Reconstructive Urology

Low Serum Testosterone Level Predisposes to Artificial Urinary Sphincter Cuff Erosion

Matthias D. Hofer, Allen F. Morey, Kunj Sheth, Timothy J. Tausch, Jordan Siegel, Billy H. Cordon, Matthew I. Bury, Earl Y. Cheng, Arun K. Sharma, Chris M. Gonzalez, William E. Kaplan, Nicholas L. Kavoussi, Alexandra Klein, and Claus G. Roehrborn

OBJECTIVE To examine the association between decreased serum testosterone levels and artificial urinary sphincter (AUS) cuff erosion.

MATERIALS AND METHODS We evaluated serum testosterone levels in 53 consecutive patients. Low testosterone was defined as <280 ng/dL and found in 30/53 patients (56.6%). Chi-square and Student *t* tests, Kaplan-Meier analysis, binary logistic regression, and Cox regression analysis were used to determine statistical significance.

RESULTS Nearly all men with AUS cuff erosions had low serum testosterone (18/20, 90.0%) compared to those without erosions (12/33, 36.4%, $P < .001$). Mean time to erosion was 1.70 years (0.83-6.86); mean follow-up was 2.76 years (0.34-7.92). Low testosterone had a hazard ratio of 7.15 for erosion in a Cox regression analysis (95% confidence interval 1.64-31.17, $P = .009$) and Kaplan-Meier analysis demonstrated decreased erosion-free follow-up (log-rank $P = .002$). Low testosterone was the sole independent risk factor for erosion in a multivariable model including coronary artery disease and radiation (odds ratio 15.78; 95% confidence interval 2.77-89.92, $P = .002$). Notably, history of prior AUS, radiation, androgen ablation therapy, or concomitant penile implant did not confound risk of cuff erosion in men with low testosterone levels.

CONCLUSION Men with low testosterone levels are at a significantly higher risk to experience AUS cuff erosion. Appropriate counseling before AUS implantation is warranted and it is unclear whether testosterone resupplementation will mitigate this risk. UROLOGY ■■: ■■–■■, 2016. © 2016 Elsevier Inc.

Implantation of an artificial urinary sphincter (AUS) remains the gold standard for the treatment of male stress incontinence in the nonneurogenic setting,[1] with postprostatectomy incontinence being accountable for the vast majority of AUS implantations.[2] At least 30% of AUS devices will have to be replaced over the course of their lifetime, usually due to urethral atrophy[2]; moreover, sphincter cuff erosions precipitate complete AUS removal in another 8%.

Whereas catheterization trauma without AUS deactivation may be responsible for some cases of cuff erosion,[3] prior urethral surgery and a history of radiation therapy have been described as causes.[2,4,5] Chronic compression, tissue ischemia, and radiation-induced obliterative endarteritis in such cases lead to corpus spongiosum atrophy, which compromises the ability of the urethra to withstand the pressurized AUS cuff. Spongiosal atrophy has been reported in up to 58% of AUS cases.[3,6]

A low serum testosterone level (LT) is not uncommon among postprostatectomy patients,[7] both due to the advanced age of the patients and secondary to androgen ablation therapy. Low androgen levels have been associated with atrophy of organs such as skeletal muscle and urinary bladder in animal models.[8,9] In the current study, we present the first reported investigation of LTs among AUS patients experiencing cuff erosion.

MATERIALS AND METHODS

Patient Cohort

After an initial clinical observation of LT in several AUS cuff erosion cases, we prospectively evaluated serum testosterone levels under an Institutional Review Board-approved protocol in 53 consecutive patients presenting for follow-up after AUS implantation for stress urinary incontinence. All patients had undergone

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From the Department of Urology, UT Southwestern Medical Center, Dallas, TX; and the Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, IL

Address correspondence to: Allen F. Morey, M.D., Department of Urology, UT Southwestern Medical Center, Moss Building, 8th Floor, Suite 124, 5323 Harry Hines Boulevard, Dallas, TX 75390-7201. E-mail: allen.morey@utsouthwestern.edu

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AUS placement at our institution by a single surgeon between 2007 and 2015 using a uniform 2-incision technique as previously described.[10] In general, patients routinely present 1.5, 3, and 12 months postoperatively and annually thereafter if their further course is uneventful, but earlier if there are complications. Serum testosterone levels were determined in a total of 53 consecutive patients who returned to clinic for follow-up during the accrual period of 2 months regardless of their clinical condition or whether they exhibited symptoms of hypogonadism (inclusion criteria). Our study cohort therefore consisted of (1) those who presented acutely with cuff erosion, and (2) those without cuff erosion presenting for routine clinic follow-up visits. As we observed from our entire AUS cohort of 352 men that the mean time to cuff erosion is 1.6 years, we excluded men without cuff erosion if <1.7 years had elapsed since AUS placement (exclusion criterion). Hence, we observed a higher rate of patients with eroded AUS than expected because they would come to our clinic outside their follow-up schedule. One testosterone measurement was taken and low testosterone was defined as serum testosterone <280 ng/dL, which was the cutoff level of the clinical laboratory at UT Southwestern Medical Center.

Statistical Analysis

Chi-square and *t* tests, Cox regression and Kaplan-Meier analysis, as well as binary logistic regression analysis were performed using SPSS 20.0 for MAC (IBM Corporation, Armonk, NY).

RESULTS

LT Is Associated With AUS Erosion

Of 53 patients who consecutively presented to our clinic for AUS follow-up, 20 (37.73%) presented with AUS erosion and 33 for routine follow-up without evidence of erosion. LTs (<280 ng/dL) were identified in 30/53 patients (56.6%) and we noted a significant lower mean serum testosterone level in men with AUS cuff erosions (161.66 ng/dL) compared to those without erosions (314.62 ng/dL, $P = .003$, Table 1). Mean time to AUS erosion in men with LT was 1.70 years (range 0.08-6.86 years) after AUS implantation. Stratified by testosterone serum level <280 ng/dL per our clinical laboratory's reference value, the vast majority of patients with AUS cuff erosions (90.0%) had testosterone serum levels below that threshold compared to those without erosion (36.4%, $P < .001$, Fig. 1A).

Interestingly, a history of pelvic radiation therapy was significantly more prevalent among patients with AUS erosion (80.0% vs 51.5%, $P = .038$, Table 1) as was coronary artery disease (36.8% vs 12.1%, $P = .047$). We did not find a significant difference in etiology of stress urinary incontinence, age, mean cuff size or placement of 3.5 cm cuff, prior AUS or sling placement, prior androgen ablation therapy, or comorbidities such as hypertension or diabetes.

LT Confers Risk for AUS Erosion Independently

Most of our 53 AUS patients with testosterone levels had a serum testosterone below 280 ng/dL (30/53 [56.6%]), and as shown in Figure 1B, had a higher rate of AUS cuff erosion (18/30, [60.0%]) compared to men with normal testosterone levels (2/23 (8.7%), $P < .001$). A Kaplan-Meier survival analysis shown in Figure 2 demonstrated a significant decrease of erosion-free follow-up time in men with decreased testosterone levels compared to men with physiologic levels ($P = .003$, log-rank). With a mean follow-up of 2.76 years (range 0.34-7.92 years), a Cox regression analysis revealed that LT portended a hazard ratio of 7.15 for AUS erosion (95% confidence interval [CI] 1.64-31.17; $P = .009$). In comparison, coronary artery disease had a hazard ratio of 2.99 (95% CI 1.15-7.76; $P = .024$) and radiation therapy of 3.19 (95% CI 1.05-9.77; $P = .041$). We also generated a multivariable regression model including

Table 1. Characteristics of patients with and without AUS erosions

	No Erosion	Erosion	*P*
N	33	20	
Mean age	71.89	71.07	0.793
Mean serum testosterone	314.62 ± 194.02	161.64 ± 119.88	**.003**
Hypogonadal	12 (36.4%)	18 (90.0%)	**<.001**
Stress urinary incontinence etiology			
Prostate Cancer—Radical Prostatectomy	29 (87.9%)	15 (75.0%)	0.226
Prostate Cancer—Primary Radiation	1 (3.0%)	3 (15.0%)	0.110
TURP	1 (3.0%)	2 (10.0%)	0.287
Mean cuff size	3.79	3.98	.086
3.5 cm Cuff	17 (51.5%)	8 (42.1%)	0.416
Prior AUS	8 (24.2%)	9 (47.4%)	0.117
Prior sling	4 (12.1%)	6 (31.6%)	0.107
XRT history*	17 (51.5%)	16 (80.0%)	**.038**
Androgen ablation therapy	6 (18.2%)	2 (10.0%)	0.420
Erectile dysfunction	19 (57.6%)	12 (60.0%)	0.862
Penile implant	10 (30.3%)	7 (36.8%)	0.723
Hypertension	21 (63.6%)	11 (55.0%)	0.533
Coronary artery disease	4 (12.1%)	7 (36.8%)	**.047**
Diabetes mellitus	5 (15.2%)	6 (31.6%)	0.196

AUS, artificial urinary sphincter; TURP, transurethral resection of the prostate; XRT, radiation therapy.
P values reaching statistical significance are in bold type.
* Patient with primary or adjuvant pelvic radiation therapy.