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Critical Analysis of the Use of Uroflowmetry for Urethral Stricture Disease Surveillance

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Abstract

OBJECTIVE—To critically evaluate the use of uroflowmetry (UF) in a large urethral stricture disease cohort as a means to monitor for stricture recurrence.

MATERIALS AND METHODS—This study included men that underwent anterior urethroplasty and completed a study-specific follow-up protocol. Pre- and postoperative UF studies of men found to have cystoscopic recurrence were compared to UF studies from successful repairs. UF components of interest included maximum flow rate (Q_m), average flow rate (Q_a), and voided volume, in addition to the novel post-UF calculated value of Q_m minus Q_a (Q_m-Q_a). Area under the receiver operating characteristic curves (AUC) of individual UF parameters was compared.

RESULTS—Q_m-Q_a had the highest AUC (0.8295) followed by Q_m (0.8241). UF performed significantly better in men ≤40 with an AUC of 0.9324 and 0.9224 for Q_m-Q_a and Q_m respectively, as compared to 0.7484 and 0.7661 in men >40. Importantly, of men found to have anatomic recurrences, only 41% had a Q_m of ≤15 mL/s at time of diagnostic cystoscopy, whereas over 83% were found to have a Q_m-Q_a of ≤10 mL/s.

CONCLUSION—Q_m rate alone may not be sensitive enough to replace cystoscopy when screening for stricture recurrence in all patients, especially in younger men where baseline flow rates are higher. Q_m-Q_a is a novel calculated UF measure that appears to be more sensitive than Q_m when using UF to screen for recurrence, as it may be a better numerical representation of the shape of the voiding curve.

Uroflowmetry (UF) is a simple, noninvasive method to evaluate voiding function in patients experiencing lower urinary tract symptoms.[1,2] It is often combined with other metrics, including the International Prostate Symptom Score, in the initial diagnosis and follow-up of

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benign prostatic hyperplasia (BPH), and other causes of obstruction.[3] In patients with urethral stricture disease (USD) who have undergone urethroplasty, UF is one of the most frequently used tests to monitor for stricture recurrence.[4] However, UF's use as a stand-alone tool to screen for recurrence following urethroplasty has never been rigorously validated.

It has been well established that the maximum flow rate (Q_m) in patients with USD is significantly diminished relative to age-matched normal controls.[5,6] This knowledge has been extrapolated to the post-urethroplasty setting, where commonly used cutpoints of a postoperative Q_m of less than 10 mL/s or a postoperative Q_m of less than 15 mL/s are used as indicators of urethral stricture recurrence.[5–7] Similarly, when UF data are available both pre- and postoperatively, a change in Q_m following surgery of less than 10 mL/s has also been suggested as a predictor of recurrence.[8] The goal for each of these UF parameters is to minimize the invasiveness of postoperative screening while maximizing the ability to find recurrences.

The purpose of this study is to rigorously evaluate the capability of individual UF parameters, such as Q_m and average flow rate (Q_a), as well as a novel hybrid measure (Q_m-Q_a) to monitor for urethral stricture recurrence. Use of Q_m-Q_a has not been described in prior literature and attempts to provide a simple method to quantify the shape of the voiding curve. The study tested two hypotheses: (1) when compared to the gold-standard cystoscopy, UF parameters will have high test (screening) sensitivity and specificity, and (2) the sensitivity and specificity of UF to screen for stricture recurrence will be diminished in older patients.

MATERIALS AND METHODS

Subjects

The Trauma and Urologic Reconstruction Network of Surgeons (TURNS) is a multi-institutional effort that aims to prospectively monitor urethroplasty outcomes. The shared, centrally located web-based TURNS database was retrospectively queried for all men who had undergone anterior urethroplasty between 2009 and 2014. Data for these men were prospectively collected under Institutional Review Board-approved protocols, with patient consent obtained prior to surgery. Study inclusion criteria included men who had a follow-up cystoscopy at 3, 6, or 12 months postoperatively and had a corresponding same-day UF study. In patients with multiple follow-up cystoscopies/UF studies, the most recent instance was used for analysis. Recurrence was defined as the inability to advance a 17 French cystoscope past the previously reconstructed portion of the urethral lumen with minimal force; neither symptoms nor requirement for secondary operations were considered in this definition.

UF

Interpretation of UF readouts was made by the surgeon of record as per study protocol. Basic parameters of UF included Q_m, Q_a, voided volume (VV), postvoid residual (PVR), and shape of the voiding curve. A novel calculated value was Q_m minus Q_a (Q_m-Q_a). The changes (Δ) between pre- and postoperative parameters were also calculated in a subset of men. UF studies with voided volumes of less than 150 mL were discarded from the analysis.

Statistics

Descriptive statistics were first used to characterize the patient demographics, location of urethral stricture, and nature of repair. Men were divided into either a cystoscopic recurrence or successful repair group, and *t* tests were used to assess the differences in pre- and postoperative UF parameters between the two groups. Receiver operating characteristic (ROC) curves were constructed to determine the predictive value of each UF parameter in diagnosing urethral stricture recurrence relative to the cystoscopic gold standard. Sensitivity, specificity, positive predictive value, and negative predictive value of UF parameters to detect cystoscopic recurrence were calculated using predetermined, commonly cited cutpoints. The patients were further stratified into >40 years or ≤40 years of age, and similar analysis was repeated. Follow-up was determined as the time from surgery to the time of the last objective (UF or cystoscopy) data point. Statistical analysis was completed using SAS® 9.3 (Cary, NC), with statistical significance set at $P < .05$.

RESULTS

Demographics

Of the 1181 men in the TURNS database, 323 men met study criteria. The majority of men were excluded because of a lack of postoperative cystoscopy data (n = 524) or an absent or poor UF study (n = 334) from the same clinic visit. Urethroplasty was performed by 7 surgeons from different academic institutions. The mean age of included patients was 44.35 ± 15.26 with a mean follow-up time of 12.84 ± 12.38 months. The most common location of stricture repair was the bulbar urethra (n = 272), followed by the penile urethra (n = 27), and the mean intraoperative stricture length was 3.62 ± 2.93 cm. The most common repair was excision and primary anastomosis (n = 139), followed by substitution ventral onlay (n = 55) and substitution dorsal onlay (n = 42). Using cystoscopic criteria, 58 (18%) of the men in the study were noted to have recurrence.

Preoperative UF Data

Preoperative UF studies were available in 189 (59%) of the men. The mean preoperative Q_m was 9.44 ± 6.82 mL/s, mean preoperative mean Q_a was 5.87 ± 4.40 mL/s, mean VV was 258.12 ± 176.50 mL, and mean PVR was 162.26 ± 198.64 mL. Preoperative UF values were not predictive of operative success nor did they correlate with age, stricture length, or stricture location.

Postoperative UF Data

Comparison of postoperative UF data between men with and without evidence of cystoscopic recurrence is shown in Table 1. The mean postoperative Q_m, Q_a, and Q_m-Q_a were significantly different between cohorts; there was no difference in postoperative VV (398.91 ± 204.33 vs 365.33 ± 205.62 mL, $P = .2584$).

ROC analysis was performed comparing UF to cystoscopy (gold standard) (Fig. 1). Postoperative Q_m-Q_a demonstrated the highest area under the receiver operating characteristic curves (AUC) of 0.8295 (95% confidence interval: 0.7426, 0.9164); postoperative Q_m followed closely behind with an AUC of 0.8241 (0.7452, 0.9031). AUC values were not significantly different between Q_m-Q_a and Q_m. Postoperative PVR demonstrated an AUC of 0.6296.

Sensitivity tables were constructed with various cutpoints to further evaluate the predictive capabilities of each parameter (Table 2). A commonly used cutpoint of Q_m < 10 mL/s had a sensitivity for detecting cystoscopic recurrence of only 21%.[7] A postoperative Q_m-Q_a < 10 mL/s was 83% sensitive and 58% specific.

Subgroup analysis stratified men into cohorts of ≤40 and >40 years of age. The recurrence rates were similar between the groups (17% vs 18%, respectively, $P = .9016$). Men ≤40 years had a higher postoperative mean Q_m (31.45 ± 13.60 mL/s) compared to men >40 years (22.18 ± 10.16 mL/s, $P < .0001$). ROC analysis revealed significantly higher AUC in men ≤40 years compared to men >40 for both Q_m-Q_a (0.9324 vs 0.7484) and Q_m (0.9224 vs 0.7661).

Men with preoperative UF studies available were used as a urethral stricture test cohort to validate the sensitivities of the cutpoints. A Q_m-Q_a < 10 mL/s was 94% sensitive (ie, 169 of 179 patients with preoperative UF had a Q_m-Q_a of <10 mL/s). Only 60% (115/189) of patients had a Q_m of <10 mL/s and 84% (158/189) had a Q_m of <15 mL/s.

DISCUSSION

The purpose of this study was to critically evaluate and compare the ability of UF parameters to independently identify cystoscopic recurrence of urethral strictures following urethroplasty. Of specific interest were the commonly cited cutpoints of postoperative Q_m < 10 mL/s, postoperative Q_m < 15 mL/s, and ΔQ_m < 10 mL/s as indicators of recurrence. In this study cohort, we did not find that these generic cutpoints were sensitive enough for use as reliable screening thresholds. In general, UF parameters did not demonstrate a high-enough sensitivity/specificity as a standalone screening test relative to cystoscopy. However, UF did appear to be a more useful screener in the younger patient population (≤40 years old).

UF is commonly used to assess bladder outlet obstruction in the context of BPH. Two studies evaluating the ability of Q_m to predict bladder outlet obstruction reported sensitivities of only 39% and 47% when a Q_m <10 mL/s cutpoint was used.[3,9] Although UF on its own does not appear to have adequate diagnostic capability in BPH to replace urodynamic studies or imaging, its ability to provide objective measurements in conjunction with other tests contributes to optimal patient management.[10] In USD, UF has taken on a similar role. Meeks et al estimated that 56% of urologists currently use UF as one of several primary tests to monitor for urethral stricture recurrence after urethroplasty.[4] Despite this, there is no consensus as to which UF parameters have the most diagnostic value and when they should be used. Validation and incorporation of UF into a standardized screening protocol have the potential to limit the need for invasive cystoscopies.

A postoperative Q_m < 10 mL/s was previously reported to have a sensitivity of only 54% in detection of recurrence.[5] If this cutpoint had been used in this population, a sensitivity of only 21% would have been achieved and 46 of the 58 recurrences would have been missed. A postoperative Q_m < 15 mL/s performed similarly poorly with a sensitivity of only 41%. Although Q_m alone is typically the parameter of interest when interpreting UF, its usage as a screening tool is hampered by the wide distribution of Q_m in the recurrence group (17.11 ± 8.31 mL/s), likely the result of heterogeneous effects from bladder dysfunction and prostatic size/obstruction. An improvement can be seen with ΔQ_m, which allows for an individually normalized value. A prior study reported that an improvement of ΔQ_m < 10 mL/s had a sensitivity of 94% with a specificity of 78%.[8] In this population, a similar improvement in sensitivity to 81% and specificity to 48% was seen with this threshold.

The novel Q_m-Q_a parameter may be superior to Q_m or ΔQ_m in monitoring for stricture recurrence (Fig. 2). ROC AUC for Q_m-Q_a (0.8295) was similar to Q_m (0.8241, P = .8089) but higher than ΔQ_m (0.7638, P = .0492). Using a cutpoint of Q_m-Q_a < 10 mL/s, a sensitivity of 83% and a specificity of 58% were seen. Unlike Q_m alone, the Q_m-Q_a is able to capture the overall shape of the curve by factoring in Q_a. A patient with a cystoscopic recurrence on the higher end of the Q_m spectrum may have a flow of 20 to 25 mL/s, yet still present with a flat voiding curve. Whereas the typical cutpoints of Q_m will fail to capture this patient, the Q_m-Q_a is more likely to identify the recurrence. Had a Q_m-Q_a of <10 mL/s been used as a standalone method to screen for recurrence in this population, 154 fewer cystoscopies would have been performed, but 10 strictures would have been missed. If the entire cohort was preoperatively considered as a group of strictures, the preoperative Q_m-Q_a < 10 mL/s would have identified 94% of strictures compared to only 60% for Q_m < 10 mL/s.

The value of Q_m correlates inversely with age, especially in the population over age 50, where there is a sharp drop off regardless of VV.[11,12] Younger patients demonstrate more robust flow due to stronger bladder contractions and less prostatic obstruction. In this study, both Q_m and Q_m-Q_a demonstrated superior predictive capability in detecting stricture recurrence in patients ≤40 years of age (AUC of 0.9224 and 0.9324, respectively) compared to patients >40 years of age (AUC of 0.7661 and 0.7484, respectively). The stronger flow of healthy younger men allows for better discrimination between a patent and strictured urethra. In an older individual, this difference may be less pronounced. Overall, UF appears to have better predictive value in the younger patient population and thus, it may be a more useful stand-alone tool for stricture monitoring in the younger group. In older individuals, where UF parameters are more profoundly affected by the size of the prostate, monitoring of patient-specific subjective measures will likely always remain important.

Limitations to the study include the strict interpretation of a urethral stricture recurrence. This study focused on the anatomical recurrence, which was specifically defined as the inability to advance a standard 17 French cystoscope past the previously reconstructed portion of the urethral lumen with minimal force. Although this is an objective measure, it does not consider the functional outcome (ie, urinary symptoms, quality of life) for the patient. For example, some patients noted as recurrences in this study were relatively asymptomatic and did not undergo secondary repair. Currently, the clinical significance of asymptomatic stricture is unknown, and thus so is the clinical utility of diagnosing them. A second limitation is that the degree of stricture was not graded in this study; longer and tighter strictures likely have a stronger correlation with impaired flow. Finally, a large number of men were excluded from analysis, most of whom had inadequate UF studies. Whereas this exclusion does not diminish the studies' ability to test UF as a stand-alone measure for diagnosing recurrence, it does highlight the fact that UF can oftentimes be difficult to administer in a busy clinic in which many men arrive with empty bladders. Thus, the clinical practicality of using UF alone must be studied further.

CONCLUSION

UF is a widely used test to monitor the integrity of the reconstructed urethra after urethroplasty, but the findings from this study suggest that when used alone, the sensitivity is unacceptably low to detect recurrences. Whereas UF appears to perform better in patients under 40 years old, utilization of a standard "cutpoint" (e.g. $Q_m < 15$ ml/s) for all patients performed poorly in this group of individuals. A refined approach will likely need to include patient-specific UF parameters that monitor Q_m over time, Q_m-Q_a values (which may be a novel way to numerically describe the shape of the voiding curve), and the addition of patient-reported outcomes measures. If a standard, noninvasive approach to monitoring the urethra is adopted widely, as has been proposed by many, further refinement will be required.[4,13,14]

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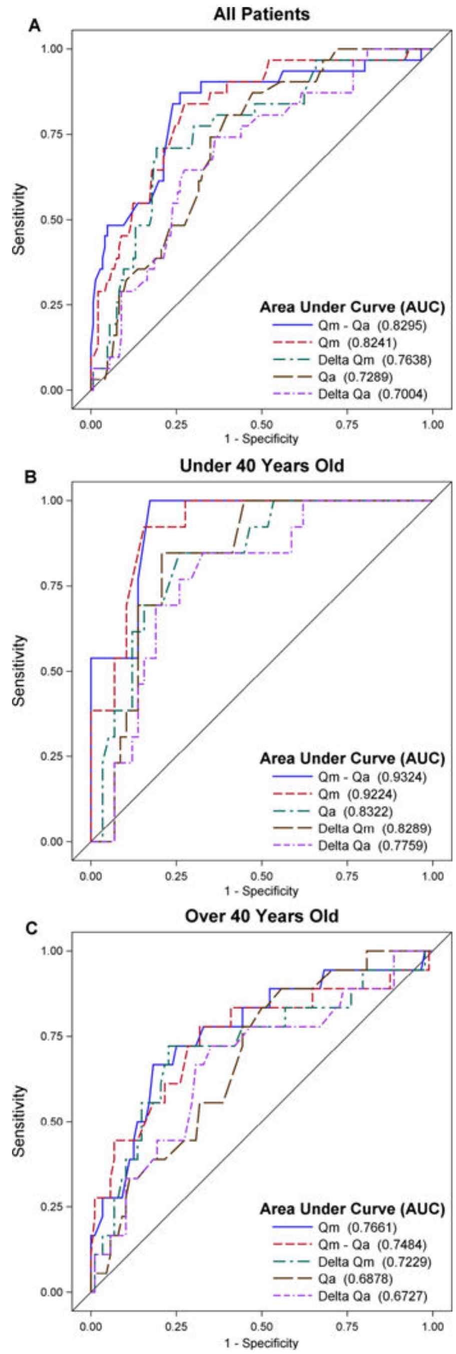

Figure 1.

(**A–C**)—ROC curves of UF parameters predicting cystoscopic urethral stricture recurrence. ROC, receiver operating characteristic; UF, uroflowmetry. (Color version available online.)

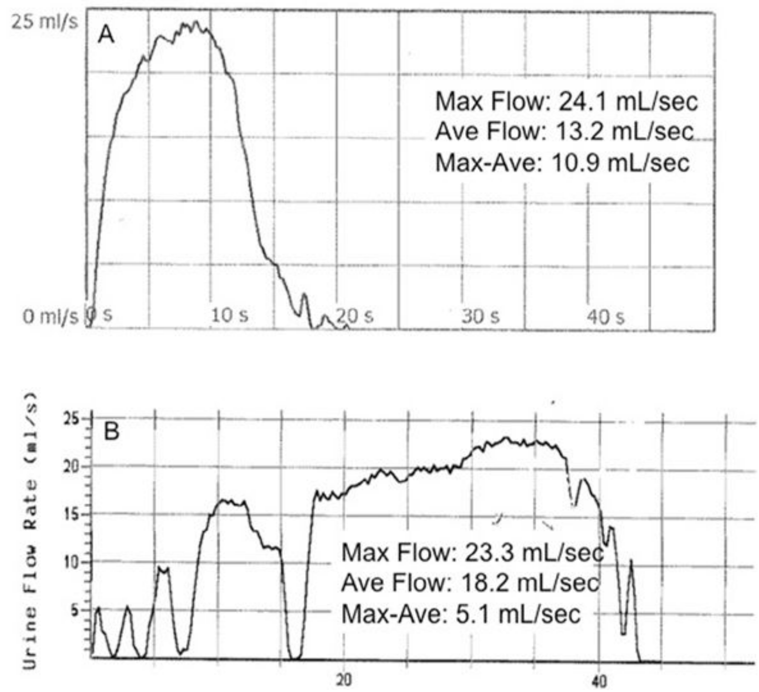

Figure 2.

Uroflowmetry tracings from two postoperative patients with high (normal) maximum flow rates. Patient **A** had a normal cystoscopy, whereas Patient **B** was found to have recurrence. Note the differences in the Q_m-Q_a between the two patients.

Table 1

Comparison of UF parameters between successful repair and recurrence groups (ranked by ROC AUC)

	Successful Repair Group		Recurrence Group			
	N	Mean ± SD	N	Mean ± SD	*P* Value	ROC AUC (vs cystoscopy)
Postoperative Q_m-Q_a (mL/s)	253	13.27 ± 8.19	57	7.42 ± 5.40	<.0001	0.8295
Postoperative Q_m (mL/s)	265	28.05 ± 12.52	58	17.11 ± 8.31	<.0001	0.8241
ΔQ_m (mL/s)	157	19.88 ± 14.30	32	8.07 ± 10.57	<.0001	0.7638
$\Delta(Q_m$ -$Q_a)$ (mL/s)	146	10.38 ± 9.14	31	4.23 ± 6.19	<.0001	0.7531
Postoperative Q_a (mL/s)	253	14.84 ± 7.47	57	9.80 ± 4.51	<.0001	0.7289
ΔQ_a (mL/s)	146	9.07 ± 8.49	31	3.74 ± 6.07	<.0001	0.7004
Postoperative PVR (mL)	244	72.64 ± 105.30	54	136.67 ± 174.00	.0116	0.6296
Postoperative VV (mL)	265	398.91 ± 204.33	58	365.33 ± 205.62	.2584	0.5647

AUC, area under the receiver operating characteristic curves; PVR, postvoid residual; Q_a, average flow rate; Q_m, maximum flow rate; ROC, receiver operating characteristic; UF, uroflowmetry; VV, voided volume.

Table 2

Sensitivity, specificity, PPV, and NPV of UF parameters to diagnose cystoscopic recurrence of urethral strictures

Cutpoints (mL/s)	Age	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Postoperative $Q_m < 10$	All	21	97	60	85
	≤40	21	100	100	86
	>40	21	95	47	84
Postoperative $Q_m < 15$	All	41	88	43	87
	≤40	33	97	73	87
	>40	47	81	36	87
Postoperative $Q_m < 20$	All	67	74	36	91
	≤40	58	91	58	91
	>40	74	61	30	91
Postoperative $Q_m < 25$	All	84	52	28	94
	≤40	79	73	39	94
	>40	88	37	24	93
Postoperative Q_m-$Q_a < 6$	All	41	85	38	87
	≤40	38	92	50	87
	>40	44	80	33	87
Postoperative Q_m-$Q_a < 8$	All	64	70	32	90
	≤40	58	79	38	90
	>40	68	63	29	90
Postoperative Q_m-$Q_a < 10$	All	83	58	30	94
	≤40	83	70	37	95
	>40	82	49	26	93
$\Delta Q_m{}^{*} < 10$	All	81	48	26	92
	≤40	83	49	26	93
	>40	79	48	25	91
$\Delta Q_m{}^{*} < 15$	All	90	37	24	94
	≤40	92	42	25	96
	>40	88	33	23	93

NPV, negative predictive value; PPV, positive predictive value; other abbreviations as in Table 1.

*ΔQ_m = change in maximum flow rate following urethroplasty.