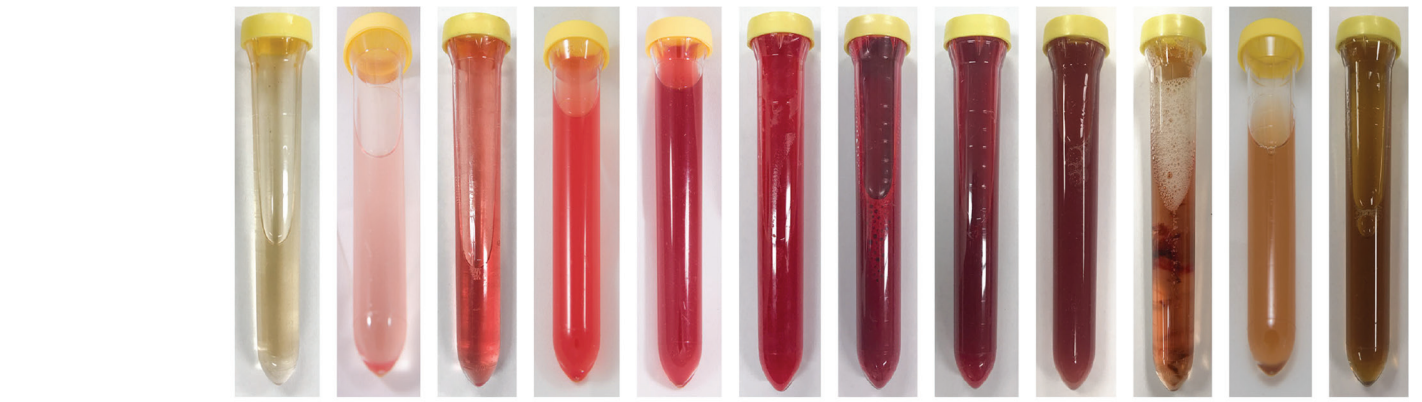

Figure 1. Twelve deidentified hematuric samples from inpatient and outpatient adult urology patients at Columbia University Medical Center, with mean severity scores for each corresponding sample.

Introduction

Gross hematuria (GH) is a common urological symptom of an array of underlying diseases, from urinary tract infection to bladder cancer.[1] As a result, GH is one of the most frequent reasons for a urological consult, second only to urinary calculi and lower urinary tract symptoms.[2] Despite this, there is no widely agreed upon classification system for GH used by providers, which makes communication about the appearance and severity of hematuria challenging. Investigators have attempted to develop methods to describe hematuria, yet the drinks rating system remains commonly used in practice, particularly among non-urological practitioners.[3-6] Nonetheless, this system has never been meaningfully validated, making its true utility unknown. This study aims to assess the performance of the drinks rating system among providers at an academic medical center.

Methods

Twelve hematuric urine samples were collected from adult urology patients (Figure 1). A survey using pictures and videos of the urine samples was distributed to various providers. Each survey included 8 randomly chosen samples. Participants were asked to provide a free-text description of the appearance of each urine sample prior to choosing a match from a predetermined list of 10 drink options: lemonade, amber, pink lemonade, rosé wine, fruit punch, cranberry juice, tea, red wine, cola, and tomato juice. Participants were also asked to rate the severity of hematuria on a 6-point scale from "no hematuria" to "severe" and if the sample contained clots. We used intra-class coefficient (ICC) to estimate the reliability of the drink descriptor and hematuria severity ratings across providers. We stratified ICC by level of training and specialty. The protocol was approved by the Columbia University Institutional Review Board.

Results

We received 105 survey responses for a response rate of 14.1%. Almost 80% of the respondents were physicians (n = 83). The majority of nonphysician participants were registered nurses (RNs; n = 18). Over half of the respondents reported internal medicine as their primary field (n = 54), and more than 35% were 30-40 years old.

Each sample was rated by an average of 67 providers using the ratings shown in the Table. Across all ratings, the most common was mild (22.4%) and least common was severe (12.5%). One hundred ninety-eight unique terms were provided across all samples (Figure 2). When describing samples in their own words, respondents commonly used the words "red," "pink," and "hematuria." The 10 most commonly used words are provided in the Table. Mean severity score was calculated for each sample and ranged from 0.0 (no hematuria) to 4.6 (severe); results

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Table. Survey responses

	Times used, No. (%)
Drink descriptors	
Lemonade	83 (10.4)
Amber	73 (9.1)
Pink lemonade	111 (13.9)
Rosé wine	92 (11.5)
Fruit punch	126 (15.8)
Cranberry juice	68 (8.5)
Tea	75 (9.4)
Red wine	57 (7.1)
Cola	26 (3.3)
Tomato juice	89 (11.1)
Severity ratings	
No hematuria	154 (19.2)
Mild	180 (22.4)
Mild-moderate	111 (13.8)
Moderate	134 (16.7)
Moderate-severe	124 (15.4)
Severe	100 (12.5)
Free-text word frequency	
Red	152 (8.2)
Pink	131 (7.1)
Hematuria	94 (5.1)
Light	89 (4.8)
Clear	83 (4.5)
Bloody	81 (4.4)
Urine	79 (4.3)
Yellow	77 (4.2)
Dark	74 (4.0)
Clots	72 (3.9)

Figure 2. Word cloud of written responses to describe appearance of hematuria. Word size reflects frequency of use.

are shown in Figure 1.

Selected ICC results are provided graphically in Figure 3. Overall inter-rater reliability for severity was good (ICC 0.75, 95% CI 0.57-0.91) and moderate for the drinks rating system (0.62 [0.42-0.85]).

Discussion

Despite being one of the most common reasons for urological consultation, there remains little standardization in the description of GH. A commonly used but unvalidated method for characterizing GH is to compare it to familiar drinks. Our study aimed to assess the agreement between providers in describing hematuria in appearances using the drinks rating system and in subjective severity.

Our observations support the need for a standardized hematuria scale, evidenced by the sheer number of words used to describe hematuria in the free-text portion of the survey (Figure 2). This highlights the lack of consensus regarding an accurate way to describe hematuria.

When asked to estimate the severity of GH, the ICCs were relatively high (ICC 0.75, 95% CI 0.57-0.91), while the ICCs for drink descriptor were almost entirely in the low-moderate to moderate range. As such, our findings highlight that conveying perceived severity is a more reliable way of communicating degree of hematuria compared to the drinks rating system. While groups of practitioners generally tend to agree on the clinical significance of hematuria, we observed differences among types of providers. Nonphysician providers were more likely to rate a particular sample as being more severe twice as often as physicians, despite both groups having similar internal reliability.

Systematic assessment of hematuria has received limited attention in the literature. Studies have previously explored GH assessment by color or severity but rarely both. One study created a point system based on the degree to which urine in catheter tubing obscured the Roman numeral "II" in increasingly large font with a corresponding blood concentration.[3] No assessment of reliability was performed. Other studies have utilized color swatch cards for comparison to hematuria.[4-6] Good reliability was found for a 6-color swatch card assessment.[4] In regard to severity, one study used a 5-point visual severity scale created by asking urologists how they would adjust continuous bladder irrigation if presented with a urine sample.[8] The resulting scale proved highly reliable among study participants, but due to a small study size (n = 43) and that over 50% of participants in the study were urological practitioners, generalizability to non-urological providers remained limited.[8]

Our study has some limitations. Due to the relatively small number of respondents, the 95% CI for all ICCs was wide. Despite this wide range, the broad conclusions remain the same: practitioners agree more on the severity of hematuria than they do on how to describe it using the drinks rating system. Another limitation is with the drinks rating system itself, specifically due to the large number of possible choices. In addition, the participants in this study were all providers at a single academic center. However, because most consults occur within an institution, the within-institution reliability is of greater relevance than that across institutions.

Our results suggest there is an opportunity to develop a standardized scale for describing hematuria which may help streamline communication about hematuria among health care providers across disciplines. While approaches such as swatch cards may be useful and reliable, a severity score requires no device or product and therefore has fewer barriers to implementation.

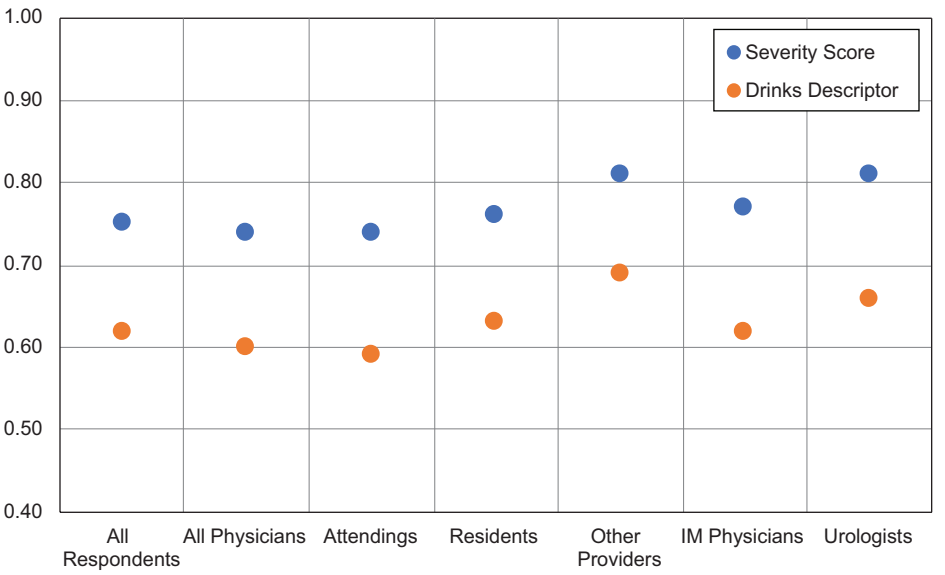

Figure 3. Selected intraclass correlation coefficient values for hematuria severity and categorical drink descriptor. IM indicates internal medicine physicians.

Conclusion

We found that practitioners tended to agree more on the subjective severity of hematuria than a description using a drinks rating scale. This suggests there are opportunities to standardize communication about hematuria and using a simple severity scale may effectively convey acuity during urological consultation. ■

1. Khadra MH, Pickard RS, Charlton M, Powell PH, Neal DE. A prospective analysis of 1,930 patients with hematuria to evaluate current diagnostic practice. *J Urol.* 2000;163(2):524-527.
2. Stoffel JT, Moinzadeh A, Hansen M. Identification of common themes from after-hour telephone calls made to urology residents. *Urology.* 2003;62(4):618-621.
3. Sakuma S, Fujita R, Komiya H. A novel method for evaluating and expressing the degree of macroscopic hematuria. *Int Urol Nephrol.* 2006;38(2):203-205.
4. Hageman N, Aronsen T, Tiselius HG. A simple device (Hemostick) for the standardized description of macroscopic haematuria: our initial experience. *Scand J Urol Nephrol.* 2006;40(2):149-154.
5. Lee JY, Chang JS, Koo KC, Lee SW, Choi YD, Cho KS. Hematuria grading scale: a new tool for gross hematuria. *Urology.* 2013;82(2):284-289.
6. Wong LM, Chum JM, Maddy P, Chan ST, Travis D, Lawrentschuk N. Creation and validation of a visual macroscopic hematuria scale for optimal communication and an objective hematuria index. *J Urol.* 2010;184(1):231-236.
7. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *J Chiropr Med.* 2016;15(2):155-163.
8. Stout TE, Borofsky M, Soubra A. A visual scale for improving communication when describing gross hematuria. *Urology.* 2021;148:32-36.

FROM THE RESIDENTS & FELLOWS COMMITTEE

Use of Artificial Intelligence in Urology

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The application of artificial intelligence (AI) in medicine has substantially grown in the past few years. Through a variety of applications, researchers are attempting to extend the use of AI to boost patient outcomes, save health care costs, and provide better patient care. Beginning in the 1970s, models were initially developed in the field of internal medicine to aid in the development of a clinical hypothesis or diagnosis based on previously recorded clinical data.[1] Today, we observe the extensive application of AI in a variety of medical disciplines, including arranging appointments or testing for patients, clinical apps suggesting diagnoses based on lab results and symptoms, and even robotic surgical systems in the operating room.

Outside of hospitals, AI is also utilized when assessing wearable technology. The Apple Watch can now detect abnormal cardiac rhythms and blood oxygen levels in newer models. For patients with epilepsy, the U.S. Food and Drug Administration approved the use of Embrace and Empatica wristbands in 2018. The bracelet uses electrodermal sensors to detect generalized tonic-clonic seizures and transmits this information together with the patient's location to caregivers and medical professionals.[2]

A number of urology subspecialties have begun to advance and integrate AI into clinical practice. AI has been used in endourology to both predict stone composition and identify stones on CT and US imaging. In 2019 Parakh and colleagues were able to develop a neural network to identify a stone in the urinary system with 90% accuracy.[3] A total of 535 adult individuals who were suspected of having urolithiasis were included in this retrospective analysis. The neural network assessed a total of 100 scans in order to accurately map the urinary tract and then the presence of a stone.

In pediatric urology, Bägli and colleagues utilized computerized artificial neural networks to assess outcomes after pyeloplasty using US imaging.[4] All US scans had been assessed by a single radiologist, and a 4-layer network representing the 4 possible outcomes—significantly improved, improved, same, and worse—was built. In each of the 16 cases, the artificial neural network successfully identified the sonographic outcomes following pyeloplasty. As we observe the incorporation of AI in benign prostatic hyperplasia care, urologic oncology, urogynecology, as well as renal transplant, urologists continue to remain at the forefront of innovation in the field of AI.

A paradigm shift toward the use of AI in clinical decision-making and surgical practice is now occurring in the medical field.[5] I believe that AI will progressively be incorporated into clinical recommendations as we continue to improve it and apply it to surgical practice. With greater technological advancements and continued research, it is surreal to be part of the growing field of urology. ■

1. Schwartz WB, Patil RS, Szolovits P. Artificial intelligence in medicine. *N Engl J Med.* 1987;316(11):685-688.
2. Regalia G, Onorati F, Lai M, Caborni C, Picard RW. Multimodal wrist-worn devices for seizure detection and advancing research: focus on the Empatica wristbands. *Epilepsy Res.* 2019;153:79-82.
3. Parakh A, Lee H, Lee J, Eisner BH, Sahani DV, Do S. Urinary stone detection on CT images using deep convolutional neural networks: evaluation of model performance and generalization. *Radiol Artif Intell.* 2019;1(4):e180066.
4. Bägli DJ, Agarwal SK, Venkateswaran S, et al. Artificial neural networks in pediatric urology: prediction of sonographic outcome following pyeloplasty. *J Urol.* 1998;160(3 Pt 2):980-983.
5. Shah M, Naik N, Somani BK, Hameed BM. Artificial intelligence (AI) in urology—current use and future directions: an iTRUE study. *Turk J Urol.* 2020;46(Suppl 1):S27-S39.

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Treating Metastatic Castrate-sensitive Prostate Cancer: Beyond Androgen Deprivation Therapy

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Androgen Deprivation Therapy

Despite a reduction in the overall incidence, the 2004-2018 SEER (Surveillance, Epidemiology, and End Results) data reveal a concerning trend of increase in the incidence of metastatic prostate cancer. It is crucial to understand the disease dynamics and the multitude of treatment options available to manage this issue effectively. Despite the advent of various novel hormonal and chemotherapy options, androgen deprivation therapy (ADT) still has an important role in the treatment of metastatic castrate-sensitive prostate cancer (mCSPC). Both surgical and medical castration are effective ADT methods with their own advantages. Attempts at decreasing toxicity (via intermittent ADT) have been unsuccessful, and continuous ADT is recommended for all patients with mCSPC. The newer gonadotropin-releasing hormone antagonists are an effective ADT method with unique advantages. They do not need a short duration of antiandrogen therapy to prevent a testosterone flare, have a rapid suppression of testosterone levels, and are associated with a decreased risk of cardiovascular disease. Despite the efficacy of ADT, a majority of mCSPC patients eventually develop ADT resistance. Addition of various novel hormonal therapy (NHT) options, like abiraterone, second-generation antiandrogens, and docetax, have been evaluated to improve outcomes in mCSPC.

Doublet Combination Therapy

Doublet therapy with docetaxel or NHT plus ADT has been proven to be superior to ADT monotherapy. While addition of docetaxel in GETUG-15 demonstrated no overall survival (OS) benefit (HR 1.01),[1] CHAARTED demonstrated an OS benefit (13.6 months, HR 0.61).[2] Preplanned subgroup analysis revealed that OS benefit with docetaxel (17 months, HR 0.63) was restricted only to patients with high-volume disease (defined as visceral metastases, and/or 4 bone metastases, 1 outside vertebral body or pelvis). STAMPEDE (arm C) refuted the prior data and demonstrated an OS benefit with the addition of docetaxel to ADT (16 months, HR 0.81) irrespective of the metastatic burden.[3]

LATITUDE demonstrated that abiraterone plus ADT resulted in an OS benefit (16 months, HR 0.66) in high-risk mCSPC.[4] High-risk status

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was defined as the presence of 2 of the 3 features (≥3 bone lesions, Gleason score ≥8, or visceral metastases). Interestingly, STAMPEDE (arm G) demonstrated that doublet therapy with abiraterone was associated with an OS benefit (33 months, HR 0.60) irrespective of the tumor burden.[5] Direct randomized comparative analysis of data from the 2 STAMPEDE trial arms indicates that abiraterone is a safe and effective alternative to docetaxel (irrespective of tumor burden). Unlike the first-generation antiandrogens, second-generation antiandrogens have an efficient role in mCSPC. Doublet therapy with enzalutamide resulted in an OS benefit in ENZAMET (HR 0.70)[6] and ARCHES (HR 0.66).[7] Apalutamide plus ADT was found to be effective in TITAN, with an OS benefit (HR 0.65).[8]

Triplet Combination Therapy

The incremental benefit of doublet combination therapy (ADT plus chemotherapy or NHT) over ADT has subsequently led to evaluation of triplet combination therapy (ADT plus chemotherapy plus NHT). Concurrent docetaxel and enzalutamide resulted in increased toxicity in ENZAMET,[6] but post hoc analysis of ARCHES reveals that sequential enzalutamide after docetaxel was a safe approach, with further data needed to determine efficacy.[7] ARASENS demonstrated a significantly longer OS with darolutamide plus ADT and docetaxel (HR 0.68) when compared to ADT and docetaxel.[9] Outcome analysis based on tumor burden is still awaited. De novo mCSPC patients on PEACE-1 treated with abiraterone plus ADT and docetaxel demonstrated an OS benefit (HR 0.75) over ADT plus docetaxel.[10] Preplanned subgroup analysis reveals that OS benefit was statistically significant in patients with high metastatic burden and immature data to demonstrate a similar benefit in patients with low-burden disease. Based on these data, darolutamide-based triplet therapy has been Food and Drug Administration approved, and both darolutamide- and abiraterone-based triplet therapies feature in the National Comprehensive Cancer Network guidelines (for high-burden mCSPC).

High- and Low-Burden mCSPC

Treatment based on the volume of metastatic disease in mCSPC remains controversial. Table 1 summarizes the important randomized clinical trials in mCSPC, and Table 2 summarizes stratified outcomes based on tumor burden. The high-volume CHAARTED definition and high-risk LATITUDE definition closely resemble a population that has been categorized as high burden. The lack of OS benefit in the CHAARTED and GETUG-15 trials could be attributed to the difference in sample size and proportion of de novo vs recurrent castrate-sensitive prostate cancer (which have varied outcomes). The consistent benefit irrespective of tumor burden in the STAMPEDE trials and other trials establishes the efficacy of doublet therapy in all mCSPC patients. Further clinical data from ARASENS and PEACE-1 will delineate the role of triplet therapy in low-burden mCSPC. While there is no proven role of radiotherapy to the prostate in all mCSPC patients, STAMPEDE demonstrated an 8% improvement in 3-year OS in oligometastatic mCSPC (<5 bone metastases).[11] PEACE-1 demonstrated the safety of radiotherapy in the triplet combination as well, but further follow-up is required to determine their clinical significance.

Points to Consider

- Despite the increased sensitivity of prostate-specific membrane antigen positron emission tomography imaging, CT scans and bone scans remain the diagnostic modality of choice to assess disease burden and metastases.
- American Society of Clinical Oncology guidelines recommend against the routine use of bone-modifying agents in mCSPC. Their role is restricted to patients with osteoporosis or high fracture risk.
- Despite their efficacy, NHTs result in increased financial toxicity and a disproportionate impact in older age and Black patients, resulting in medication nonadherence.[12]

Conclusion

Treatment paradigms of mCSPC have moved beyond ADT monotherapy, and doublet and triplet

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Table 1. Randomized Controlled Trials Evaluating Doublet and Triplet Therapy in Metastatic Castrate-sensitive Prostate Cancer

Intervention	Control	Trial	OS	HR (95% CI)
ADT + docetaxel	ADT	CHAARTED[2]	57.6 vs 47.2 mo	0.61 (0.47-0.80)
		STAMPEDE[3]	59.1 vs 43 mo	0.81 (0.69-0.95)
		GETUG-15[1]	58.9 vs 54.2 mo	1.01 (0.75-1.36)
ADT + abiraterone	ADT	LATITUDE[4]	53.3 vs 36.5 mo	0.66 (0.56-0.78)
		STAMPEDE[5]	79 vs 46 mo	0.60 (0.50-0.71)
ADT + enzalutamide	ADT	ARCHES[7]	71% vs 57% (4-y OS)	0.66 (0.53-0.81)
		ENZAMET[6]	67% vs 57% (5-y OS)	0.70 (0.58-0.84)
ADT + apalutamide	ADT	TITAN[8]	65.2% vs 37.9% (4-y OS)	0.65 (0.53-0.79)
ADT + darolutamide + docetaxel	ADT + docetaxel	ARASENS[9]	62.7% vs 50.4% (4-y OS)	0.68 (0.57-0.80)
ADT + abiraterone + docetaxel		PEACE-1[10]	NR vs 4.43 y	0.75 (0.59-0.95)

Abbreviations: ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival.

Table 2. Stratification of Metastatic Castrate-sensitive Prostate Cancer Randomized, Controlled Trial Outcomes Based on Metastatic Burden

Intervention	Trial	High tumor burden		Low tumor burden	
		OS	HR	OS	HR (95% CI)
ADT + docetaxel	CHAARTED[a]	51.2 vs 34.4 mo	0.63 (0.50-0.79)	63.5 mo vs NR	1.04 (0.70-1.55)
	STAMPEDE (C arm)	39.9 vs 35 mo	0.81 (0.64-1.02)	93.2 vs 76.7 mo	0.76 (0.54-1.07)
ADT + abiraterone	LATITUDE[b]	49.7 vs 33.3 mo	0.62 (0.52-0.78)	93.2 vs 76.7 mo	0.76 (0.54-1.07)
	STAMPEDE (G arm)	49% vs 28% (5-y OS)	0.54 (0.43-0.69)	72% vs 55% (5-y OS)	0.54 (0.40-0.74)
ADT + enzalutamide	ENZAMET	55% vs 49% (5-y OS)	0.79 (0.63-0.98)	80% vs 66% (5-y OS)	0.54 (0.39-0.74)
ADT + apalutamide	TITAN	NR vs 34 mo	0.57 (0.45-0.73)	NR vs NR	0.76 (0.54-1.07)
ADT + abiraterone + docetaxel	PEACE-1	4.1 vs 1.6 y	0.47 (0.30-0.72)	NR vs 2.7 y	0.58 (0.29-1.15)

Abbreviations: ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival.
[a] CHAARTED high-volume definition: visceral metastases, and/or 4 bone metastases (at least 1 outside the vertebral bodies and pelvis).
[b] LATITUDE high-risk definition: presence of 2 of 3 high risk features (≥3 bone lesions, Gleason score ≥8, or visceral metastases).

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combination therapies have established themselves as safer and more effective interventions across clinical and quality of life end points. The Figure depicts a proposed treatment algorithm for mCSPC. For all high-burden mCSPC, triplet combination therapy is recommended over doublet therapy (if tolerable). For low-burden mCSPC, triplet combination therapy can be considered in a young, fit individual, with doublet therapy and consideration of radiation to the prostate being an acceptable alternative. Shared decision-making with the patients, financial toxicity of NHTs, and potential clinical trial eligibility will be critical in choosing the right treatment. ■

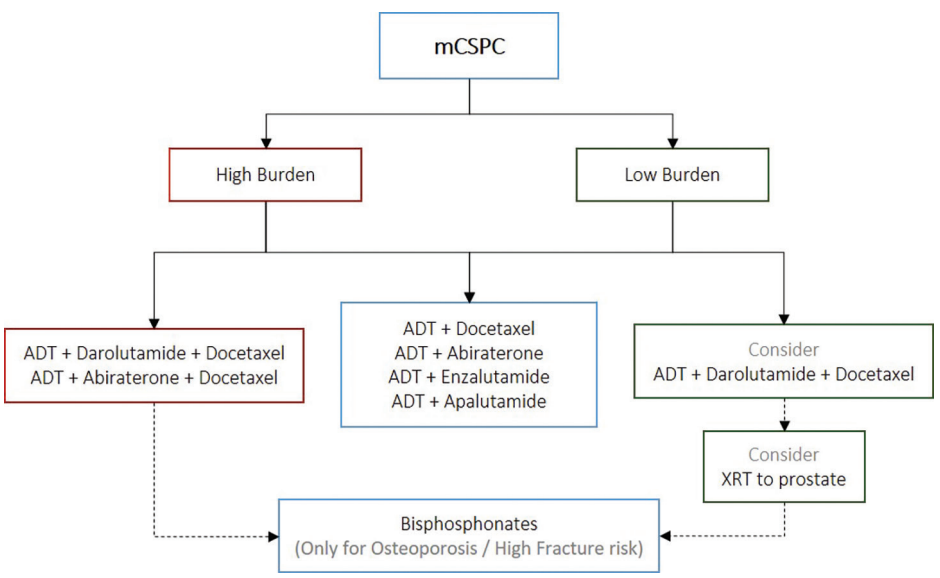

Figure. Treatment algorithm. ADT indicates androgen deprivation therapy; mCSPC, metastatic castrate-sensitive prostate cancer; XRT, radiation therapy.

1. Gravis G, Fizazi K, Joly F, et al. Androgen-deprivation therapy alone or with docetaxel in non-castrate metastatic prostate cancer (GETUG-AFU 15): a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2013;14(2):149-158.
2. Sweeney CJ, Chen Y-H, Carducci M, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. *N Engl J Med.* 2015;373(8):737-746.
3. James ND, Sydes MR, Clarke NW, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet.* 2016;387(10024):1163-1177.
4. Fizazi K, Tran N, Fein L, et al. Abiraterone plus prednisone in metastatic, castration-sensitive prostate cancer. *N Engl J Med.* 2017;377(4):352-360.
5. James ND, de Bono JS, Spears MR, et al. Abiraterone for prostate cancer not previously treated with hormone therapy. *N Engl J Med.* 2017;377(4):338-351.
6. Davis ID, Martin AJ, Stockler MR, et al. Enzalutamide with standard first-line therapy in metastatic prostate cancer. *N Engl J Med.* 2019;381(2):121-131.
7. Armstrong AJ, Szmulewitz RZ, Petrylak DP, et al. ARCHES: a randomized, phase III study of androgen deprivation therapy with enzalutamide or placebo in men with metastatic hormone-sensitive prostate cancer. *J Clin Oncol.* 2019;37(32):2974-2986.
8. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for metastatic, castration-sensitive prostate cancer. *N Engl J Med.* 2019;381(1):13-24.
9. Smith MR, Hussain M, Saad F, et al. Darolutamide and survival in metastatic, hormone-sensitive prostate cancer. *N Engl J Med.* 2022;386(12):1132-1142.
10. Fizazi K, Foulon S, Carles J, et al. Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design. *Lancet.* 2022;399(10336):1695-1707.
11. Parker CC, James ND, Brawley CD, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. *Lancet.* 2018;392(10162):2353-2366.
12. Joyce DD, Sharma V, Jiang DH, et al. Out-of-pocket cost burden associated with contemporary management of advanced prostate cancer among commercially insured patients. *J Urol.* 2022;208(5):987-996.

High Infertility Rates and Pregnancy Complications in Female Physicians Indicate a Need for Culture Change

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Female physicians are at increased risk of infertility, miscarriage, and pregnancy complications due to a multitude of factors. Physicians undertake long training and experience stressful work environments during optimal childbearing years. Female physicians commonly experience maternal discrimination,[1,2] and pregnancy complications and negative influences on family planning represent work-home conflicts that may increase the risk of burnout and career dissatisfaction.[3]

Prior reports indicating female physicians have children at an older age[4-6] and have fewer children[4,7] are limited by small sample sizes or are constrained to certain specialties. To identify contemporary pregnancy trends in a large sample of female physicians, an anonymous electronic survey querying pregnancy demographics and complications, infertility diagnosis and treatment, workplace environment, and prior education on these topics was distributed through private female physician social media groups. The results were compared to general population data[8-10] and between medical and surgical specialties.

A total of 4,533 female physicians completed the survey: 1,089 surgeons and 3,444 medical specialists. Compared with the general population, female physicians had children significantly later in life (31.8 vs 23.6 years; $P < .0001$), were more likely to have had a miscarriage (40.7% vs 19.7%; $P < .0001$), to have undergone infertility evaluation (35.2% vs 8.8%; $P < .0001$) or infertility treatment (28.1% vs 12.7%; $P < .0001$), or to have had a pre-term birth (20.4% vs 10.2%; $P < .0001$).

Forty-two percent of those surveyed were discouraged from starting a family during training or practice, 49% experienced negative workplace attitudes regarding pregnancy, and only 8% received education during medical training regarding the risks of delaying pregnancy. Those who received education were more likely to have pregnancies earlier in their career and were less likely to have had a miscarriage (33% vs 41%, $P = .0017$), infertility evaluation (27% vs 35%, $P = .0012$), or infertility treatment (23% vs 29%, $P = .0179$).

Compared with medical specialists, surgeons reported fewer children, older age at first pregnancy, longer working hours, and more pre-term births. Surgeons also reported less support for pregnancy and breastfeeding (58% vs 66%, $P < .0001$) and shorter maternity leave (8.6 vs 10.9 weeks, $P < .0001$) compared with non-surgeons. On multivariate analysis, with every hour more worked per week, there was a 1% higher chance of having a major pregnancy complication ($P < .001$).

> "These findings highlight that female physicians have a significantly greater incidence of miscarriage, infertility, and pregnancy complications than the general population."

These findings highlight that female physicians have a significantly greater incidence of miscarriage, infertility, and pregnancy complications than the general population. Compared with non-surgeons, surgeons are of even older maternal age and are more likely

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HIGH INFERTILITY RATES AND PREGNANCY COMPLICATIONS

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to experience discrimination in the workplace regarding pregnancy, breastfeeding, and family planning. Finally, and most importantly, education on the consequences of delaying pregnancy during training was found to mitigate many of these risks.

It is predictable that female physicians often find themselves delaying having children.[4-6] Physicians at all levels of training and practice often face pregnancy-related discrimination, stringent board training requirements, limited workforce redundancy, and brief parental leaves.[11,12] Guilt related to burdening colleagues who may be asked to cover leave and pressure to preserve professional reputation may also dissuade physicians from starting a family.

Over 40% of respondents were discouraged from starting a family and nearly 50% experienced negative workplace attitudes regarding pregnancy. These results reflect a pervasive culture throughout medicine that has changed very little over the past decade. Prior studies found only 16% of physicians reported their workplace to be supportive of pregnancy,[13] 36% of residency program directors actively discouraged pregnancy during residency,[11] and among practicing physician mothers, 78% reported gender and/or maternal discrimination.[1]

The culture of medicine and surgery must evolve to better support family planning and childbearing for physicians. Paid parental leave of adequate duration is a clear metric of parental support. Adequate paternal leave is associated with reduced post-partum depression, infant mortality, and maternal rehospitalization.[14] In a survey of 243 female urologists, those who took 9 weeks or longer of maternity leave were 3.8 times more likely to report satisfaction.[15] Despite these facts, over 70% of academic medical centers offer less than 6 weeks of paid parental leave.[16]

Lower rates of miscarriage and infertility were reported in those who received education while in training regarding the risks of delaying pregnancy. Such curricula should be provided during medical school and early residency to encourage trainees to make evidence-based decisions about timing of family planning and allow them to explore options for fertility preservation. Adequate and supported parental leave and early education of trainees are only 2 facets of culture change. Building on the work of recent studies,[4,17,18] key practical recommendations for system improvement are outlined in the Figure.

> "The culture of medicine and surgery must evolve to better support family planning and childbearing for physicians."

These changes would improve the health and well-being of childbearing female physicians and may reduce burnout seen in those suffering from infertility, pregnancy complications, and miscarriages.[19] As physician burnout is increasingly recognized for its adverse impact on quality of patient care, professionalism, physicians' own care and safety, and the viability of health care systems,[20] efforts to improve physician wellness must consider improved family benefits, education, and support for family planning for female physicians. ■

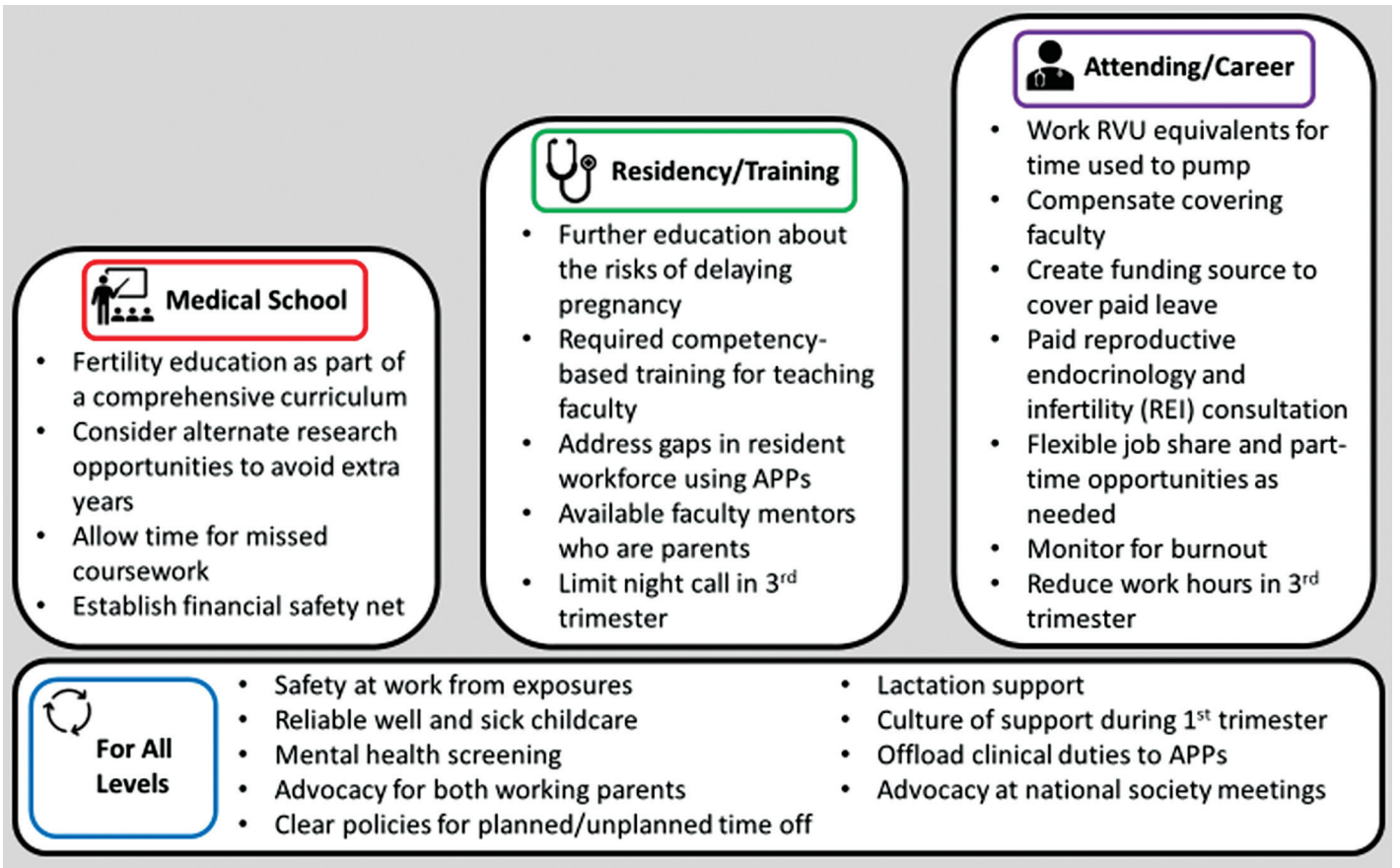

Figure. Solutions for culture change across all levels of medical training/practice. APP indicates advanced practice provider; RVU, relative work unit.

1. Adesoye T, Mangurian C, Choo EK, et al. Perceived discrimination experienced by physician mothers and desired workplace changes: a cross-sectional survey. *JAMA Intern Med.* 2017;177(7):1033-1036.
2. Halley MC, Rustagi AS, Torres JS, et al. Physician mothers' experience of workplace discrimination: a qualitative analysis. *BMJ.* 2018;363:k4926.
3. West CP, Dyrbye LN, Shanafelt TD. Physician burnout: contributors, consequences and solutions. *J Intern Med.* 2018;283(6):516-529.
4. Rangel EL, Castillo-Angeles M, Easter SR, et al. Incidence of infertility and pregnancy complications in US female surgeons. *JAMA Surg.* 2021;156(10):905-915.
5. Stentz NC, Griffith KA, Perkins E, Jones RD, Jagsi R. Fertility and childbearing among American female physicians. *J Women's Health (Larchmt).* 2016;25(10):1059-1065.
6. Cusimano MC, Baxter NN, Sutradhar R, et al. Delay of pregnancy among physicians vs nonphysicians. *JAMA Intern Med.* 2021;181(7):905-912.
7. Phillips EA, Nimeh T, Braga J, Lerner LB. Does a surgical career affect a woman's childbearing and fertility? A report on pregnancy and fertility trends among female surgeons. *J Am Coll Surg.* 2014;219(5):944-950.
8. U.S. Department of Health and Human Services. *National Survey of Family Growth 2015-2017.* Centers for Disease Control and Prevention; 2018. https://www.cdc.gov/nchs/data/nsfg/NSFG_2015_2017_UserGuide_MainText.pdf.
9. Rossen LM, Ahrens KA, Branum AM. Trends in risk of pregnancy loss among US women, 1990-2011. *Paediatr Perinat Epidemiol.* 2018;32(1):19-29.
10. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK. Births: Final data for 2019. *Natl Vital Stat Rep.* 2021;70(2):1-51.
11. Cole S, Arnold M, Sanderson A, Cupp C. Pregnancy during otolaryngology residency: experience and recommendations. *Am Surg.* 2009;75(5):411-415.
12. Pearson ACS, Dodd SE, Kraus MB, et al. Pilot survey of female anesthesiologists' childbearing and parental leave experiences. *Anesth Analg.* 2019;128(6):e109-e112.
13. Sinal S, Weavil P, Camp MG. Survey of women physicians on issues relating to pregnancy during a medical career. *J Med Educ.* 1988;63(7):531-538.
14. Van Niel MS, Bhatia R, Riano NS, et al The impact of paid maternity leave on the mental and physical health of mothers and children: a review of the literature and policy implications. *Harv Rev Psychiatry.* 2020;28(2):113-126.
15. Lerner LB, Baltrushes RJ, Stolzmann KL, Garshick E. Satisfaction of women urologists with maternity leave and childbirth timing. *J Urol.* 2010;183(1):282-286.
16. Itum DS, Oltmann SC, Choti MA, Piper HG. Access to paid parental leave for academic surgeons. *J Surg Res.* 2019;233:144-148.
17. Durfey SNM, White J, Adashi EY. Pregnancy and parenting in medical school: highlighting the need for data and support. *Acad Med.* 2021;96(9):1259-1262.
18. Bamdad MC, Hughes DT, Englesbe M. Safe and supported pregnancy: a call to action for surgery chairs and program directors. *Ann Surg.* 2022;275(1):e1-e2.
19. Győrffy Z, Dweik D, Girasek E. Reproductive health and burn-out among female physicians: nationwide, representative study from Hungary. *BMC Womens Health.* 2014;14:121.
20. West CP, Dyrbye LN, Erwin PJ, Shanafelt TD. Interventions to prevent and reduce physician burnout: a systematic review and meta-analysis. *Lancet.* 2016;388(10057):2272-2281.

AUA Patient Perspectives Program

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Is there a role for including patients and patient advocates in professional society meetings like the annual AUA meeting? And what should that role be? This article discusses my experience as an inaugural presenter in the AUA Patient Perspectives Program at the annual AUA meeting and provides my answers to those questions.

The AUA in 2021 announced its inaugural Patient Perspectives Program at its annual meeting as "an opportunity for patients and/or patient advocates to address the disparities that may exist between urological professionals' recommended treatment plans and patients' quality-of-life preferences" and for "patient advocates and urologic healthcare providers to improve communication and seek to close the gap between best medical treatment practices and patient quality-of-life considerations." Urologic oncologist Dr Angie Smith reached out in June 2021 to ask if I was interested in entering a submission for the inaugural program. Given my passion for patient-researcher partnerships and keen interest in attending professional society meetings, I was intrigued by the possibilities. I also felt strongly that the work that she, fellow urologic oncologist Dr John Gore, Bladder Cancer Advocacy Network Director of Education and Advocacy Stephanie Chisolm, and I had done deserved a wider audience. Therefore, I submitted the required abstract.

Our project met the research on patient-specific urological health issue criterion. We had constructed and conducted a patient survey using the BCAN (Bladder Cancer Advocacy Network) Patient Survey Network to query patient preferences regarding study design, outcomes, and conduct between radical cystectomy and bladder-preserving chemoradiation. In my role, I applied lived and research advocacy experiences to provide critical feedback to design a survey that queries patient preferences regarding study design, outcomes, and conduct. That feedback included the addition of sexual and bowel function outcomes and logistical burden (eg, transportation, time off work), order of listed patient outcomes, word selection (eg, urinary symptoms changed to urinary function), and clarification that cystectomy may also include additional organ removal (eg, prostate, uterus, vagina).

The template was straightforward, given my advocacy and science experience: Introduction, Materials and Methods, Results, and Conclusion. With the generous support of my colleagues (particularly, Dr Smith), the required 2,280-character abstract was prepared. Character limits were somewhat familiar to me from my advocacy work, but I had no experience submitting content with character counts myself. I learned quickly how to reveal word and character count (with and without spaces!) using Microsoft Word.

In July 2021, my abstract was accepted for the Las Vegas meeting in September. I made travel arrangements and awaited guidance. However, the Delta variant of COVID took hold and it became clear that an in-person meeting was not possible. The meeting itself was recalibrated to a virtual format, but the Patient Perspectives Program was delayed to the following year.

In February 2022, I was advised that presentations would be held as planned during the May New Orleans meeting. Logistical communications in February were followed in March by a draft abstract for *AUANews*. I was also asked to pre-record my presentation in late March. All was well until I noticed the last line of instructions:

"It may be time to consider including patients as panel members and presenters in select sessions and including 1 or more patients in program planning."

Your other slides [after title slide] "should be your virtual poster from which you will present."

I had forgotten (or missed) the requirement for a poster! I had seen dozens of posters during my advocacy work and knew how difficult a poster would be to construct using PowerPoint. I desperately needed a template and reached out to my AUA contact for one. I received a screenshot of a typical scientific poster and later a blank screenshot with a poster outline. Nothing editable.

Undeterred, I reached out to my researcher colleagues who are in the business of routinely generating posters. Dr Smith came to my rescue with an editable PowerPoint template. I then leveraged the prepared poster to create related slides and record my presentation. A bit of a perfectionist about recorded presentations and with no video editing software option, I had to repeatedly re-record to get 1 acceptable 6-minute presentation. I had plenty of practice.

Nine awardees, including me, arrived in May at the Dome Arena (2 additional awardees had pre-recorded presentations). We presented to about 25 people in a somewhat busy and noisy setting open to the exhibit hall but off to the side. Acoustics reflected the inherent challenges of the setting: acceptable though not optimal.

Presentations were followed by Q&A, where I received one very technical, though logical, design question on the planned clinical trial. It was well beyond my capabilities and role. I deferred to my clinician colleagues who had been very generous with their time and were in the audience. Dr Gore came to the rescue.

After debriefing with AUA staff and connecting with the other attendees, I joined sessions focused on my bladder cancer research advocacy context and networked with research colleagues. As my second in-person meeting post-COVID, it was exciting and meant a lot to see people in person despite my KN95 mask.

The program evolved in its second year. Universal poster creation challenges led to an AUA decision to remove them from the 2023 process. The abstract outline was modified to be less "researchy" and more familiar to patients. While not completely successful, these improvements were directionally on target and more patient-friendly.

"Discussions on patient engagement goals and exploration of how to optimize that engagement would be very productive and illuminating. It may be time to consider including patients as panel members and presenters in select sessions and including 1 or more patients in program planning."

Going forward, a higher level of patient engagement in the design and execution of the program should be considered. The goals and submission collateral should be recalibrated with patient partner input to ensure alignment with the intent and create entry collateral consistent with the skills of patient partners. Discussions on patient engagement goals and exploration of how to optimize that engagement would be very productive and illuminating. It may be time to consider including patients as panel members and presenters in select sessions and including 1 or more patients in program planning. This would better anchor the goals and outcomes of the meeting to the real-world challenges of facing off to patients and advancing urology through research and clinical trials. Contexts which have taken these steps have found that they pay significant dividends. ■

AUA Patient Perspectives Demonstrates Urology's Commitment to Empowering Patients

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NYU Langone Health, New York

In 2017, I underwent gender affirming phalloplasty after years of planning and waiting. Prior to 2017, the closest surgeon was hundreds of miles away from the typically health care–saturated New York City. I was lucky to live there and gain access to care at that time, as many parts of the United States still do not have genital gender affirming surgeons 5 years later.[1] Beyond distance, I was experiencing a more intractable barrier to care: unaddressed questions about the patient experience of surgery. I worked in health care and did a deep dive through the clinical literature and online peer support groups. Technical details and individual narratives about the recovery process helped me decide that surgery was the right choice for me, yet despite my overall certainty about surgery, there were still aspects of my surgical decision-making which felt like throwing a dart at the board. I had benefited from many informal patient-led efforts to collect reviews of surgeons and techniques, yet I knew that this was not comparable with an evidence-based medicine approach. Robust information about the patient experience of surgery was a resource I needed, but it was not present in the literature.[2]

These barriers motivated me to create peer health education resources, undertake gender affirming surgery research, and now study medicine as a first-year student at the University of Michigan Medical School. I experienced health care impacted by a "literature gap," and like many other transgender people, this experience was further compounded by occasional mistreatment in health care settings, the downstream effects of social stigma,[3] and lack of gender affirming care content in medical education.[4] When I set out on this path, I believed that if I didn't create the evidence-based care my community needed, no one in the institution of medicine ever would. I hear this same refrain from the incredible group of transgender medical trainees and junior researchers I am in contact with: we need to take care of each other, as the institution had not demonstrated a capacity to take care of us.

I still believe that increasing transgender and nonbinary-identified leadership in academic medicine will bring vital skills and energy; however, I'm starting to change my narrative about baseline institutional capacity. The surgical care I received as a patient has been impeccable, a truth about the commitment of the surgeons and care providers involved, which now lives in my body. The quality of this care, and the compassion it was delivered with, is what grants me the personal well-being needed to sustainably return this care to my future patients. Beyond the joy medicine has granted me in my own body, I've had the honor to begin research work I want to see in the world now, rather than delaying for years of training and gaining institutional access.

In 2021, I joined with urological surgeons and researchers at the TRANS-ARC summit (www.trans-arc.org), a Eugene Washington Engagement Award funded project of the Patient-Centered Outcomes Research Institute. We convened an engagement conference which created comparative effectiveness research questions sourced from a diverse group of patients and stakeholders. Providing researchers with these questions is the first step to using the resources of academic medicine to enrich critically needed care, but more fundamental to my own intentions, it allowed transgender people to use their voices to participate in the care of each other. Dr Geolani Dy, the project lead, alongside her collaborators in academic medicine, had labored through the grant writing, planning, convening, and report writing process with this express goal in mind. We transgender people need to take care of each other, and through TRANS-ARC, I have learned that the institution has the capacity to support this.

> "The surgical care I received as a patient has been impeccable, a truth about the commitment of the surgeons and care providers involved, which now lives in my body."

Figure. Gaines Blasdel presents on TRANS-ARC at the Patient Perspectives Program at AUA2022.

When I submitted a presentation on our work to the AUA Patient Perspectives program, I hoped that urologists working with other populations could learn from our successful initiative,[5] and understood that urology was a field with many foundational patient-centered engagement initiatives to learn from.[6] I was supported by the AUA, which served as a fantastic partner in guiding the process, ensuring that attending and presenting was stress-free. When meeting the additional presenters, I was struck by the many pairs of clinician-investigators with their patient-advocate colleagues, collaborators like Dr Dy and myself, presenting on similar work in diverse fields. The care and support of these institutional investigators for their peer-advocate partners was palpable in the time leading up to the presentations. During the session, I was further moved by how thoughtful and engaged the AUA attendees were. I saw reflections of the collaborative future being built with TRANS-ARC, which was then refracted and magnified through the excitement of the diverse urologists in the audience.

In addition to witnessing the wide buy-in of urology to the importance of patient perspectives, an unexpected benefit was fostering solidarity with groups affected by other conditions. In particular,

> "During the session, I was further moved by how thoughtful and engaged the AUA attendees were."

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AUA PATIENT PERSPECTIVES DEMONSTRATES UROLOGY'S COMMITMENT

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Tight Lipped (https://www.tightlipped.org/), a vulvovaginal and pelvic pain advocacy group, was working on overlapping issues. Our respective clinical diagnoses were each recently moved from the chapter on mental and behavioral disorders in ICD (International Classification of Disease)-10 to a chapter on conditions related to sexual health in ICD-11.[7] While it is materially useful to connect and create specific, cross-applicable resources on pathologization and access to care, it was also meaningful to have a group of fellow travelers building many of the same bridges. In addition to the support of the field of urology, patient groups supporting each other's initiatives and gaining traction together will make a big difference. At the AUA Patient Perspectives session, it was clear that urology is a field with a commitment to empowering patients to be a partner in the future of academic medicine. ■

1. Kang CO, Kim E, Cuccolo N, et al. A critical assessment of the transgender health care workforce in the United States and the capacity to deliver gender-affirming bottom surgery. *Ann Plast Surg.* 2022;89(1):100-104.
2. Clennon EK, Martin LH, Fadich SK, et al. Community engagement and patient-centered implementation of patient-reported outcome measures (PROMs) in gender affirming surgery: a systematic review. *Curr Sex Health Rep.* 2022;14(1):17-29.
3. Poteat T, German D, Kerrigan D. Managing uncertainty: a grounded theory of stigma in transgender health care encounters. *Soc Sci Med.* 2013;84:22-29.
4. Nolan IT, Blasdel G, Dubin SN, Goetz TG, Greene RE, Morrison SD. Current state of transgender medical education in the United States and Canada: update to a scoping review. *J Med Educ Curric Dev.* 2020;7:238212052093481.
5. Dy GW, Blasdel G, Downing JM. Centering transgender and nonbinary voices in genital gender-affirming surgery research prioritization. *JAMA Surg.* 2022;157(7):628.
6. Smith AB, Chisolm S, Deal A, et al. Patient-centered prioritization of bladder cancer research. *Cancer.* 2018;124(15):3136-3144.
7. World Health Organization. *ICD-11 for Mortality and Morbidity Statistics.* World Health Organization; 2018. https://icd.who.int/browse11/l-m/en.

CASE REPORT

Double-graft Urethroplasty: Surgical Technique and Outcomes

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Introduction

Urethral stricture is a pathology often complex and difficult to manage. Various techniques have been developed to treat it, ranging from primary anastomosis to tissue flaps and grafts.[1] Traditionally, short-segment obliterative bulbar strictures (<2 cm) are managed by excision and end-to-end anastomosis urethroplasty. However, bulbar urethral strictures (>2 cm) that are not amenable to end-to-end anastomosis urethroplasty can be managed by augmentation urethroplasty.[2] Currently, the preferred tissue for grafts is the oral mucosa due to its excellent physical characteristics and because harvesting is simple and with low rates of morbidity.[1] A combined dorsal and ventral onlay augmentation urethroplasty technique was described by Palminteri et al for bulbar urethral reconstruction.[3]

Clinical Case

In 2021, a 67-year-old male with a history of open prostatectomy presented with a recurrence of urinary symptoms associated with an epididymo-orchitis episode and urinary retention during the early postoperative period. In emergency care and given the impossibility of passing a urethral catheter, transurethral cystoscopy and cystography were performed which documented a penobulbar narrowing of 90% of the lumen, making it necessary to perform a suprapubic cystostomy. Single-graft urethroplasty was performed in December 2021 with early reappearance of the symptoms and a new episode of urinary retention with a transurethral cystoscopy and cystography that showed reappearance of the narrowing, making it necessary to perform a suprapubic cystostomy again (Figure 1). A double-graft urethroplasty was performed evidencing the previous graft with contracture and occlusion of 100% of the urethral lumen, with significant associated spongiofibrosis and a defect with a total length of 4 cm.

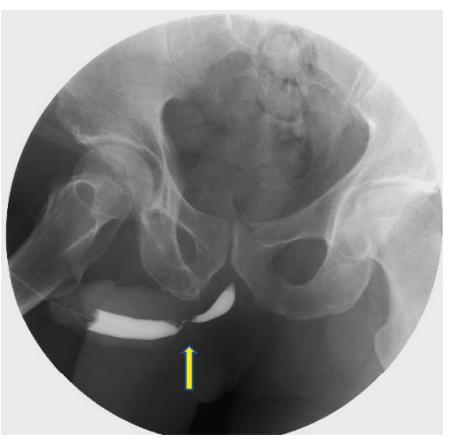

Figure 1. Cystography with evidence of penobulbar stricture (arrow).

Surgical Technique

The operative procedure was performed under general anesthesia with nasotracheal intubation. Retrograde and anterograde urethroscopy was performed with a flexible cystoscope to assess the urethral stricture and its length. Buccal mucosa graft (BMG) was used for augmentation of the urethra. BMG was harvested from the inner cheek and the donor site was closed with interrupted polyglactin sutures (3/0). A midline perineal incision was created. The bulbospongiosus muscle was identified and incised in the midline to expose the bulbar urethra. Ventral sagittal urethrotomy was performed opening the urethra and the stricture and extended 1 cm distally and proximally to the normal urethral lumen. The dorsal urethral plate was incised with a scalpel in the midline until the tunica albuginea of the corpora cavernosa. An elliptical area was created for the dorsal inlay graft (Figure 2), and the BMG was harvested and quilted in this area over the dorsal urethral plate with running polydioxanone (5/0) sutures (Figure 3). Subsequent to the dorsal urethral augmentation, the second BMG was sutured laterally to the left mucosal margin of the urethral plate with a running polydioxanone

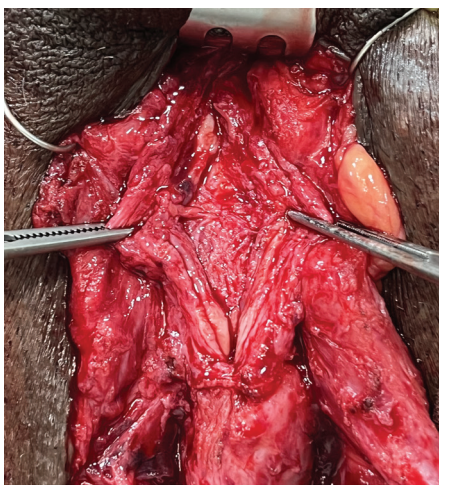

Figure 2. Creation of elliptical area for the dorsal inlay graft.

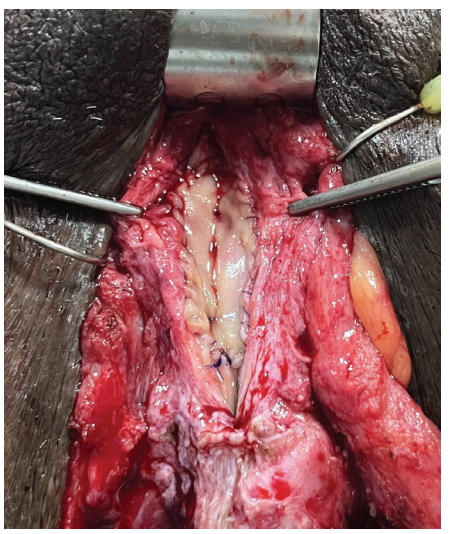

Figure 3. Buccal mucosa graft harvested and quilted over the dorsal plate.

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DOUBLE-GRAFT URETHROPLASTY: SURGICAL TECHNIQUE AND OUTCOMES

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(5/0) suture. The catheter was inserted, and finally the graft was rotated and sutured laterally to the right mucosal margin (Figure 4). Finally, spongioplasty was performed with running polydioxanone (4/0) suture (Figure 5).

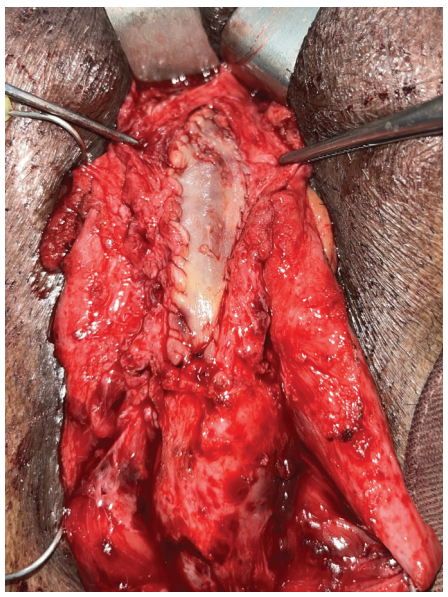

Figure 4. Second buccal mucosa graft sutured laterally to the mucosal margin of the urethral plate.

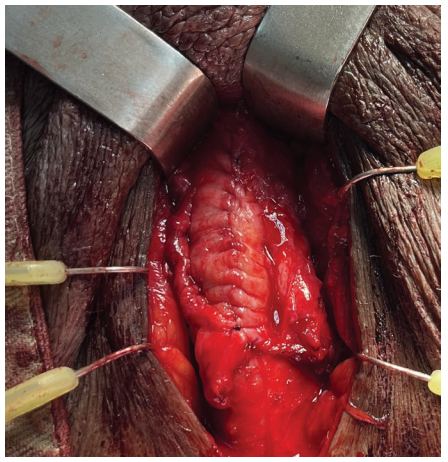

Figure 5. Spongioplasty.

Follow-up and Outcomes

Catheter removal was done 3 weeks after surgery. The patient was followed with AUA Symptom Score, uroflowmetry, and ultrasound with post-void residual urine every 3 months for the first year and every 6 months thereafter without evidence of recurrence of emptying symptoms to date (Figure 6).

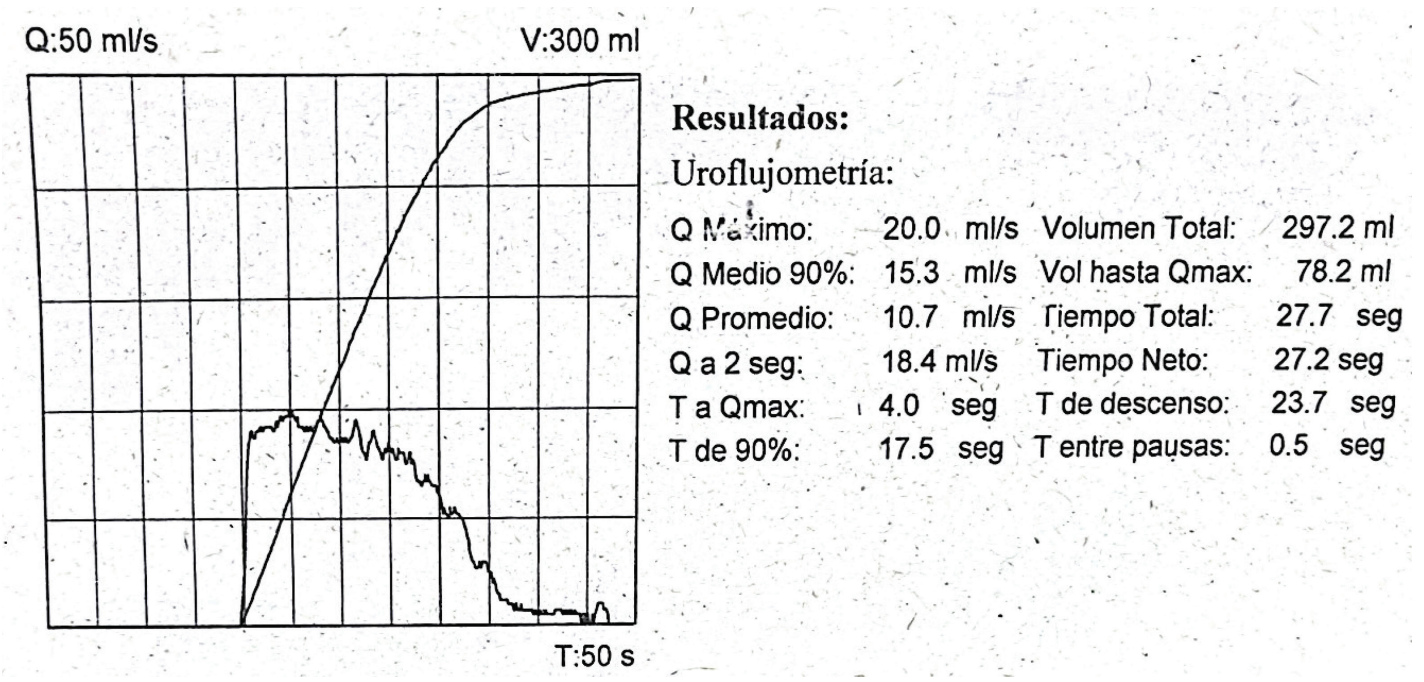

Figure 6. Postoperative uroflowmetry. Q indicates flow rate; Qmax, maximum flow rate; T, time; V, voided volume.

Discussion

Several surgical techniques have been described to treat bulbar urethral strictures based on stricture length. Traditionally, short urethral strictures are treated with excision and end-to-end anastomosis, whereas longer strictures are repaired by patch graft urethroplasty, preferably using BMG. The graft can be placed dorsally or ventrally by using dorsal or ventral urethrotomy approaches.[4] The advantages of BMG, compared to penile skin flaps or other kind of grafts such as genital/extragenital skin or bladder/intestinal mucosae, include a cosmetically superior incision, decreased operative time, low harvest morbidity, and better histological characteristics of the graft.[3] One of the reasons for surgical failure is retraction of the graft, which may occur around 30% of the grafted tissue. In more extensive cases of stenosis, when the caliber of the urethra is narrower, a graft of greater diameter is required, hence the risk of stenosis is greater. Double grafts have been used to maximize success in these cases.[1] The technique described by Palminteri et al offers the possibility of a wide urethral lumen with good urinary outcomes and preservation of sexual function.[3] This technique has the following advantages: (1) the ventral approach is technically easy, (2) there is no mobilization or rotation of the urethra, which preserves the vascular erectile function, (3) preservation of the urethral plate with watertight urethral mucosa and graft augmentation can be performed with a wide urethral lumen, and (4) both dorsal and ventral grafting can be performed depending on the narrow urethral plate.[2] In conclusion, the double-face augmentation urethroplasty is a feasible and versatile technique that can be considered in many circumstances, including long and complex strictures and failed urethroplasty, with satisfactory outcomes.[5] ■

> "The advantages of BMG, compared to penile skin flaps or other kind of grafts such as genital/extragenital skin or bladder/intestinal mucosae, include a cosmetically superior incision, decreased operative time, low harvest morbidity, and better histological characteristics of the graft."

> "The technique described by Palminteri et al offers the possibility of a wide urethral lumen with good urinary outcomes and preservation of sexual function."

1. Barroso U Jr, Prado F. A new double graft technique in urethroplasty for complex urethral stenosis: preliminary findings. *Int Braz J Urol.* 2021;47(4):856-860.
2. Enganti B, Reddy MS, Chiruvella M, et al. Double-face augmentation urethroplasty for bulbar urethral strictures: analysis of short-term outcomes. *Turk J Urol.* 2020;46(5):383-387.
3. Palminteri E, Manzoni G, Berdondini E, et al. Combined dorsal plus ventral double buccal mucosa graft in bulbar urethral reconstruction. *Eur Urol.* 2008;53(1):81-90.
4. Palminteri E, Berdondini E, Florio M, et al. Two-sided urethra-sparing reconstruction combining dorsal preputial skin plus ventral buccal mucosa grafts for tight bulbar strictures. *Int J Urol.* 2015;22(9):861-866.
5. Enganti B, Chiruvella M, Bendigeri MT, et al. Double-face augmentation urethroplasty for bulbar urethral strictures: technical implications and short-term outcomes for a dorsal versus ventral approach. *Eur Urol Open Sci.* 2021;26:10-13.

CASE REPORT

Late Relapse in Germ Cell Testicular Cancer

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Introduction

Germ cell tumors are the most common cause of cancer in men between the ages of 15 and 35. They are one of the most curable solid tumors, with a survival rate greater than 80%.[1,2] However, approximately 10% of all patients will experience relapse of the disease during follow-up, the majority presenting in the first 2 years of follow-up and only 1% to 6% beyond 2 years. The approximate incidence according to the histology of the tumor is 3.2% in nonseminomatous tumors and 1.4% in seminoma.[2-4] This reinforces the importance of long-term follow-up of this pathology. Additionally, in those patients with late relapse, a more aggressive biology of the tumor has been demonstrated, requiring multimodal management.[2]

Late relapses of testicular cancer occur beyond 2 years after initial successful treatment.[2] Most patients experience this relapse during the first 5 years of follow-up, with reports in the literature of exceptional cases where relapse occurrence exceeds 10 years. This is why it is valuable to expand the knowledge about the characteristics of this type of presentation, as well as the treatment modalities used and the response.

Clinical Case

A 57-year-old male patient with a history of nonseminomatous testicular cancer diagnosed in 1989, with a histological diagnosis of teratoma + embryonal carcinoma + choriocarcinoma (involving 90% of the testicle), who was treated with orchiectomy without adjuvant chemotherapy or radiotherapy presented with late tumor relapse (31 years).

In May 2020, the patient presented with pelvic pain radiating to the lower limbs, accompanied by urinary symptoms and macroscopic hematuria with expulsion of clots. A renal and urinary tract US was performed showing a pelvic mass, and via cystoscopy it was possible to see the mass bulging through the right ureter, with biopsy revealing atypical urothelial cells suggestive of a reactive process.

CT urography found dilatation in the collecting system and proximal two-thirds of the right ureter, with decreased enhancement of the right renal parenchyma secondary to the presence of a pelvic mass with irregular and well-defined contours measuring 82×60×69 mm in diameter.

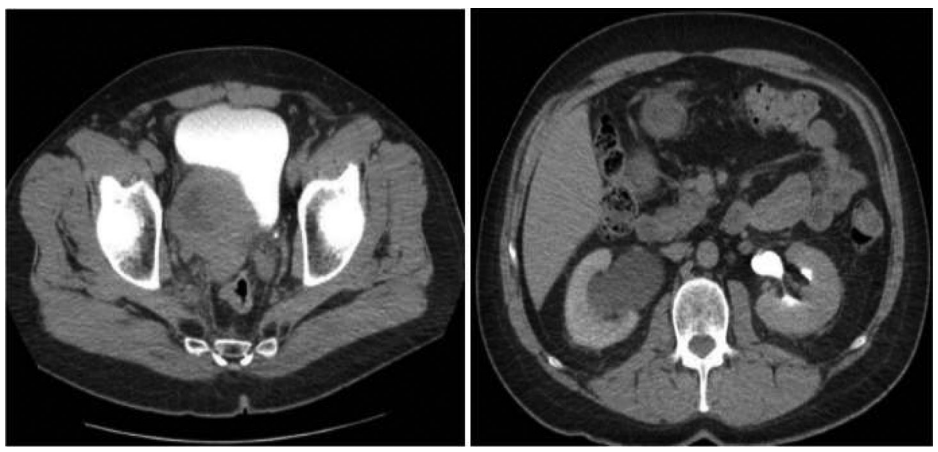

Figure 1. Urography, July 2020.

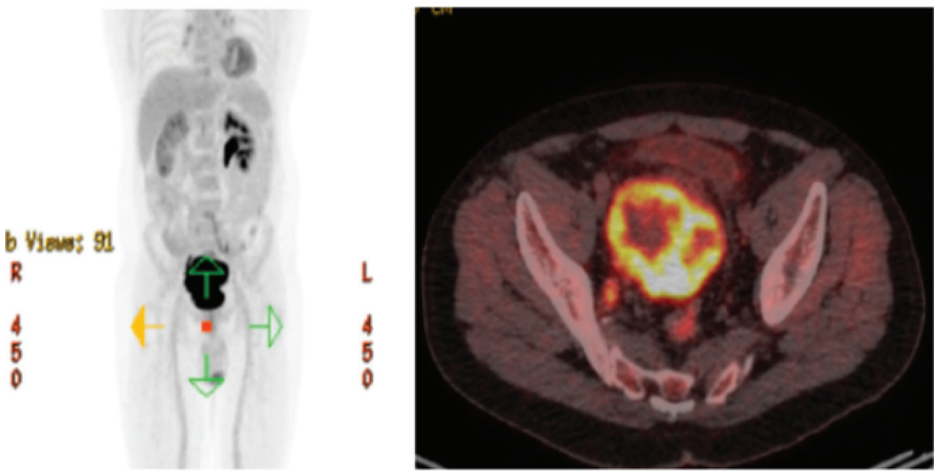

Figure 2. Positron emission tomography-CT, July 2020.

This mass involved the distal third of the right ureter, as well as the ureterovesical junction, the right posterior and lateral wall of the bladder, the right lobe of the prostate gland, and the right seminal vesicle (Figure 1).

Positron emission tomography (PET)-CT elucidated a pelvic mass located in the vesicorectal space of approximately 65×90×59 mm, with peripheral uptake of 16.52 standardized uptake value of radiotracer, with malignant appearance and behavior and signs of tumor necrosis or cystic degeneration. Intense uptake of radiotracer compromised the distal portion of the right internal iliac artery and right renal cortical artery, associated to hydronephrosis, probably caused by obstruction. The right ureter was dilated and lost within the described mass in the vesicorectal space. There was no abnormal uptake in the left testicle (Figure 2).

The patient was taken to laparoscopy and biopsy, which revealed germinal nonseminomatous tumor with morphology consistent with embryonal carcinoma and endodermal sinus tumor. He started treatment with bleomycin, etoposide, and cisplatin, and after 3 cycles, PET-CT revealed rectovesical space mass with significant metabolic intensity decrease (74% in relation to a partial metabolic response). No enlarged lymph nodes or hypermetabolic adenopathies were identified (Figure 3).

The patient had an excellent response to treatment both from the clinical and biomarker point of view, with initial α-fetoprotein (AFP) of 217 and post-treatment AFP of 7.3. Therefore, he was scheduled to undergo urological surgery for resection of residual mass and ureter reanastomosis.

After 2 years of follow-up of the previous treatment for testicular cancer relapse, the patient presented with an elevated PSA of 13 ng/mL with a normal digital rectal examination and pre-biopsy prostate MRI with PI-RADS (Prostate Imaging-Reporting Data System) 4 lesions, for which he underwent prostate fusion biopsy on August 23, 2022 with the discovery of grade group 3 prostate adenocarcinoma, with unfavorable NCCN (National Comprehensive Cancer Network) intermediate-risk disease staging (Figures 4 and 5). PET-prostate-specific membrane antigen was negative for metastatic lesions, so treatment with curative intent was performed with radical prostatectomy and standard lymphadenectomy on October 19, 2022 with final disease staging pT3aN0M0R0 grade group 3 with 65% Gleason 4 and present cribriform glands. Currently PSA is undetectable.

Discussion

This is a rare and challenging case of a very late relapse of nonseminomatous germ cell tumor-embryonal carcinoma and endodermal sinus tumor 31 years

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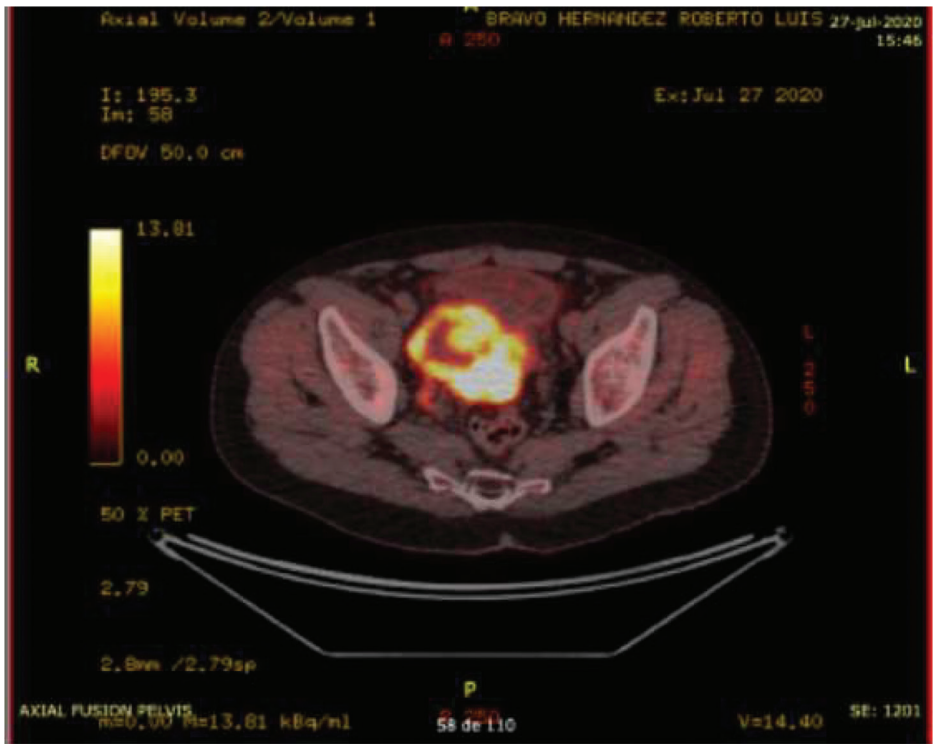

Figure 3. Positron emission tomography-CT, October 2020.

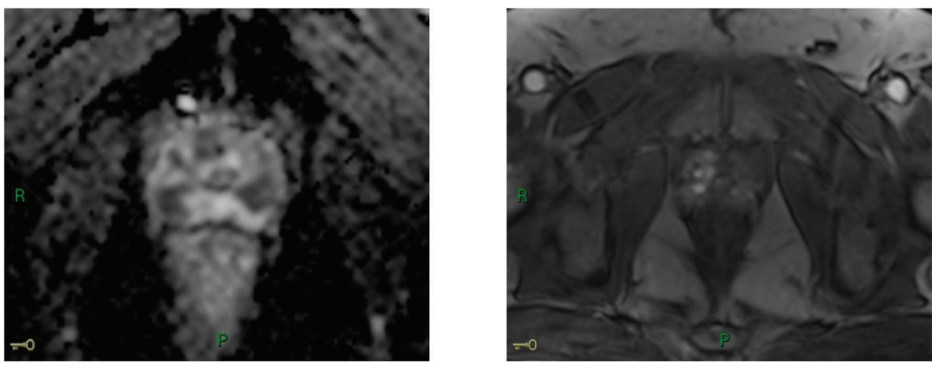

Figure 5. Multiparametric nuclear MRI of the prostate, July 2022.

after orchiectomy, which also had an atypical clinical presentation of a mass in the pelvic region with involvement of the ureter's distal third suggesting a urothelial origin.

Only a few cases of relapses occurring 20 years after the initial presentation are reported in the literature. For example, Ansari and Hajigholami,[5] and Arafat et al[4] described patients with nonseminomatous germ cell tumors with very late relapse at 27 years after the initial presentation. These cases emphasize the importance of lifelong surveillance of patients with germ cell tumors, even patients with extremely low risk for late relapse, including those with clinical stage I disease.

In order to anticipate the appearance of these late relapses, there are widely documented risk factors for the development of metastatic disease in patients with stage I testicular cancer, such as lymphovascular invasion and the percentage of embryonal carcinoma in nonseminomatous tumors.[2,3] Some biomarkers are currently being studied to predict relapses, finding utility in proteins such as MIB-1, CXCL12, β-catenin, and possibly CXCR4; however, their validation is lacking in larger, multicenter, well-defined studies.[3]

Screening is usually carried out during routine follow-up examinations, either by elevated serum markers such as AFP or human chorionic gonadotropin, radiographic findings, or clinical symptoms[6] such as low back pain or a palpable abdominal mass. It should be noted that early detection will have an impact on prognosis, since symptoms in the initial presentation have been associated with lower cancer-specific survival and overall survival.[2]

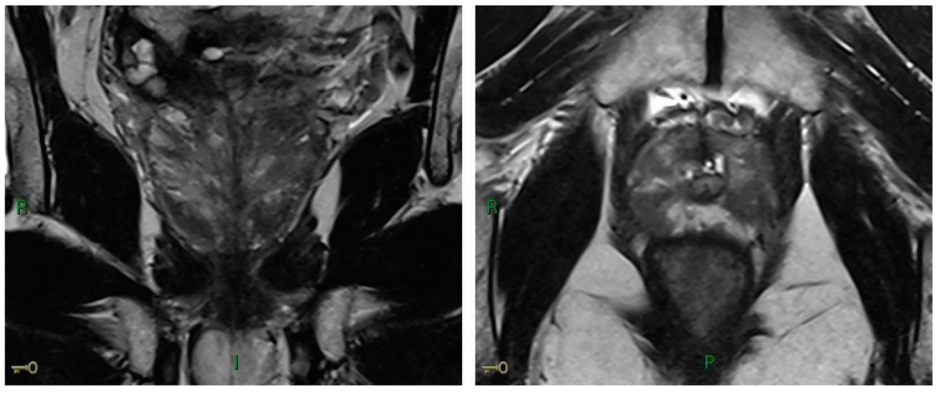

Figure 4. Multiparametric nuclear MRI of the prostate, July 2022.

Regarding the histology of late relapse, it is known that it is usually biologically more aggressive than that found during retroperitoneal lymphadenectomy for primary tumors. Teratoma is usually found in approximately 20% to 30% of positive node specimens at primary lymphadenectomy and in 40% of patients with post-chemotherapy lymphadenectomy.[2]

Given the high rate of chemoresistance in late relapsed tumors, the cornerstone of treatment is complete surgical excision, although salvage chemotherapy regimens have been described, such as platinum, ifosfamide, paclitaxel, etoposide, and epirubicin, although with low complete response rates,[7] at 20.7% for late response and 42.1% for early relapse. Therefore, the aim of follow-up beyond 5 years shifts to the detection of late side effects of treatment.[8]

Just as platinum-based chemotherapy has increased cancer-specific and overall cancer-free survival, it has also been associated with secondary neoplasms.[9] Studies have shown an increased risk of second malignancies among testicular cancer survivors (TCS),[10] especially after radiation therapy (RT) and chemotherapy, with an increased relative risk of approximately 1.4-fold of developing subsequent prostate cancer, among other second cancer types.[10] Zhang et al presented a cohort of 282 TCS, with data extracted from the SEER (Surveillance, Epidemiology, and End Results) database controlling for age at the time of diagnosis and era of diagnosis of prostate cancer.[11] The standardized risk ratio analysis showed no statistically significant increased risk for grade of the disease among TCS who had received prior RT (radiotherapy) compared with TCS with no prior RT. The latency between the 2 diagnoses ranged from 12 to 443 months, with a median of 211 months. In our case, 33 years elapsed, almost twice as long as described in the literature. However, it is known that testicular cancer survivors with subsequent diagnosis of prostate cancer are more likely to be detected at a younger age than those men with primary prostate cancer (with a median age of 69, $P < .001$), with detection rates of 65.2% vs 37.6% for age ≤65, and

"Studies have shown an increased risk of second malignancies among testicular cancer survivors (TCS),[10] especially after radiation therapy (RT) and chemotherapy, with an increased relative risk of approximately 1.4-fold of developing subsequent prostate cancer, among other second cancer types."

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34.8% vs 62.4% for age >65 ($P <$ .001).[11] Although the exact reason for this observation is not clear, this difference may be multifactorial, including cancer susceptibility at a younger age in TCS and/or the result of earlier detection under routine cancer surveillance as part of survivorship care after testicular cancer treatments.

A prospective historical cohort by Hellesnes et al of 5,625 TCS shows an increased risk of solid neoplasia after 2 or more cycles of platinum-based chemotherapy when compared to surgery as single management of up to 72%.[9] Both the L-field technique and paraaortic RT were associated with 1.6-fold increased risks for second cancer in comparison to surgery only. On the other hand, follow-up studies imply radiation exposure in constant CT scans, with an association of increased risk of second cancer.[12,13]

In view of these data, it is debatable if regular follow-up of all testicular cancer patients beyond 5 years is a good use of medical resources as well as keeping health professionals alert about the risk of secondary solid neoplasms in this population, emphasizing careful evaluations to ensure a timely diagnosis. ■

1. Mortensen MS, Lauritsen J, Kier MGG, et al. Late relapses in stage I testicular cancer patients on surveillance. *Eur Urol.* 2016;70(2):365-371.
2. O'Shaughnessy MJ, Feldman DR, Carver BS, Sheinfeld J. Late relapse of testicular germ cell tumors. *Urol Clin North Am.* 2015;42(3):359-368.
3. Lobo J, Gillis AJM, van den Berg A, Looijenga LHJ. Prediction of relapse in stage I testicular germ cell tumor patients on surveillance: investigation of biomarkers. *BMC Cancer.* 2020; 20(1):728.
4. Arafat W, Albany C, Ulbright TM, Foster R, Einhorn LH. Very late relapse of germ cell tumor as a teratoma: a case report and review of the literature. *J Surg Case Rep.* 2014;2014(6):rju051-rju051.
5. Ansari H, Hajigholami A. Too late relapse of testicular cancer after 27 years; a case report. *J Nephropathol.* 2018;7(1):19-21.
6. Oldenburg J, Martin JM, Fosså SD. Late relapses of germ cell malignancies: incidence, management, and prognosis. *J Clin Oncol.* 2006; 24(35):5503-5511.
7. Akar E, Tural D, Arslan D, Başsorgun Cİ, Yıldız Ö. Late relapse of testicular cancer: recurrence after 24 years and treatment with chemotherapy alone. *J Cancer Res Ther.* 2015; 11(3):661.
8. Ondrusova M, Suchansky M, Psota M, Zeleny T, Ondrus D. Late relapse in stage I of nonseminomatous germ cell testicular cancer on surveillance. *Bratisl Lek Listy.* 2018;119(1):3-5.
9. Hellesnes R, Kvammen Ø, Myklebust TÅ, et al. Continuing increased risk of second cancer in long-term testicular cancer survivors after treatment in the cisplatin era. *Int J Cancer.* 2020;147(1):21-32.
10. Travis LB, Fosså SD, Schonfeld SJ, et al. Second cancers among 40 576 testicular cancer patients: focus on long-term survivors. *J Natl Cancer Inst.* 2005;97(18):1354-1365.
11. Zhang H, Yang H, Bandyopadhyay S, et al. Increased risk of high-grade prostate cancer among testicular cancer survivors. *PLoS One.* 2022;17(2):e0263573.
12. Brenner DJ, Hall EJ. Computed tomography–an increasing source of radiation exposure. *N Engl J Med.* 2007;357(22):2277-2284.
13. Tarin TV, Sonn G, Shinghal R. Estimating the risk of cancer associated with imaging related radiation during surveillance for stage I testicular cancer using computerized tomography. *J Urol.* 2009;181(2):627-633.

Frontiers in Vaginal Reconstruction: Current Issues and Issues on the Horizon

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Pelvic organ prolapse (POP) is extremely common and prevalence rates have been reported as high as 50%. Of the women who have POP, approximately 10% will have surgical correction for their condition and 1 in 3 women will have multiple surgeries.[1] Women with POP often present with multi-compartmental defects and associated urinary and bowel symptoms. A rectocele can cause symptoms of vaginal bulge with subsequent need for a woman to perform vaginal splinting in order to evacuate her rectum; however, significant defecatory dysfunction and symptoms of obstructed defecation are usually not due to rectocele alone. Development of obstructed defecation following hysterectomy can be indicative of enterocele or rectal prolapse, and it has been reported that between 21% and 34% of women who present with rectal prolapse have concurrent POP.[2] Fortunately there is increasing awareness that women presenting with POP and defecatory dysfunction should have a multidisciplinary evaluation for possible concomitant urogynecologic and colorectal surgical repair. A study based on the American College of Surgeons National Surgical Quality of Improvement Program (ACS NSQIP) database reported that the number of concomitant POP and rectal prolapse surgeries increased from 2.6% to 7% over an almost 10-year period.[3]

At a minimum, evaluation for women with POP includes history and physical examination. While physical examination can assess for vault prolapse, the degree of associated enterocele or rectal prolapse and/or intussusception can be underappreciated. Dynamic MRI of the pelvis should be considered for women with significant defecatory dysfunction or obstructed defecation complaints as it provides both anatomical and functional information. Images are obtained at rest and with Valsalva to visualize prolapse of the small and large bowel. Women with complaints such as feeling their bowel movements are blocked at a certain point, pelvic pressure alleviated with bowel movements, and pushing on the perineum to evacuate their bowels may have an enterocele, rectal kinking from redundant sigmoid colon, and/or rectal prolapse (Figures 1 and 2). Crane et al reported that at 1 year following robotic sacrocolpopexy with and without rectocele repair, 44% of women had persistent outlet constipation regardless of whether rectocele repair was performed.[4] A subsequent study reports no change in the Colorectal-Anal Distress Inventory (CRADI-8) or Colorectal Anal Impact Questionnaire (CRAIQ-7) for obstructed defecatory symptoms after sacrocolpopexy with posterior repair, and the authors state that they cannot recommend posterior compartment surgery as providing any patient benefit.[5] On the contrary, when sacrocolpopexy and rectopexy are performed together both bowel function and quality of life are improved.[6] These studies are thought-provoking as to whether preoperative dynamic MRI for the women who only had rectocele repair would have been useful in identifying an anatomical abnormality such as sigmoid intussusception or rectal kinking such that correction would have resolved the constipation and obstructed defecation symptoms.

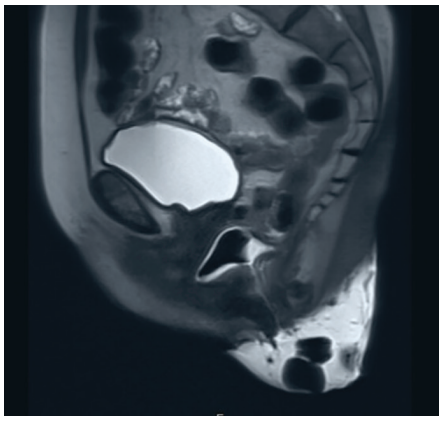

Figure 1. Sagittal T2 MRI image at rest of woman with vault prolapse and symptoms of obstructive defecation.

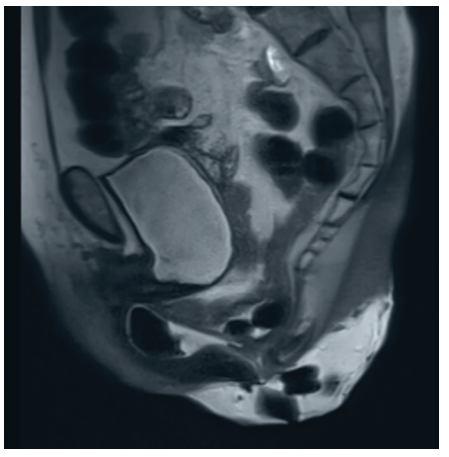

Figure 2. Sagittal T2 "dynamic" MRI image with Valsalva showing large enterocele.

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FEMALE PELVIC FLOOR RECONSTRUCTION: A MULTIDISCIPLINARY APPROACH

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Women with both urogynecologic and colorectal anatomical abnormalities should be considered for a multidisciplinary surgical approach that may include concomitant ventral mesh rectopexy with or without sigmoid resection, sacrocolpopexy, transvaginal rectocele repair, and a procedure to correct stress incontinence. Due to concerns for possible bowel anastomotic leak if sigmoid resection is performed and/or unrecognized intraoperative bowel injury, these procedures can be performed with a biologic graft; however, the theoretical increased risk with synthetic mesh is tempered by a relatively high recurrence rate (unpublished data). Furthermore, although the data are limited regarding complications of ventral mesh rectopexy with mesh, complication rates are low and have been reported between 0% and 2.4%.[7] Considering the recurrence rate exceeds reported complication rates with mesh, synthetic mesh should be considered unless there is significant concern for bowel contamination or there is another contraindication.

There is increasing evidence supporting the safety and feasibility of performing simultaneous sacrocolpopexy and rectopexy with low complication rates.[8] Prior studies have shown that no added morbidity has been demonstrated with addition of sacrocolpopexy to rectopexy, although the surgical time required to perform these 2 procedures certainly takes longer than when only 1 is performed.[3] In our practice, we work closely with our colorectal colleagues and frequently perform concomitant robotic sacrocolpopexy with ventral rectopexy. When performing the combined procedure, the surgical dissection starts at the sacral promontory to ensure adequate exposure of the anterior longitudinal ligament. If a hysterectomy is performed, the supracervical approach is preferred assuming no contraindication to reduce the risk of a mesh complication.[9] Following dinal ligament and hysterectomy (if performed), the colorectal surgeon mobilizes the sigmoid colon and rectum, then sutures mesh to the anterior rectum. Mobilization of the colon and rectum facilitates creation of peritoneal flaps that will eventually cover the rectopexy and colpopexy grafts. Next, a Y-shaped mesh is sutured to the cervix and anterior and posterior vagina in standard fashion for the colpopexy. Finally, the tails of the Y-mesh and the rectopexy mesh are both sutured to the anterior longitudinal ligament.

In conclusion, it is important to carefully evaluate a female patient who presents with POP and defecatory dysfunction as there may be an underlying colorectal disorder that also requires surgical correction. Close collaboration between vaginal reconstructive surgeons, colorectal surgeons, and radiologists can provide the best outcomes for these women. ■

1. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. *Obstet Gynecol.* 1997;89(4):501-506.
2. Altman D, Zetterstrom J, Schultz I, et al. Pelvic organ prolapse and urinary incontinence in women with surgically managed rectal prolapse: a population-based case-control study. *Dis Colon Rectum.* 2006;49:28-35.
3. Geltzeiler CB, Birnbaum EH, Silviera ML, et al. Combined rectopexy and sacrocolpopexy is safe for correction of pelvic organ prolapse. *Int J Colorectal Dis.* 2018;33(10):1453-1459.
4. Crane AK, Geller EJ, Matthews CA. Outlet constipation 1 year after robotic sacrocolpopexy with and without concomitant posterior repair. *South Med J.* 2013;106(7):409-414.
5. Arunachalam D, Hale DS, Heit MH. Posterior compartment surgery provides no differential benefit for defecatory symptoms before or after concomitant mesh-augmented apical suspension. *Female Pelvic Med Reconstr Surg.* 2018;24(2):183-187.
6. Watadani Y, Vogler SA, Warshaw JS, et al. Sacrocolpopexy with rectopexy for pelvic floor prolapse improves bowel function and quality of life. *Dis Colon Rectum.* 2013;56(12):1415-1422.
7. Van der Schans EM, Boom MA, El Moumni M, Verheijen PM, Broeders IAMJ, Consten ECJ. Mesh-related complications and recurrence after ventral mesh rectopexy with synthetic versus biologic mesh: a systematic review and meta-analysis. *Tech Coloproctol.* 2022;26(2):85-98.
8. Wallace SL, Kim Y, Lai E, et al. Postoperative complications and pelvic organ prolapse recurrence following combined pelvic organ prolapse and rectal prolapse surgery compared to pelvic organ prolapse only surgery. *Am J Obstet Gynecol.* 2022;227(2):317.
9. Dallas K, Taich L, Kuhlmann P, et al. Supracervical hysterectomy is protective against mesh complications after minimally invasive abdominal sacrocolpopexy: a population-based cohort study of 12,189 patients. *J Urol.* 2022;207(3):669-676.

JU INSIGHT

Outcomes of Active Surveillance of Low-grade Prostate Cancer: A Landmark Approach

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Timilshina N, Alibhai SMH, Tomlinson G, Sander B, Cheung DC, Finelli A. Long-term outcomes following active surveillance of low-grade prostate cancer: a population-based study using a landmark approach. *J Urol.* 2023;209(3):540-548.

Study Need and Importance

Treatment options for low-risk prostate cancer (PC) commonly include active surveillance (AS), surgery, and radiation therapy, but no high-level evidence has shown any one treatment strategy to be superior to another in

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Table. Cox Proportional Survival Model of Metastasis, Overall Mortality, and Prostate Cancer-specific Mortality (Landmark Analysis and Propensity Score Matched Analysis)

Variables	Primary landmark analysis		Propensity score matched analysis	
	Hazard ratio (95%CI)	*P* value	Hazard ratio (95%CI)	*P* value
Outcome 1: Metastasis				
Active surveillance vs initial treatment	1.34 (1.15-1.57)	< .001	1.28 (1.08-1.51)	< .001
Outcome 2: Overall mortality				
Active surveillance vs initial treatment	1.12 (1.01-1.24)	.038	1.12 (1.01-1.25)	.036
Outcome 3: Prostate cancer–specific mortality				
Active surveillance vs initial treatment	1.66 (1.15-2.39)	.007	1.87 (1.24-2.82)	.003

Abbreviation: CI, confidence interval.
Each analysis was adjusted for age, diagnosis year, Johns Hopkins Adjusted Clinical Groups comorbidity score, disease characteristics at diagnosis (PSA, positive core, and maximum % of core), rurality, patient income, and provider-related characteristics (hospital type, physician type, physician and institution volume tertile).

OUTCOMES OF ACTIVE SURVEILLANCE OF LOW-GRADE PROSTATE CANCER

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low-grade PC. Although reports from single academic institutions on long-term outcomes for AS have been promising, with excellent PC-specific survival of 99%-100% at 10 years, cogent population-level data are lacking. Generally, published studies feature highly selected patients with very low–risk PC, protocol-based follow-up, and median follow-up of roughly 5 years. No study has published long-term oncologic outcomes of AS at a population level.

What We Found

In this retrospective, population-based study, we compared long-term cancer outcomes of 21,282 men with low-grade PC managed with AS to those with initial treatment. We used 2 complementary analytical approaches to reduce bias. Our results (with a median follow-up of 10 years) suggest that AS was associated with slightly worse long-term metastasis-free survival, overall survival, and PC-specific survival compared with initial treatment (see Table).

Limitations

Our study lacks data on some prognostic variables such as cancer staging and PSA that may influence treatment choice and outcome.

Interpretation for Patient Care

In this real-world study of long-term outcomes in men with low-grade PC, AS is associated with excellent long-term metastasis-free survival and overall survival. However, long-term PC-specific survival was slightly inferior to initial treatment (1% worse at 10 years with AS); this must be balanced against known harms of overtreatment. Minor differences in long-term outcomes may be due to less restrictive inclusion criteria, less rigid follow-up, or the effects of initial treatment. With more contemporary use of MRI and transperineal biopsy, the results of AS will also likely improve and reduce any differences with radical treatment. ■

UPJ INSIGHT

Postoperative Opioid Prescribing Following Outpatient Male Urethral Surgery: Evidence for Change

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Findlay BL, Bearrick EN, Hebert KJ, et al. Postoperative opioid prescribing following outpatient male urethral surgery: evidence for change. *Urol Pract.* 2023;10(2):138-145.

Study Need and Importance

Surgeons play a central role in the opioid epidemic. Inappropriate overprescribing of opioids is a major contributor to this epidemic. While major headway has been made with enhanced recovery after surgery pathways following other major urological procedures, there is a dearth of data regarding male urethral surgery pain pathways.

What We Found

A total of 116 patients underwent outpatient anterior urethroplasty between August 2017 and January 2021. One-third of patients did not use opioids postoperatively, and nearly 78% of patients used ≤5 tabs (see Figure). Overall, the median number of opioid tablets used was 2, with a median of 8 tablets overprescribed. Those receiving tramadol reported a greater reduction in pain and higher satisfaction with their outpatient surgery experience. The only predictor for use of >5 tabs was preoperative opioid use (75% vs 25%, $P < .01$), although only 6 patients were considered opioid exposed.

Limitations

This was a single-surgeon experience, with involvement of a highly trained team who provide extensive perioperative counseling regarding expectations of surgery. Additionally, surveys were conducted by the care team at the postoperative visit, which was conducted 3 weeks following surgery. This inevitably introduces a large degree of recall bias given that patients were asked to comment on 72-hour postoperative pain scores. Surveys did not elucidate potential etiologies contributing to pain (ie, incisional, catheter related, or buccal mucosal graft harvest when applicable), nor did they capture potential postoperative complications, which could have contributed to greater narcotic utilization.

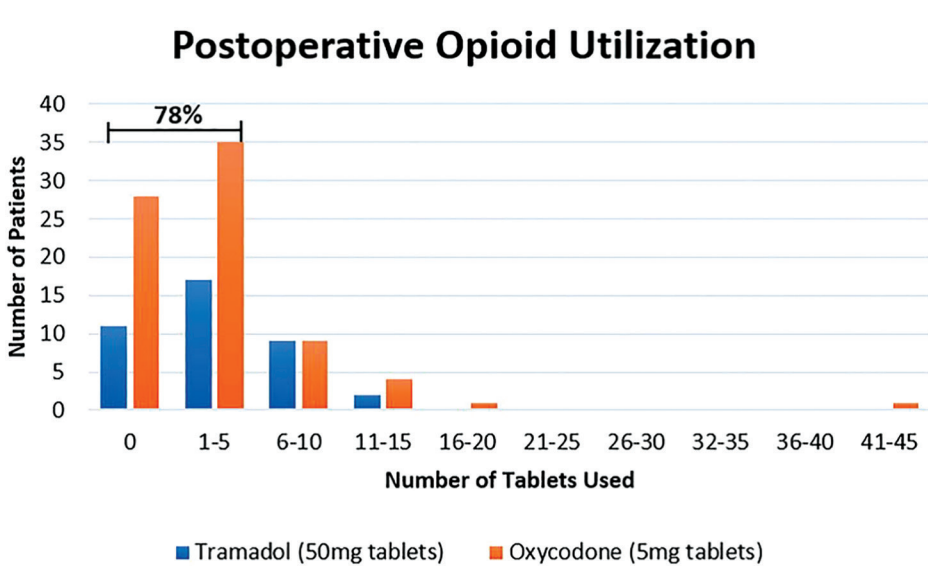

Figure. Postoperative opioid utilization comparing tramadol and oxycodone.

Interpretation for Patient Care

A multimodal, limited opioid pain management pathway using a small quantity of adjunctive opioid provides adequate pain control after outpatient urethroplasty. However, the ultimate goal is to optimize multimodal pain pathways and perioperative patient counseling in order to transition to a fully narcotic-free pathway. ■

MEDICAL STUDENT COLUMN

The Use of Magnetic Resonance Imaging-derived Radiomic Models in Prostate Cancer Risk Stratification

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In recent years, the advancement of precise medical imaging has facilitated the establishment of radiomics, a computer-based method of extracting and quantifying subvisual imaging characteristics.[1] These features (ie, qualities of intensity, texture, shape, or wavelet) can be extracted from a variety of medical images (CT, MRI, or positron emission tomography) using advanced mathematical algorithms, aggregated into predictive models via machine learning, and applied to enhance personalized therapies. In the last decade, several studies have highlighted the enormous potential of radiomics in enhancing care for a variety of diseases. These include, but are not limited to, cancers of the gastrointestinal tract, lung, brain, and (more recently) the genitourinary tract.

In prostate cancer, MRI is a standard clinical tool used for diagnosis, prognosis, and treatment planning. As a key part of the prostate cancer clinical care pathway, MRI represents an opportune point of intersection for the use of radiomics. In this regard, the number of research articles on MRI-derived prostate radiomics has predictably increased since 2017 (see Figure), accounting for 218 original articles in the last 5 years. However, as the technology is still evolving, the exploration of radiomic-based models in prostate cancer has thus far largely been sequestered within the fields of radiation oncology, radiology, and biomedical imaging. Even further, most of these investigations have concentrated on screening or diagnostic uses—ie, the correlation of radiomic models with PI-RADS (Prostate Imaging Reporting and Data System) lesions, in confirming biopsy findings, or in prostate cancer screenings. However, as prostate cancer is highly heterogeneous, the use of radiomics could be further extended to enable prediction beyond initial diagnosis and toward risk stratification, prognostication, and prediction of therapy response.

Of the 218 articles published on MRI-derived prostate radiomics in the last 5 years, 42 (19.3%) have utilized MRI-derived radiomics specifically for prostate cancer risk stratification and prognostication. Prediction of Gleason grade group and adverse pathologies, including seminal vesicle invasion, extraprostatic extension, and lymph node involvement, were primary endpoints in 21 (50%) and 11 (26.2%) published articles from 2017 to 2022. In studies predicting Gleason score, radiomic models differentiated well between Gleason score risk groups and in predicting Gleason grade group upgrading (ROC AUC 0.63-0.89).[2,3] Studies predicting adverse pathology also yielded high ROC AUC values between 0.83 and 0.91 for radiomic models, outperforming clinical nomograms in 2 comparative studies.[4,5]

While these results support the potential use of radiomics in initial risk stratification, final pathology following radical prostatectomy would likely still dictate treatment strategy. As such, the natural progression for clinical integration of radiomics has shifted toward prognostication and prediction of treatment response. Of the 42 articles above, 4 (9.5%) and 6 (14.3%) investigations have highlighted the use of MRI-derived radiomics in predicting post-surgical recurrence and post-radiation failure, respectively. ROC AUCs for these models ranged from 0.71 to 0.73 in the post-surgical and post-radiation cohorts,[6,7] values which are comparable to the Memorial Sloan Kettering Cancer Center Pre-Radical Prostatectomy Nomogram and the University of California San Francisco CAPRA (Cancer of the Prostate Risk Assessment) scores for predicting recurrence following surgery. However, given the recency of these studies, only 2 groups have included external validation of their radiomic models, and it is clear that further exploration is required before clinical integration can be considered.

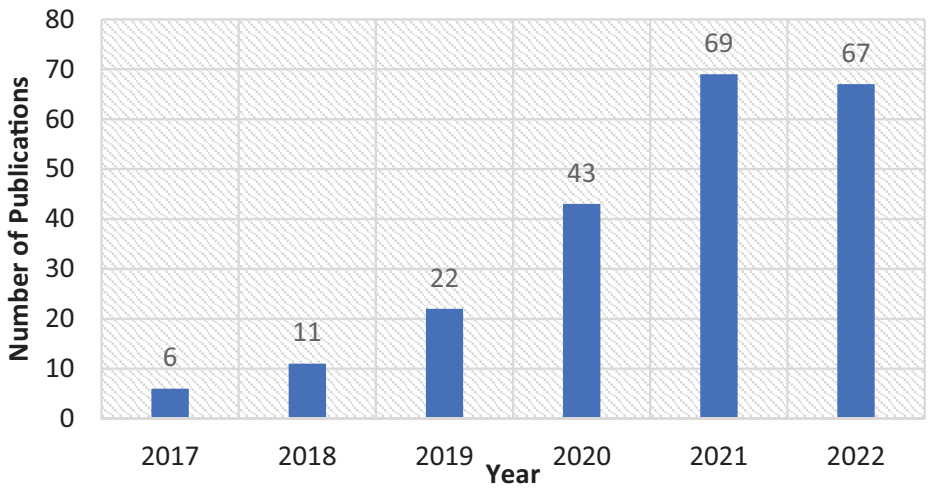

Figure. Number of prostate cancer radiomics publications from 2017 to 2022.

As an MD/PhD scholar at the University of Nebraska Medical Center, my thesis dissertation project centers on increasing applicability of radiomic technologies to prostate cancer prognostication. Working with Dr Michael Baine in the Department of Radiation Oncology has enabled me to shape a project that integrates the technology of imaging-derived radiomics with the clinical care pathway in prostate cancer. Internal development of these radiomic models has yielded promising preliminary findings with high sensitivity in predicting prostate cancer recurrence following radical prostatectomy. Over the coming months, we hope to further enhance the predictive capability of our models by integrating patient demographics and clinical characteristics with the radiomic features. Furthermore, as the project grows, we will continue recruiting other institutions to externally validate our model and its findings.

Overall, prostate cancer radiomics presents as an emerging research field with the potential to offer noninvasive, imaging-based biomarkers for risk stratification and prediction of treatment response. Given the high heterogeneity of prostate cancer, the quantitative characterization of tumor heterogeneity and identification of imaging-based biomarkers may enable disease-tailored treatment planning. Direct application of radiomics to prediction of treatment outcomes, however, remains an ongoing investigation. As these studies mature and reach potential for clinical integration, concerted efforts to standardize methodology and systematically validate these radiomic models must be undertaken. ■

1. Shur JD, Doran SJ, Kumar S, et al. Radiomics in oncology: a practical guide. *Radiographics.* 2021;41(6):1717-1732.
2. Abdollahi H, Mofid B, Shiri I, et al. Machine learning-based radiomic models to predict intensity-modulated radiation therapy response, Gleason score and stage in prostate cancer. *Radiol Med.* 2019;124(6):555-567.
3. Losnegård A, Reisæter LAR, Halvorsen OJ, et al. Magnetic resonance radiomics for prediction of extraprostatic extension in non-favorable intermediate- and high-risk prostate cancer patients. *Acta Radiol.* 2020;61(11):1570-1579.
4. Cuocolo R, Stanzione A, Faletti R, et al. MRI index lesion radiomics and machine learning for detection of extraprostatic extension of disease: a multicenter study. *Eur Radiol.* 2021;31(10):7575-7583.
5. Ma S, Xie H, Wang H, et al. MRI-based radiomics signature for the preoperative prediction of extracapsular extension of prostate cancer. *J Magn Reson Imaging.* 2019;50(6):1914-1925.
6. Li L, Shiradkar R, Leo P, et al. A novel imaging based nomogram for predicting post-surgical biochemical recurrence and adverse pathology of prostate cancer from pre-operative bi-parametric MRI. *EBioMedicine.* 2021;63:103163.
7. Zhong QZ, Long LH, Liu A, et al. Radiomics of multiparametric MRI to predict biochemical recurrence of localized prostate cancer after radiation therapy. *Front Oncol.* 2020;10:731.

RADIOLOGY CORNER

Bochdalek Hernia With an Intrathoracic Kidney: A Rare Kidney Ectopia

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A 58-year-old male presented to the emergency department with severe left flank pain that had been worsening over the last 5 months. The pain radiated to his left upper quadrant and left anterior ribs and was associated with significant nausea and vomiting. He had a prior history of a congenital diaphragmatic hernia repaired as an infant, without other significant medical history. His lab work showed a creatinine of 1.25 mg/dL without a known baseline. Imaging in the emergency department revealed a left sided Bochdalek hernia, a congenital defect of the diaphragm through which abdominal organs can herniate into the thoracic cavity. In this patient's case, nearly his entire left kidney was found to be intrathoracic with compression of his ureteropelvic junction by the left diaphragmatic crus, causing severe hydronephrosis (Figures 1 and 2). Given these findings, the decision was made to place a left percutaneous nephrostomy tube for immediate decompression, which resulted in near immediate pain relief. Antegrade pyelogram showed retention of contrast without drainage at the ureteropelvic junction, confirming obstruction.

The hernia was ultimately repaired with a transabdominal, robotic downward nephropexy (Figure 3). Robotic trocars were placed in the upper left quadrant after laparoscopic access. Very few adhesions were seen and the lower pole of the kidney was identified within the hernia sac. Circumferential mobilization of the kidney and the hilum within the hernia sac was performed and the kidney was fixated to the psoas fascia. Given the redundant ureter and narrowing of the ureteropelvic junction, a dismembered pyeloplasty was performed with stent placement. The case was performed in conjunction with thoracic surgery, which robotically repaired the Bochdalek hernia with mesh through the same trocars. The patient recovered well after surgery and was discharged home on postoperative day 3.

Bochdalek hernias are an incredibly rare condition with an incidence of only 0.17%. They occur due to failure of closure of the posterolateral foramina of the diaphragm and various abdominal organs can herniate into the thoracic cavity, including the kidney, liver, colon, spleen, and stomach. They occur on the left side of the diaphragm 85% of the time, on the right side of the abdomen in roughly 13% of cases, and are bilateral in only 3%-6% of cases.[1] When examining all types of ectopic kidneys, intrathoracic kidney is the rarest type of ectopia, occurring in less than 5% of cases.[2] Many Bochdalek hernias are identified early in infancy as they can result in pulmonary complications and respiratory distress. However, in adults they can be found incidentally or can present symptomatically with abdominal or chest pain or dyspnea.[3] If the patient is asymptomatic, the hernia can be managed conservatively with labs and imaging to monitor for progression and surgical intervention is not necessarily warranted.[4] In one review of 33 patients with Bochdalek hernias, only 2 patients had documented impaired renal function, 6 cases had normal renal function, and 25 reports did not comment on renal function.[5] In the same series, surgical repair was found to be uncommon. Diaphragmatic repairs were performed in 12% of patients, partial nephrectomy occurred in 3% of patients, and emergency laparotomy and thoracotomy were performed in 3% of cases. Minimally invasive surgical intervention specifically for urinary obstruction is even rarer, with a case report in 2019 noting that there had only been 3 reported cases of Bochdalek hernias leading to obstruction and their case was the first case of obstruction resolved by laparoscopy.[6]

Overall, data on Bochdalek hernias are rare and mostly limited to case reports and case series due to the extremely low incidence of the condition. Our patient represents a very small percentage of patients

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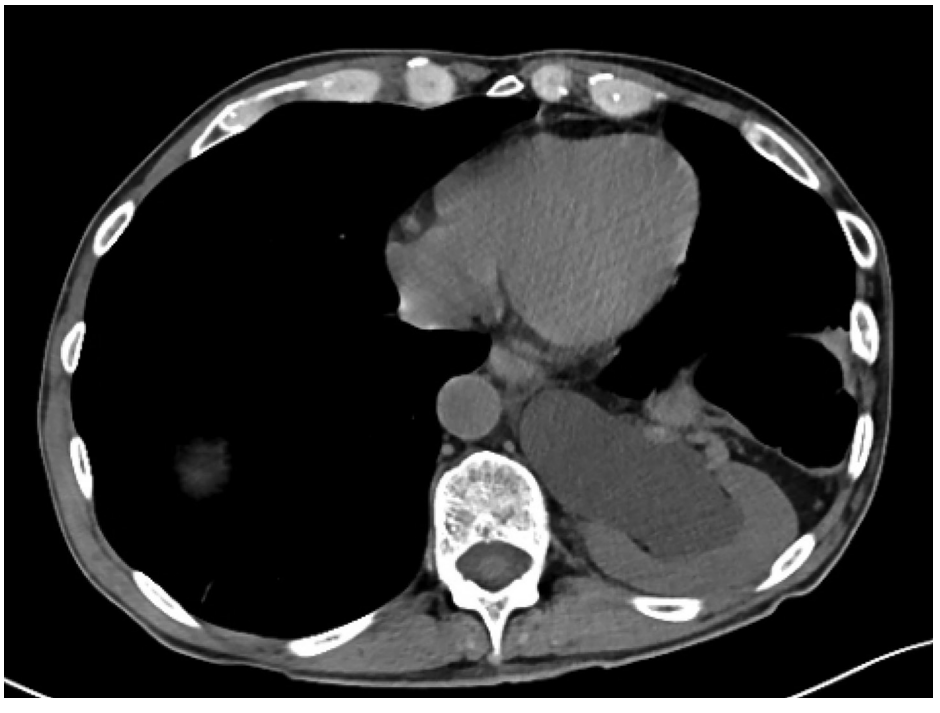

Figure 1. Axial CT image at presentation demonstrating intrathoracic kidney with severe hydronephrosis due to compression of the ureteropelvic junction by the diaphragmatic crus.

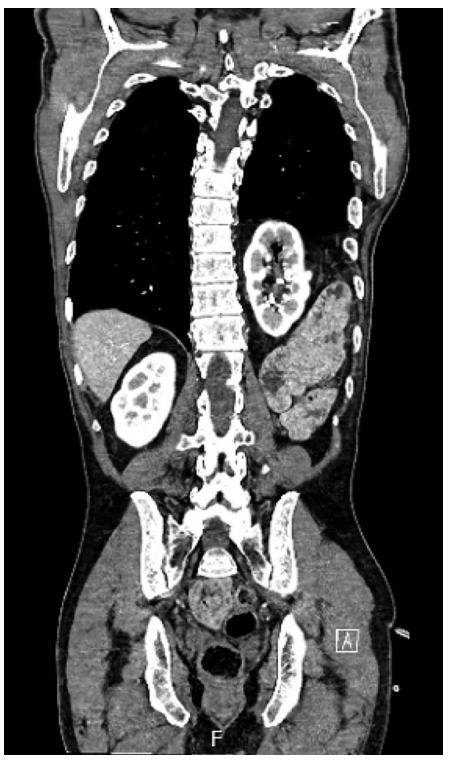

Figure 2. Coronal CT image after percutaneous nephrostomy placement prior to hernia repair and nephropexy.

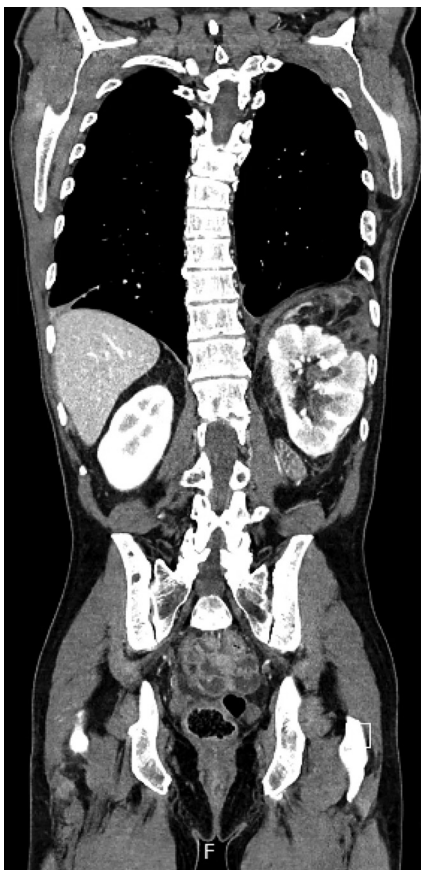

Figure 3. Postoperative coronal CT image with intra-abdominal kidney.

BOCHDALEK HERNIA WITH AN INTRATHORACIC KIDNEY

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presenting with urinary obstruction for which surgical repair was indicated and successfully performed. ■

1. Brock PB, Davis SS Jr. Repair of congenital diahernias: Morgagni and Bochdalek. In: Davis SS Jr, Dakin G, Bates A, eds. *The SAGES Manual of Hernia Surgery*. Springer; 2019:573-582.
2. Shah AD, Ajay S, Adalia M, Rathi A. Bochdalek hernia with intrathoracic kidney. *Lung India*. 2012;29(4):373-375.
3. Akita M, Yamasaki N, Miyake T, et al. Bochdalek hernia in an adult: two case reports and a review of perioperative cardiopulmonary complications. *Surg Case Rep*. 2020;6(1):72.
4. Lin FC, Lin JS, Kim S, Walker JR. A rare diaphragmatic ureteral herniation case report: endoscopic and open reconstructive management. *BMC Urol*. 2017;17(1):26.
5. Navaratnarajah A, Barry V, Charif R. Bochdalek hernias associated with intrathoracic kidney: a case report and systematic review of outcomes including renal function. *Clin Nephrol Case Stud*. 2020;8:1-11.
6. Alliende C, Oporto S, Mandujano F, Sáez ID, Coz F. Laparoscopic repair of Bochdalek hernia, presenting as renal colic. *Urology*. 2019; 132:e11e2.

OFFICE & SURGICAL TECHNOLOGIES

Applications of Single-port Robotic Surgery in Urology

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Since the description of employment of laparoscopic cholecystectomy in the 1980s, urologists have consistently been at the forefront of the advancement of laparoscopic technology and techniques.[1] The goal of continuing to improve surgical outcomes and laparoscopic techniques eventually led to the creation of robotic surgical systems, and in 2000 the da Vinci Surgical System became the first robotic surgery system approved by the U.S. Food and Drug Administration for general laparoscopic surgery. There has been development of additional systems, but the da Vinci is the overwhelmingly dominant system being used.[2,3]

Even with use of the multiport da Vinci, surgeons continued attempts to improve morbidity of surgery. Use of robotic systems allowed for R-LESS (robot-assisted laparoendoscopic single-site) surgery as it helped to overcome limitations of LESS (laparoendoscopic single-site), and while still technically challenging was still an improvement over a pure laparoscopic approach due to better vision and better arm/instrument maneuverability.[4] However there were limitations due to the multiport design of the system, including arm collisions, difficulty triangulating target tissue, inability to use a fourth arm, and difficult access for the bedside assistant.[2] Nevertheless, this ultimately led to the development of the of da Vinci single-port (SP) surgical system, with the SP robotic platform receiving approval by the U.S. Food and Drug Administration in 2018.

With the da Vinci SP surgical system, all instruments and the camera are placed in a single 25 mm cannula in one of 4 channels located at the 12, 3, 6, and 9 o'clock positions, which helps to maximize work space and minimize arm collisions, which is an improvement over previous LESS and R-LESS procedures.[2] In addition, instruments have the benefit of an additional joint that can serve as a flexible elbow along with the typical EndoWrist joint. This can help prevent arm collisions as well as negotiate around the target anatomy or difficult to reach locations. The smaller visual field, however, requires adaptation by the surgeon, but the articulation allows for camera angulation of 0° to 30°, which, at least in part, helps offset the limitation.[2]

As with most minimally invasive options, the goal of an SP robotic procedure would be to reduce postoperative pain, reduce narcotic analgesic use, reduce hospital stay, and reduce the time to return to normal activities, in addition to a better cosmetic outcome. Unfortunately, there are currently limited comparative studies to evaluate this. In addition, as minimally invasive procedures evolve, some of the gains may only be marginal and be more difficult to measure.

Due to the still emerging nature of this technology, current literature is still largely limited to smaller case series and retrospective studies with additional investigation still being needed. More information involving the SP system is associated with its use in radical prostatectomies. Systematic literature reviews have shown that short-term oncologic (ie, positive surgical margins) and functional outcomes as well as safety are similar between SP and multiport systems, while some studies suggest decreased pain and shorter hospital stays.[5-7] In another study involving high-volume surgeons, initial operative times were only slightly longer with the SP system after 3 cases or fewer, suggesting relative ease of adapting to the new system, at least in the context of an experienced surgical team.[8]

Extraperitoneal and transperineal radical prostatectomies have also been shown to be feasible using the SP system and may make access to the prostate somewhat easier than with a typical multiport system given the increased angulation and articulation of the camera and instruments. In a single-institution study there were promising results with regard to initial recovery, complications, and narcotic use.[9]

Additional smaller studies have similarly shown the SP system to be viable with partial and radical nephrectomies, pyeloplasty, simple prostatectomies, and cystectomies.[10] Although larger numbers are needed, current literature reviews again suggest overall surgical complications are likely to at least be comparable to those associated with multiport robotic surgeries in these cases as well.[10]

With any new technology, the cost/benefit ratio must always be assessed. Each SP system costs approximately $2 million with instruments costing around $5,000-$7,500 apiece (each instrument having 20-25 uses).[2] The development of other robotic systems, such as the Telelap ALF-X, REVO-I, and Avatera, may help to lower these costs in the future.

While additional prospective, randomized, controlled trials that also include more long-term outcomes and cost analysis are warranted, SP robotic surgery appears to be an exciting, safe, and feasible alternative to the more traditional multiport robotic-assisted laparoscopic approaches. ■

1. Mikhail D, Sarcona J, Mekhail M, Richstone L. Urologic robotic surgery. *Surg Clin North Am*. 2020;100(2):361-378.
2. Garbens A, Morgan T, Cadeddu JA. Single port robotic surgery in urology. *Curr Urol Rep*. 2021;22(4):22.
3. Yaxley JW, Coughlin GD, Chambers SK, et al. Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study. *Lancet*. 2016;388(10049):1057-1066.
4. White MA, Haber GP, Autorino R, et al. Robotic laparoendoscopic single-site radical prostatectomy: technique and early outcomes. *Eur Urol*. 2010;58(4):544-550.
5. Fahmy O, Fahmy UA, Alhakamy NA, et al. Single-port versus multiple-port robot-assisted radical prostatectomy: a systematic review and meta-analysis. *J Clin Med*. 2021;10(24):5723.
6. Lai A, Dobbs RW, Talamini S, et al. Single port robotic radical prostatectomy: a systematic review. *Transl Androl Urol*. 2020;9(2):898-905.
7. Bertolo R, Garisto J, Bove P, et al. Perioperative outcomes between single-port and "multi-port" robotic assisted radical prostatectomy: where do we stand?. *Urology*. 2021;155:138-143.
8. Agarwal DK, Sharma V, Toussi A, et al. Initial experience with da Vinci single-port robot-assisted radical prostatectomies. *Eur Urol*. 2020;77(3):373-379.
9. Aminsharifi A, Sawczyn G, Wilson CA, et al. Technical advancements in robotic prostatectomy: single-port extraperitoneal robotic-assisted radical prostatectomy and single-port transperineal robotic-assisted radical prostatectomy. *Transl Androl Urol*. 2020;9(2):848-855.
10. Garisto J, Bertolo R, Reese SW, et al. Minimizing minimally invasive surgery: current status of the single-port robotic surgery in urology. *Actas Urol Esp (Engl Ed)*. 2021;45(5):345-352.

Subcutaneous Penile Implants

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As many people reading this article are urologists, it is likely that you have been asked by your male patients, "Hey Doc, is there anything new to make my penis bigger?"

As a male sexual medicine specialist, this happens to me every week. Historically, my response was that there was nothing reliable available and that most of the reported options such as injections of fat, polymethyl methacrylate, hyaluronic acid, or fat grafts were compromised by reabsorption or significant complications.

Even if there are viable treatment options to enhance penile size, one persistent question remains among urologists: Is it not odd that men want a bigger penis? There are certainly many published papers examining this question.[1-4] In fact, one study reported that up to 91% of men who believed their penis to be smaller than average desired a bigger penis.[5] There is no doubt that most men if given the opportunity to magically have a bigger penis would gladly accept it, but what about the men who actually pursue this treatment? They have often been given the diagnosis of body dysmorphic disorder or, more specifically, penile dysmorphic disorder. Although there are men who are seriously obsessed with the appearance of their penis, that has not been my typical experience since I began offering Penuma implantation in early 2019. In fact, a recently published article showed that only 5.5% of 1,641 men surveyed had a severely low genital self-image, with 11.3% considering undergoing cosmetic genital surgery.[3] Mondaini et al in their evaluation of men pursuing penile size augmentation found that 85% had a normal size penis.[6] This suggests that these men simply want to be bigger as they feel this will enhance their self-esteem and sexual relationships.

Currently, the Penuma device is available as a surgically implanted soft silicone insert, which first came on the market well over a decade ago, and as of May 2022, it is the only Food and Drug Administration–cleared device to provide cosmetic enhancement of the penis. It is designed to enhance flaccid and erect penile girth as well as flaccid penile length. It is NOT designed or marketed to enhance erect length.

It appears that the ideal candidates for this procedure are circumcised men with normal erectile function who may also have a retractile penis, insecurity or embarrassment about penis size, mild penile curvature or shaft indentation, or a normal penile length with decreased girth.[7] All men interested in Penuma surgery undergo an initial intake questionnaire and telephone screening to rule out those who are clearly not good candidates including those who expect increased erect length, have unrealistic expectations, are active smokers, have uncontrolled diabetes, have moderate to severe curvature caused by Peyronie's disease, or have undergone any prior enhancement procedure such as subcutaneous injections or grafting. These men then fill out a series of validated questionnaires primarily focused on body dysmorphic disorder as well as a SHIM (Sexual Health Inventory for Men) survey to confirm satisfactory erectile function. If there are any questions about a man's psychological candidacy for this cosmetic surgery of the penis, they are referred to a licensed sex therapist before seeing one of the surgeons in the Penuma Network.

To date approximately 5,000 Penuma devices have been implanted, the majority in Beverly Hills by Dr James Elist, who developed the device and has been offering this procedure since 2004. Dr Elist, has now trained 9 Penuma surgeons who are performing this surgery in the U.S.

As surgeons, we know any procedure has possible risks, and this is especially important when performing elective cosmetic surgery. Possible risks discussed with the patient include infection and erosion which would necessitate removal of the device. Other less severe complications include seroma formation, which is also encountered following other subcutaneous implants such as in the face, gluteal area, calf, and breast. Device dislodgment/displacement and visible distal flaring of the implanted device have become uncommon since enhancements have been made in the implantation technique. The Penuma Surgeons Network is quite interactive, and as a result of sharing personal modifications in technique, much progress has been made to improve cosmetic outcomes as well as reduce infection and erosion rates. For instance, a lateral scrotal incision has supplanted the original infrapubic incision and is now the preferred approach which has reduced seroma rates but also provides a more cosmetic concealed scar (Figures 1-4). The implantation technique is nicely described in the recently

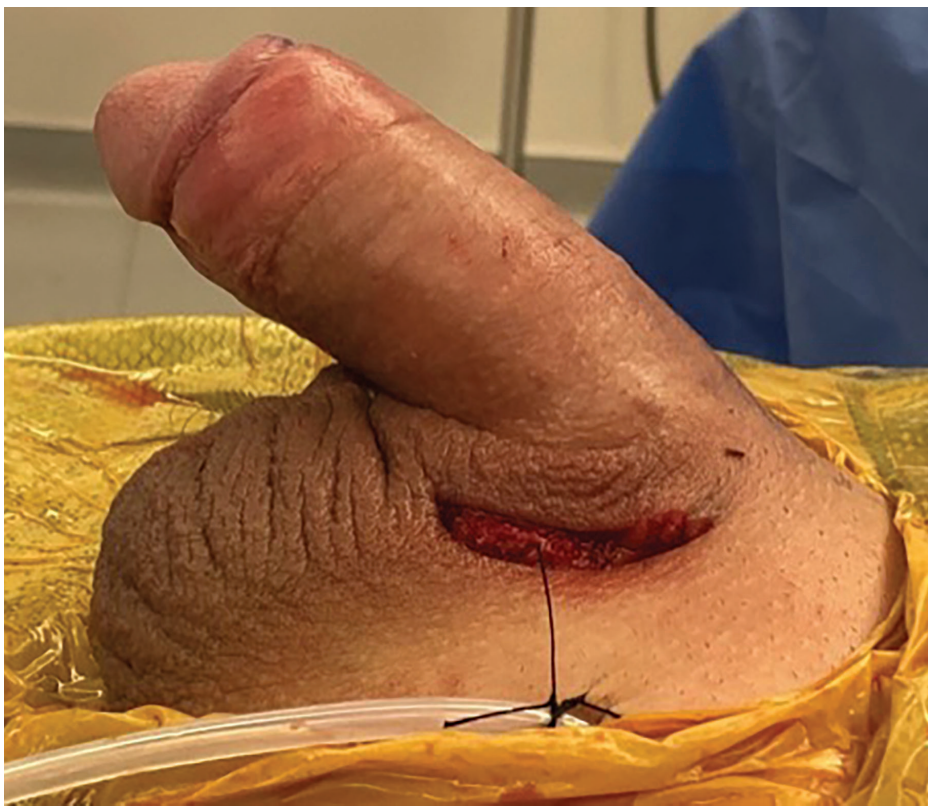

Figure 1. Lateral scrotal incision for implantation of Penuma shown prior to closure.

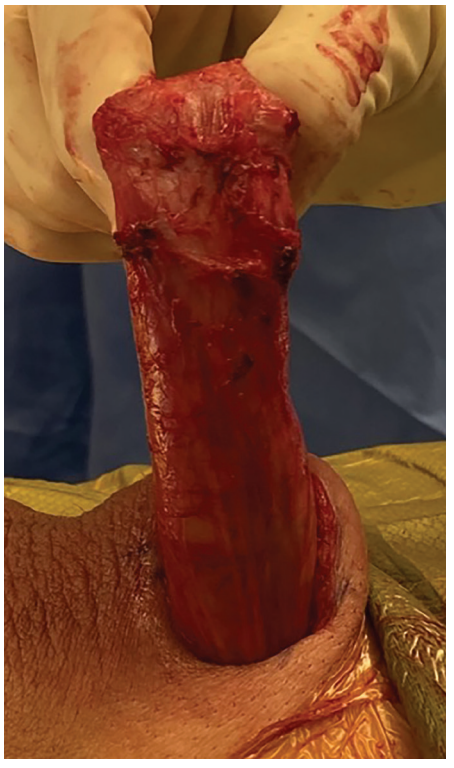

Figure 2. Penis everted through lateral scrotal incision with dissection exposing subcoronal sulcus.

Figure 3. Penuma device sutured to subcoronal sulcus with 2-0 Ethibond.

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SUBCUTANEOUS PENILE IMPLANTS

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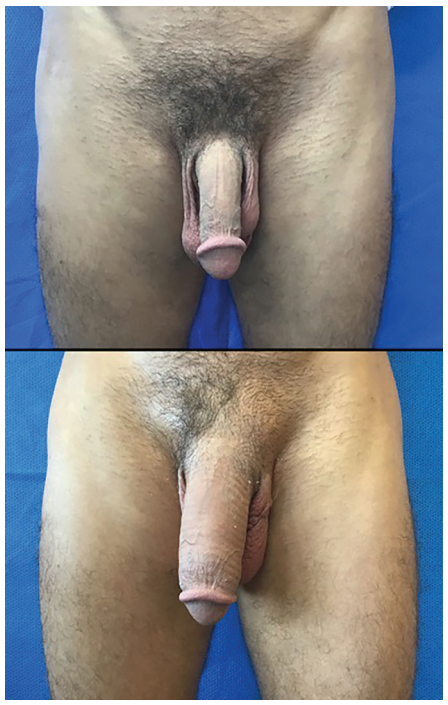

Figure 4. Example of pre- and postoperative result.

published article by Siegal et al.[7] Cautery is not used when developing the plane between Dartos and Buck fascia, which likely has reduced seroma and erosion rates as well, and a variety of medications are given perioperatively and during irrigation of the field which has also reduced seroma, infection, and erosion. Infection and erosion have historically been reported at a combined 2%-4% rate requiring device removal, which is clearly devastating. To address this, a post-Penuma removal protocol was developed which can help return the penis to its pre-insertion state more efficiently.[8]

Part of the goal of the Penuma Scientific Advisory Board was to develop a registry of men undergoing this surgery so we could report on their outcomes. One difficulty with this is that because there are only a few implanters nationwide, postoperative assessment is often compromised as these men are frequently lost to follow-up. The manufacturer, International Medical Devices (Beverly Hills, California) is sponsoring the development of a more robust registry which should include outcomes from all Penuma surgeons.

In the meantime, the available published data indicate that men can expect to see an increase in postoperative flaccid length and girth of 52% and 40%, respectively, as found in the recently published, 49-patient study by Siegal et al.[7] This study compared nicely to the 2018, 400-patient report by Elist et al, where flaccid length and girth increased 24% and 57%, respectively.[9] In our Chicago experience, we developed a nonvalidated, Penuma-specific, postoperative satisfaction survey used in 40 men who were at least 6 months out from their surgery to allow for implant-related changes, including feel and sensation, to stabilize. We found that 55% were dissatisfied with their sexual relationship prior to surgery compared to 18% after the implant. Importantly, 68% endorsed being dissatisfied or very dissatisfied with the appearance of their penis prior to surgery, compared to 82% who reported being satisfied or very satisfied with the appearance of their penis after surgery.[10]

In conclusion, it appears that many men simply want a bigger penis and are willing to pay out of pocket for a variety of procedures to obtain that goal. Historically, injecting fillers and grafting procedures have been complicated with reabsorption and occasionally serious adverse results. The Penuma device is now being offered by well-trained urologists to men who are thoroughly evaluated to make sure they are appropriate candidates and counseled about the potential risks of the procedure, which like penile protheses for erectile dysfunction can still result in serious complications over 50 years since penile implants were first introduced. Relatively speaking, Penuma is early in its journey, and with further attention to surgical technique, device enhancements, as well as appropriate patient selection, we will see in upcoming reports evidence that men who want a bigger penis can realize this with the Penuma device. Currently, the Penuma device appears to provide a durable, natural-appearing penis with enhanced girth and flaccid length. It does not interfere with normal penile function including erection, sensation, orgasm, ejaculation, and urination. Most importantly, in the limited presented and published reports, there is evidence of high patient satisfaction. ■

1. Gaither TW, Allen IE, Osterberg EC, et al. Characterization of genital dissatisfaction in a national sample of U.S. men. *Arch Sex Behav.* 2017;46(7):2123-2130.
2. Veale D, Miles S, Read J, et al. Phenomenology of men with body dysmorphic disorder concerning penis size compared to men anxious about their penis size and to men without concerns: a cohort study. *Body Image.* 2015;13:53-61.
3. Hustad IB, Malmqvist K, Ivanova E, Rück C, Enander J. Does size matter? Genital self-image, genital size, pornography use and openness toward cosmetic genital surgery in 3503 Swedish men and women. *J Sex Med.* 2022;19(9):1378-1386.
4. Lever J, Frederick D, Peplau L. Does size matter? Men's and women's views on penis size across the lifespan. *Psychol Men Masc.* 2006;7(3):129-143.
5. Sharp G, Oates J. Sociocultural influences on men's penis size perceptions and decisions to undergo penile augmentation: a qualitative study. *Aesthet Surg J.* 2019;39(11):1253-1259.
6. Mondaini N, Ponchietti R, Gontero P, et al. Penile length is normal in most men seeking penile lengthening procedures. *Int J Impot Res.* 2002;14(4):283-286.
7. Siegal AR, Zisman A, Sljivich M, Razdan S, Valenzuela RJ. Outcomes of a single center's initial experience with the Penuma® penile implant. *Urology.* 2023;171:236-243.
8. Wilson SK, Picazo AL. Update on the Penuma an FDA-cleared penile implant for aesthetic enhancement of the flaccid penis. *Int J Impot Res.* 2022;34(4):369-374.
9. Elist JJ, Valenzuela R, Hillelsohn J, Feng T, Hosseini A. A single-surgeon retrospective and preliminary evaluation of the safety and effectiveness of the Penuma silicone sleeve implant for elective cosmetic correction of the flaccid penis. *J Sex Med.* 2018;15(9):1216-1223.
10. Salkowski M, Alter K, Levine LA. Outcomes and satisfaction after penile silicone implant surgery. *J Urol.* 2022;207(Suppl 5):e907.

FROM THE EDUCATION COUNCIL

Assessing the Educational Needs of the Urological Care Team Managing Overactive Bladder Patients

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AUA Office of Education Chair

"The length of a film should be directly related to the endurance of the human bladder" – Alfred Hitchcock

The AUA Office of Education works with our members through year-round educational needs assessment research to ensure we are providing what you need.

In 2022, the AUA conducted Phase I of an overactive bladder (OAB) needs assessment to better understand the educational needs of the urological care team who manage OAB patients. These comprehensive needs assessments include one-on-one interviews, multiple focus groups, and thereafter an online survey sent out to the broader AUA membership. For this OAB survey, a total of 759 surveys were completed for a response rate of 7%. Nearly all urology health care providers responding to this survey (95%) indicate they personally manage OAB patients.

A key observation from the one-on-one interviews and focus groups was that the prescribing habits of urology health care providers was quite consistent. For the most part, almost all providers initially started patients on an anticholinergic medication. This was attributable to the insurance approval process for coverage of β3 agonist medications which often required failure of an anticholinergic prior to initiating a β3 agonist. The Figure summarizes the biggest barriers associated with the prescribing of OAB medications.

Based on these barriers, over half of urological health care providers (53%) indicated that the greatest educational need for OAB related to the insurance approval process

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ASSESSING THE EDUCATIONAL NEEDS OF THE UROLOGICAL CARE

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and documentation for β3 agonists. Other areas noted as OAB educational needs include review of the AUA/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction guideline and amendment, the role of combination therapy (anticholinergic plus β3 agonist), and management of comorbid conditions. In addition, only 38% of respondents indicated they are very familiar with the term "anticholinergic burden."

The Office of Education invests all of this time and resources to ensure that the education we provide is directed at what our members need. To that end, I want to share with you the education that is currently available to meet these identified needs.

If you need some immediate education, I would recommend the online CME (Continuing Medical Education) course, "Live From AUA2022: Highlights in Overactive Bladder" housed in AUAUniversity (https://auau.auanet.org/content/live-aua2022-highlights-overactive-bladder). This is a great course which provides a summary of all of the most important OAB updates from AUA2022, including relevant plenary content, abstracts, and instructional courses.

Figure. Barriers to prescribing overactive bladder medication.

At AUA2023, there will be several in-person educational opportunities. First, Dr Victor Nitti will be joining the Advanced Practice Provider 2-day program on Saturday, April 29, to review these data and discuss the treatment modalities for OAB. Later that day, Dr Eric Rovner will lead a very popular session titled, "Contemporary Pharmacotherapy for Overactive Bladder 2023: Monotherapy and Combined Pharmacotherapy to Optimize Treatment." This 2-hour Instructional Course will cover many of the issues highlighted in the needs assessment including (1) the similarities and differences between the various oral pharmacotherapies for OAB, (2) the principles of physiology and pharmacotherapy for currently available agents (including antimuscarinics, β3 agonists, and combination therapy), and (3) analyzing the clinical (and theoretical) advantages and limitations of currently available agents. This is always a well-attended course which I highly recommend.

We would like to thank the 750+ members who took the time to respond to AUA's needs assessment survey as well as to Victor W. Nitti, MD and Lynn Allmond, NP for their contribution and leadership to this activity. The AUA would also like to thank Urovant Sciences, Inc for providing an independent educational grant in support of this educational needs assessment.

If you have any questions about this survey, please email education@auanet.org, and if you ever receive one of our email invitations, I encourage you to take a few minutes to share your thoughts with us. It is invaluable for us to improve the programming for our membership. ■

What Is Reconstructive Urology? The Evolution of the Field and Fellowship Training

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Reconstructive urology has historically been a difficult subspecialty to define with overlap into other aspects of urology including oncology, andrology, prosthetics, incontinence, voiding dysfunction, pediatrics, robotics, and plastic surgery.[1] Perhaps sadly, Wikipedia may provide the best definition of reconstructive urology as a "specialized field of urology that restores both structure and function to the genitourinary tract."[2] Historically, much of reconstructive urology has focused on urethral reconstruction. But in addition to urethral disease, the genitourinary reconstruction umbrella often includes genital surgery, gender affirming surgery, male incontinence, cancer survivorship, erectile dysfunction, Peyronie's disease, neurogenic bladder, urinary diversion, transitional urology, urological trauma, and urinary fistulae. While this practice variability exists, historically urethral reconstruction has been the "tie that binds" reconstructive urology.

The first formal fellowship training program in adult and pediatric genitourinary reconstructive surgery was formed in 1975 at Eastern Virginia Medical School by Dr Charles Devine. Thereafter, the male genitourinary reconstruction and trauma fellowship at University of California, San Francisco, was created by Dr Jack McAninch in 1989. Shortly afterward, a fellowship in reconstructive urology was founded at Duke University by Dr George Webster. For many years, these 3 programs were the pillars of male reconstructive urology training, at least in North America. Each fellowship was unique in its training experience. Additionally, equally diverse and distinguished fellowships existed in Europe throughout this time frame. In the early 2000s, as the understanding of genitourinary diseases, anatomy, tissue transfer, and surgical techniques evolved, reconstructive urology blossomed while "standing on the shoulders of these giants." In the 2000s, the number of fellowship programs grew dramatically. In response to the growth of reconstructive urology worldwide, the Society of Genitourinary Reconstructive Surgeons (GURS) developed a formal fellowship match program. For the 2012 cycle, GURS began developing a formal reconstructive match, which initially offered 13 different programs and has grown to 27 programs during the most recent 2023 match.

GURS fellowship training typically offers a robust clinical experience. Recent case log analysis from 25 different programs over 11 years of the GURS match has shown increases in urethral reconstruction, genital reconstruction, abdominal reconstruction, and male sexual dysfunction (I. Calvo,

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WHAT IS RECONSTRUCTIVE UROLOGY?

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unpublished data, 2023). The typical urethroplasty experience for a GURS program is a mean volume of 88 cases/y, 16 cases/y for genital reconstruction, and a mean of 24.5 cases/y for abdominal reconstruction. Programs also provide a mean of 32.7 cases/y for male sexual health with a stable number of male incontinence cases at a mean of 30.5 cases/y. Despite an increase in the number of fellowship programs, the GURS fellow operative experience remains robust. This growth likely reflects the growth of reconstructive urology as a discipline combined with consolidation of cases to academic centers and expansion of service lines offered by GURS surgeons in areas such as gender-affirming surgery, robotics, and adult congenital care.

GURS fellowship training is also of high quality. In a recent survey of GURS fellowship graduates, 92% reported being pleased with their training, 100% felt competent to enter unsupervised reconstructive urology practice, 100% readily found employment in reconstructive urology, 92% practice in a location that they consider one of their top 3 destinations, and 92% were satisfied with their clinical practice as a reconstructive urologist.[3] While generally a satisfying and robust experience for fellows and fellowship program directors, there is significant variability among fellowship programs, likely reflecting the growing diversity of reconstructive urology practice. Rather than programs potentially withdrawing from GURS because of an inability to satisfy any one specific case log threshold, the consensus of program directors has been to adopt this emerging diversity in training. Urethral reconstruction remains a mainstay of GURS training with 76% of program directors identifying this as a mandatory category for fellowship qualification. However, GURS training has recently been redefined by consensus into 4 main categories including urethral reconstruction, genital reconstruction, abdominal/pelvic reconstruction, and genitourinary prosthetics with associated necessary case log thresholds.

As reconstructive urology continues to grow and evolve, there will be a need to educate more broadly. Work is actively underway to develop an online reconstructive urology curriculum to ensure every graduating fellow and otherwise interested GURS member possesses a core set of reconstructive knowledge and technical skills. Additionally, in order to address the substantial need to train internationally, GURS will work to develop mini-fellowship programs and establish formal exchanges between centers to help disseminate technical advances in reconstructive urology worldwide. Since the majority of GURS fellowships are in North America, further worldwide outreach and collaborative creation of new fellowship programs in other regions will help address the large international need in reconstructive urology. ■

> "As reconstructive urology continues to grow and evolve, there will be a need to educate more broadly."

1. Saavedra AA, Rourke KF. Training in reconstructive urology: the past, present and future. *Transl Androl Urol.* 2018;7(4):666-672.
2. Wikimedia Foundation Inc. *Wikipedia: The Free Encyclopedia.* 2004. Accessed December 13, 2022. https://en.wikipedia.org/wiki/Urology.
3. Cotta BH, McCammon KA, Rourke K, Rosenstein D, Buckley JC. Training genitourinary reconstructive surgeons: a survey of graduated fellows and fellowship directors. *Urology.* 2019;131:36-39.

What Is Good Publication Practice and Why Should It Matter to Urologists?

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Urology, like all other medical specialties, values the quality of its peer-reviewed evidence base. Although editorial groups like the International Committee of Medical Journal Editors (ICMJE) and the World Association of Medical Editors began providing detailed advice about the quality and reporting of publications during the twentieth century, the specific challenges of collaborative research and authoring with company sponsors also needed attention. This need prompted the development of the original Good Publication Practice (GPP) guideline by Wager, Field, and Grossman.[1]

GPP

The original GPP guideline was intended to function similarly to other types of "good practice," like Good Clinical Practice, which was first released by the International Committee on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use in 1996.[1] A few years later, the ICMJE expressed reservations about data transparency and the ability of authors to be accountable for published study results. Notably, to protect intellectual property rights, investigators and other authors were often denied access to study data. In addition, it could be difficult to identify different studies and patient cohorts because there was no regularized way of registering studies so that peer reviewers could identify them. Other elements of study conduct and the role of contract research organizations were not always disclosed.[2]

Wager and colleagues said that company-sponsored research should be held to the same ethical standards as any biomedical publication. The initial GPP document adopted the measures suggested by ICMJE and strongly encouraged attention to transparency, maintaining authorship standards and clearly explaining the publication process for company-sponsored research.[1]

The International Society of Medical Publication Professionals, founded in 2005, adopted the GPP guidelines and has sponsored periodic updates to keep up to date with developments in publishing.[3,4] These iterations introduced new information about day-to-day practices in publication planning and development, such as the role of steering committees, as well as providing advice as the field expanded. The ICMJE guidelines[5] and the CONSORT (Consolidated Standards of Reporting Trials) statement[6] provided an important basis for these GPP iterations, which focused primarily on publications of clinical trial data.[3,4]

The 2022 GPP Update

The 2022 update of GPP, also known as GPP 2022, reflects developments in the publication profession, which now extends beyond clinical trial publications to cover all scientific areas.[7] GPP has expanded its focus beyond CONSORT to other disciplines covered by the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) network.

The GPP 2022 supplement describes best practices for publication planning, such as establishing steering committees, developing a publication plan, and determining whether contributors have met applicable authorship criteria. Advice is also given about the leadership that publication professionals should show, such as developing policies and training teams. The supplement now gives insight into publication professional roles that can be useful to authors and academic partners. Recommendations for including patients in the publication process, working in corporate alliances, enhanced publication content, and plain language summaries are also provided. Hot topics, such as best use of preprints to serve medical and scientific needs, are also included.[7]

A primary focus of GPP 2022 is inclusivity. An example of this inclusivity is that regional investigators should be included in author bylines. The supplement was redesigned to provide an overview suitable for novices or students, and an emphasis on enhanced content, plain language summaries, and patient inclusion in the publication process all support this general aim. For instance, GPP now recommends that patients be treated as full participants when they contribute to publications or serve on steering committees.[7]

Focus on Urology

Of course, GPP can only offer general advice, which means that subject matter experts, editors, investigators, and other academics also have important roles to play in applying the GPP principles. Only experts working within a specific area can determine how the GPP principles should be applied in specialized situations. For instance, journal editors can set guidelines for authorship, number of authors, plain language summaries, enhanced content, and peer review. Investigators can comment on how much time and effort will be needed to follow the guidelines in GPP.

> "Urology as a medical specialty has shown leadership in considering its own best publication practices."

> "The GPP 2022 supplement describes best practices for publication planning, such as establishing steering committees, developing a publication plan, and determining whether contributors have met applicable authorship criteria."

Urology as a medical specialty has shown leadership in considering its own best publication practices. Further leadership is possible. For instance, GPP does not include advice for conducting peer review: this is an area that is worthy of comment by peer reviewers within specific expert areas like urology.

We hope that the American Urological Association will adopt GPP 2022 and will encourage its members to share best practices for authorship and publishing, including areas like peer review that are not included in GPP. ■

1. Wager E, Field EA, Grossman L. Good publication practice for pharmaceutical companies. *Curr Med Res Opin.* 2003;19(3):149-154.
2. Davidoff F, DeAngelis CD, Drazen JM, et al. Sponsorship, authorship, and accountability. *Ann Intern Med.* 2001;135(6):463-466.
3. Graf C, Battisti WP, Bridges D, et al. Good publication practice for communicating company sponsored medical research: the GPP2 guidelines. *BMJ.* 2009;339:b4330.
4. Battisti WP, Wager E, Baltzer L, et al. Good publication practice for communicating company-sponsored medical research: GPP3. *Ann Intern Med.* 2015;163(6):461-464.
5. International Committee of Medical Journal Editors. *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals.* December 2021. https://www.icmje.org/recommendations.
6. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Int J Surg.* 2012;10(1):28-55.
7. DeTora LM, Toroser D, Sykes A, et al. Good Publication Practice (GPP) guidelines for company-sponsored biomedical research: 2022 update. *Ann Intern Med.* 2022;175(9):1298-1304.

FROM THE YOUNG UROLOGISTS COMMITTEE

Young Urology Events at AUA2023

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The upcoming American Urological Association annual meeting has much to look forward to in Chicago. Members of the Young Urologists' (YUs') Committee (YUC) have crafted an agenda for the Young Urology Forum (being held on Saturday, April 29, 2023, from 10 am-12 pm) which will provide insight YUs can put to immediate use in their day-to-day practices. More specifically, a key topic that continues to envelop much of social media and routine conversation within our specialty is optimization of practice environment and mitigation of burnout. Accordingly, "Cultivating Longevity in Practice" has been conceived by this year's YUC as the theme of the 2023 Young Urology Forum.

This topic matter is designed to help YUs navigate the challenges of building successful and sustainable careers in our field. The Young Urology Forum will have a wide array of speakers offering insights into building resiliency in practice, providing a multitude of perspectives. How can I stay engaged and motivated in my work over the long term? How can I build and maintain strong relationships with my peers? How can I prevent musculoskeletal injuries and other physical strain while performing surgery? What can I do to stay engaged in my professional development throughout my career? All of these questions will drive this year's Young Urology Forum. The agenda includes 5 distinguished speakers, all inspirational experts on this subject matter. Dr Eila Skinner (@ecskinner53), Dr Gina Badalato (@GMBadalato), Dr Christopher Anderson (@CBAnderson2014), Dr David Canes (@CanesDavid), and Dr Amy Park (@DrAmyPark) will speak on their experiences optimizing and cultivating longevity in practice.

An inaugural event also planned by the YUC for this year's AUA meeting is the "Meet the Leaders" program. An idea originally conceived by the YUC several years ago but put on hold due to the pandemic, this event is a unique opportunity for our YU members to gain valuable insights on career advancement within the AUA from recognized leaders of the organization. During this interactive session, YUs will have the opportunity to ask questions and engage in a roundtable format with candid conversation with some of the most respected and influential leaders in our field. These leaders will share their career experiences crafting pathways toward engagement within the AUA. In addition to gaining valuable insights, this is also a great opportunity for YUs to make meaningful connections and network with their peers and mentors. In short, the "Meet the Leaders" event is a chance to build lasting relationships with recognized leaders in our specialty and pave the way for future professional growth. Please note that this program will require sign-up in advance to participate. We encourage interested YU members to be on the lookout for this and secure time at this exciting event.

In addition, a third event planned and organized by the YUC for YUs at AUA2023 is the Speed Mentoring program. This program has quickly become a longstanding annual tradition at the AUA meeting. Residents and fellows sign up as "mentees" and discuss a wide range of topics with pre-selected YU mentors in short, "speedy" 10-minute conversations. Mentees then rotate to have similar short-burst conversations with additional mentors who are subject matter experts in the topic areas of interest. No issue is off limits in this no-holds-barred conversation; for example, previously, mentees have discussed fellowship/job advice, career choice, employment contract issues, and career goals.

We hope this has given you a sense of the valuable opportunities and experiences that await YUs at AUA2023. From the Young Urology Forum's "Cultivating Longevity in Practice," to "Meet the Leaders" and "Speed Mentoring," the YU program has been tailored so there is something for all YUs to engage with and benefit from. We look forward to seeing you at this year's meeting and hope that you will take advantage of all that it has to offer. We would like to extend a heartfelt thank you to the AUA leadership and staff for their hard work and dedication in planning these events. Without their tireless effort and support, the YU program would not be possible. ■

VOICES

Bridging the Gap: Evolution of the Diversity & Inclusion Task Force to AUA Diversity, Equity, and Inclusion Committee

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In December 2020, the AUA Board of Directors charged a diversity and inclusion (D&I) task force to identify and prioritize potential strategies the AUA could realistically implement for enhancing D&I within the AUA and within urological practices/institutions and to make recommendations for education, research, and/or advocacy initiatives that AUA could pursue, in collaboration with others, to help enhance diversity, equity, and inclusion (DEI) within these settings. Widespread, systemic change is required to challenge structures and norms that perpetuate such disparities for our patients and individuals who are underrepresented in the urological workforce.[1] As a leading professional organization in urology, the AUA has a duty to recognize the scope of these issues related to justice, diversity, equity, and inclusion, and to guide the change that is needed to advance our field.

Under the leadership of Dr Tracy Downs as chair and Dr Simone Thavaseelan as vice chair, as well as then Executive Vice President of Public Policy Kathy Shanley, PhD, the task force carried out its charge through structural competency development and training via an experiential, interactive, and transformative curriculum to establish

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BRIDGING THE GAP: EVOLUTION OF THE DIVERSITY & INCLUSION

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common understanding and foundations around DEI work, didactics and small group discussion, readings, and reflection for members to further develop DEI expertise.

The task force delivered 14 recommendations to the AUA Board, all of which were accepted with the exception of voting rights for the chief diversity officer.[2] The establishment of a new and standing D&I committee as approved by the AUA Board of Directors was to address the lack of an existing, centralized structure, beyond the Board's D&I Task Force, directly charged with making recommendations for and executing ongoing D&I initiatives. Previously, the AUA took a decentralized approach to D&I with departments or program areas sponsoring various D&I activities and initiatives without centralized oversight or communications effort within the organization or with affiliated societies. With regards to voting rights for the chief diversity officer, the Board elected to address the urgent need of diversification of the AUA governance structures though efforts at the Section level to promote representational diversity and create leadership reflective of both changing workforce and population demographics.

With the appointment of Dr Larissa Bresler as chief diversity officer and creation of the D&I Committee, the AUA has begun to operationalize these recommendations in short order. Dr Bresler has met with multiple stakeholders across the DEI space in urology already, and has further engagement planned. Members of this newly formed committee represent broad diversity within urology and across social identifiers of race, gender, ethnicities, sexual orientation, religion, language, and age, as well as AUA Section and subspeciality and clinical or academic focus (see Figure). The committee has chairpersons, program directors, society presidents, and specialty society DEI chairs; more than half of the committee is bilingual, several are double-boarded in either urological subspecialty or another medical discipline, and several are funded researchers. This intentional decision to include intersectional identities across the urology workforce is demonstrative of the practice of inclusive excellence.

Figure. AUA Diversity & Inclusion Committee.

In addition, the executive vice president and chief human resources officer serves as the AUA liaison for the committee. Four workgroups have been established in the D&I Committee: Education and Research, Unity and Collaboration, Media and Publication, and Pipeline, each with the following goals:

The Education and Research Workgroup:

- Collaborate with Education and Research council chairs including Dr Jay Raman and relevant committee chairs to increase the scope of DEI and health care disparities education within the AUA.
- Connect with Dr Cheryl Lee from American Board of Urology to create educational content/videos on health care disparities to be included in the recertification process and lifelong learning process.

The Media and Publication Workgroup:

- Assigned initial tasks to collaborate with the AUA media team to work on publications, podcasts, and editorial opportunities.
- Plan and execute future podcasts, 100 posts, and publications such as *AUANews*, journals, podcasts, etc.
- Collaborate with key AUA directors Caitlin Lukacs and Jennifer Regala (AUA Communications and Publications departments, respectively).

Unity and Collaboration Workgroup:

- Coordinate efforts with AUA sections and specialty societies to avoid duplicate efforts, reinventing the wheel, and provide best practices to guide organizations in their internal D&I efforts.

The Pipeline Workgroup:

- Assigned initial tasks to advance pipeline programs for underrepresented in medicine and underrepresented in urology groups by building strong national programs for first- and second-year medical students.
- Develop the "Prospect" Pipeline mentoring program as a long-term program designed for underrepresented in medicine students to learn of urology and develop intentional mentoring, sponsorship, and networking to successfully pursue a match and career in urology.
- Execute a career-day mentoring program at the annual meeting location to encourage students of nearby medical schools to attend the meeting with a urologist mentor.

Urology and its organized leadership are not diverse and this will not change passively. Amid the COVID-19 pandemic and recognition in particular of racial inequity, many organizations have found they are poorly equipped to institute change and that their governance structures are no longer designed to fully support their strategic visions. There is an urgent need to modernize these cultures and the structure, policy, practice, norms, and values associated with them. The evolution of organizational with the transition from the AUA D&I Task Force to the standing AUA D&I Committee has been swift, consistent with the AUA's commitment to advancing DEI goals as part of its strategic mission. Professional medical societies are uniquely poised to evolve themselves to remove barriers to advancement and accelerate health equity by creating a more just and inclusive urological community for the betterment of our patients. ■

1. Simons ECG, Thavaseelan S, Saigal C, Downs T. Diversifying graduate medical education & the urology workforce: re-imagining our structures, policies, practices, norms, & values. *Urology*. 2022;162:128-136.

2. Thavaseelan S, Burnett AL 2nd, Chang S, et al. AUA Diversity & Inclusion Task Force: blueprint and process for justice, equity, diversity and inclusion. *J Urol*. 2022;208(3):498-504.

Working Towards Gender Equity Together: Allyship in Urology

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Gender Inequities In Urology

Women urologists in training and in practice face a number of distinct challenges. Microaggressions, societal expectations about interactions with women, expectations about family/mother roles, lack of representation in leadership, fertility–the list goes on.

Despite the growing number of women in the field, there are still significant data that suggest women are promoted at a slower rate than male colleagues,[1] are paid less even when controlling for work hours,[2] and may have fewer academic opportunities when it comes to publications, awards and recognition.[3] On top of this, women physicians face hurdles in their daily work environment. The National Academies of Sciences, Engineering, and Medicine reported that 20%-50% of women trainees reported sexual harassment or assault.[4] Discussion surrounding work environment for women and perceptions of equity in the workplace are important steps towards achieving inclusion and ultimately success.[5] While these topics are frequently discussed amongst women, in order to exact meaningful change these conversations need to include our male peers.

What Is Allyship?

In 2021, Dictionary.com identified "allyship" as its Word of the Year, defined as "the status or role of a person who advocates and actively works for the inclusion of a marginalized or politicized group in all areas of society, not as a member of that group, but in solidarity with its struggle and point of view, and under its leadership."[6] With respect to women in the urological workforce, this definition implies that allies should be working towards greater inclusion for women within urology. Inclusion goes beyond simply increasing the number of women in the field (ie, increasing representation); inclusion means that women who are urologists have equal access to opportunities, are given a seat at the table, and are valued within our historically male-dominated specialty.

An important and related concept is "sponsorship," typically where a more senior individual uses their connections and experience to help create greater access to opportunities for individuals not as far along in their career pathway. Finally, another important term in this space is "upstander," which Elisa van Dam defines as an individual who speaks or acts on behalf of someone else, especially when that person is being ignored or attacked. In addition, an upstander can be a person with influence who works to undo systems and/or structures with inherent bias.[7]

Why Is Allyship Important?

Allyship is important for a number of reasons. Individuals within marginalized groups, such as women in urology, often lack access to power or influence that can overcome inherently biased structures in the workplace, whereas allies may be more readily able to change these structures. For example, if a women urologist is experiencing harassment by staff in the operating room, an ally in a position of power can act to help identify the negative behaviors and address the infrastructure of the biased system to put a stop to the harassment. Additionally, an inclusive work culture should not impose the burden of demolishing structural and cultural biases upon members of the groups most disadvantaged by those biases.

> "Individuals within marginalized groups, such as women in urology, often lack access to power or influence that can overcome inherently biased structures in the workplace, whereas allies may be more readily able to change these structures."

How Can I Be an Ally?

Allyship is a continuous journey of learning and advocacy, even for individuals with a long history of allyship. Here are some easy actions to incorporate allyship into your practice:

1. Learn about becoming an effective ally by reading. Numerous resources about allyship are available online, in print, and potentially at your local institution. It is important to recognize that allies understand the burden of learning is on those seeking to become an ally, rather than asking members of marginalized groups how to be an ally.
2. Learn about your implicit biases. Everyone has implicit (sometimes call unconscious) biases; in many ways these biases are absorbed from societal expectations, media, or personal experiences, even as early as childhood. One way to gain insight into your own unconscious biases is to take an Implicit Association Test (free at https://implicit.harvard.edu/implicit/takeatest.html).
3. Do a network and mentorship biopsy. Examine the demographics of individuals you have mentored and/or sponsored over the past 5-10 years. How many of those individuals are women? How many are from other marginalized groups? If you have few or no women among those individuals, that suggests an opportunity for you to increase your knowledge and experience as an ally for women.
4. Listen to the experiences of women who you work with. Your colleagues have lived experiences that may differ from yours, and spending some time listening is helpful in establishing yourself as a trusted ally.

> "For urology to continue to thrive as a field, particularly in the setting of the twin demographic challenges of an aging workforce and an aging patient population (which will increasingly require urological care), it is important for our specialty to embrace inclusion of women and other minoritized and marginalized groups."

An excellent way of listening and supporting is by lending your voice to women in the room. For example, sometimes women experience their ideas being dismissed or repurposed in a meeting or conference. As an ally, you can lend support to those ideas, and make sure credit is given where credit is due.

5. Speak up when you witness offensive comments and microaggressions. Being a supportive ally entails being able to support someone when you see harmful behavior, and calling out negative treatment. It is okay to use your position to raises concerns with leaders to identify necessary changes to policies and practices as well as organizational climate and culture.

Be an upstander!

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WORKING TOWARDS GENDER EQUITY TOGETHER

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6. Transparency is key in achieving equity. Transparency is often lacking in medicine, whether it's salary structure, administrative support, or even leadership advancement/opportunities.

All salaries, incentive structures, and support should be made public within your group. Although potentially uncomfortable, the pay gap in urology will never be closed until we know exactly how much people are getting paid for their work.

All leadership, funding, and promotional opportunities should be advertised publicly. Although it feels easy to tap a colleague you trust for a position, the opportunity to apply should be made available to all who are interested. This process will help improve opportunities to women, and urologists from historically marginalized groups, who may be overlooked.

7. Be intentional about sponsorship. Sponsorship is the active support to help someone's career advancement goals. Mentorship is different from sponsorship in that it focuses on guidance and can come from colleagues at any career level.

Some intentional ways to be an ally and a sponsor:

- Nominate women for positions of leadership within your group/department/institution.
- Nominate women for awards. Data show that women are underrepresented in AUA career recognition awards, and the process towards equity starts with nominations.
- If you are unable to give a talk or attend a meeting, suggest a woman take your place.
- If you are invited to give a talk and the panel lacks diversity, recommend a woman or diverse speaker joins the panel. It is okay to withdraw or say no to an all-male panel.

8. Support fair pregnancy/parental leave/lactation practices.

Other Marginalized Groups in Urology

While the focus of this article is allyship for women within urology, it is critically important to recognize that individuals from many backgrounds remain marginalized within urology. Individuals from minoritized racial or ethnic groups, gender diverse urologists, LGBTQ individuals, and others often face structural and implicit biases in their work life and beyond. Importantly, women who also belong to another minoritized group (eg, Black women) can face multiple disadvantages from biases and barriers in the workplace, which is termed "intersectionality."

For urology to continue to thrive as a field, particularly in the setting of the twin demographic challenges of an aging workforce and an aging patient population (which will increasingly require urological care), it is important for our specialty to embrace inclusion of women and other minoritized and marginalized groups. Allyship is an important way that everyone can contribute to the growth and future success of urology–take the first step to becoming an ally today! ■

1. Breyer BN, Butler C, Fang R, et al. Promotion disparities in academic urology. *Urology.* 2020;138:16-23.
2. Spencer ES, Deal AM, Pruthi NR, et al. Gender differences in compensation, job satisfaction and other practice patterns in urology. *J Urol.* 2016;195(2):450-455.
3. Wenzel J, Dudley A, Agnor R, et al. Women are underrepresented in prestigious recognition awards in the American Urological Association. *Urology.* 2022;160:102-108.
4. National Academies of Sciences, Engineering, and Medicine. *Sexual Harassment of Women Climate, Culture, and Consequences in Academic Sciences, Engineering, and Medicine (2018).* The National Academies Press; 2018.
5. Martin LH, Haslam RE, Agnor R, Collins A, Bassale S, Seideman CA. Perceptions of gender equity by urologic subspecialty. *Urology.* 2023:S0090-4295(23)00050-X.
6. Dictionary.com. *Dictionary.com's 2021 Word Of The Year Is ….* Published December 6, 2021. https://www.dictionary.com/e/word-of-the-year-2021/.
7. MacKenty Brady S, van Dam E, Lee L. *The Inclusive Leader's Playbook: The Work of the Inclusive Leader.* Institute for Inclusive Leadership; 2021.

Have You Read?

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Sunaryo PL, May PC, Holt SK, Sorensen MD, Sweet RM, Harper JD. Ureteral strictures following ureteroscopy for kidney stone disease: a population-based assessment. *J Urol.* 2022;208(6):1268-1275.

Special thanks to Drs Ahmad Hefnawy and Omer Acar at the University of Illinois at Chicago.

Ureteroscopy is the most common procedure to treat renal and ureteral stones in the U.S., but we have lacked information about ureteral strictures following it on a large population level. These authors used the IBM MarketScan research database to study the outcomes of over 300,000 patients who underwent ureteroscopy or shock wave lithotripsy for treatment of upper tract stones between 2008 and 2019. Those receiving ureteroscopy or shock wave lithotripsy were nearly evenly split a bit under half and half, and about a tenth were treated with both.

Patients undergoing ureteroscopy alone or with shock wave lithotripsy had a near 3% rate of ureteric stricture, nearly twice that of those who had shock wave lithotripsy alone. Risk factors for stricture included concurrent kidney and ureteral stones, preoperative hydronephrosis, history of ureteroscopy and shock wave lithotripsy in the past year, and age. More than half of those who developed ureteral stricture following ureteroscopy or shock wave lithotripsy underwent a secondary procedure to manage stricture-related problems. Interestingly, during the decade studied, ureteroscopy to treat upper tract urolithiasis climbed from about 2 out of 5 to nearly 3 out of 5.

What do we do with this information? Ureteroscopy is obviously here to stay, but the prevalence and morbidity of ureteral stricture disease following it feels higher than anticipated. Let's keep this in the back of our minds as we plan our approaches for upper tract stones and counsel our patients.

Mulloy E, Li S, Belladelli F, Del Giudice F, Glover F, Eisenberg ML. The risk of cardiovascular and cerebrovascular disease in men with a history of priapism. *J Urol.* 2023;209(1):253-260.

Special thanks to Drs Jason Huang and Mahmoud Mima at the University of Illinois at Chicago.

Erectile dysfunction has a well-established correlation with future cardiovascular disease and is a clear indicator of vascular health. But what about erections that last too long? Here for the first time investigators studied the association of priapism and the development of cardiovascular and other vascular diseases by applying advanced statistics to evaluate a cohort of over 10,000 men in a commercial insurance database.

Across the board compared to control groups men who had priapism had about a quarter higher risk of future cardiovascular disease, nearly a third higher risk of cerebrovascular disease, and about a quarter higher risk of other forms of heart disease.

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These conclusions were consistent throughout subgroup analyses, such as including only those with ischemic priapism or excluding patients with sickle cell disease. Recurrence of priapism was associated with increased risk of vascular diseases in a dose-dependent fashion, which further validates the association.

This first study of its kind is definitely thought provoking and begs for others to investigate it. If confirmed, recommendations of the American Urological Association and Sexual Medicine Society of North America guidelines for ischemic priapism could include evaluation for vascular disease as well.

Shee K, Washington SL III, Cowan JE, et al. Gleason grade 1 prostate cancer volume at biopsy is associated with upgrading but not adverse pathology or recurrence after radical prostatectomy: results from a large institutional cohort. *J Urol.* 2023;209(1):198-207.

Special thanks to Drs Marcin Zuberek and Simone Crivellaro at the University of Illinois at Chicago.

What is the real clinical significance of Gleason grade group 1 prostate cancer? Its management and guidelines have greatly evolved: once it was believed to be a malignancy that needed immediate treatment; now it can be watched over a period of time. Yet urologists and pathologists continue to struggle with sampling and diagnostic inadequacies that may leave clinically meaningful cancer behind. What happens to patients in whom clinically significant cancer is missed on the premise of being characterized as Gleason grade group 1? That's the question these authors sought to answer.

In this retrospective study of over 1,000 patients with Gleason grade group 1 on initial biopsy, patients with 20% of positive cores or more were 1.31 times more likely to be upstaged to Gleason grade group 2 after radical prostatectomy. Yet despite the upstaging of pathology, there was no difference in the recurrence rate or adverse pathology.

> "What happens to patients in whom clinically significant cancer is missed on the premise of being characterized as Gleason grade group 1?"

The authors acknowledge several limitations to their study, namely its retrospective nature and lack of a uniform testing protocol. Still, these findings provide another important piece to the puzzle of Gleason grade group 1 prostate cancer. High-volume disease should prompt discussion with patients that there might be remaining undiscovered clinically significant cancer and consideration of more active surveillance, additional testing to further characterize the disease, or treatment. ■