Am J Clin Exp Urol 2021;9(5):367-377
www.ajceu.us /ISSN:2330-1910/AJCEU0135783

*Original Article*

# Irregular bladder shapes identified in women with overactive bladder: an ultrasound nomogram

Rui Li[1], Anna S Nagle[1], Kaitlyn M Maddra[2], Naomi Vinod[2], Suzanne A Prince[1], Sarah I Tensen[1], Devina Thapa[2], Blessan Sebastian[2], Dhruv Sethi[2], Abraham Alattar[1], Laura R Carucci[3], Adam P Klausner[2], John E Speich[1]

*[1]Department of Mechanical and Nuclear Engineering, Virginia Commonwealth University College of Engineering, Richmond 23284, VA, USA; [2]Department of Surgery, Division of Urology, Virginia Commonwealth University School of Medicine, Richmond 23298, VA, USA; [3]Department of Radiology, Virginia Commonwealth University School of Medicine, Richmond 23298, VA, USA*

Received May 28, 2021; Accepted July 28, 2021; Epub October 15, 2021; Published October 30, 2021

**Abstract:** In this study, an ultrasound-based bladder shape nomogram was developed using data from women without overactive bladder (OAB) and tested in women with OAB to identify irregular bladder shapes. The goal was development of a nomogram that can ultimately be used for non-invasive identification of a bladder shape-associated OAB phenotype. Transabdominal 3-dimensional (3D) bladder ultrasound images were collected at 1-minute intervals during urodynamics studies and at 5-10-minute intervals during oral hydration studies. These prospective studies enrolled women with and without OAB based on International Consultation on Incontinence questionnaire on OAB (ICIq-OAB) question 5a (OAB 5a≥2, without OAB 5a<2). Bladder perimeters were manually traced and refined using GE 4D-View software. Nomograms for the transverse, sagittal and coronal perimeter-volume relationships were developed for women without OAB. A power model was used to approximate upper and lower nomogram bounds with 95% confidence intervals. Nomograms were tested using data from women with OAB, and each participant was classified as having an irregular bladder shape based on the number of perimeter values outside the nomogram bounds. Nomograms were developed using 533 images from 27 women without OAB (14 from urodynamics and 13 from hydration studies) and were tested using 264 images from 24 women with OAB (16 urodynamics and 8 hydration). The sagittal perimeter nomogram provided the best results, with irregular sagittal perimeters identified in 6/24 (25%) women with OAB and 0/27 (0%) without OAB. An irregular sagittal perimeter was significantly associated with OAB (P<0.05). Ultrasound-based nomograms may enable feasible, non-invasive identification of a subgroup of women with bladder shape-associated OAB.

**Keywords:** Urodynamics, lower urinary tract symptoms, phenotype, ultrasound imaging

## Introduction

Overactive Bladder (OAB) is a subjective, symptom-based syndrome defined by an urgent desire to void and often includes increased urinary frequency and/or nocturia [1]. This condition impairs the quality of life of millions of individuals [2], and is responsible for a substantial economic burden [3]. Medical treatments for OAB have limited long-term efficacy and are poorly tolerated [4, 5]. One explanation for this lack of efficacy is that OAB is almost certainly an array of different conditions that manifest with a common set of symptoms.

Therefore, a key problem in OAB science is the use of a "kitchen sink" approach in which all OAB patients are treated similarly using an algorithmic trial-and-error system [6]. In this regard, an individual with theoretical "OAB phenotype A" would be expected to respond differently than an individual with "OAB phenotype B", and the paradigm shift in OAB research can only come through the development of new metrics to improve diagnostic phenotyping. In addition, invasive urodynamics studies are often used to investigate refractory OAB cases, and there is a recognized need to develop less invasive OAB diagnostics [7]. The present study addresses the needs for both improved OAB phenotyping and non-invasive diagnostics using ultrasound imaging.

Transabdominal ultrasound imaging is a relatively low-cost and non-invasive technology that is widely used to measure post void residual volumes [8, 9]. Ultrasound has also been utilized to measure bladder wall thickness to assess bladder outlet obstruction [10] and a nomogram for bladder wall thickness was recently developed for evaluating detrusor underactivity [11]. Furthermore, two recent studies emphasize the potential value of ultrasound to quantify changes in bladder shape associated with overactive bladder [12, 13]. Gray et al. used ultrasound to quantify bladder shape changes that correlated with detrusor overactivity in women with OAB [13]. Glass et al. used ultrasound to identify bladder height-to-width ratios that were abnormal in a subgroup of women with OAB compared to age and BMI-matched controls without OAB [12].

Building upon these studies, the objectives of the present study were to (1) develop a bladder shape nomogram using bladder perimeter measurements in a group of women without OAB, and (2) test the ability of the nomogram to identify irregular bladder shapes in a group of women with OAB.

## Materials and methods

### *Participant groups*

Women with and without OAB were recruited for prospective ultrasound urodynamics and oral hydration studies approved by an Institutional Review Board (Approval #: IRB HM200-00453). Inclusion/exclusion criteria: all participants were required to be at least 21 years old and have no cognitive impairment. After completing the informed consent process, participants were enrolled in the study and completed the validated International Consultation on Incontinence questionnaire on Overactive Bladder (ICIq-OAB) [14]. From this questionnaire, the urgency question (5a: 'Do you have to rush to the toilet to urinate?') was used to determine two participant groups. Women were categorized into groups with OAB (responses ≥2, 'sometimes', 'most of the time' and 'all of the time') and without OAB (responses <2, 'never' and 'occasionally'). Age and body mass index (BMI) were recorded for all participants.

### *Ultrasound imaging during urodynamics and hydration protocols*

Transabdominal 3-dimensional (3D) ultrasound images (**Figure 1**) were collected during prospective urodynamics and oral hydration studies using a GE Voluson™ E8 ultrasound system with a 4-8 MHz abdominal probe. During the urodynamics studies, bladders were filled at 10% of cystometric capacity per minute based on the capacity of a previous fill, and ultrasound images were collected at 1-minute intervals throughout filing [15]. During the hydration studies, participants completed 2-4 fill-and-void cycles with ultrasound images collected at 5-10-minute intervals throughout filling [16].

### *Image analysis*

Beginning with the transverse plane, a trained technician manually traced the perimeter of each bladder image in six cross-sectional planes 30° apart (**Figure 1**) using GE 4D-View software [17], as previously described [18, 19]. The virtual organ computer-aided analysis (VOCAL) feature in the software automatically combined these cross-sections to generate a rendered 3D model. Then, the perimeter tracing of each plane was manually refined as necessary to match the contours of the bladder wall and update the 3D model. From this model, geometric parameters, including the volume and the inner perimeters in transverse, sagittal and coronal planes (**Figure 1**) were calculated using the built-in features of the GE 4D-View software and recorded for subsequent analysis [17].

### *Nomogram development*

Linear, second order polynomial, exponential decay and power functions for the relationship between bladder perimeter and volume were evaluated for nomogram development. Each function was fit to the perimeter data for the transverse, sagittal and coronal planes, and the power model provided the best fit for each of the three planes (**Figure 2**). For each of the three planes, upper and lower prediction bounds based on 95% confidence intervals were derived for the power model using all perimeter data from the participants without OAB (**Figure 3**, left panels).

### *Nomogram validation and testing*

The perimeter-volume nomograms were validated and tested for the volume range of 100 ml to 500 ml for all participants who had at least three ultrasound measurements with volumes greater than 100 ml. The nomograms were validated by identifying the number of perimeter values outside the nomogram bounds for each participant without OAB (**Figures 3** and **4**, left panels). In addition, the nomograms were tested by identifying the number of perimeter values outside the nomogram bounds for each participant with OAB (**Figures 3** and **4**, right panels). Validation and testing were performed on three groups of data points between 100 and 500 ml: (1) data for all volumes, (2) data for the four largest volumes, and (3) data for the three largest volumes (**Table 1**). In addition, thresholds of 3, 2 and 1 perimeter values outside the nomogram bounds were considered when determining the number of outlying values needed to identify a bladder with an irregular shape (**Table 1**). The smaller groups and thresholds were tested in an attempt to identify the minimum number of images needed to identify OAB participants with irregular bladder shapes without identifying any participants without OAB.

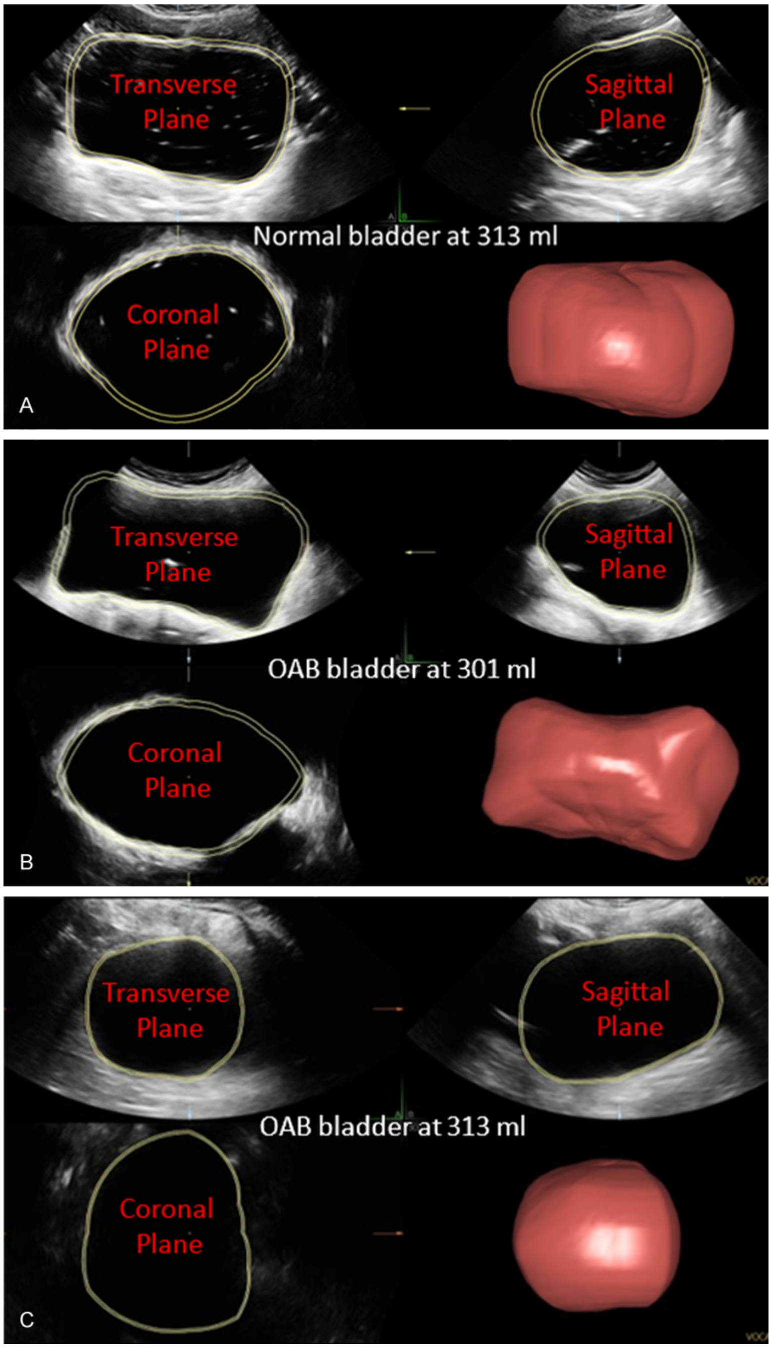


**Figure 1.** Examples of bladder ultrasound images at similar volumes from a participant without overactive bladder (OAB) (A) and two participants with OAB (B, C) with irregular bladder shapes. Inner and outer perimeters were traced in the transverse, sagittal and coronal planes and a 3D model was generated. Compared to the typical bladder in (A), the bladder in (B) has a smaller sagittal perimeter and is wider and shorter in the transverse plane, and the bladder in (C) has a larger sagittal perimeter and is taller in the coronal plane.

*Data analysis*

Development, validation and testing nomogram were conducted using MATLAB R2019a, and statistical analysis were performed in IBM SPSS Statistics 26. T-tests, Mann-Whitney U-tests and Fisher's exact tests were used to determine differences, as appropriate, and a comparison with a *P* value of less than 0.05 was considered statistically significant. Participant demographic results were expressed in the format of mean ± standard error of the mean (**Figure 5**).

## Results

*Participant demographic data*

A total of 51 female participants enrolled in this study and had complete data sets for analysis,

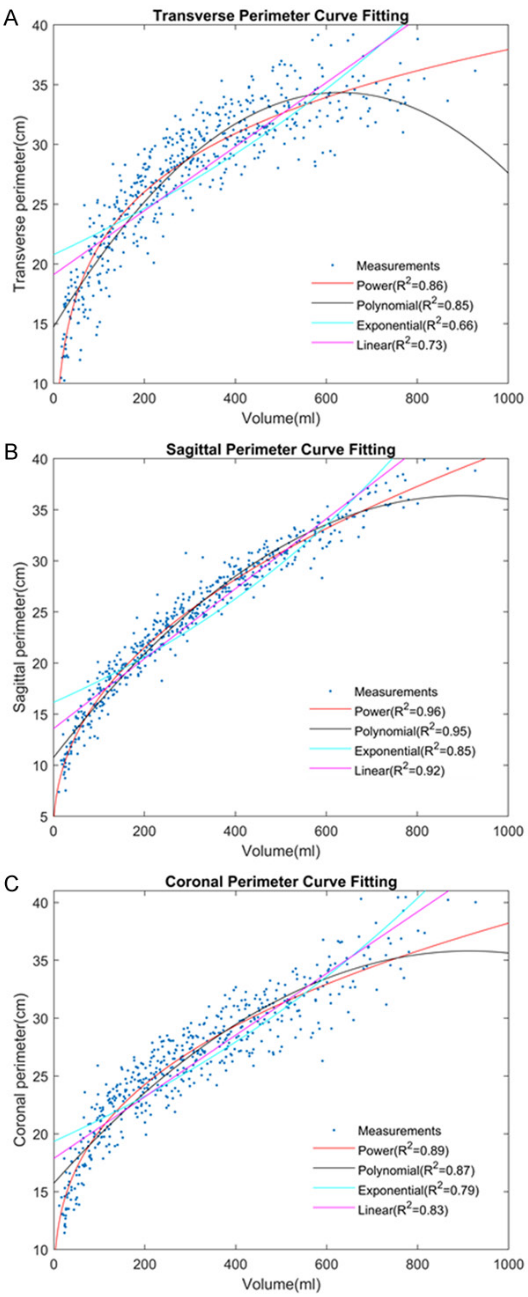


**Figure 2.** Curve fitting using polynomial, power, exponential and linear functions for transverse (A), sagittal (B) and coronal (C) perimeters for participants without overactive bladder. The power function had the highest $R^2$ values in all three planes, and the sagittal perimeter fit with the power function had the highest $R^2$ of 0.96.

including at least three ultrasound measurements with volumes greater than 100 ml. Data from 24 participants with OAB and 27 without OAB were analyzed. Demographic data are shown in the (**Figure 5**). As expected, statistically significant differences were observed in the ages and bladder capacities between the two groups, and BMI was not statistically different (**Figure 5**).

*Nomogram development*

Perimeter-volume nomograms were developed using perimeter data from 533 ultrasound images from 27 women without OAB, including 14 urodynamic studies and 13 hydration studies (**Figure 3A**, **3C** and **3E**). The equations for the volume (V)-perimeter (P) nomograms were as follows:

Transverse nomogram upper and lower bounds:

$P=35.12*V^{0.109}-32.02$, $P=39.47*V^{0.101}-45.78$

Sagittal nomogram upper and lower bounds:

$P=1.75*V^{0.445}+5.60$, $P=1.81*V^{0.441}+0.19$

Coronal nomogram upper and lower bounds:

$P=3.11*V^{0.342}+8.87$, $P=3.30*V^{0.335}+1.12$.

*Nomogram testing and validation*

The perimeter-volume nomograms were tested using 264 sagittal perimeter measurements from 24 women, including 16 from urodynamics studies and 8 from hydration studies. Nomograms were tested for each of the three ultrasound planes using the three groups of data points and three thresholds for the number of outlying points listed in **Table 1** (rows labeled "OAB"). To check the validity of the nomograms, data from women without OAB were also tested for the three groups of data points and three thresholds for the number of outlying points listed in **Table 1** (rows labeled "without OAB").

When testing all data points between 100 and 500 ml, none of the participants without OAB had three or more perimeter values outside the nomogram bounds for any of the three imaging planes (**Figure 3A**, **3C** and **3E**). In contrast, multiple participants with OAB had three or more perimeter values outside the nomogram bounds (**Figure 3B**, **3D** and **3F**), including sagittal perimeters for five OAB participants (**Table 1**, All points, 3 outside, *P=0.018). When the threshold number of perimeter values used to identify an outlier was decreased from

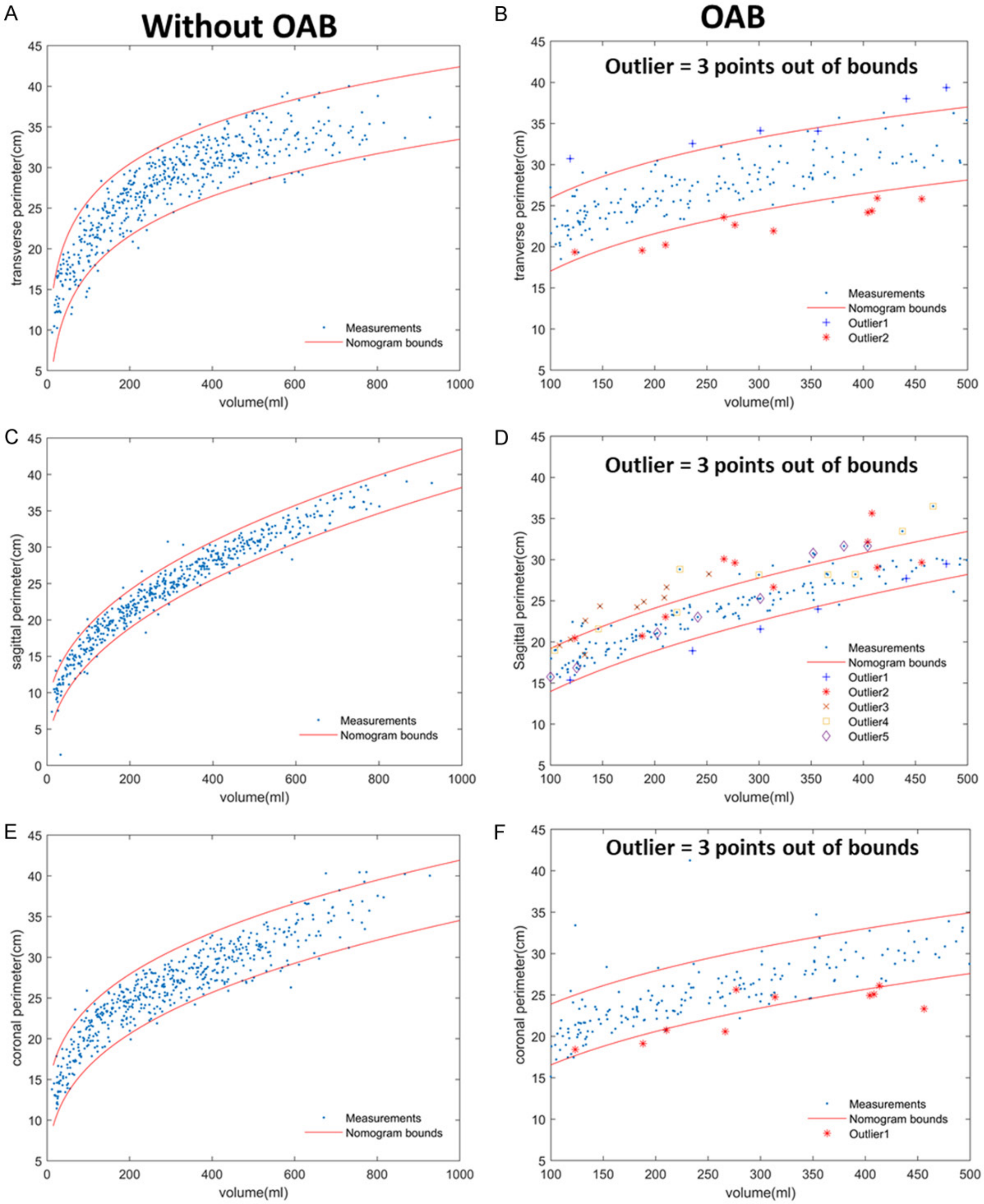


**Figure 3.** Nomograms were generated using 95% confidence intervals for bladder perimeter-volume data from participants without overactive bladder (OAB) for the transverse (A), sagittal (C) and coronal (E) planes. Nomograms were tested using bladder perimeter-volume data in the 100-500 ml volume range from OAB participants for the transverse (B), sagittal (D) and coronal (F) planes. Using a threshold of three or more perimeter values out of the nomogram bounds to define an irregular bladder shape, the transverse and coronal nomograms (B, F) detected two and one OAB participants, respectively, and the sagittal nomogram (D) detected five OAB participants with irregular bladder shapes. The participants without OAB were also tested to verify the nomograms, and none of them had three or more perimeter values outside the nomogram bounds.

three to two, additional participants with OAB were identified as outliers, but multiple participants without OAB were also identified (**Table 1**, All points, 2 outside).

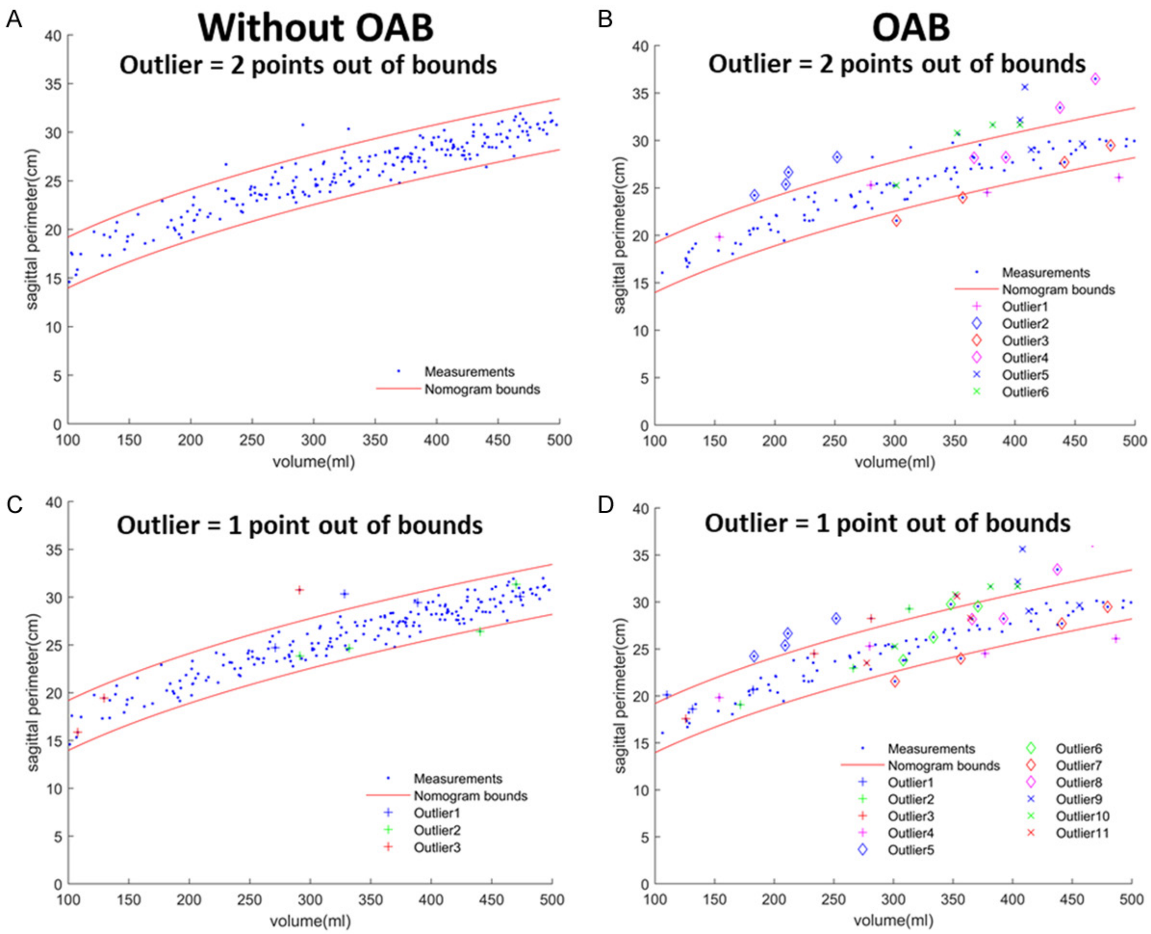


**Figure 4.** The perimeter-volume nomograms presented in **Figure 3** were also tested using a threshold of two or more (A, B) and one or more (C, D) perimeter values for the four largest volumes outside of the nomogram bounds to define an irregular bladder shape. Using bladder perimeter-volume data in the 100-500 ml volume range from overactive bladder (OAB) participants, the sagittal nomograms (B, D) detected six and eleven OAB participants using the threshold of two or more and one or more perimeters respectively. However, during verification of the algorithm using data from the participants without OAB with threshold of one or more perimeters, the sagittal nomogram detected three participants without OAB with irregular shapes (C). None of the participants without OAB were detected using the threshold of two or more perimeter values (A).

**Table 1.** Perimeter nomograms validation and testing results

| Groups of points tested | | All points | | 4 points largest vol | | 3 points largest vol | |
|---|---|---|---|---|---|---|---|
| Number of outlying points | | 3 outside | 2 outside | 2 outside | 1 outside | 2 outside | 1 outside |
| Transverse | Without OAB (n=27) | 0 | 2 (7%) | 0 | 2 (7%) | 0 | 2 (7%) |
| | OAB (n=24) | 2 (7%) | 3 (13%) | 2 (7%) | 5 (21%) | 2 (7%) | 5 (21%) |
| Sagittal | Without OAB (n=27) | 0 | 2 (7%) | 0 | 3 (13%) | 0 | 3 (13%) |
| | OAB (n=24) | 5 (21%)* | 6 (25%) | 6 (25%)** | 11 (46%)Ω | 4 (17%) | 11 (46%)Ω |
| Coronal | Without OAB (n=27) | 0 | 2 (7%) | 1 (4%) | 2 (7%) | 1 (4%) | 2 (7%) |
| | OAB (n=24) | 1 (4%) | 2 (7%) | 1 (4%) | 4 (17%) | 1 (4%) | 4 (17%) |

*P=0.018, **P=0.008, ΩP=0.011. vol.=volume, OAB=overactive bladder.

When testing the nomograms using only the images with the four largest volumes for each participant, no participants without OAB and six participants with OAB were identified with two or more sagittal perimeters outside the nomogram bounds (**Figure 4A**, **4B** and **Table 1**,

| | Participants | UD Fills | HYD fills | US measurements | BMI (kg/m$^2$) | Age (year) | Capacity (ml) |
|---|---|---|---|---|---|---|---|
| Without OAB | 27 | 14 | 43 | 533 | 26.2±1.5 | 26.4±1.7 | 559±40 |
| OAB | 24 | 16 | 14 | 264 | 29.5±2.0 | 42.3±3.4 | 440±38 |

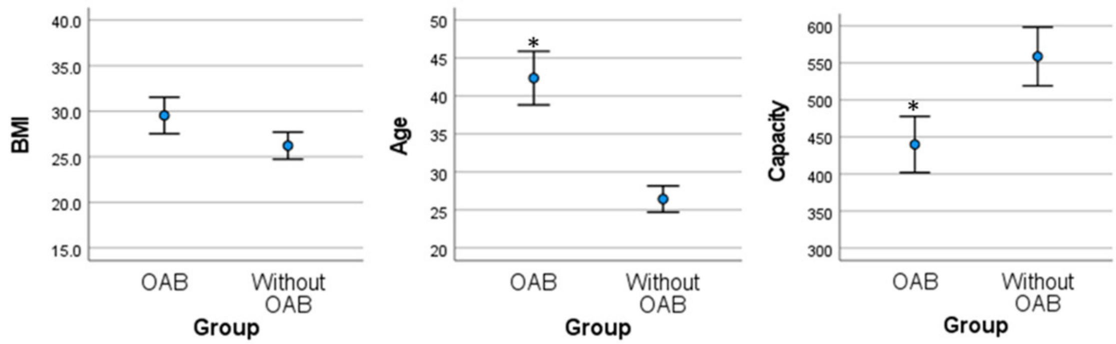


**Figure 5.** Participant characteristics for the groups without and with overactive bladder (OAB), including the type of filling, urodynamics (UD) or oral hydration (HYD), numbers of ultrasound images analyzed, body mass index (BMI), age and bladder capacity. BMI was not different for the two groups (P>0.05). Age and bladder capacity were different for the two groups (*P<0.05).

**P=0.008). Five out of the six (83%) OAB participants with irregular bladder shapes had smaller sagittal perimeters, and the other one (17%) had a larger sagittal perimeter (**Figure 4B**). Furthermore, when the threshold number of perimeter values used to identify an outlier was decreased from two to one, eleven participants with OAB were identified with outlying sagittal perimeters, but three participants without OAB were also identified (**Figure 4C**, **4D** and **Table 1**, ΩP=0.011). Similarly, nomogram testing was completed using only the images with three largest volumes for each participant, but fewer outliers with OAB were identified (**Table 1**).

## Discussion

The present study employed a systematic method to develop a perimeter-volume nomogram to identify irregular bladder shapes. Linear, second-order, exponential and power functions were considered for the shape of the model, and the power function was identified as having the best fit to the data. Nomograms were developed for the transverse, sagittal and coronal perimeters, and the sagittal perimeter nomogram provided the best performance, with 6 out of 24 (25%) OAB participants and none of the 27 (0%) participants without OAB identified as having an irregular bladder shape. These results indicate that some women with OAB have irregularly shaped bladders, and that an ultrasound-based nomogram can be implemented to non-invasively identify these individuals. The clinical significance of these findings is that non-invasive ultrasound could potentially be used to improve the way we diagnose and subcategorize OAB.

The sagittal perimeter-volume nomogram identified five OAB participants with smaller sagittal perimeters and one OAB participant with larger sagittal perimeter values (**Figure 4B**). **Figure 1** shows an example of a bladder from an OAB participant with a smaller sagittal perimeter that is wider and shorter in the transverse plane (**Figure 1B**) and an example of an OAB participant with a larger sagittal perimeter that is taller in the coronal plane (**Figure 1C**) compared to the normal example (**Figure 1A**). These results are consistent with a previous study that examined bladder height-to-width ratios to assess differences of bladder shapes in participants with and without OAB [12]. That study identified 5 out of 11 (45%) OAB participants with irregular bladder shapes, including three with larger height-to-width ratios and two with smaller height-to-width ratios [12]. A major advantage of ultrasound assessments of the bladder is that they can be performed during non-invasive oral hydration studies that have recently been developed for assessing bladder sensation [16, 20-23].

Bladder shape and material properties affect filling mechanics [24, 25], and further studies are needed to determine whether specific OAB symptoms or other conditions such as detrusor overactivity correlate with irregular bladder shapes. A recent study identified a relationship between detrusor overactivity and the acutely regulated bladder material property of dynamic elasticity [26, 27]. Furthermore, conceptual models have been developed to relate bladder wall elasticity to muscle strain and activation histories [25, 26, 28, 29]. Based on these studies, we speculate that bladders with poor contractility may have poor regulation of dynamic elasticity and as a result exhibit insufficient wall stiffness to maintain a normal shape during filling. This hypothesis is consistent with recent studies that demonstrated changes in dynamic elasticity were induced by bladder shape changes through external bladder compression in an ex-vivo perfused pig bladder model [30, 31]. Ultrasound has also been used to identify bladder wall micromotion during urodynamics [32], and future studies could also seek to identify whether bladder wall micromotion affects bladder shape in a manner similar to detrusor overactivity [13].

Measurement of bladder wall thickness may aid in evaluating detrusor underactivity [11]; however, Rachaneni et al. found that bladder wall thickness and detrusor overactivity were not related [33]. Gray et al. showed that bladder shape changes correlated with detrusor overactivity in women with OAB [13], and the present study associated irregular bladder shapes with OAB. Thus, quantification of bladder shape may have more value than bladder wall thickness in the assessment of OAB and detrusor overactivity.

Perimeter-volume nomogram testing was performed for the volume range of 100-500 ml because ultrasound volume measurements are less accurate below 100 ml [19]. In addition, most patients, especially those with OAB, do not reach bladder capacities above 500 ml. An important step toward making the sagittal perimeter nomogram clinically feasible is to minimize the number of ultrasound images required for analysis. The best results for the present nomogram were achieved when analyzing only the sagittal plane images for the four largest volumes for each participant, and analyzing images from only the three largest volumes also produced similar results without identifying any participants without OAB. This suggests that three images at relatively large volumes near capacity may be sufficient to accurately identify a bladder with an irregular shape.

The six OAB participants identified with irregular bladder shapes (**Figure 4B**) were all from ultrasound images taken during urodynamics, which raises the concern that a difference in body posture in the urodynamics chair compared to the chair used for hydration studies may affect bladder shape. The data employed to generate nomogram included a relatively balanced number of participants from urodynamics and hydration, which should reduce the potential of bias. Furthermore, the irregular bladder shapes detected during urodynamics were from participants with relatively severe OAB based on ICIq-OAB scores. Additional studies are needed to confirm any influence that postural changes might have on the bladder shape nomogram results. Pressure from the ultrasound probe can affect bladder sensation [16], and this will also need to be considered when incorporating ultrasound into any assessment of bladder function.

The sagittal perimeter-volume nomogram was verified using the same data from participants without OAB that were used to develop the nomogram. Future studies are needed to validate the nomogram using data from new normal participants and additional participants with OAB. Our preliminary work indicates that bladder shape measurements are repeatable [34]; however, future studies are needed to specifically evaluate the repeatability of the bladder shape parameters from one visit to another and minimize the number of images needed for analysis. Furthermore, the sagittal perimeter does not fully characterize the shape of the bladder, and future studies could examine the effectiveness of incorporating additional parameters, such as the transverse/coronal perimeter ratio into a bladder shape nomogram. Finally, to make bladder shape metrics clinically feasible, machine learning could be implemented in the analysis of bladder images to reduce processing time and potentially improve reliability [35].

In summary, this study developed a novel bladder shape nomogram based on ultrasound-measured perimeters and identified 25% women with OAB as having irregular bladder shapes compared to 0% of women without OAB. The results indicate that some women with OAB may have irregularly shaped bladders, and this novel nomogram may provide a non-invasive and cost-efficient approach to identify these individuals as a shape-associated OAB subgroup.


## Acknowledgements

This study was supported by NIH grant R01DK101719 and the VCU School of Medicine Summer Research Fellowship Program. The authors thank ultrasound technologist Jary Varghese, registered nurse Sandra Smith, research coordinators Kimberly Bradley and Meagan Miller, doctoral student Zachary Cullingsworth and medical students Hameeda Naimi, Hiren Kolli, and Derek Sheen for their important contributions to this study.

## Disclosure of conflict of interest

None.



**Address correspondence to:** Dr. John E Speich, Department of Mechanical and Nuclear Engineering, Virginia Commonwealth University, 401 West Main Street, PO Box 843015, Richmond 23284, Virginia, USA. Tel: 804-827-7036; E-mail: jespeich@vcu.edu


## References


[1] Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, van Kerrebroeck P, Victor A and Wein A; Standardisation Sub-committee of the International Continence Society. The standardisation of terminology of lower urinary tract function: report from the standardisation Sub-committee of the international continence society. Neurourol Urodyn 2002; 21: 167-178.

[2] Milsom I, Kaplan SA, Coyne KS, Sexton CC and Kopp ZS. Effect of bothersome overactive bladder symptoms on health-related quality of life, anxiety, depression, and treatment seeking in the United States: results from EpiLUTS. Urology 2012; 80: 90-96.

[3] Coyne KS, Wein A, Nicholson S, Kvasz M, Chen CI and Milsom I. Economic burden of urgency urinary incontinence in the United States: a systematic review. J Manag Care Pharm 2014; 20: 130-140.

[4] Sexton CC, Notte SM, Maroulis C, Dmochowski RR, Cardozo L, Subramanian D and Coyne KS. Persistence and adherence in the treatment of overactive bladder syndrome with anticholinergic therapy: a systematic review of the literature. Int J Clin Pract 2011; 65: 567-585.

[5] Kelleher C, Hakimi Z, Zur R, Siddiqui E, Maman K, Aballea S, Nazir J and Chapple C. Efficacy and tolerability of mirabegron compared with antimuscarinic monotherapy or combination therapies for overactive bladder: a systematic review and network meta-analysis. Eur Urol 2018; 74: 324-333.

[6] Gormley EA, Lightner DJ, Faraday M and Vasavada SP; American Urological Association; Society of Urodynamics, Female Pelvic Medicine. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. J Urol 2015; 193: 1572-1580.

[7] Gammie A, Speich JE, Damaser MS, Gajewski JB, Abrams P, Rosier P, Arlandis S, Tarcan T and Finazzi Agro E. What developments are needed to achieve less-invasive urodynamics? ICI-RS 2019. Neurourol Urodyn 2020; 39 Suppl 3: S36-S42.

[8] Asimakopoulos AD, De Nunzio C, Kocjancic E, Tubaro A, Rosier PF and Finazzi-Agrò E. Measurement of post-void residual urine. Neurourol Urodyn 2016; 35: 55-57.

[9] Alrabadi A, Al Demour S, Mansi H, AlHamss S and Al Omari L. Evaluation of voiding position on uroflowmetry parameters and post void residual urine in patients with benign prostatic hyperplasia and healthy men. Am J Mens Health 2020; 14: 1557988320938969.

[10] Franco G, De Nunzio C, Leonardo C, Tubaro A, Ciccariello M, De Dominicis C, Miano L and Laurenti C. Ultrasound assessment of intravesical prostatic protrusion and detrusor wall thickness--new standards for noninvasive bladder outlet obstruction diagnosis? J Urol 2010; 183: 2270-2274.

[11] De Nunzio C, Lombardo R, Cicione A, Trucchi A, Carter S, Tema G, Nacchia A, Vicentini C and Tubaro A. The role of bladder wall thickness in the evaluation of detrusor underactivity: development of a clinical nomogram. Neurourol Urodyn 2020; 39: 1115-1123.

[12] Glass Clark S, Nagle AS, Bernardo R, Vinod N, Carucci L, Carroll A, Speich J and Klausner AP. Use of ultrasound urodynamics to identify differences in bladder shape between individuals with and without overactive bladder. Female Pelvic Med Reconstr Surg 2020; 26: 635-639.

[13] Gray T, Phillips L, Li W, Buchanan C, Campbell P, Farkas A, Abdi S and Radley S. Evaluation of bladder shape using transabdominal ultrasound: feasibility of a novel approach for the detection of involuntary detrusor contractions. Ultrasound 2019; 27: 167-175.

[14] Abrams P, Avery K, Gardener N and Donovan J; ICIQ Advisory Board. The international consultation on incontinence modular questionnaire: www.iciq.net. J Urol 2006; 175: 1063-1066; discussion 1066.

[15] Nagle AS, Klausner AP, Varghese J, Bernardo RJ, Colhoun AF, Barbee RW, Carucci LR and Speich JE. Quantification of bladder wall biomechanics during urodynamics: a methodologic investigation using ultrasound. J Biomech 2017; 61: 232-241.

[16] Sheen D, Kolli H, Nagle AS, Cullingsworth Z, Vinod NN, Naimi HA, De Wachter SG, Mazzeo SE, Stothers L, Speich JE and Klausner AP. Validation of a real-time bladder sensation meter during oral hydration in healthy adults: repeatability and effects of fill rate and ultrasound probe pressure. Low Urin Tract Symptoms 2019; 11: 224-231.

[17] GE Healthcare, 4DView User Manual, H48-671BL, 2010.

[18] Nagle AS, Bernardo RJ, Varghese J, Carucci LR, Klausner AP and Speich JE. Comparison of 2D and 3D ultrasound methods to measure serial bladder volumes during filling: steps toward development of non-invasive ultrasound urodynamics. Bladder (San Franc) 2018; 5: e32.

[19] Vinod NN, Nagle AS, Naimi HA, Kolli H, Sheen D, Nandanan N, Carucci LR, Speich JE and Klausner AP. Bladder volume correction factors measured with 3D ultrasound and BladderScan. Can J Urol 2019; 26: 9829-9834.

[20] Lai HH, Naliboff B, Liu AB, Amundsen CL, Shimony JS, Magnotta VA, Shaffer JJ, Gilliam RL, Wiseman JB, Helmuth ME, Andreev VP, Kirkali Z and Harte SE; LURN Study Group. The LURN research network neuroimaging and sensory testing (NIST) study: design, protocols, and operations. Contemp Clin Trials 2018; 74: 76-87.

[21] De Wachter SG, Heeringa R, Van Koeveringe GA, Winkens B, Van Kerrebroeck PE and Gillespie JI. "Focused introspection" during naturally increased diuresis: description and repeatability of a method to study bladder sensation non-invasively. Neurourol Urodyn 2014; 33: 502-506.

[22] Naimi HA, Nagle AS, Vinod NN, Kolli H, Sheen D, De Wachter SG, Speich JE and Klausner AP. An innovative, non-invasive sensation meter allows for a more comprehensive understanding of bladder sensation events: a prospective study in participants with normal bladder function. Neurourol Urodyn 2019; 38: 208-214.

[23] Nagle AS, Speich JE, De Wachter SG, Ghamarian PP, Le DM, Colhoun AF, Ratz PH, Barbee RW and Klausner AP. Non-invasive characterization of real-time bladder sensation using accelerated hydration and a novel sensation meter: an initial experience. Neurourol Urodyn 2017; 36: 1417-1426.

[24] Damaser MS and Lehman SL. The effect of urinary bladder shape on its mechanics during filling. J Biomech 1995; 28: 725-732.

[25] Habteyes FG, Komari SO, Nagle AS, Klausner AP, Heise RL, Ratz PH and Speich JE. Modeling the influence of acute changes in bladder elasticity on pressure and wall tension during filling. J Mech Behav Biomed Mater 2017; 71: 192-200.

[26] Cullingsworth ZE, Klausner AP, Li R, Nagle AS, Carroll AW, Roseman JT 2nd and Speich JE. Comparative-fill urodynamics in individuals with and without detrusor overactivity supports a conceptual model for dynamic elasticity regulation. Neurourol Urodyn 2020; 39: 707-714.

[27] Colhoun AF, Klausner AP, Nagle AS, Carroll AW, Barbee RW, Ratz PH and Speich JE. A pilot study to measure dynamic elasticity of the bladder during urodynamics. Neurourol Urodyn 2017; 36: 1086-1090.

[28] van Duyl WA. A model for both the passive and active properties of urinary bladder tissue related to bladder function. Neurourology and Urodynamics 1985; 4: 275-283.

[29] van Duyl WA and Coolsaet BLRA. Biomechanics of the urinary bladder: spontaneous contraction activity and micromotions related to accommodation. Int Urol Nephrol 2021; 53: 1345-1353.

[30] Balthazar A, Cullingsworth ZE, Nandanan N, Anele U, Swavely NR, Speich JE and Klausner AP. An external compress-release protocol induces dynamic elasticity in the porcine bladder: a novel technique for the treatment of overactive bladder? Neurourol Urodyn 2019; 38: 1222-1228.

[31] Duval DLM, Weprin S, Nandanan N, Cullingsworth ZE, Swavely NR, Balthazar A, Mangino MJ, Speich JE and Klausner AP. Regulation of bladder dynamic elasticity: a novel method to increase bladder capacity and reduce pressure using pulsatile external compressive exercises in a porcine model. Int Urol Nephrol 2021; 53: 1819-1825.

[32] Nagle AS, Cullingsworth ZE, Li R, Carucci LR, Klausner AP and Speich JE. Bladder wall micromotion measured by non-invasive ultrasound: initial results in women with and without overactive bladder. Am J Clin Exp Urol 2021; 9: 44-52.

[33] Rachaneni S, McCooty S, Middleton LJ, Parker VL, Daniels JP, Coomarasamy A, Verghese TS, Balogun M, Goranitis I, Barton P, Roberts TE, Deeks JJ and Latthe P. Bladder ultrasonography for diagnosing detrusor overactivity: test accuracy study and economic evaluation. Health Technol Assess 2016; 20: 1-150.

[34] Maddra K, Swavely N, Li R, Nagle A, Vinod N, Prince S, Tensen S, Naimi H, Weprin S, Sheen D, Kolli H, Carucci L, Klausner A and Speich J.

Abstracts: Ultrasound-defined bladder shape parameters for improved overactive bladder phenotyping: a repeatability study using healthy volunteers. Neurourol Urodyn 2020; 39: S1: S181.

[35] Bentellis I, Guérin S, Khene ZE, Khavari R and Peyronnet B. Artificial intelligence in functional urology: how it may shape the future. Curr Opin Urol 2021; 31: 385-390.