Overcoming the challenges of characterizing normal urodynamic parameters in middle-aged and older women

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Introduction: *To describe urodynamic study (UDS) findings in middle-aged and older women with various lower urinary tract symptoms (LUTS) who were found to have a normal study interpretation.*

Materials and methods: *Following institutional review board approval, UDS tracings of non-neurogenic women who were tested for various LUTS and whose study was interpreted as normal were reviewed. Demographic data, indications for UDS, and UDS parameter findings were extracted. UDS was conducted according to an established protocol using a 6F dual-lumen catheter (ICS guidelines) with a Laborie system and interpreted with a pre-existing template to standardize each reading. The fill-void study was frequently repeated during the same UDS session to confirm normal findings. Study interpretation was done by a neutral reviewer with UDS expertise.*

Results: *From 2000-2012, 42 middle-aged women, who had been coded as having a normal study, were retrospectively reviewed from a database of over 2200 studies. The majority were Caucasian, with mean age 63 (range 42-85), mean body mass index 24.5 (20-37), mean parity 2 (0-4), and 67% were post-menopausal. Of the 42 patients, 28 underwent a second fill-void study. UDS findings were reported based on clinical indication for UDS: 1) incontinence, 2) pelvic organ prolapse, or 3) other LUTS symptoms. UDS findings were consistent between first and second studies.*

Conclusions: *UDS parameters from a cohort of middle-aged and older women with normal findings could serve as reference values when interpreting urodynamic studies or for designing an age-comparable nomogram.*

Key Words: urodynamics, normal female voiding, pressure flow study, reference values

Introduction

Contrary to men for whom an extensively studied bladder outlet obstruction (BOO) nomogram exists,[1] BOO in women is not as firmly established with only one nomogram attempt.[2,3] It is indeed striking how little has been published about "normal" or "normative values" for urodynamic study interpretation in women so far. There is a reason behind this apparent lack of data. One of the challenges is to design a prospective study to enroll a large number of uncomplaining volunteers to provide the necessary data with appropriate test-retest reliability to overcome situational variations. In the absence of such normative values obtained from a large group of fairly asymptomatic older women, an age-comparable nomogram cannot be realistically attained.

Yet, although ideal, such an esteemed study is beyond reasonable expectations. Many aging women develop lower urinary tract symptoms (LUTS), even though those may be mild and not very bothersome. In fact, a UDI-6 questionnaire study in asymptomatic, non-complaining, older women identified a real baseline level of questionnaire score elevation for incontinence and voiding symptoms in that population,[4] hindering the feasibility of obtaining trustworthy "control" data in this older age group related to urodynamic studies.

So, if control values in older women are needed to create a reliable nomogram, but such an older group is unlikely to have totally normal controls comparable to those which have already been studied in a younger population[5] for their urodynamic parameters, one therefore forced to consider some alternative options.

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A "surrogate" approach could consist in reviewing large urodynamic study (UDS) datasets from recent NIH trials conducted in middle-aged women scheduled to undergo surgical correction for stress-predominant urinary incontinence (SUI). Using data from the SISTER[6] and the TOMUS[7] trials, a recent publication outlined differences in filling and voiding UDS parameters between older women over the age of 65 versus their younger counter-parts.[8] However, these women were not strictly speaking "normal" as their incontinence condition may have affected their storage and voiding mechanisms.

In this study, we adopted a different approach by investigating the UDS data of middle-aged and older women who underwent UDS for LUTS but with a resultant normal study interpretation, even when the study was repeated a second time during the same session. By better characterizing the range of normal values during UDS in an older population, we could better interpret UDS studies in that age group and also possibly use this data to build a more accurate BOO nomogram in women of all ages.

Materials and methods

Following institutional review board approval, a large urodynamic database from a single institution was queried from 2000 to 2012 for middle-aged (> 40 years old) and older (> 65 years old) women who had received a post-UDS study code of "normal study". In essence, the UDS was performed for clinical indications including incontinence, prolapse or voiding dysfunction, but the study was completely normal, even when repeated a second time, and did not reproduce or unmask their presenting symptoms. The main exclusion criteria were a neurogenic condition by history and/or symptomatology, and a urodynamic study interpretation limitation like a voided volume of less than 100 mL or a non-plausible tracing (catheter lost during study, erroneous value outside expected range).

Our urodynamic study protocol has already been reported.[9,10] In brief, each study was conducted by a trained urodynamicist using a Laborie Aquarius XLT system (Laborie Medical Technologies, Toronto, ON Canada). On the day of the study, the woman was instructed to arrive with a reasonably full bladder and voided in privacy for a non-invasive uroflowmetry. A 6 French dual-lumen urethral catheter was then inserted to measure the post-void residual. Collected urine was tested to exclude a urinary tract infection. Following the urethral catheter insertion, a 9 French rectal catheter and surface patch electrodes were placed. After verifying proper recording of each catheter by a cough and recording the baseline resting pressure in the bladder,[11] the filling cystometrogram was started at an initial fill rate of 50 mL/min with the patient in standing position. Women with symptomatic prolapse first underwent UDS testing (filling and voiding) with a pack to reduce the prolapse and then a second time afterwards with the pack removed.[12] The volume at the first sensation to void was recorded. Cough and valsalva maneuvers were carried out at 200 mL to assess for urodynamic SUI, and repeated at 100 mL increments until maximum cystometric capacity (MCC) was reached. Occurrence of urgency and urinary urge incontinence due to detrusor overactivity was also assessed throughout the study. Once at MCC, the patient was asked to sit and the transducers were readjusted. Prior to voiding, a short run of the tracing was obtained whenever possible to establish a new pressure baseline, followed by a cough to confirm proper recording of each pressure line. During voiding (pressure flow study or PFS), maximum flow (Qmax), detrusor pressure at maximum flow (pdetQmax), voided volume, and post-void residual (PVR) volume were recorded. After voiding, a repeat cough confirmed proper recording of both pressure lines. Because women in this series presented with LUTS, a large number of them were re-tested a second time in the same session looking to reproduce their symptoms.

UDS data was extracted manually from the UDS tracing rather than relying on computer readings. The studies were performed and interpreted in accordance to Good Urodynamic Practice guidelines[13] and all UDS definitions were in accordance with the International Continence Society (ICS) guidelines.[14]

The study interpretation was performed by the urodynamicist at the completion of the UDS procedure, then reviewed by the referring surgeon, and each tracing was re-analyzed for this study by a trained third party investigator not related to the care of these patients. A filling cystometrogram was considered normal when baseline parameters were within normal range, no detrusor overactivity or compliance changes were observed until MCC was reached, and no incontinence was demonstrated during repeated stress maneuvers.[15]

A voiding cystometrogram was considered normal when following a baseline recording and adequate cough spike, a normal flow curve was obtained with no straining at the start or end of the voiding phase, and the catheters were recording adequately during the whole process. Only patients who were found to have normal tracings during their filling and voiding phases on one run, if only one was performed, or both runs, were included in this report.

Descriptive statistics for categorical measures were found using frequencies and percentages, and continuous measures were found using means, standard deviations, and ranges. Unpaired t-tests were used to assess for any differences in urodynamic findings based on symptomatology group or age group (above and below age 65). Paired t-tests were used to test for differences between the first PFS run and the second PFS run, as well as the first PFS run compared to NIF findings. Box and whisker plots were used to assess variations in PFS parameters between runs 1 and 2, Figure 1. Multiple comparisons were not adjusted for. Non-parametric alternatives for the parametric tests used in this analysis were considered, but did not result in any changed statistical conclusions. All statistical analyses were performed using SAS 9.3 for Windows (SAS Institute Inc., Cary, NC, USA).

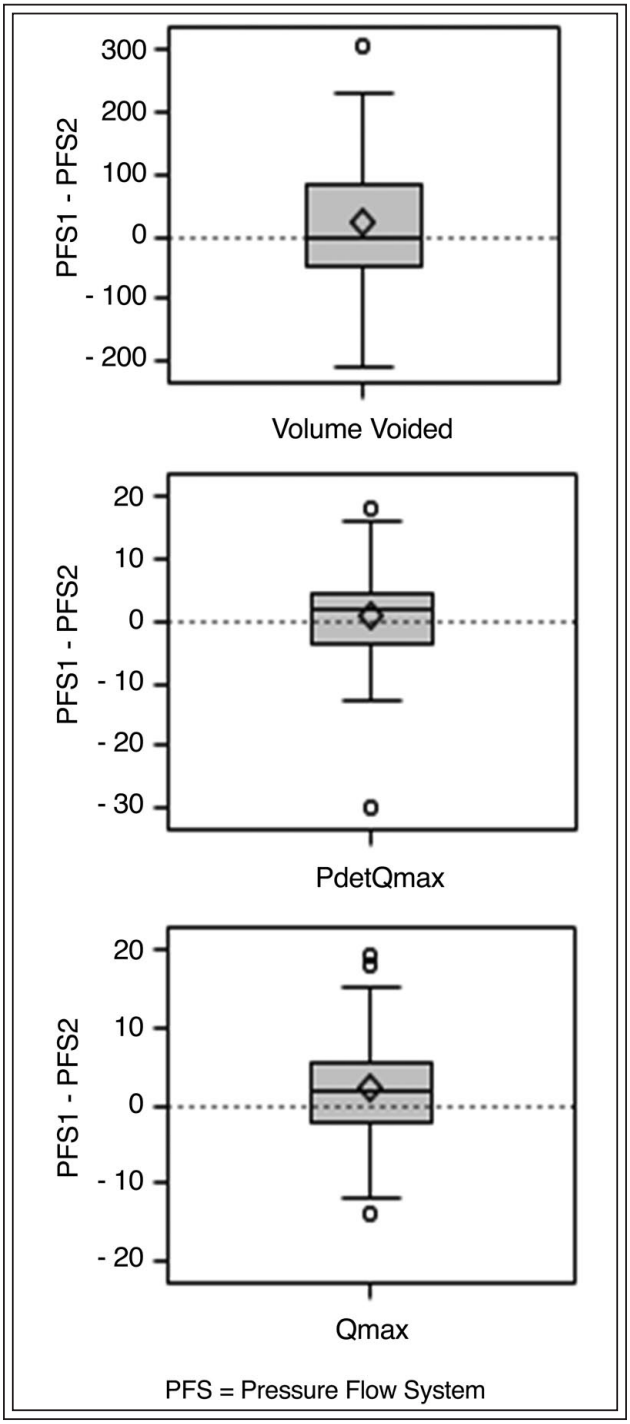

Figure 1. Box and whisker plots of the difference between PFS 1 (run 1) and PFS 2 (run 2).

TABLE 1. **Patient characteristics**

Demographic characteristics	
Age (years): mean (s.d.)	63.4 (11.2)
Body mass index: mean (s.d.)	26.6 (4.4)
Gravida: mean (s.d.)	2.3 (1.1)
Parity: mean (s.d.)	1.9 (1.0)
Vaginal births: mean (s.d.)	1.9 (1.0)
Racial and ethnicity group: N (%)	
Caucasian	40 (95.2%)
Hispanic	1 (2.4%)
Unknown	1 (2.4%)
Prior hysterectomy: N (%)	23 (54.8)
Abdominal	18 (42.9)
Vaginal	5 (11.9)
Prior pelvic/urologic surgery: N (%)	28 (65.1)
Prior sling	8 (18.4)
Symptomatic indications for UDS: N (%)	
Incontinence	
Mixed urinary incontinence	12 (27.9)
Stress urinary incontinence	8 (18.6)
Urgency urinary incontinence	1 (2.3)
Not specified	4 (9.3)
Prolapse symptoms	12 (28.6)
Voiding symptoms	
Intermittent stream	3 (7.0)
Incomplete emptying	2 (4.7)
Storage/irritative symptoms	
Urgency	3 (7.0)
Frequency	3 (7.0)
Nocturia	3 (7.0)
Bladder spasms	1 (2.3)
Dysuria	1 (2.3)
Recurrent UTI	2 (4.7)
Pain	2 (4.7)
Greater than 1 symptom	10 (23)

UDS = urodynamic study
UTI = urinary tract infection

TABLE 2. **Urodynamic findings**

	Group 1 (incontinence)	Group 2 (POP)	Group 3 (all others)	All groups combined 1st void	All groups combined 2nd void
Patients studied (N)	16	12	14	42	29
Age (years)	64 ± 11	61 ± 8	65 ± 14	63 (42-85)	---
NIF (N)	9	10	9		
Qmax	22.3 ± 11.2	18.5 ± 9.5	20.4 ± 7.3	---	---
VV	274.4 ± 170.4	284.0 ± 181.0	284.4 ± 176.9	---	---
PVR	29.4 ± 36.9	65.5 ± 47.5	61.0 ± 127.7	---	---
PFS (N)	16	12	14		
MCC	330.1 ± 69.1	355.8 ± 127.6	374.6 ± 196.4	352.3 ± 136.8	345.2 ± 114.2
Qmax	22.2 ± 5.9	17.1 ± 3.9	20.5 ± 10.3	20.2 ± 7.3	18.1 ± 7.1
PdetQmax	22.5 ± 6.9	20.5 ± 11.6	20.2 ± 7.5	21.2 ± 8.5	19.9 ± 9.5
VV	365.3 ± 74.8	425.3 ± 165.5	405.8 ± 203.3	395.7 ± 150.6	357.8 ± 137.2
PVR	6.4 ± 15.3	1.9 ± 6.6	11.1 ± 32.5	6.6 ± 20.7	7.6 ± 25.6

Second run was performed in 9/16 (group 1), 10/12 (group 2), and 10/14 (group 3).
All urodynamics data expressed as mean + s.d.
PFS = pressure flow study; NIF = non-invasive flow, s.d. = standard deviation; POP = pelvic organ prolapse; MCC (mL) = maximum cystometric capacity; Qmax (mL) = maximum flow rate; PdetQmax (cmH_2O) = detrusor pressure at maximum flow rate; VV (mL) = volume voided; PVR (mL) = post-void residual

Results

From over 2200 UDS tracings in the current database, 44 studies in women labeled as "normal" were identified. One subject with myasthenia gravis and another one with multiple sclerosis were excluded, leaving 42 non-neurogenic women in the final study analysis. Patient demographics were reported in Table 1. The noted mean and median age were 63.4 and 63 years old respectively, consistent with reported ages in literature series on SUI and POP.

Indications for urodynamic testing in this cohort of women were summarized in Table 1. Ten of 42 (24%) patients had more than one LUTS. For comparative analysis, this cohort was divided into three groups according to their symptoms: incontinence, prolapse, and all others. Comparison between the three groups using an unpaired t-test showed no statistical difference with 95% confidence for all measured urodynamic parameters, except for Qmax between the incontinence and prolapse groups, Table 2. Sixty nine percent of the patients had a second study done and 35 patients had noninvasive flow data (of which 7 were excluded for having a voided volume < 100 mL). Cumulative results of the first and second trials for all patients with normal urodynamic findings were summarized in the two final columns of Table 3. The filling and pressure-flow values from the first and second trials were compared using a paired t-test and were also found to show no statistical difference with 95% confidence. Urodynamic tracings with presence of vaginal packing in cases of prolapse were not significantly different compared to the tracings obtained during the second fill-void study without a pack in place.

The average maximum cystometric capacities, maximum flow, and detrusor pressure at maximum flow were 352 mL ± 136.8 mL, 20.2 mL ± 7.3 mL, and 21.2 cm ± 8.5 cm H_2O, respectively. The voided volume had a mean of 395.7 mL ± 150.6 mL and post-void residual volume of 6.6 mL ± 20.7 mL. While there was no statistical difference between the Qmax from the pressure flow study and the NIF, the difference in voided volume (PFS1-NIF) was 125.2 ± 233.6, a difference that was significant ($p = 0.0099$). The post-void residual volume was statistically higher for the NIF compared to the PFS (PFS1-NIF = -46.4 + 63.5, $p = 0.0008$). The UDS findings of all patients were summarized in Table 2. In addition, no difference was observed in urodynamic parameters between the group younger than 65 and their older counterparts, Table 4.

TABLE 3. **Comparison of urodynamic findings between PFS runs 1 and 2 and NIF in all groups combined**

Urodynamic variable	PFS run 1-run 2	Paired t-test p value	PFS run 1-NIF	Paired t-test p value
MCC	13.1 ± 120.0	0.5361	---	---
Qmax	2.2 ± 7.0	0.0865	0.2 ± 10.8	0.9309
PdetQmax	0.6 ± 9.6	0.7412	---	---
VV	21.6 ± 115.4	0.3060	125.2 ± 233.6	0.0099
PVR	0.8 ± 11.4	0.7181	-46.4 ± 63.5	0.0008

All urodynamics data expressed as mean + s.d.
PFS = pressure flow study; NIF = non-invasive flow; s.d. = standard deviation; MCC (mL) = maximum cystometric capacity; Qmax (mL) = maximum flow rate; PdetQmax (cmH_2O) = detrusor pressure at maximum flow rate; VV (mL) = volume voided; PVR (mL) = post-void residual

Discussion

Middle-aged and older women with LUTS constitute a significant proportion of the female urology population. Although this group of patients are frequently evaluated with UDS, there is a dearth of information related to normative values to interpret these UDS studies. Therefore we studied a cohort of women over the age of 40 who presented with LUTS and produced a completely normal UDS study from which we extracted values for use in the interpretation of urodynamic studies in this age group.

Some studies have tried to define normative UDS parameters in middle-aged and older women, Table 5. Barapatre et al analyzed the uroflowmetry data of 308 women without any LUTS.[16] Although the sample size was adequate, their patient population was considerably younger with a mean age at 33.7 years (13-47). Lemack et al reported on normative value for pressure-flow studies in 20 asymptomatic women and compared these values with patient with SUI[5] but here again these patients were much younger (mean age 41.7 years, range 30-70). The pooled analysis of the SISTER and TOMUS trials compared voiding parameters of women less than 65 years with those 65 years old or greater and this data can be useful for women with predominant SUI. Finally, Blaivas and Groutz used a control group consisting of "20

TABLE 4. **Comparison of urodynamic findings between patients younger and older than 65**

	< 65 years old	≥ 65 years old	p value
Patients studied (N)	23	19	
Age (years)	55 ± 6	74 ± 5	
NIF (N)	17	11	
Qmax	21.6 ± 10.3	18.3 ± 7.3	0.3530
VV	298.4 ± 185.0	254.3 ± 147.4	0.5119
PVR	41.2 ± 42.7	69.9 ± 115.8	0.4457
PFS (N)	23	19	
MCC	358.5 ± 148.1	344.7 ± 125.3	0.7486
Qmax	20.5 ± 8.6	19.7 ± 5.7	0.7267
PdetQmax	21.1 ± 9.6	21.3 ± 7.3	0.9342
VV	418.0 ± 171.8	369.9 ± 121.1	0.3140
PVR	1.9 ± 6.2	12.0 ± 29.2	0.1552

All urodynamics data expressed as mean + s.d.
PFS = pressure flow study; NIF = non-invasive flow; s.d. = standard deviation; MCC (mL) = maximum cystometric capacity; Qmax (mL) = maximum flow rate; PdetQmax (cmH_2O) = detrusor pressure at maximum flow rate; VV (mL) = volume voided; PVR (mL) = post-void residual

TABLE 5. **Summary of studies investigating normative urodynamic study values in females**

	Blaivas et al[3]		**Nager et al[11]**		**Zimmern et al[8]**	
Age (years)	67.6	52	< 65 group	> 65 group	< 65 group	≥ 65 group
Mean (range)	(range)	(28-81)		55 (42-64)	74 (65-85)	
Number of pts	20	588	849	96	23	19
NIF						
Qmax	24.4 + 8.8	25.5 + 11.2	26.2 + 0.4	22.0 + 1.3	21.6 ± 10.3	18.3 ± 7.3
VV	250.0 +113.0	309.0 + 134.0	310.9 + 4.8	294.4 + 14.0	298.4 ± 185.0	254.3 ± 147.4
PVR	30.0 + 49	25.0 + 38	22.2 + 1.5	20.0 + 4.4	41.2 ± 42.7	69.9 ± 115.8
PFS						
MCC	---	392.0 + 138.0	375.6 + 4.7	371.8 +13.6	358.5 ± 148.1	344.7 ± 125.3
Qmax	13.3 + 6.3	21 .0 + 10.0	22.7 + 0.4	20.7 + 1.1	20.5 ± 8.6	19.7 ± 5.7
PdetQmax	17.9 + 7.5	19.0 + 13.0	19.5 + 0.6	14.0 + 1.7	21.1 ± 9.6	21.3 ± 7.3
VV	312.0 + 131.0	393.0 + 160	392.9 + 5.7	376.6 + 16.4	418.0 ± 171.8	369.9 ± 121.1
PVR	103.0 + 100.0	---	---	---	1.9 ± 6.2	12.0 ± 29.2

All urodynamics data expressed as mean + s.d.
PFS = pressure flow study; NIF = non-invasive flow; s.d. = standard deviation; MCC (mL) = maximum cystometric capacity; Qmax (mL) = maximum flow rate; PdetQmax (cmH_2O) = detrusor pressure at maximum flow rate; VV (mL) = volume voided; PVR (mL) = post-void residual

women with LUTS, but whose urodynamic study was normal".[3] So they used an approach similar to ours, but with no age or demographic information provided on these patients, and no evidence presented for data consistency since repeat studies were not performed.

In our study, we demonstrated consistency in the UDS results. In women with a normal first UDS run, a second run was frequently repeated hoping to elicit their presenting symptomatology; but they produced a second run with nearly identical parameters as they did in the first run as confirmed on box and whisker plots. Although there was no difference observed between indications for UDS in the three subgroups identified, the numbers in each group were relatively small and did not allow to reach a firm conclusion.

Age did not impact the findings, with no difference observed in the group above 65 compared to their younger counterparts. The effect of voided volume on flow parameters was noteworthy and suggested no influence from the presence of the small size urethral catheter. Like finding a needle in a haystack, the study has limitations as it originates from a relatively small cohort of women extracted from a very large database. Nonetheless, at present, it provides robust data on the range of normal filling and voiding UDS values in middle-aged and older women.

Conclusion

There is no widely accepted UDS nomogram for women mostly due to the absence of age-comparable data. UDS parameters from this cohort of middle-aged and older women with normal findings are now available as an additional resource when interpreting urodynamic studies or for a better design of an age-related nomogram. □

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