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OBSTRUCTIVE UROPATHY INDUCED BLADDER DYSFUNCTION CAN BE REVERSIBLE: BLADDER COMPLIANCE MEASURES BEFORE AND AFTER TREATMENT

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ABSTRACT

Purpose: We demonstrated that abnormal bladder compliance in the setting of obstructive uropathy can be improved by relief of bladder outlet obstruction.

Materials and Methods: A cohort of 9 men with nonneurogenic lower urinary tract symptoms and videourodynamics proven bladder outlet obstruction were identified prospectively from a university urology practice. Study exclusion criteria ensured absence of active urinary infection, hematuria and neurourological pathology. Testing specifically focused on assessment of the bladder compliance curve, and a compliance value was calculated (ml./cm. H_2O). Treatment intervention consisted of transurethral incisions or resection of the prostate in 8 cases and transurethral balloon dilation of a urethral stricture in 1. Followup videourodynamics testing was performed 1 month after treatment to confirm relief of outlet obstruction and reassess bladder compliance.

Results: Mean patient age was 75.2 $\pm$ 6.16 years. Pretreatment mean bladder compliance $\pm$ SE was 3.06 $\pm$ 0.45 ml./cm. H_2O. At 1 month after treatment videourodynamics testing confirmed relief of obstruction in the cohort. Posttreatment mean bladder compliance $\pm$ SE was 13.53 $\pm$ 0.45 ml./cm. H_2O. Nonparametric paired t test analysis determined that the difference between pretreatment and posttreatment bladder compliance was statistically significant at $p = 0.0117$.

Conclusions: This pilot study suggests that relief of obstructive uropathy even in elderly patients with long-standing lower urinary tract symptoms, can significantly improve bladder compliance.

KEY WORDS: compliance, bladder, urinary tract, urodynamics

Diagnosis and treatment of lower urinary tract symptoms and obstructive uropathy due to benign prostatic hyperplasia are growing concerns for modern societies. In 2000 it was estimated that there were approximately 6.5 million American men between the ages of 50 and 79 years with such symptoms and pathology.[1] In other words a significant portion of health care resources will need to be dedicated to treat this growing segment of the population.

Key questions about the natural history and sequelae of obstructive uropathy remain unsatisfactorily answered. While it is well established that outlet obstruction in the setting of a neurogenic bladder poses a serious risk of eventual upper urinary tract deterioration,[2,3] the same principle has not yet become widely accepted with regard to the nonneurogenic bladder condition. In this report we discuss nonneurogenic bladder outlet obstruction as it specifically relates to the common entities of benign prostatic hyperplasia, obstructive uropathy and urethral stricture disease.

Because of the known risk that high pressure neurogenic bladders pose to the upper urinary tract, bladder compliance measures are routinely assessed. According to the International Continence Society, compliance is a urodynamic measurement defined as change in bladder volume per unit of detrusor pressure (ml./cm. H_2O). Therefore, compliance offers a reliable measure of bladder storage function and can be readily obtained from office cystometrography.

Clearly there is a need to address bladder storage dysfunction with nonneurogenic bladder outlet obstruction. We frequently treat a subset of patients with severe lower urinary tract symptoms whose symptoms persist unabated despite relief of presumed or proven obstruction. At the other end of the spectrum we also treat a subset of patients with so-called "silent prostatism." Although the latter group presents without a significant history of bothersome lower urinary tract symptoms, the worst case scenario involves massive urinary retention due to detrusor decompensation, bilateral hydronephrosis and renal insufficiency, which reminds us that the obstructive process can be quite morbid.[4]

METHODS

We evaluated a prospective series of men with lower urinary tract symptoms who presented to a university urology practice. After the necessary history and physical examination excluded the possibility of urinary infection, hematuria and neurourological pathology, videourodynamics testing was performed. Using a 10Fr triple lumen catheter intravesical infusion of radiopaque contrast material proceeded at a rate of 50 ml. per minute. Study inclusion criteria for this subset series analysis required absence of neurourological pathology, absence of identifiable bladder pathology (for example urinary tract infections or bladder carcinoma), ability to void during before and after treatment testing, and docu-

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mentation of abnormal bladder compliance and bladder outlet obstruction during testing.

Our analysis focused on the calculation of bladder compliance of cystometry filling curves followed by simultaneous fluoroscopic and urodynamic observation of the voiding phase. In contrast to the classic definition of bladder compliance, we opted to use a different volume end point for calculation. This deviation from the standard was necessary in large part because the nature of these voiding study urodynamics tracings would not consistently offer a clear transition point between the end of filling and onset of a detrusor contraction. For consistency in determining an end point value we chose the point on the curve at which urethral relaxation before the onset of voiding was demonstrated (fig. 1).

Simultaneous fluoroscopic observation allowed for the identification of the site of outlet obstruction. The subset of patients identified as having bladder outlet obstruction and abnormal bladder compliance was then offered surgical relief of outlet obstruction as deemed appropriate. Followup videourodynamics testing was performed in 9 patients in this cohort at a minimum of 1 month after treatment. The objective was to reassess prospectively the bladder compliance curve in the setting of urodynamically proven bladder outlet obstruction relief.

RESULTS

Mean patient age was 75.2 ± 6.16 years. Of the 9 patients with bladder outlet obstruction 8 underwent transurethral incision or resection of the prostate and 1 underwent transurethral balloon dilation of a urethral stricture. All 9 patients were reevaluated with videourodynamics testing 1 month after treatment.

As described previously bladder compliance was calculated by using the data point of maximum bladder capacity at onset of urethral relaxation as the numerator and maximum bladder pressure at onset of urethral relaxation as the denominator. Raw data calculations for each cohort subject are shown in table 1. After pretreatment and posttreatment cohort values were averaged statistical analysis was performed using the nonparametric paired t test (Wilcoxon signed rank test) as shown (table 2). Statistical analysis revealed that differences in pretreatment and posttreatment measures of bladder compliance and voiding pressure were indeed significant (table 3 and fig. 2).

DISCUSSION

A large body of experimental and clinical data shows that nonneurogenic bladder outlet obstruction eventually leads to bladder hypertrophy. To characterize this hypertrophic state further, quantification of the impact on overall bladder storage function is important. If we were to apply the lessons learned from neurogenic bladder outlet obstruction then quantitative measures of bladder compliance should be routinely assessed in our evaluation for nonneurogenic. However, to date most discussions of urodynamics testing of obstructive uropathy overlook the concept of bladder compliance. Only recently have a few investigators sought to correlate male lower urinary tract symptoms and obstructive uropathy with alterations in bladder compliance.[5] Their analysis suggests a linear relationship between increasing bladder outlet obstruction and decreasing bladder compliance.

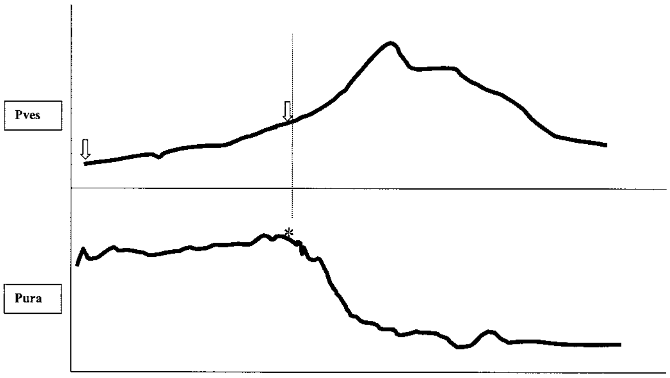

FIG. 1. Sample urodynamics tracing with designated points for calculation of modified bladder compliance quotient. *Pves,* vesical pressure. *Pura,* urethral pressure.

Does impaired bladder compliance place a nonneurogenic urinary system at risk? Comiter et al described a cohort of patients with urodynamics proven obstructive uropathy and identified a high risk subset. Their analysis suggests a strong association between impaired bladder compliance and increased incidence of azotemia.[6] Such clinical and urodynamics observations lend support to the argument that bladder compliance also represents a significant risk factor in the nonneurogenic bladder outlet obstruction system. If larger scale assessments corroborate this correlation between abnormal bladder compliance and insidious deterioration of renal function then the general practice of watchful waiting may need to be revised. Capturing this high risk subset of patients would necessitate more uniform screening. Most importantly this subset of patients would benefit most from timely transurethral surgery.

The followup question is then whether bladder outlet obstruction induced changes can be reversed. Numerous animal studies offer experimental models of bladder outlet obstruction and its ensuing effects, describing a scenario of acute ischemia triggering cellular/molecular signals that lead to bladder hypertrophy. There are some compelling animal data to suggest that bladder hypertrophic changes are reversible to varying degrees after relief of obstruction[7–9] but little comparable human data. Kojima et al attributed the scarcity of human data to the "lack of a reliable tool capable of evaluating the degree of bladder hypertrophy quantitatively in clinical settings."[10] Using ultrasonography they demonstrated that careful estimates of bladder weight could be translated into the degree of bladder hypertrophy.[11] Using this ultrasonographic tool to reassess the group after surgical relief of obstruction, they detected significant changes in bladder weight interpreted as reversal of preexisting bladder hypertrophy in 88% (29 of 33) of the cohort. However, their study was limited by the lack of urodynamics confirmation of bladder outlet obstruction in the pretreatment cohort.

Our primary goal in this study was to capture a group of patients with urodynamically proven bladder outlet obstruction plus abnormal bladder compliance. As explained previously, we opted to modify the standard International Continence Society definition of bladder compliance (fig. 1), which is compliance = (detrusor pressure at end of filling − detrusor pressure at onset of filling)/volume infused. Within the context of a pressure flow voiding study the transition point (detrusor pressure at the end of filling) on the cystometrography curve can be difficult to ascertain. In an effort to arrive at a reliable data point for calculation in this population, we chose the point on the cystometrography curve at which urethral relaxation ensues. With this alternate end point we thought that a more meaningful, reproducible and, albeit, modified "compliance quotient" could be derived.

We routinely use data points from vesical pressure tracings rather than from detrusor pressure, since use of rectal balloon catheters is generally avoided in male voiding studies at our facility. Because the physician is always present during urodynamics testing, the investigator can confirm the absence of significant artifactual contribution of abdominal pressure to the voiding study, and in such settings detrusor pressure and vesical pressure are essentially comparable.

Treatment in our series consisted of transurethral incision

TABLE 1. *Raw data for the study cohort*

Pt.—Age	Bladder Capacity/Bladder Pressure (ml./cm. H_2O compliance)		Before Treatment Voiding Pressure (cm. H_2O)	After Treatment Voiding Pressure (cm. H_2O)
	Before Treatment	After Treatment		
HAb—76	160/76 (2.1)	100/11 (9.09)	76	N/a
HA—75	343/82 (4.18)	284/48 (5.91)	82	48
IK—75	300/60 (5)	350/30 (11.67)	60	30
TL—70	259/58 (4.47)	147/37 (3.97)	58	37
HL—63	310/83 (3.7)	270/30 (9)	83	30
HR—78	200/70 (2.86)	240/25 (9.6)	70	25
ES—85	130/142 (0.92)	80/8 (10)	142	8
RT—75	200/97 (2.1)	300/5 (60)	97	N/a
RW—80	140/64 (2.19)	100/40 (2.5)	64	40

TABLE 2. *Statistical analysis using Wilcoxon signed rank test (nonparametric t-test)*

	Bladder Compliance Before Treatment (ml./cm. H_2O)	Bladder Compliance After Treatment (ml./cm. H_2O)	Voiding Pressure Before Treatment (cm. H_2O)	Voiding Pressure After Treatment (cm. H_2O)
Mean	3.06	13.53	79.86	31.14
SD	1.35	17.69	29.15	12.73
SE	0.45	5.9	11.02	4.81
Low CI	2.02	−0.07	52.9	19.37
High CI	4.1	27.12	106.8	42.92

TABLE 3. *Comparison of pretreatment and posttreatment urodynamic study variables*

	Mean Bladder Compliance (ml./cm. H_2O)	Mean Detrusor Voiding Pressure (cm. H_2O)
Pretreatment	3.06 ± 2.05	81.33 ± 8.65
Posttreatment	13.53 ± 5.9	31.14 ± 4.81
Statistical significance (p value)	0.0117	0.0156

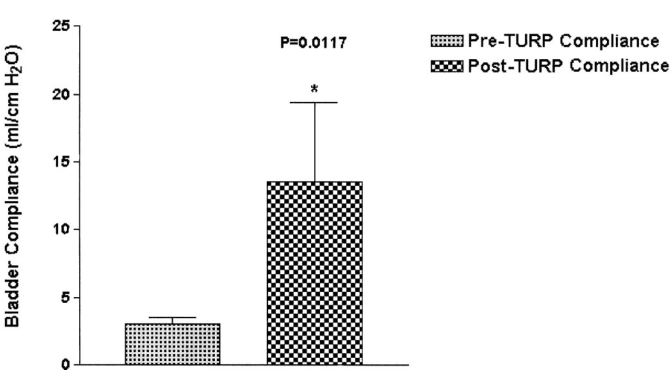

FIG. 2. Statistical analysis shows differences in measures of bladder compliance before (*Pre-TURP*) and after (*Post-TURP*) transurethral resection of prostate.

or resection of the prostate and transurethral balloon dilation. Bladder compliance was reassessed no sooner than 1 month after treatment and we were impressed to find that a subset of patients demonstrated significant improvement in bladder compliance. Even more intriguing was the suggestion that a sense of subjective improvement of lower urinary tract symptoms appeared to correlate with objective improvement of bladder compliance. Conversely, lack of subjective symptom improvement correlated with urodynamic evidence that abnormal bladder compliance had not been significantly altered. However, this subjective assessment was anecdotal rather than rigorously defined by questionnaire.

As this was a small pilot study conducted to detect bladder compliance changes after surgical intervention, the full panoply of possible test variables, that is International Prostate Symptom Score, prostate volume, uroflowmetry, post-void residual volume, passive urethral resistance ratio, blood urea nitrogen/creatinine and so forth, was not collected and registered as in a clinical trial. Whether lower urinary tract symptoms as defined by the International Prostate Symptom Score correlate with commonly used objective parameters remains a point of debate.[12] However, we do believe that this strong clinical observation merits further large-scale investigation.

Despite a plethora of literature on this subject, fundamental questions remain unanswered. Does the current practice of watchful waiting place an unrecognized subset of symptomatic patients at risk for irreversible bladder storage dysfunction and/or upper urinary tract compromise? More commonly we also recognize that a significant fraction of patients will not experience appreciable relief of lower urinary tract symptoms after surgical or medical intervention. It is a clinical observation that remains poorly explained at the basic science and clinical levels. Closer inspection of the raw data describing our study cohort supports that observation (table 1). For some individuals the degree of change in bladder compliance is quite dramatic and for others it is much less so. One might speculate that the likelihood of bladder compliance reversibility corresponds to the duration of obstructive uropathy incurred damage to the detrusor. Unfortunately we lack the longitudinal data necessary to test such a hypothesis. What might be the various outcome pathways in the natural history of untreated bladder outlet obstruction progression? Furthermore, convincing, large-scale epidemiological data are still lacking, hampering efforts to ascertain the magnitude of the clinical problem.

The recent findings of Madersbacher et al would suggest that lower urinary tract symptoms and bladder outlet obstruction have much to do with bladder compliance.[5] Comiter et al identified a high risk group of patients with bladder outlet obstruction, azotemia and abnormal bladder compliance.[6] In this imagined timeline of developing obstructive uropathy it is important to learn when and if intervention can restore or preserve bladder storage function. Our study suggests that for some patients abnormal bladder compliance can be improved with appropriate treatment. As Lemack and Zimmern stated in their review of the subject, "It is imperative to know which, if any, of the pathologic sequelae of bladder outlet obstruction are potentially reversible."[13] Therefore, bladder compliance measures could serve as that much needed quantitative tool in further studies. Thus within the clinical realm of lower urinary tract symptom evaluation, incorporation of bladder compliance can provide us with a consistent, reproducible measurement of bladder storage function or dysfunction.

CONCLUSIONS

Bladder compliance curves obtained during routine urodynamics evaluation can help to convey the degree of bladder storage function injury sustained as a result of developing obstructive uropathy. Unlike some test measures, this urodynamics parameter is unaffected by patient anxiety about the test situation or episodic urethral sphincter activity. Thus, it offers a reliably reproduced measure of bladder storage dysfunction. We describe a practical modification of the classically defined bladder compliance quotient for the purposes of our evaluation of abnormal bladder compliance detected during pressure flow voiding studies.

This pilot study revealed that impaired bladder storage function as measured by bladder compliance can significantly improve upon relief of outlet obstruction. Given that the imagined timeline for development of the obstructive process is measured in years if not decades, it is exciting to witness reversal of bladder storage dysfunction within a matter of weeks after institution of treatment. However, there must certainly be a point in the process beyond which bladder storage dysfunction is unsalvageable. Further clinical investigation is warranted to corroborate these findings suggestive of a linear relationship between bladder compliance and degree of bladder outlet obstruction. Additionally, further analysis of pretreatment and posttreatment compliance changes may help to build a data base of predictive variables regarding the natural history of bladder outlet obstruction and its sequelae.

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