

# Underactive bladder and detrusor underactivity represent different facets of volume hyposensitivity and not impaired contractility

Phillip P. Smith<sup>1,2,3\*</sup>, Gerard Pregoner<sup>1</sup>, Andrew Galffy<sup>3§</sup>, George A. Kuchel<sup>2</sup>

<sup>1</sup>Department of Surgery, <sup>2</sup>Center on Aging and <sup>3</sup>Department of Obstetrics and Gynecology, University of Connecticut Health Center, Farmington, CT, USA

<sup>§</sup>Current address: Providence Medical Group, Medford, OR, USA

\*Corresponding author: Phillip P. Smith, MD, Email: ppsmith@uchc.edu

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Abbreviations used: UAB, underactive bladder; OAB, overactive bladder; UI, urinary incontinence; DU, detrusor underactivity; DO, detrusor overactivity; BOO, bladder outlet obstruction; SUI, stress urinary incontinence; IS, increased sensations; DHIC, detrusor hyperreflexia with impaired contractility; DV, dysfunctional voiding; WF, Watts factor; PVR, post void residual (bladder) volume; FS, First sensation; FD, First desire; ND, Normal desire; SD, Strong desire

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## ABSTRACT

**OBJECTIVES:** Underactive bladder (UAB) and detrusor underactivity (DU) are receiving increasing clinical and research attention. Although lacking a formalized definition, UAB is described as a symptom complex, while DU is a standardized statement of urodynamic function. Both terms nominally suggest impaired detrusor contractility leading to disordered emptying. We sought to evaluate the relationship between UAB, DU and detrusor contractility.

**METHODS:** A chart review of 256 urodynamic records from clinical practice was conducted. Data about symptoms and urodynamic performance were extracted and analyzed, comparing measures of sensory and motor function among groups based on symptoms and urodynamic observations.

**RESULTS:** One hundred and ninety eight complete urodynamic studies met ad hoc defined criteria for inclusion. UAB is specific (0.90) for, but not sensitive (0.22) to, DU. Increased post-void residual volume is common to both UAB and DU, but neither is associated with impaired contractility as measured by Watts factor. Patients with UAB and DU demonstrate higher sensation volume thresholds than do those without these symptoms or observations.

**CONCLUSIONS:** The symptom complex of UAB is not a reliable predictor of the urodynamic observation of DU, and neither condition is associated with a diminished Watts factor. Our results suggest that UAB and DU are typically disorders of volume hyposensitivity rather than of impaired contractility, and may differ in their relationship to bladder perceptions. Thus, these terms should not be used interchangeably.

**Keywords:** underactive bladder, detrusor underactivity, urodynamics

## INTRODUCTION

Normal voiding is a social and behavioral experience in addition to representing a physiologic process. In response to a critical level of afferent activity associated with increasing volume in the low-pressure bladder, voiding is consciously activated, permitting sphincteric relaxation and detrusor smooth muscle contraction. The relationship of detrusor contraction force to urethral resistance to opening determines typical pressure-flow characteristics [1]. Sustained efferent input and sufficient detrusor muscular metabolic processes are required to complete bladder emptying. The perception of normal voiding is the feeling of complete bladder emptying with a continuous and good stream under voluntary control.

Defects in voiding performance arise through inadequate detrusor contractile performance relative to urethral resistance to flow. Insuffi-

cient detrusor force can result from inadequate efferent stimulation and/or deficient force generation as a result of problems such as damaged contractile mechanisms, thermodynamic inefficiency, metabolic/respiratory changes, or insufficient substrate delivery. The term “impaired contractility” has been used in both animal and human research to denote diminished detrusor contraction force despite presumptions of sufficient stimulation and substrate supply [2-4].

Detrusor underactivity (DU) is the urodynamic observation of a voiding contraction of reduced strength and/or duration, with prolonged and/or incomplete bladder emptying [5]. While impaired contractility has been regarded as the cause of DU [6], this has not been established. Furthermore, whether or not DU is always pathologic is not known, due a lack of knowledge of its prevalence in asymptomatic populations and the application of voiding normative values to populations in whom published norms may not be applicable (e.g. the frail elderly).

The perception of DU is the central idea behind underactive bladder (UAB), a term which currently lacks formal definition but has recently been suggested to include prolonged urination often with altered sensation, impaired sense of emptying, and a slow stream suggesting DU [7]. As a perception of abnormal function, UAB must be regarded as a symptom complex and therefore always abnormal.

UAB, DU and impaired contractility have been used somewhat interchangeably despite their more specific meanings as a symptom complex (UAB), as a urodynamic observation (DU), and as a pathophysiologic etiology (impaired contractility). If, as nominally suggested, UAB and DU represent clinical presentations of impaired contractility, efforts to treat these conditions should continue to be aimed at discovering ways to improve detrusor force during voiding. We therefore explored the hypothesis that UAB, DU and impaired contractility describe the same population in a cohort of symptomatic patients who have been urodynamically characterized.

## METHODS

A total of 256 consecutive urodynamic files from our adult clinical laboratory representing all studies conducted from November 2011 through December 2013 were retrospectively abstracted, following an IRB approved protocol. All urodynamics were conducted interactively by the same experienced urodynamicist, who at the time of the examination prepared a report including a brief history of patient symptoms and indication for study (confirmed with the patient by the urodynamicist), a statement regarding the technical adequacy and interpretability of the study, a summary of the observations and a urodynamic impression. The electronic urodynamics files including these reports over an 18 month period were the documents reviewed for this study.

Videourodynamic studies were conducted on a Laborie Aquarius TT system, in conformance with the standards recommended by the International Continence Society [8] except where specifically noted. Testing was performed with the patient in a sitting position, using a filling rate of 50ml/min of room temperature CystoConray II, with transducers zeroed to atmosphere at the level of the pubic symphysis. Sensation volume thresholds were recorded at responses to standard questions: First Sensation (FS): “when you can first sense something in your bladder; that may or may not be a desire to empty.”; First Desire (FD): “when you have the first thought of a desire to empty your bladder.”; Normal Desire (ND): “when you normally go urinate if not busy.”; Strong Desire (SD): “when you would interrupt a good conversation, meal, or show to go empty your bladder.”

Urodynamic observations were recorded consistent with ICS Terminology [5]. Patients with non-obstructive impairment of efficient voiding evidenced by low voiding detrusor pressure in the absence of high flow, and/or poorly sustained detrusor voiding contraction were considered to have DU. Patients unable to generate a detrusor contraction for voiding were not included in DU. Patients with detrusor overactivity but otherwise normal voiding were grouped as DO. Patients with both DO and DU were classified as DHIC (“detrusor hyperreflexia with impaired contractility”), and were not included in the DU group. The primary observation of low volume sensation thresholds in the absence of DO was grouped as Increased Sensations (IS) regardless of symptoms. Patients were grouped as stress incontinence (SUI) if leakage in response to increased intraabdominal pressure in the absence of detrusor

contraction was the only abnormality of bladder filling and voiding. Any study demonstrating non-neurogenic detrusor-sphincteric dyssynergia was classified primarily as dysfunctional voiding (DV). Bladder outlet obstruction (BOO) was diagnosed in men having voids plotting into Schaefer Zone 2 or greater on the eponymous nomogram. Due to the lack of widely accepted nomograms in women, diminished flow (< ca. 15 ml/sec) in the presence of normal or elevated pressures (ca. > 19 cm.w) especially with a history of anterior vaginal/peri-urethral surgery, was classified as BOO in females.

From each urodynamic record, age, sex, primary symptom and urodynamic observation, volume at each sensation and post-void, start and end fill bladder pressure (Pves) were recorded in an Excel spreadsheet. Consistent with available definitions [5, 9-11], symptoms were categorized according the primary symptom reported: Underactive Bladder (UAB) - hesitancy, slow/intermittent stream, and/or sensations of incomplete emptying. Overactive Bladder (OAB) – frequency, urgency, and/or nocturia. Urinary Incontinence (UI) – involuntary loss of urine, any reported incontinence. Other primary symptoms recorded were Pain and Other. Detrusor voiding contractility was recorded as maximum Watts Factor (WF), as calculated by the urodynamic software after limiting the analysis to the voiding contraction and flow. This measure is chosen as it is derived from detrusor pressure, detrusor shortening velocity, and considerations of the thermodynamics of muscle contraction, and has been shown to be independent of outlet resistance [12]. Records from patients having a known neurologic condition, findings consistent with structural abnormality, inability to void, uninterpretable study, and symptoms of Pain or Other were excluded from further analysis (n = 58).

For statistical analysis, OAB and UI were grouped as Non-UAB, and all non-DU urodynamic observations were grouped together to allow four-way comparisons between UAB, non-UAB, DU and non-DU groups. Comparison among symptom/finding groups for maximum WF and postvoid residual volume (PVR) were made.

Cut-off values of WF defining impaired contractility have not been previously reported, yet as a measure of contractility it should be possible to define a value. Therefore, we based our definition of impaired contractility on two descriptive evaluations of the lower end of the distribution of WF values we obtained from our cohort. First, we defined impaired contractility as a WF in the bottom quartile of all the values. Second, we also normalized this data through a logarithmic transformation, defining impaired contractility as presence of WF values one standard deviation below the mean. Based on these definitions of impaired contractility, two contingency tables were created to assess the relationship between UAB/non-UAB, DU/non-DU and impaired contractility. Since the terminology suggests impaired contractility and incomplete emptying are characteristics of UAB and DU, Fisher Exact Test was used to test the strength of association between UAB and DU, with and without impaired contractility (by both definitions), and the predictive value of UAB for DU. ROC curves were calculated for WF and PVR to evaluate potential cut-off values and to test these measures of voiding performance (contraction strength and efficiency) as predictors of symptoms and observations relating to non-obstructive voiding impairment. Based on reports suggesting a continuous, quasi-linear progression of bladder volume vs. reported sensations [13,14], sensory volume thresholds were regarded as ordinal (1 = FS, 2 = FD, 3 = ND, 4 = SD) and plots of volume vs the ordinal scale were prepared for symptoms and observation categories. Linearity of sensory volume threshold and wall stress function plots were checked by Pearson r and

linear regression used to compare slopes and intercepts. Symptom and urodynamic observation (UAB, non-UAB; DU, non-DU) were compared at each sensory volume threshold and in our linear model.

GraphPad software was used for analysis,  $P < 0.05$  considered statistically significant.

**Table 1. Patient characteristics.**

	Overall			Female			Male			Female vs male
	n	Years	s.d.*	n	Years	s.d.	n	Years	s.d.	P
Overall	198	59.8	17.5	142	57.8	17.4	56	64.9	16.8	0.009
<b>Symptom</b>										
UAB	59	61.3	17.9	26	55.8	17.3	33	65.5	17.5	0.037
OAB	58	55.8	17.1	43	53.8	17.2	15	61.8	15.6	0.107
UI	81	61.5	17.3	73	60.8	17.3	8	67.8	17.2	0.307
<b>Urodynamics</b>										
DU	27	68.4	14.5	20	67.5	14.5	7	71	15.6	0.614
DHIC	9	79.6	10.2	6	82	10	3	74.7	10.6	0.377
DU+DHIC	36	71.2	14.3	26	70.8	14.8	10	72.1	13.8	0.814
DO	20	58.9	18.1	16	54.7	17.8	4	75.8	5.7	0.001
SUI	37	59.1	16.9	32	58.4	17	5	63.6	17.8	0.567
IS	6	62.3	12.4	6	62.3	12.4	0	-	-	-
DV	50	68.4	14.5	43	67.5	14.5	7	71	15.6	0.151
BOO	49	63.5	14.3	19	58.2	12.5	30	66.8	14.5	0.033

\*s.d., standard deviation

**Table 2. Contingency Table relating Underactive Bladder, Detrusor Underactivity, and Impaired Contractility.** Top panel defines Impaired contractility as WFmax  $< 4.7$  (25 percentile cutoff), bottom panel defines Impaired Contractility as WFmax as  $< 3.36$  (one S.D. below mean). For neither definition were UAB, DU and Impaired Contractility significantly related.

		UAB +	UAB -
<b>Impaired Contractility: Watts Factor <math>&lt; 3.35</math></b>			
DU +	Imp Cont +	2	3
	Imp Cont -	11	10
DU -	Imp Cont +	6	14
	Imp Cont -	40	89
<b>Impaired Contractility: Watts Factor <math>&lt; 4.7</math></b>			
DU +	Imp Cont +	4	4
	Imp Cont -	9	10
DU -	Imp Cont +	11	30
	Imp Cont -	35	95

## RESULTS

One hundred and ninety eight urodynamic records were analyzed. The distribution of age, sex, symptoms and findings are shown in **Table 1**. Fifty nine (26 females and 33 males) patients reported primary symptoms categorized as UAB, and 27 (20 females and 7 males) patients

had DU as the primary urodynamic finding. Overall males were older than females (64.9 vs 57.8 yrs,  $P = 0.009$ ) and males were older than females for UAB, DO and BOO. UAB vs. non-UAB symptom groups did not differ in age for females, males, and overall. DU patients were older than non-DU patients, overall (68.5 vs 58.4 yrs,  $P = 0.006$ ) and for females (67.6 vs 57.1 yrs,  $P = 0.007$ ). Sensory volume threshold, WF and PVR means for all symptom and observation groups are shown in **Figure 1**. Sensation volume thresholds, WF and PVR data were not normally distributed, therefore Kruskal-Wallis nonparametric one-way analysis of variance with Dunns posthoc test was used for across-group comparisons.

For WF, the 25th percentile value of the non-normally distributed data was 4.70. Following normalization of WF data by logarithmic transformation, the antilog of the log (WF) one standard deviation below the mean was determined, 3.35. Contingency tables created are shown in **Table 2**. In neither case was a statistically significant relationship between UAB or DU with impaired contractility found.

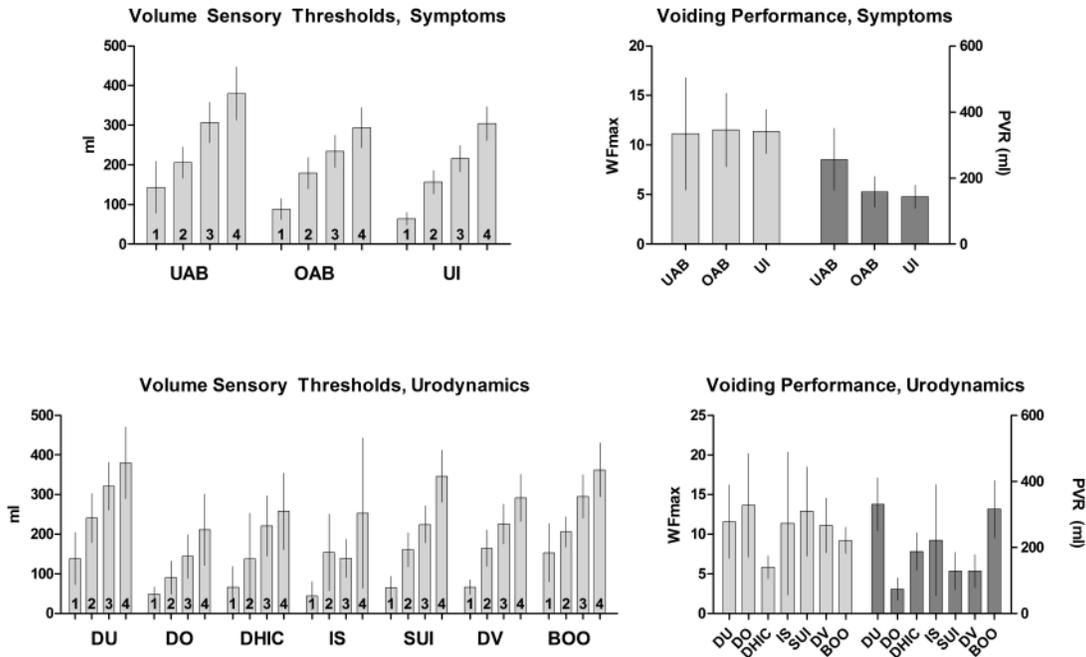
Considering only symptoms (UAB) and the voiding dysfunction suggested by that term (DU), the sensitivity and specificity of UAB symptoms for the urodynamic finding of DU in the overall group and for males and females were calculated. UAB was significantly associated with DU ( $P = 0.04$ ) only for the combined group; sensitivity and specificity of 0.22 (0.12–0.35) and 0.90 (0.84–0.94), respectively. Broken down by sex, sensitivity was 0.27 and 0.18 and specificity was 0.87 and 0.96 for females and males respectively, however these associations did not achieve statistical significance.

The mean WF did not significantly differ among UAB/non-UAB/DU/non-DU groups. The mean PVR was significantly larger in UAB

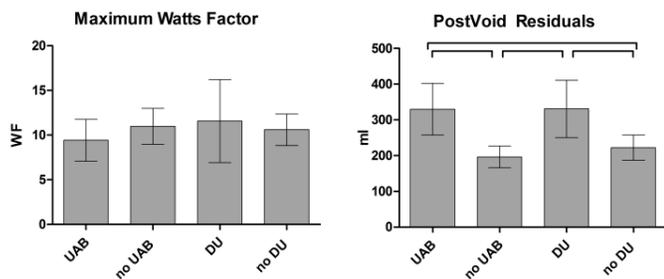
and DU than in non-UAB and non-DU. These data are shown in **Figure 2**. WF did not significantly correlate with PVR by Spearman ranked correlation. ROCs of PVR and WF for UAB and DU were determined. Only PVR for UAB and DU showed significantly an area under the curve greater than 0.5. The greatest likelihood ratio for DU was 2.22 (59% sensitive/73% specific) at 309 ml, and for UAB was 6.4 (14% sensitive, 98% specific) at 623 ml (at 309 ml, sensitivity = 47%/specificity = 77%, likelihood ratio 2.1). On this basis, the data were sorted by PVR into > 309 and < 309 ml and plotted against ordinal sensations. All sensations occurred at significantly higher volumes in the high PVR group than in the low PVR group, and the slope of high PVR was significantly larger

( $94 \pm 6.6$  vs  $76 \pm 1.7$ ,  $P = 0.032$ ).

The sensory volume threshold data are shown in **Figure 3**. The relationship of volume to ordinal sensations for both symptoms and findings proved to be highly linear (coefficients shown in the Figure). For both symptoms and urodynamics the y-intercept of the volume/sensations curve was significantly greater for UAB and DU than the alternate group, but the slopes were similar. UAB patients had greater volumes at FS and ND, whereas only ND was significantly larger for DU than non-DU. UAB did not differ from DU at any threshold, nor did non-UAB from non-DU.



**Figure 1. Bladder filling and voiding data for symptom and urodynamic groupings.** For volume sensations, 1 = First Sensation, 2 = First Desire, 3 = Normal Desire, 4 = Strong Desire. Means  $\pm$  +/- 95% CI of the mean.



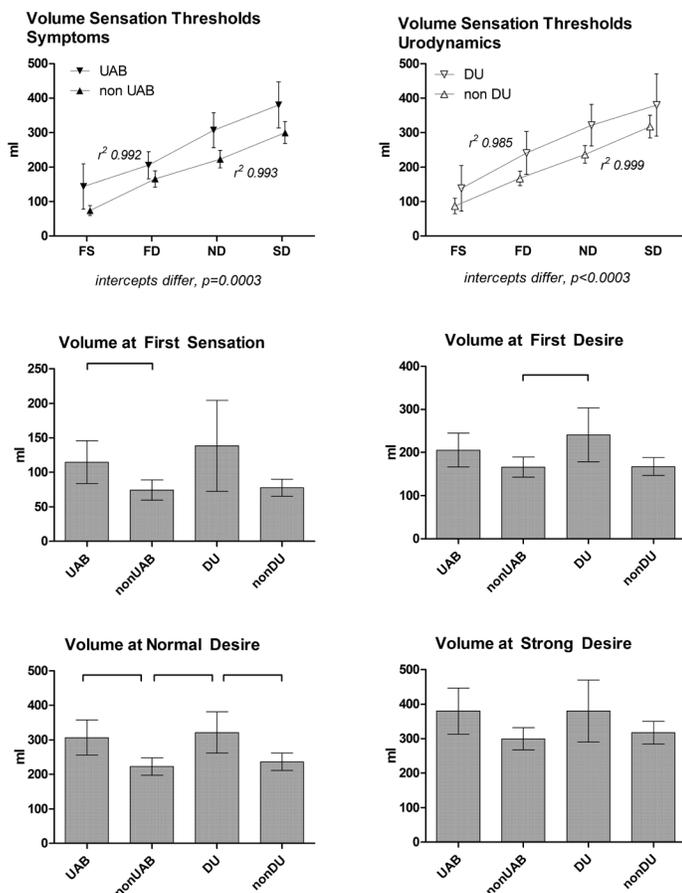
**Figure 2. Analysis of volume sensation thresholds based on symptoms (UAB +/-) and urodynamics (DU +/-).** Means  $\pm$  95% CI of the mean. Brackets denote significant differences,  $P < 0.05$  (Kruskal-Wallis test with Dunns post-hoc).

## DISCUSSION

Other than Detrusor Underactivity, the terminology pertaining to diminished detrusor performance is without formal definition. For this study we defined UAB as a symptom complex, and assessed detrusor contraction strength (here equated with “contractility”) with a standard urodynamic measure. As a retrospective study concerning a little researched topic, our results must be viewed as preliminary. However, we have demonstrated that symptoms of impaired voiding, detrusor underactivity, and diminished contractility cannot be assumed to co-exist and therefore may have differing etiologies.

Neither UAB nor DU is associated with a different WF than the other groups, nor is there a predictive WF for UAB or DU, thereby demonstrating that loss of contractility is neither a requisite nor uniquely associated with UAB and/or DU. UAB and DU are both characterized by diminished volume sensitivity during bladder filling, however UAB is not a good predictor of DU. While the populations with UAB and

DU do somewhat overlap, the strength of association is not strong, and in this study only achieves statistical significance for grouped male/female. Overall and by sex, UAB is not sensitive for DU, but specificity is good, suggesting UAB is experienced in response to multiple functional pathologies and that DU might commonly result in UAB especially in men. Finally, examination of the data in Table II, showing the distributions of all binary combinations of symptom, observation, and contractility status for both WF cutoff values reveals that the concurrence of UAB, DU and impaired contractility is the unusual situation rather than the expected. We therefore reject our hypothesis that UAB, DU and impaired contractility are different aspects of the same population.



**Figure 3. Analysis of voiding performance, maximum WF and post-void residual volume, based on symptoms (UAB +/-) and urodynamics (DU +/-). Means  $\pm$  95% CI of the mean. Brackets denote significant differences,  $P < 0.05$  (Kruskal-Wallis test with Dunns post-hoc).**

UAB patients do not differ in mean age, whereas DU patients are older than non-DU patients, suggesting that DU may relate to aging whereas UAB is a common term in a limited perceptual vocabulary. Our retrospective categorization of primary symptom into filling, voiding, and incontinence centered categories lacks sufficient resolution to determine if the experience of UAB is shared across age and categories of dysfunction. Given the broad overlaps of the individual data point distributions for all measures, it seems reasonable to expect that UAB might be further phenotyped, allowing subcategorizations which could carry some diagnostic value.

As expected, UAB and DU are associated with increased PVR. While this is almost tautologic in the case of DU, neither the formal ICS definition nor our urodynamics laboratory consider elevated PVR by itself to be a marker of DU. Some have suggested that incomplete emptying (in the absence of urodynamic data) should be an inclusion point for UAB especially in the presence of voiding symptoms, and our data would agree even though the sensitivity is small and greatest likelihood ratio occurred at an obviously large volume ( $> 600$  ml for UAB).

Postvoid residual volumes are the result of lack of sufficient contractile strength and/or loss of detrusor stimulation required to overcome urethral resistance to opening. Maintaining efferent stimulation of the detrusor for voiding is logically dependent upon a continued afferent data stream accurately related to bladder volume, as suggested by animal modelling [15]. The diminished volume sensitivity (especially seen in the higher intercept of the line connecting the volume sensory thresholds) and the lack of association with impaired contractility, suggest that UAB and DU are primarily sensory, rather than detrusor motor, pathologies. As a symptom complex, UAB means that voiding impairment is perceived. Its association with elevated PVR suggest this perception may be accurate, and thus the pathology may be post-perceptual. In this case, cessation of detrusor contraction must arise from either central failure to generate parasympathetic outflow in response to afferent sensory information and/or detrusor exhaustion due to inadequate metabolic supply. Detrusor underactivity does not necessarily produce UAB, therefore in the absence of UAB could represent impaired volume transduction or central registration of afferent activity, i.e., is a pre-perceptual problem. This is highly speculative especially since the prevalence of detrusor underactivity and any relationship to PVR in an asymptomatic population is unknown. However these considerations suggest that the concurrence of UAB and DU are indicative of a more global problem in managing bladder volumes.

There are two concerns regarding urodynamic observations of DU. First, the observed similarities of the sensory volume thresholds for DU and BOO suggest the possibility of some overlap of the sensory pathologies of these two disorders; indeed, at low pressure/low flow states characteristic of DU it is very difficult to assess hydraulic obstruction. Diagnostic confusion may exist. Second, we define DHIC as the combined finding of DU and DO in the same patient in our laboratory, as has been described previously [16]. The original description of DHIC diagnosed impaired contractility by voiding efficiency  $< 50\%$  in patients with presumed centrally-mediated DO [17]. These are similar but not identical definitions, since voiding efficiency depends upon the physiologic realities of detrusor contraction strength (i.e. contractility) and duration, whereas DU is a urodynamic observation without etiologic content (as is DO). Equating DHIC with the DU + DO (as defined by ICS) is clinically justified as the intention of the term DHIC seems to be to reflect detrusor-based findings of both impaired storage and emptying in symptomatic persons in the absence of obstruction. However we did not include DHIC with DU as it is not clear that DHIC is a pathophysiologic subset of DU. The suggestion that DHIC represents a more severe form of DU is hard to reconcile with our findings; it has in fact recently been suggested that DHIC may represent an evolution of increased sensations (presenting as OAB) on the way to DU [18], following up on Resnick's original suggesting that DHIC is an evolution of DO [17]. Both of these areas deserve further investigation.

Our results are dependent upon the definitions of UAB and DU, our interpretation and implementations of those definitions, and the

reliability of sensation reporting and urodynamics. UAB lacks a formal definition, however impaired voiding function is implicit in all published suggestions, and thus can be viewed as the voiding phase counterpart to the filling phase syndrome of overactive bladder (OAB). Interpretation of all studies by the same urodynamicist potentially results in a consistently biased interpretation of the ICS definition of DU, and it is possible that data obtained from other urodynamicists may not yield the same results. However the ICS definition offers no specific numerical cut-offs and exactly what constitutes “DU” is therefore subject to some interpretation. Bias could also be introduced by sensation prompting by the urodynamicist; in our lab, each patient is informed of the next sensation to report but no further prompting is utilized, minimizing this risk. Studies of sensations (such as this one) are predicated on an accurate perceptual process and a degree of statistical reliability in patient reporting of sensations. We excluded patients with neurologic diagnoses to minimize the risk of impaired perceptual processes contaminating the reliability of sensory volume thresholds. Both urodynamic results [19] and sensation reporting [20] show good reliability, and potential problems with inter- or intra-observer reliability were avoided by using only data obtained in the original history and interpretation of each urodynamic study.

## CONCLUSIONS

Our ad hoc definition of UAB as a symptom complex is consistent with that described in recent publications. DU is a standardized statement of urodynamic function. Impaired contractility lacks a firm definition but generally implies poor contraction strength attributable to the detrusor muscle. UAB is not a good predictor of DU, and neither are associated with contractility by a standard urodynamic calculation. UAB and DU are both characterized by system volume hyposensitivity although probably due to differing reasons, as UAB is a perception and DU is a measure of function. UAB and DU define differing constructs as well as populations, and are not reporters of impaired contractility. These terms should not be used interchangeably.

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