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Effect of Urethroplasty on Anxiety and Depression

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Purpose: To our knowledge anxiety and depression in patients with urethral stricture disease and the impact of urethroplasty on mental health has never been explored. We hypothesized that patients with urethral stricture disease would have higher than normal anxiety and depression levels, and urethroplasty would improve mental health.

Materials and Methods: We retrospectively reviewed the records of patients in a multi-institutional reconstructive urology database who underwent anterior urethroplasty. Preoperative and postoperative evaluation of anxiety and depression, and overall health was recorded using the validated EQ-5D™-3L Questionnaire. Sexual function was evaluated with the IIEF (International Index of Erectile Function) and the MSHQ (Men's Sexual Health Questionnaire). Stricture recurrence was defined as the need for a subsequent procedure.

Results: Median followup in the 298 patients who met study inclusion criteria was 4.2 months. Preoperative anxiety and depression was reported by 86 patients (29%). Those with anxiety and depression reported higher rates of marijuana use, a worse preoperative IIEF score (17.5 vs 19.6, $p = 0.01$) and a lower image of overall health (66 vs 79, $p \leq 0.001$). Improvement or resolution of anxiety and depression was experienced by 56% patients treated with urethroplasty while de novo postoperative anxiety and depression were reported by 10%. These men reported a decreased flow rate (16 vs 25 ml per second, $p = 0.01$). Clinical failure in 8 patients (2.7%) had no effect on the development, improvement or resolution of anxiety and depression.

Conclusions: Of patients with preoperative anxiety and depression 56% reported improvement or resolution after urethroplasty. Although new onset anxiety and depression was rare, these patients had a significantly lower postoperative maximum flow rate, possibly representing a group with a perceived suboptimal surgical outcome. A urethral stricture disease specific questionnaire is needed to further elucidate the interplay of urethral stricture disease with anxiety and depression.

Key Words: urethral stricture, reconstructive surgical procedures, treatment outcome, anxiety, depression

Abbreviations and Acronyms

AD = anxiety and depression
IIEF = International Index of Erectile Function
MSHQ = Men's Sexual Health Questionnaire
PVR = post-void residual volume
SHIM = Sexual Health Inventory for Men
TURNS = Trauma and Urologic Reconstruction Network of Surgeons
USD = urethral stricture disease

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MENTAL health illnesses are common and treatable disorders that have a significant impact on the American population. Approximately 20% of the adult population of the United States is affected by mental illness each year.¹ AD represents the 2 most pervasive mental health disorders in the United States.

In the field of reconstructive urology the relationship between surgery and mental illness remains under explored. Recent studies have shown the prevalence of urinary urgency and incontinence in patients with USD and the significant impact of these symptoms on quality of life and emotional well-being.^{2,3} In addition, erectile dysfunction can develop in patients treated with urethroplasty⁴ and erectile dysfunction has a previously well documented bidirectional association with depression.^{5,6}

To our knowledge the prevalence of mental health disorders and the effect of urethroplasty on the natural history of mental health disorders has never previously been published. In this study we investigated the prevalence of baseline AD and the effect of urethroplasty on AD. We hypothesized that 1) USD would be associated with a higher prevalence of AD compared to the national average, 2) urethroplasty would lead to resolution or improvement in AD and 3) patients with de novo AD would have a poor image of overall health and decreased sexual function.

METHODS

Study Population

Institutional review board approval was obtained. From a prospectively maintained multi-institutional database we retrospectively identified patients who underwent 1-stage anterior urethroplasty between June 2013 and May 2016 as performed by a total of 6 surgeons who are members of the TURNS. Patients who undergo urethroplasty are followed according to a previously described TURNS specific protocol.⁷ Patient demographics, USD etiology and postoperative complications were recorded. The most recent evaluation was used for postoperative analysis.

Study Outcomes

A total of 298 men completed a preoperative and a postoperative assessment of AD. Mental health and the personal image of overall health were evaluated by the validated EQ-5D™-3L questionnaire.⁸ For anxiety/depression (EQ-5D-3L item 5) patients reported symptoms as absent, moderate or extreme. Patients were asked to quantify the personal image of overall health on a scale of 1 to 100 with 1 representing the worst imaginable health state and 100 indicating the best imaginable health state. Sexual function was evaluated by the IIEF (International Index of Erectile Function)⁹ and ejaculatory function was evaluated by the MSHQ.¹⁰

Stricture Recurrence

The TURNS study protocol recommends followup 3 to 6 months after surgery, at 12 months and yearly thereafter. At followup visits questionnaires are completed in addition to uroflowmetry, PVR and cystoscopy. For study purposes a functional definition of success was used with clinical failure defined as the need for any additional stricture related procedure.

Statistical Analysis

Patients were stratified into groups according to absent, moderate or extreme baseline AD. New onset AD was defined as reports of moderate or extreme AD postoperatively by patients who initially reported absent AD preoperatively. Improved or resolved AD was defined as reports of moderate or extreme AD initially by patients who experienced improvement to moderate AD or resolution of symptoms (absent AD).

Univariate analysis was performed to evaluate potential differences in baseline characteristics in patients with the presence or absence of preoperative AD. Statistical analysis included a combination of the chi-square test, the Fisher exact test, the Student t-test or ANOVA as appropriate. All statistical analyses and data management were performed in R using R Studio®. Significance was considered at $\alpha = 0.05$ and p values were 2-sided.

RESULTS

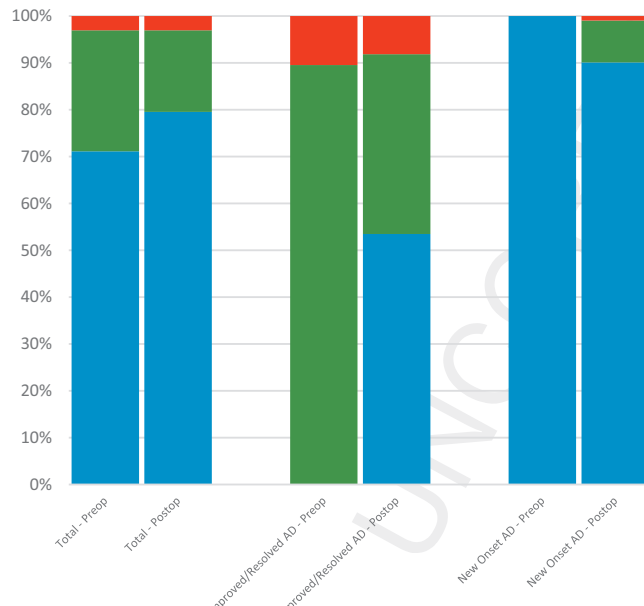
A total of 298 patients met study inclusion criteria with complete information on AD in preoperative and postoperative questionnaires. Median followup was 4.2 months. Of the 298 patients 86 (29%) reported preoperative AD. At baseline the group reporting preoperative AD was similar to those without AD in age and prevalent comorbidities. There was no

Table 1. Background characteristics of patients with and without preoperative anxiety or depression

	Total	Anxiety or Depression		p Value
		Present	Absent	
No. pts (%)	298	86 (28.9)	212 (71.1)	—
No. procedure:				1
Excision + primary anastomosis	87	25	62	
Onlay	211	61	150	
Baseline characteristics:				
Mean age	47	46.8	47.2	0.86
Mean body mass index (kg/m ²)	30.4	30.2	30.3	0.9
No. diabetes (%)	26	10 (11.6)	16 (7.5)	0.37
No. hypertension (%)	89	32 (37.2)	57 (26.9)	0.1
No. hyperlipidemia (%)	67	20 (23.3)	47 (22.2)	0.96
No. coronary artery disease (%)	22	7 (8.1)	15 (7.1)	0.94
Mean preop overall health image	75.8	66.2	78.9	<0.001
Urological factors:				
No. prior urethroplasty (%)	64	24 (27.9)	40 (18.9)	0.12
No. previous dilation (%)	134	40 (46.5)	94 (44.3)	0.35
No. previous direct vision internal urethrotomy (%)	71	19 (22.1)	52 (24.5)	0.21
Mean preop av flow rate (ml/sec)	5.1	5.25	5.05	0.72
Mean preop PVR (ml)	93.5	92.43	93.98	0.95
Mean preop MSHQ score	12.7	11.8	13.1	0.059
Mean preop SHIM score (268 pts)	19.02	17.53	19.63	0.01

difference between the groups in the underlying USD etiology, previous treatments or preoperative urinary function parameters such as PVR and the average flow rate. The group reporting preoperative AD had a worse mean preoperative SHIM score (17.5 vs 19.6, $p = 0.01$) and a lower image of overall health (66 vs 79, $p < 0.001$, table 1) than those without preoperative AD. Patients with preoperative AD also had a higher rate of marijuana use (6 vs 3, $p = 0.03$). The limited number of patients reporting use limited the power of this finding despite statistical significance.

Nine and 77 patients in the cohort of 298 reported preoperative extreme and moderate AD, respectively. Postoperatively 52 and 9 patients reported moderate and extreme AD, respectively. On subgroup analysis in the 86 men who reported preoperative AD 48 (56%) improved or resolved, 35 (41%) remained the same and 3 (3%) experienced worsening AD (see figure). Due to the small cohort of patients who reported worsening AD no further statistical analysis was performed in this group. Patients with improved/resolved AD reported a significantly more optimistic image of overall health on the preoperative questionnaires compared to those without AD improvement or resolution (72 vs 58, $p = 0.001$, supplementary table, <http://jurology.com/>). Each group experienced an improved health image after urethroplasty. However, there was no statistically significant difference in the mean change in patient perceived overall health between any of the groups analyzed ($p = 0.2$).



Distribution by EQ-5D-3L classification of extreme (red bars), moderate (green bars) or absent (blue bars) anxiety or depression preoperatively and postoperatively in 298 patients, including 86 in improved/resolved and 212 in new onset AD subgroup analyses.

Table 2. Univariate analysis of factors predicting new onset anxiety or depression in 212 patients

	Anxiety or Depression		p Value
	New Onset	Absent	
No. pts (%)	21 (9.9)	191 (90.1)	—
No. procedure:			0.86
Excision + primary anastomosis	7	55	
Onlay	14	136	
Mean baseline demographics:			
Age	53.8	46.5	0.03
Body mass index (kg/m ²)	29.9	30.4	0.73
Preop overall health image	64	80.5	0.003
Postop overall health image	63.5	85.5	<0.001
Urological factors:			
No. prior urethroplasty (%)	6 (28.6)	34 (17.8)	0.37
No. previous dilation (%)	4 (19.0)	90 (47.1)	0.003
No. previous direct vision internal urethrography (%)	3 (14.3)	49 (25.7)	0.17
Mean preop av flow rate (ml/sec)	5.7	5	0.74
Mean postop max flow rate (ml/sec)	16.3	24.7	0.01
Mean preop PVR (ml/sec)	38.3	97.9	0.051
Mean postop PVR (ml/sec)	124.2	63.8	0.3
Mean preop MSHQ score	9.9	13.4	0.03
Mean postop MSHQ score	10.3	15.7	0.002
No. worse SHIM (%)*	6 (28.6)	32 (16.8)	0.25
No. postop complication (%):			
Urine leak	1 (4.8)	8 (4.2)	1
Total excluding leak	2 (9.5)	29 (9.9)	1
No. clinical failure (%):			0.14
Postop procedure required	2 (9.5)	5 (2.6)	
No postop procedure required	19 (90.5)	186 (97.4)	

* Decrease of 3 or greater.

On subgroup analysis of the 212 patients who reported absent AD preoperatively de novo AD developed after urethroplasty in 21 (10%) (table 2). These patients were older (age 54 vs 47 years, $p = 0.03$) and had a lower preoperative health image (64 vs 81, $p = 0.002$) than patients who remained free of AD postoperatively. Surgical intervention further increased the health image divide between the groups (64 vs 86 patients, $p < 0.001$). Men with de novo AD had a lower preoperative MSHQ score (9.9 vs 13.4, $p = 0.03$) and experienced minimal improvement after surgery compared to their counterparts (10.3 vs 15.7, $p = 0.002$). A higher proportion of men (28.6% vs 16.8%) experienced SHIM worsening of 3 or greater but this difference failed to reach statistical significance ($p = 0.25$). Patients with new onset AD had a decreased postoperative maximum flow rate (16 vs 25 ml per second, $p = 0.01$), although there was no difference in clinical failure between the depression onset groups (2 vs 5, $p = 0.14$). There was no difference in the complication rate between any of the groups.

DISCUSSION

To our knowledge this report represents the first study of the mental health of the population of patients with USD and the effect of urethroplasty on anxiety and depression. We hypothesized that

1) patients with USD would have a higher prevalence of AD than the national average, 2) urethroplasty would lead to AD resolution or improvement and 3) patients with de novo AD would have a poor image of overall health and decreased sexual function. Our results confirmed our hypotheses. The prevalence of AD in our population was 28.9%, significantly higher than the combined 24.8% national average of anxiety and depression.¹¹ Despite this increased prevalence a remarkable 56% of men experienced AD improvement or resolution after urethroplasty. Finally, our study revealed 2 major predictors of postoperative de novo AD, including decreased sexual function and a poor patient reported image of overall health.

The 28.9% AD prevalence was higher in our population than the national average. To our knowledge the underlying etiology of the increased prevalence that was observed is currently unknown. Voiding dysfunction may have a role in these men and it could explain in part why most patients who undergo urethroplasty report improvement or resolution following surgery. Alternatively preoperative AD could be related to surgical intervention itself with improvement experienced after resolution of the psychological stressor. In men who do not experience improved mental health after urethroplasty we hypothesize that a more severe organic form of AD unrelated to USD symptoms may be present.

In our population decreased sexual function and a lower health image were associated with preoperative AD. As stated, there is a well documented bidirectional relationship of mental health with erectile function. Thus, the association of preoperative depression and erectile dysfunction is not surprising. Additionally, a poor health image was a strong predictor of preoperative depression. Given the similar medical comorbidities between the groups, this patient reported outcome measure could represent a poor body image that predisposes to AD symptoms rather than a true reflection of overall health. Regardless of etiology, the patient image of health had a pervasive effect on all outcomes, including the prediction of preoperative AD, the improvement/resolution of AD and the development of de novo AD. Alternatively a more optimistic health image appeared to have a protective effect against de novo AD and it was strongly associated with AD resolution after urethroplasty.

In regard to the clinical application this patient reported preoperative parameter represents an important tool to identify men at risk for baseline AD or the development of postoperative AD and an opportunity to identify patients who might benefit from AD treatment. Our study design limited the ability to determine a causative relationship between AD and health image or determine associations with other

EQ-5D questions. Future studies with a study design dedicated to further characterize the interplay between AD and health image as well as possible associations with other facets of EQ-5D such as pain, mobility and self-care are needed to improve our understanding of this patient population.

Men with new onset AD reported decreased ejaculatory function on the MSHQ before and after surgery. Urethroplasty was previously shown to have a minimal effect on ejaculatory function¹² and, thus, surgical intervention is not expected to improve this preoperative indicator. Sexual function appears to have less of an effect on AD resolution as the men who experienced AD resolution postoperatively had similar sexual health at baseline and improvement was noted after surgery compared to men without AD resolution. Palminteri et al previously reported significant preoperative anxiety regarding the effect of surgery on sexual life in a population of men undergoing bulbar urethroplasty.¹³ Thus, the psychological relief of maintained sexual function postoperatively could represent one of the causal factors leading to AD resolution.

Men with AD preoperatively had a short-term surgical success rate greater than 95%. In this cohort 56% of the men reported improvement/resolution of AD after surgical intervention. This remarkable improvement rate suggests that USD was a significant psychological stressor contributing to preoperative mental health and urethroplasty may alleviate this cause of AD. Therefore, men who report preoperative AD may be counseled that most patients experience an improvement in mental health symptoms after urethroplasty. Conversely men with de novo AD experienced a higher rate of clinical failure than their counterparts (14% vs 3%, $p = 0.07$). In a larger population of patients clinical failure may have achieved conventional statistical significance. The decreased postoperative maximum flow rate observed in this group could be representative of a suboptimal surgical outcome. Further studies with a more in-depth analysis of this patient population would help determine whether postoperative AD is due in part to a poor surgical outcome. Nonetheless, the knowledge that 10% of patients may experience new feelings of anxiety or depression postoperatively, potentially as a result of a suboptimal surgical outcome, emphasizes the importance of postoperative screening by surgeons and referral for further evaluation if necessary.

The strengths of this study include the relatively large, multi-institutional population of patients and the prospective nature of data collection using validated patient reported outcome questionnaires. The lack of preoperative and postoperative data on selective serotonin reuptake inhibitors is a weakness and a potential confounder of the postoperative resolution of

AD. However, we believe that this weakness was likely mitigated by our decision to evaluate patients at early followup after urethroplasty to best evaluate the immediate impact of surgery on AD.

The incorporation of anxiety and depression into a single questionnaire item could also be interpreted as a limitation. However, the presentation and manifestation of mental health disorders often overlap. Depression and anxiety share a number of diagnostic criteria and carry a significant level of comorbidity.¹⁴ With this knowledge in the context of a previously validated questionnaire we determined that our methods were appropriate for a streamlined analysis of mental health in patients with USD treated with urethroplasty.

The absence of a control group in our study design limited the ability to definitively conclude that the observed AD improvement was unique to the USD population and due exclusively to urethroplasty. Future studies including a control group

(ie observation or nonurethroplasty intervention) would further clarify whether our findings are unique to the USD population and due to urethroplasty alone.

CONCLUSIONS

Most patients with baseline AD experienced improvement in or resolution of AD after urethroplasty. Preoperative sexual dysfunction and a poor image of overall health are associated with baseline AD as well as new onset postoperative AD. Although new onset AD was rare, patients experienced a decreased maximum flow, suggesting a perceived suboptimal surgical result. Identifying patients at risk for AD who may benefit from referral for further evaluation is important. A more comprehensive USD specific patient questionnaire is needed to elucidate the interplay between USD and AD.

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