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Three-Dimensional Ultrasound Bladder Characteristics and Their Association with Prostate Size and Lower Urinary Tract Dysfunction among Men in the Community

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Abstract

Purpose—To characterize ultrasound bladder measures, and to determine if these measures were associated with Measures of lower urinary tract dysfunction.

Methods—Three-dimensional ultrasounds were used to assess bladder surface area (SA), bladder wall thickness (BWT), and estimated bladder weight (EBW) in a random sample of the Olmsted County, Minnesota male population. Uroflowmetry was used to determine maximum urinary flow rates, and ultrasound was used to assess post-void residual volume. Prostate volume was assessed with transrectal ultrasound and prostate specific antigen (PSA) levels were assessed from serum samples. Correlation and linear regression analyses assessed relationships between bladder measures and prostate volume, PSA, maximum flow rate, and post-void residual.

Results—Among 259 men, median bladder SA was 228 cm² (25th, 75th percentiles: 180, 279), median BWT was 2.3 mm (25th, 75th percentiles: 1.8, 2.7), and median EBW was 48.5 g (25th, 75th percentiles: 43.7, 53.0). Decreased bladder SA was correlated with increased PSA level, increased prostate volume, higher AUASI scores ($r_s = -0.13$ to -0.21 ; p values = 0.03 to 0.001), and decreased maximum flow rate ($r_s = 0.21$, $p = 0.001$). Increased BWT was correlated with increased PSA level ($r_s = 0.22$, $p = 0.0003$), increased prostate volume ($r_s = 0.17$, $p = 0.01$), and decreased maximum flow rate ($r_s = -0.14$, $p = 0.03$). EBW was correlated with increased maximum flow rate ($r_s = 0.14$, $p = 0.03$), and decreased AUASI score ($r_s = -0.13$, $p = 0.04$).

Conclusions—Decreased SA and EBW were modestly associated with decreased maximum flow rate and increased AUASI scores, suggesting that such measures may provide insight into detrusor dysfunction.

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Keywords

bladder; prostatic hyperplasia; urinary retention

Introduction

Lower urinary tract dysfunction is common as men age and can significantly impair quality of life.^{1,2} It is often characterized by lower urinary tract symptoms (LUTS) that can be storage (e.g., increased frequency) or voiding (e.g., weak stream) related and by a decreased maximum urinary flow rate. Bladder outlet obstruction (BOO) from benign prostatic hyperplasia is thought to lead to decreased functional bladder capacity from detrusor overactivity, fibrosis, and hypertrophy.^{1,3} However, changes in bladder morphology and function, apart from BOO-related changes, may also be involved in the development of lower urinary tract dysfunction as men age. Decreased functional bladder capacity from detrusor overactivity, detrusor underactivity during voiding, and decreased bladder compliance may be responsible for this decline.⁴ Improved characterization of the bladder may therefore provide insight into mechanisms of lower urinary tract dysfunction in older men. Unfortunately, besides invasive urodynamic studies, there are limited tools available to determine the etiology of lower urinary tract dysfunction.

Three-dimensional ultrasound provides non-invasive direct measures of two bladder characteristics: bladder surface area (SA) and bladder wall thickness (BWT).⁵ Estimated bladder weight (EBW) is then calculated from the product of bladder SA and BWT. These characteristics have the potential to provide insight into the pathogenesis of lower urinary tract dysfunction since the bladder is both the storage vessel and mechanical force (detrusor muscle) for voiding. Previous studies have indicated that men presenting with BOO or acute urinary retention in urology practice settings have an increased EBW.⁶⁻⁸ While three-dimensional ultrasound is non-invasive, an important advantage for studying bladder characteristics, its application and interpretation in the general community is not well understood.⁹ Therefore, the goal of this study was to describe normal ultrasound characteristics of the bladder in elderly men and to determine whether these characteristics were associated with prostate volume or measures of lower urinary tract dysfunction.

Methods

Study Population

The details of our study have been published previously.¹⁰ Briefly, a cohort of Caucasian men (ages 40-79 years) was randomly sampled from the Olmsted County, Minnesota general population. After excluding men with a history of prostate or bladder surgery, urethral surgery or stricture, or medical or other neurological conditions that could affect normal urinary function, 3874 men were asked to join the study, and 2115 (55%) agreed to participate. A 25% random sub-sample participated in an intensive in-clinic examination. The cohort was actively followed on a biennial basis for sixteen years using a similar protocol to the initial examination. During the second and third round of visits, a random sample of 158 replacement men was added to the in-clinic subset. In the eighth round, a random sample of 133 men who had previously been receiving questionnaires was added to the in-clinic subset. This study received approval from the Mayo Clinic and Olmsted Medical Center Institutional Review Boards.

Three-Dimensional Ultrasound Bladder Measures

During the 9th round of follow-up (2006), three-dimensional ultrasound measures of the bladder were obtained with the BladderScan™ BVM 6500 ultrasound machine (Diagnostic

Ultrasound Corp., Bothell, WA), including bladder SA and BWT to estimate bladder weight.⁵ Men were instructed to come to the clinic exam with a full bladder. If they did not have a normal urge to void, they were orally hydrated with water and completed other aspects of the clinic visit until they had an urge to void (at functional bladder capacity). Trained nurses then placed the ultrasound probe on a gel pad 3 cm above the pubic symphysis. The images were processed using ScanPoint™ software (Diagnostic Ultrasound Corp., Bothell, WA) and the operator was prompted to readjust the probe if the bladder was not fully contained in the conical image. The probe contains a rotating transducer and image processing software calculates bladder volume and bladder SA. The BWT was automatically calculated as the distance between the outer and inner surface of the anterior bladder wall. EBW was then calculated using the formula: $EBW = SA \times BWT \times \rho$, where $\rho = 0.957 \text{ g/ml}$ (specific gravity of the bladder).

Lower Urinary Tract Dysfunction Measures

Following the bladder ultrasound, maximum urinary flow rates and voided volume were measured with a Dantec 1000 uroflowmeter (Dantec Medical, Santa Clara, California). Participants were asked to complete a previously validated questionnaire that contained a slightly modified version of the American Urologic Association Symptom Index (AUASI),¹¹ and responses to these questions were used to assess overall LUTS severity, as well as presence of storage and voiding symptoms. After voiding, post-void residual (PVR) was assessed with the three-dimensional ultrasound. Decreased maximum flow rate, increased AUASI score, and increased PVR were considered measures of lower urinary tract dysfunction.

Prostate Size Measures

Prostate volumes were measured with transrectal ultrasonography using a 7.5 MHz biplanar endorectal transducer approximating an ellipsoid shape. Prostate serum antigen (PSA) levels were determined with the Tandem-R assay (Hybritech Inc, San Diego, CA) using serum samples obtained prior to any prostatic manipulations.

Statistical Analysis

For 64 men with multiple three-dimensional ultrasound bladder measures, the coefficient of variation (CV) was calculated from the standard deviation divided by the mean of the two to three sequential bladder measures obtained prior to voiding. Characteristics were compared between men for whom ultrasound bladder measures could or could not be obtained using the Wilcoxon rank sum test. Spearman correlation coefficients were estimated to assess the associations between bladder measures (voided volume, SA, BWT, and EBW). Associations between bladder measures and prostate volume, AUASI score, maximum flow rate, and post-void residual volumes were also assessed with Spearman correlation coefficients. Linear regression models, stratified by prostate volume, were used to model the relationships between bladder measures and maximum flow rate, AUASI scores, and post-void residual volumes. Statistical interactions between bladder measures and prostate volume were assessed. Because of skewed distributions (maximum flow rate, SA, BWT, and EBW), measures were log-transformed in regression analyses.

Results

A total of 349 men completed a full in-clinic exam. Bladder SA, BWT, and EBW measures were obtained on 259 (74.2%) of these men. Median (interquartile range; IQR) coefficients of variation were 6.9% (25th, 75th percentiles: 3.9%, 14%) for bladder SA, 9.8% (25th, 75th percentiles: 4.9%, 14%) for BWT and 7.9% (25th, 75th percentiles: 4.0%, 11%) for EBW. Characteristics of the men with or without three-dimensional ultrasound bladder measures were similar (Table 1), and further analyses were limited to the 259 men with complete bladder

measures. Median SA, BWT, and EBW measures were 228 cm², 2.3 mm, and 48.5 g, respectively (Table 1).

Correlations between the three-dimensional ultrasound measures of the full bladder were calculated. Bladder SA had a negative correlation with BWT ($r_s = -0.83$, $p < 0.001$, Figure 1A). EBW, calculated from the product of bladder SA and BWT, had a positive correlation with bladder SA ($r_s = 0.50$, $p < 0.001$, Figure 1B) but there was no evident association with BWT ($r_s = 0.002$, $p = 0.97$, Figure 1C). Bladder SA had a positive correlation with voided volume ($r_s = 0.56$, $p < 0.0001$) and with voided volume plus PVR ($r_s = 0.59$, $p < 0.0001$).

Correlations between the bladder measures with prostate volume, PSA level, maximum flow rate, AUASI score, and post-void residual were more modest (Table 2). Bladder SA had a negative correlation with PSA level, prostate volume, and AUASI score ($r_s = -0.13$ to -0.21), and a positive correlation with maximum flow rate ($r_s = 0.21$). BWT had a positive correlation with PSA level ($r_s = 0.22$) and prostate volume ($r_s = 0.17$), and a negative correlation with maximum flow rate ($r_s = -0.14$). EBW was not associated with PSA level or prostate volume, but EBW had a positive correlation with maximum flow rate ($r_s = 0.14$), and a negative correlation with AUASI score ($r_s = -0.13$). Bladder measures were not significantly associated with post-void residual volume.

The extent to which the associations between bladder measures and maximum flow rate and AUASI score were modified by prostate volume were assessed (Table 3). The correlations between bladder measures and maximum flow rate were stronger in men with smaller prostates (≤ 30 ml) than in men with larger prostates (> 30 ml). Additionally, the correlations between bladder measures and AUASI score were also stronger in men with smaller prostates; however, none of the interaction terms were statistically significant.

Comment

In this study, we used three-dimensional ultrasound to characterize the bladder in older community men not actively seeking urologic care. Additionally, we found that of the three ultrasound bladder measures, SA and EBW were associated with both decreased maximum flow rate and increased AUASI score. These correlations were stronger among men with smaller prostates. However, these correlations were still modest and the utility of these bladder scan measures for predicting prostate size or lower urinary tract dysfunction may be inadequate for routine clinical management of individual patients.

The strongest correlations were between the three-dimensional ultrasound and voided volume characterizations of the bladder. Pre-void bladder SA is directly proportional to the functional bladder capacity and as expected SA had a reasonably high correlation with voided volume plus post-void residual ($r_s = 0.59$). The negative correlation between bladder SA and BWT ($r_s = -0.83$) is consistent with contraction and stretching of the detrusor muscle at different levels of functional capacity. Surprisingly, there was no association between BWT and EBW ($r_s = 0.002$). This raises the possibility that among predominantly normal men, changes in EBW are compensated by proportional changes in functional bladder capacity. For example, a decreased EBW from detrusor atrophy would be expected to decrease the BWT, unless a proportional decrease in bladder SA at functional bladder capacity also occurred.

Taken together, our study provides bladder scan measures among a random, population-based sample of men, and may assist other investigators in determining whether ultrasound bladder measures in populations with urologic conditions are disease- or condition-related. The BWT measures observed among the men in our study (median 2.3 mm) are similar to those observed by other investigators in healthy populations.^{6,12,13} However, our median EBW of 48.5 g in this sample of men is similar to or higher than the EBWs seen in previous studies of men with

severe LUTS, acute urinary retention, and those requiring surgery for urologic symptoms.^{6-8, 14} These higher than expected EBW values may be due to the way EBW was calculated for this study compared to previous studies. Previous studies have estimated EBW under the assumption that the bladder is circular in shape; however, ultrasound images suggest that this assumption is incorrect, as the bladder frequently resembles a flattened ellipse. In our study, the bladderscan software calculated a three-dimensional SA of the bladder using a computer graphics algorithm.¹⁵ This method of calculating bladder SA results in higher average SA measurements than those calculated under the spherical bladder assumption, resulting in correspondingly higher EBW measurements.⁵ However, previous studies of bladder ultrasound characteristics were frequently conducted primarily in Asian populations. Other studies have indicated that prostate volumes tend to be larger in Japanese populations compared to men in our population,¹⁶ and it is possible that bladder measures may also differ by race or ethnicity.

Overall, correlations between bladder measures and measures of lower urinary tract dysfunction (low maximum flow rate and elevated AUASI score) were modest, ranging from $r_s = -0.13$ to 0.21 . Additionally, correlations between SA and maximum flow rate and AUASI score were stronger than BWT correlations with these outcomes, suggesting that SA might be more useful as a measure of bladder function than BWT. The association of decreased bladder SA at functional capacity with decreased maximum flow rate and increased symptoms is consistent with detrusor overactivity contributing to lower urinary tract dysfunction. Finally, correlations between EBW and maximum flow rate or AUASI score were similar to SA correlations with these measures, suggesting that calculated EBW may be a reasonable surrogate measure of bladder function as well. The association of decreased EBW with decreased maximum flow rate and increased symptoms suggests detrusor atrophy (possibly from neuromuscular disease) may also contribute to lower urinary tract dysfunction.

We also found that correlations between bladder measures and maximum flow rate and AUASI score strengthened among men with smaller prostates (although the interaction terms were not statistically significant). These observations are in accord with previous studies that have found relatively modest correlations between prostate volume and urologic symptoms in population-based samples,¹⁷⁻²¹ indicating that physiologic changes apart from increased prostate volume are likely also involved in development of LUTS and decreased maximum flow rates. Our data suggest that bladder changes alone (as measured by decreased SA or EBW) may account for decreases in maximum flow rates and increases in AUASI scores.

Finally, we found that increased prostate volume was correlated with decreased SA and increased BWT (Table 2). These results are similar to previous studies, as Hakenberg et al. also found that BWT was increased in men with elevated lower urinary tract symptoms and prostatic enlargement compared to controls.²² There are a number of plausible mechanisms by which a prostatic disease pathway would be characterized by decreased detrusor function. These include bladder outlet obstruction from the prostate leading to cholinergic denervation of the detrusor,²³ detrusor hypoxia with reperfusion injury,²⁴ and changes in the electrical properties of detrusor smooth muscle cells.²⁴ In this study, we found that the correlations between bladder measures and urologic outcomes decreased in men with enlarged prostates, suggesting that bladder changes in men with enlarged prostates may be less important than the enlarged prostate volume itself in contributing to decreased flow rates or elevated symptoms.

There were several potential limitations to consider with this study. The hypothesized mechanisms relating ultrasound bladder measures to lower urinary tract dysfunction need to be confirmed with urodynamic measures of bladder function, as it is not currently clear how well ultrasound measures reflect physiologic bladder function. Additionally, three-dimensional ultrasound bladder scans could not be obtained on approximately 25% of the study sample, though there were no characteristics that suggested persons with scans were different from

persons without scans (Table 1). Finally, this study consisted entirely of Caucasian men, and results may not be representative of bladder measures in other populations with a different racial or ethnic composition.

Conclusions

This study describes characteristics of the bladder and their association with both prostate size and lower urinary tract dysfunction measures among older men in the general community. While these associations are probably too weak to justify routine clinical use, three-dimensional ultrasound bladder measurements may be helpful for gaining insight into disease mechanisms. Decreased SA and increased BWT were modestly associated with decreased maximum flow rate and increased AUASI scores, suggesting that such measures may provide insight into detrusor dysfunction. Longitudinal studies assessing changes in these bladder measurements and their prediction of urological outcomes are needed to further explore mechanisms of detrusor dysfunction and determine the clinical utility, if any, of these measurements.

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Figure 1A

Figure 1B

Figure 1C

Figure 1. Scatterplots comparing full bladder measures among 259 men from Olmsted County, Minnesota: A) Bladder wall thickness compared to bladder surface area, B) Bladder surface area compared to estimated bladder weight, and C) Bladder wall thickness compared to estimated bladder weight.

Table 1

Characteristics of men from Olmsted County, Minnesota in which complete three-dimensional ultrasound bladder measures could or could not be obtained.

	Complete 3D-ultrasound bladder measures (n=259)	Incomplete 3D-ultrasound bladder measures (n=90)	
Characteristic	Median (25 th , 75 th percentiles)	Median (25 th , 75 th percentiles)	p [*]
Age, y	66 (61, 71)	65 (60, 72)	0.90
Body mass index, kg/m ²	29 (27, 32)	29 (26, 32)	0.67
Full bladder measures			
Surface area (SA), cm ²	228 (180, 279)	-	-
Bladder wall thickness (BWT), mm	2.3 (1.8, 2.7)	-	-
Estimated bladder weight (EBW), g	48.5 (43.7, 53.0)	-	-
Prostate size measures			
PSA, ng/ml	1.3 (0.7, 2.3)	1.1 (0.6, 1.8)	0.35
Prostate volume, ml	32.5 (26.2, 45.3)	30.1 (25.5, 37.2)	0.07
Lower urinary tract dysfunction measures			
AUASI score	8.2 (4.0, 13.0)	8.0 (4.0, 12.0)	0.55
Storage symptom score	4.0 (2.0, 6.0)	3.5 (2.0, 5.0)	0.69
Voiding symptom score	4.0 (1.0, 7.0)	4.0 (1.0, 6.0)	0.52
Maximum urinary flow rate, ml/s	16.5 (11.8, 22.7)	15.5 (10.9, 22.6)	0.36
Post-void residual, ml	38.0 (18.0, 104.0)	47.0 (22.0, 100.0)	0.79

* Rank-sum p-value

Table 2

Spearman correlations between bladder measures and prostate and voiding measures among 259 men from Olmsted County, Minnesota.

Characteristic	Full Bladder Measures		
	Bladder surface area	Bladder wall thickness	Estimated bladder weight
	r, p	r, p	r, p
Age, y	-0.05, 0.45	0.02, 0.80	-0.06, 0.38
Prostate size measures			
PSA	-0.21, 0.001	0.22, 0.0003	-0.05, 0.43
Prostate volume	-0.15, 0.02	0.17, 0.01	-0.02, 0.78
Lower urinary tract dysfunction measures			
Maximum urinary flow rate	0.21, 0.001	-0.14, 0.03	0.14, 0.03
AUASI score	-0.13, 0.03	0.05, 0.38	-0.13, 0.04
Storage symptom score	-0.15, 0.02	0.07, 0.24	-0.14, 0.02
Voiding symptom score	-0.09, 0.14	0.03, 0.67	-0.09, 0.14
Post-void residual	0.07, 0.25	-0.05, 0.46	0.01, 0.84

Table 3 Linear relationship of maximum urinary flow rate and AUASI score predicted by bladder measures, stratified by prostate volume.

	Maximum Urinary Flow Rate*			AUASI Score		
	Volume ≤30 mls	Volume >30 mls	P value (interaction between volume and bladder measure)	Volume ≤30 mls	Volume >30 mls	P value (interaction between volume and bladder measure)
	β, p value	β, p value		β, p value	β, p value	
Bladder surface area *	0.37, 0.01	0.12, 0.32	0.18	-5.34, 0.01	-0.92, 0.54	0.07
Bladder wall thickness *	-0.33, 0.06	-0.13, 0.44	0.42	3.34, 0.19	0.79, 0.71	0.44
Estimated bladder weight *	0.45, 0.02	0.12, 0.52	0.23	-7.85, 0.01	-1.12, 0.61	0.07

* Measurement log-transformed prior to regression analysis.