Received: 10 December 2018 | Revised: 12 February 2019 | Accepted: 4 March 2019

DOI: 10.1002/nau.23982

ORIGINAL CLINICAL ARTICLE

WILEY Neurourology Urodynamics ICS SUFU

Urodynamic factors associated with the large capacity bladder and incomplete emptying after prolapse repair (2009-2015)

Amy D. Dobberfuhl MD, MS[1] | Robyn K. Shaffer BA[2] | Steven N. Goodman MD, PhD[3] | Bertha H. Chen MD[2]

[1]Department of Urology, Stanford University School of Medicine, Stanford, California

[2]Department of Obstetrics and Gynecology, Stanford University School of Medicine, Stanford, California

[3]Department of Health Research and Policy, Stanford University School of Medicine, Stanford, California

Correspondence
Amy D. Dobberfuhl, MD, MS, Department of Urology, Stanford University School of Medicine, 300 Pasteur Dr, Grant S-287, Stanford, CA 94305.
Email: adobber@stanford.edu

Funding information
Stanford Medical Scholars Program; SUFU Foundation; CIRM, Grant/Award Numbers: TRAN1-10958, DISC1-08731; NIH, Grant/Award Numbers: 1L30DK115056-01, 5UL1RR025742, 5KL2TR001083-05

Abstract

Aims: To identify the clinical and urodynamic factors associated with the large capacity bladder and incomplete bladder emptying after prolapse repair.

Methods: We identified 592 women who underwent anterior and/or apical prolapse repair at our institution from 2009 to 2015. Women were stratified by urodynamic capacity. The primary outcome was incomplete emptying at the longest follow-up (postvoid residual [PVR] > 200 mL). Data were analyzed in the Statistical Analysis System software.

Results: Two hundred and sixty-six women (mean age, 61 years) had preoperative urodynamic tracings available for review. After surgery, there were 519 PVRs in 239 women recorded at up to 2949 days (mean, 396) and nine time points (median, 2; IQR, 1-3). The receiver operator curve for predicted probability of longest follow-up PVR greater than 200 mL (area under curve = 0.67) identified the 600 mL cutpoint which defined large capacity bladder. Large capacity bladders (capacity, >600 mL [n=79] vs ≤600 mL, [n=160]) had a mean: detrusor pressure at maximum flow (21 vs 22 cm H_2O; $P = 0.717$), maximum flow rate (19 vs 17 mL/s; $P = 0.148$), significantly elevated PVR (202 vs 73 mL; $P < 0.001$), and significantly lower voiding efficiency (VE) (74 vs 82%, $P < 0.05$). Following prolapse repair, elevated PVR was associated with large capacity (PVR 101 vs 49 mL, $P < 0.05$). Large bladders had a two- to three-fold risk of longest follow-up PVR greater than 200 mL (14.3%-20.3% [capacity, >600 mL] vs 4.1%-7.0% [capacity, ≤600 mL]). VE was similar after surgery regardless of the capacity (87% vs 88%, $P = 0.772$).

Conclusions: The decision to pursue prolapse repair should be individualized and take into account, the bladder capacity and goals for PVR improvement after surgery.

Abbreviations: BCI, bladder contractility index (BCI = *P*det@*Q*max + 5 × *Q*max); BOOI, bladder outlet obstruction index (BOOI = *P*det@*Q*max − 2 × Qmax); CI, confidence interval; CPT, current procedural terminology; HR, hazard ratio; ICD, international classification of disease; IQR, interquartile range; OR, odds ratio; *P*det@*Q*max, detrusor pressure at maximum flow; POP-Q, pelvic organ prolapse quantification-staging vaginal examination; PVR, postvoid residual; Qmax, maximum flow rate; REDCap, research electronic data capture; UDS, urodynamics; VE, voiding efficiency (VE = voided volume ÷ capacity).

KEYWORDS
female, prolapse, urinary bladder, urinary retention, urodynamics

1 | INTRODUCTION

Pelvic organ prolapse (POP) can result in kinking of the bladder neck and bladder outlet obstruction.[1] Incomplete bladder emptying can be caused by a weak bladder and/or bladder outlet obstruction.[2] Surgical correction of anterior and/or apical prolapse results in anatomic unkinking of the bladder outlet by realigning the bladder with the bladder neck and urethra, which in theory corrects anatomic outlet obstruction. Since bladder symptoms are a considerable driver of a patient's decision to pursue prolapse repair, and incomplete bladder emptying is one of the most common lower urinary tract dysfunctions encountered in these patients, preoperative expectations are a major driver of a patient's perception of a successful surgical outcome. As such, urodynamic pressure flow evaluation has been a standard for ascertaining a patient's likelihood of spontaneous void following prolapse repair.[3]

The most commonly cited female obstruction nomogram was published by Blaivas and Groutz,[4] which classified women into three grades of obstruction, based on the voiding detrusor pressure cutpoints of 57 and 107 cm H_2O for differentiating mild, moderate, and severe obstruction. However additional nomograms have identified much lower pressure cutpoints (20-25 cm H_2O) than Blaivas and Groutz,[4] and have included the addition of flow cutpoints (11-15 mL/s) and fluoroscopic criteria (Chassagne et al,[5] Nitti et al,[6] Lemack and Zimmern,[7] Defreitas et al[8]). What is not defined by these nomograms is the influence of large-bladder capacity on voiding efficiency (VE) in the setting of POP.

VE is a measure of voided volume expressed as a percentage of bladder capacity. Given the lack of quantification of bladder capacity by traditional nomograms, improvements in postvoid residuals (PVR) and VE following prolapse repair in patients with a large capacity bladder have been poorly defined. We sought to describe outcomes associated with the large capacity bladder in women who subsequently underwent anterior and/or apical prolapse repair at our institution over a 6-year period.

2 | MATERIALS AND METHODS

After obtaining the Institutional Review Board approval, we identified 592 sequential patient records, which contained anterior and/or apical prolapse repair Current Procedural Terminology (CPT) codes at our single institution from 2009 to 2015. We then identified 358 records from this group with possible preoperative urodynamic CPT codes. Our bioinformatics data core exported demographic codes, International Classification of Disease codes (ICD-9 and 10), and additional CPT billing codes. A two-reviewer case-by-case retrospective chart review of each medical record was performed on the 358 patients and data extracted into research electronic data capture (REDCap)[9] for demographics; urodynamic parameters; rereview of urodynamic tracings; preoperative prolapse stage; date of surgery; type of surgery; the date and volume of all PVRs after surgery. Urodynamics (UDS) was performed by multiple providers according to their standard practice before surgical repair of prolapse. Following chart review, we identified 266 women with preoperative UDS followed by prolapse repair.

The aim of our study was to identify clinical and urodynamic factors associated with the large capacity bladder and incomplete bladder emptying after prolapse repair. Our primary outcome was incomplete emptying at longest follow-up (PVR > 200 mL), as reported by many investigators and more consistently detected by bladder ultrasound than a postoperative PVR greater than 100 mL.[10] A receiver operator curve for predicted probability of longest follow-up PVR greater than 200 mL stratified by preoperative bladder capacity was used to identify the cutpoint for the large capacity bladder (Figure 1C). This approach identified the 600 mL cutpoint, which was used to define the large capacity bladder, and corresponded to the third tertile of capacity.

Comorbid covariates were identified by ICD code and included diabetes, hyperlipidemia, neuropathy, obesity, and any instance of urinary tract infection. Data were analyzed in Statistical Analysis System software (SAS, Cary, NC) using χ^2 (categorical variables), t test (continuous variables, pooled test if equal variance, and Satterthwaite test if unequal variance), logistic regression, and Kaplan-Meier methods. A $P < 0.05$ was defined as significant. The Kaplan-Meier cumulative incidence analysis with the Cox hazard ratio (HR) was performed to look at the association between time and longest follow-up PVR.

3 | RESULTS

266 women (mean age, 61 years) had preoperative urodynamic tracing and surgical data available for analysis. Comorbid conditions (Table 1) included any diagnosis of

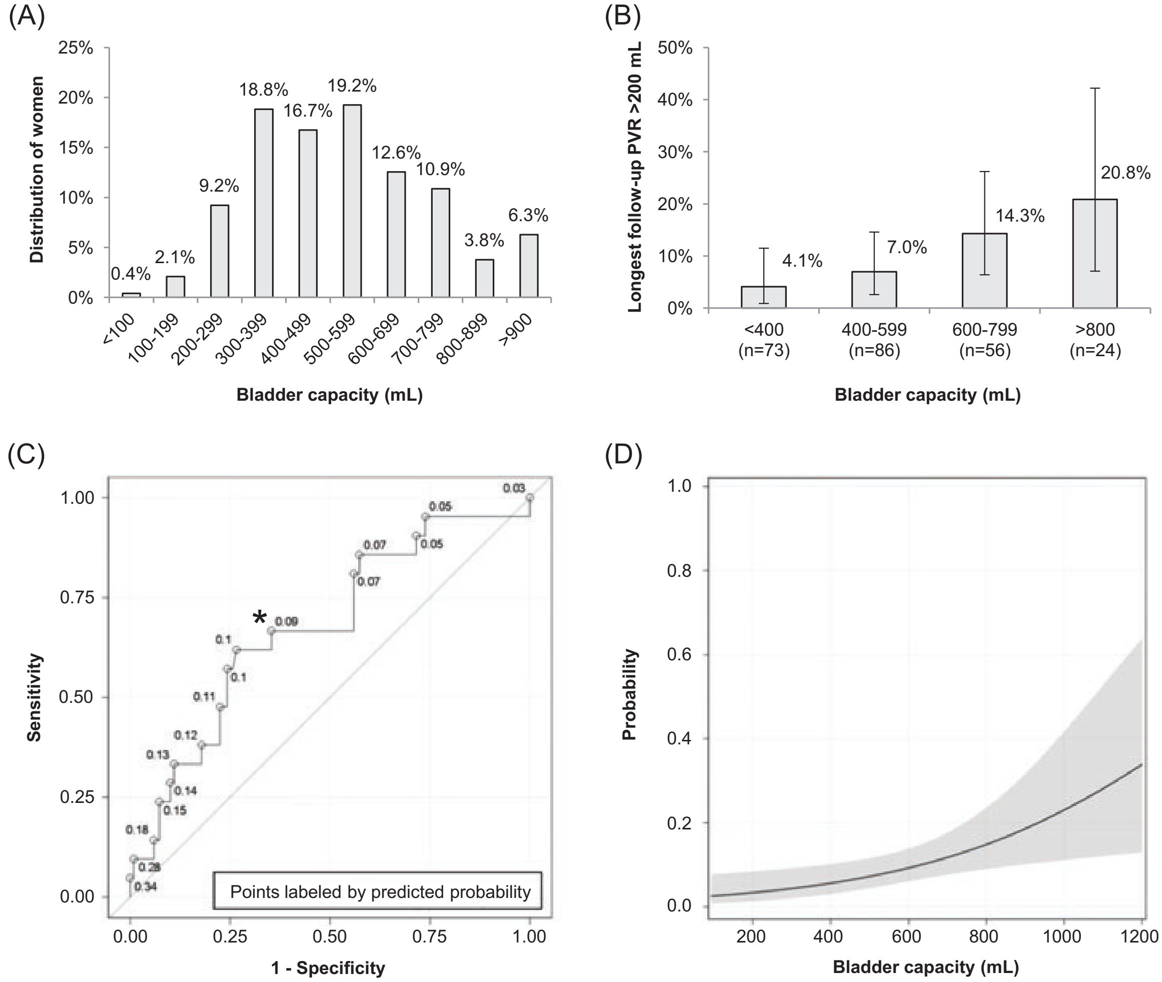

FIGURE 1 A, Distribution of women by preoperative urodynamic bladder capacity. B, Percent of women with postvoid residual (PVR) greater than 200 mL at the longest follow-up after surgery, stratified by preoperative urodynamic bladder capacity. Data presented for women who have at least one PVR available for analysis (n = 239). Error bars = 95% confidence intervals (CI). C, Receiver operator curve for predicted probability of longest follow-up PVR greater than 200 mL stratified by preoperative bladder capacity (area under the curve = 0.67); *600 mL cutpoint (9.2% predicted probability). D, Predicted probability of the longest follow-up PVR greater than 200 mL graphed for bladder capacity (mL) as a continuous variable, with 95% CI envelope

urinary tract infection (45%), hyperlipidemia (34%), obesity (17%), diabetes (14%), and neuropathy (6%). Preoperative UDS revealed a mean: capacity 529 mL (interquartile range [IQR] 370-659, SD = 207), detrusor pressure at maximum flow (*P*det@Qmax) 22 cm H_2O (IQR 12-30, SD = 14), maximum flow rate (*Q*max) 18 mL/s (IQR 11-23, SD = 11), and PVR 120 mL (IQR 5-160, SD = 173). Women with prolapse [overall POP-Q prolapse stage: I (n = 5, 2%), II (n = 92, 35%), III (n = 150, 56%), IV (n = 19, 7%)] underwent anterior only (n = 115, 43%), combination anterior-apical (n = 110, 41%), or apical only (n = 41, 15%) prolapse repair (Table 1). Sling placement was performed in 56% of women at the time of prolapse repair. Following prolapse repair, 239 out of 266 patients had at least one follow-up PVR recorded. There were a total of 519 PVR values recorded at up to 2949 days (mean, 396; SD = 659) and nine time points (median, 2; IQR, 1-3) after surgery. Mean PVR at longest follow-up was 66 mL (SD = 120).

A receiver operator analysis was then performed for the predicted probability of longest follow-up PVR greater than 200 mL stratified by preoperative bladder capacity. This was used to identify the cutpoint for the large capacity bladder. The distribution of women by preoperative urodynamic bladder capacity was plotted and noted to be slightly right skewed (Figure 1A). The third tertile preoperative urodynamic bladder capacity cutpoint was 600 mL. Similarly, the second tertile range for bladder capacity was 424 to 600 mL. The proportion of women with elevated residual (PVR > 200 mL) at longest follow-up after surgery was noted to increase by approximately 7% for each 200 mL increase in preoperative bladder capacity greater than 600 mL (Figure 1B). In bladders smaller than the third

TABLE 1 Preoperative, urodynamic, surgical and follow-up characteristics (n = 266)

	Mean ± SD/n (%)
Age, y	60.8 ± 11.8
Comorbid medical conditions	
Urinary tract infection	120 (45)
Hyperlipidemia	91 (34)
Obesity	44 (17)
Diabetes	37 (14)
Neuropathy	17 (6)
Overall POP-Q prolapse stage	
Stage I	5 (2)
Stage II	92 (35)
Stage III	150 (56)
Stage IV	19 (7)
Preoperative UDS	
Bladder capacity, mL	529 ± 207
*P*det@*Q*max, cm H_2O	22 ± 14
*Q*max, mL/s	18 ± 11
Preoperative PVR, mL	120 ± 173
Preoperative PVR > 200 mL	54 (20)
Preoperative VE, %	79 ± 26
BCI (*P*det@*Q*max + 5 × *Q*max)	111 ± 55
BOOI (*P*det@*Q*max − 2 × *Q*max)	−14 ± 28
Prolapse repair	
Anterior only	115 (43)
Anterior and apical repair	110 (41)
Apical only	41 (15)
Sling placement	150 (56)
Sling removal	13 (5)
Follow-up, women with at least one recorded PVR (n=239)	
Longest follow-up, d	396 ± 659
Number of PVRs recorded (per patient)	2.0 ± 1.6
PVR at longest follow-up, mL	66 ± 120
PVR > 200 mL at longest follow-up	21 (9)
VE at longest follow-up, %	87 ± 20

Abbreviations: BCI, bladder contractility index; BOOI, bladder outlet obstruction index; *P*det@*Q*max, detrusor pressure at maximal flow; POP-Q, pelvic organ prolapse quantification-staging vaginal examination; PVR, postvoid residual; *Q*max, maximal flow; SD, standard deviation; UDS, urodynamics; VE, voiding efficiency.

tertile of capacity, only 4.1% (<400 mL) to 7.0% (400-599 mL) of patients had a PVR greater than 200 mL at longest follow-up, compared with 14.3% (600-799 mL) to 20.3% (>800 mL) of women in the third tertile of bladder capacity.

To further characterize the association between specific bladder capacity cutpoints and the probability of elevated PVR greater than 200 mL at longest follow-up, a univariate logistic regression receiver operator curve was generated (Figure 1C). Individual predicted probabilities for bladders near the third tertile cutpoint of 600 mL were calculated, with a 9.2% probability of incomplete bladder emptying (longest follow-up PVR > 200 mL) noted for a bladder capacity of 600 mL. Individual predicted probabilities for each of the women with the longest follow-up PVR available for analysis were then plotted as a continuous variable with a 95% confidence interval (CI) envelope (Figure 1D). A non-linear relationship and relatively tight CI are noted up to 600 mL. Above the 600-mL bladder capacity threshold, the CI begins to widen. In accordance with the above histogram and confidence envelope distribution, and the clinical relevance of a two- to three-fold increase in the risk of elevated PVR after surgery for the third tertile capacity bladder (vs 400-599 mL), the 600 mL bladder capacity cutpoint was selected as the preoperative statistical strata of interest.

Univariate and multivariate logistic regression was utilized to identify preoperative factors associated with elevated PVR after prolapse repair. Two hundred and thirty-nine out of 266 women had at least one PVR recorded after surgery. The 27 women with missing values were excluded from the longest follow-up PVR logistic regression analysis. On univariate logistic regression (Table 2), the presence of urinary tract infection (odds ratio [OR], 3.85; CI, 1.36-10.90; $P = 0.011$), bladder capacity greater than 600 mL (OR, 3.74; CI, 1.48-9.46; $P = 0.005$), and preoperative PVR greater than 200 mL (OR, 2.82; CI, 1.10-7.28; $P = 0.031$) were significantly associated with the longest follow-up PVR greater than 200 mL. None of the following were significantly associated at the $P < 0.05$ level with longest follow-up PVR greater than 200 mL: surgical characteristics pertaining to the type of repair (anterior, apical, combination), sling placement or removal, and any instance of diabetes, hyperlipidemia, neuropathy, or obesity. Since it was not known if urinary tract infection occurred before or after UDS and/or prolapse repair, infection was excluded from the multivariable adjustment. In our final multivariate regression model (Table 2), preoperative bladder capacity greater than 600 mL (OR, 3.09; CI, 1.04-9.17, $P = 0.042$) was significantly associated with the outcome longest follow-up PVR greater than 200 mL.

Patient characteristics were then stratified by preoperative bladder capacity at the 600 mL cutpoint (Table 3). Large capacity bladders (capacity >600 mL [n=79] vs ≤600 mL, [n=160]) had a mean: capacity (766 vs 413 mL; $P < 0.001$),

TABLE 2 Univariate and multivariate logistic regression for outcome longest follow-up PVR greater than 200 mL (n=239)

	Univariate		Multivariate	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age, y	0.98 (0.94-1.02)	0.294	0.99 (0.95-1.03)	0.648
Comorbid medical conditions				
Urinary tract infection	3.85 (1.36-10.9)	0.011	–	–
Hyperlipidemia	0.70 (0.26-1.89)	0.485	0.65 (0.19-2.23)	0.497
Obesity	1.58 (0.54-4.59)	0.400	1.20 (0.34-4.24)	0.779
Diabetes	2.04 (0.69-5.98)	0.196	2.26 (0.64-7.97)	0.204
Neuropathy	1.42 (0.30-6.70)	0.654	1.10 (0.19-6.53)	0.913
POP-Q stage				
Stage I	3.58 (0.36-36.10)	0.279	–	–
Stage II	1.66 (0.68-4.10)	0.267	0.83 (0.14-4.94)	0.835
Stage III	0.57 (0.23-1.41)	0.221	0.52 (0.09-2.86)	0.452
Stage IV	0.73 (0.09-5.83)	0.766	–	–
UDS strata				
Bladder capacity (>600 mL)	3.74 (1.48-9.46)	0.005	3.09 (1.04-9.17)	0.042
Preoperative PVR (>200 mL)	2.82 (1.10-7.28)	0.031	1.83 (0.61-5.53)	0.284
Prolapse repair				
Anterior only	1.48 (0.60-3.63)	0.393	1.76 (0.33-9.29)	0.508
Anterior and apical repair	0.86 (0.34-2.16)	0.746	1.49 (0.28-7.96)	0.643
Apical only	0.57 (0.13-2.56)	0.463	–	–
Sling placement	0.80 (0.33-1.97)	0.632	0.80 (0.29-2.18)	0.657
Sling removal	3.87 (0.96-15.6)	0.057	2.96 (0.59-14.8)	0.186

Abbreviations: CI, confidence interval; OR, odds ratio; POP-Q, pelvic organ prolapse quantification-staging vaginal examination; PVR, postvoid residual; UDS, urodynamics.

*P*det@*Q*max (21 vs 22 cm H_2O; $P = 0.717$), *Q*max (19 vs 17 mL/s; $P = 0.148$), and PVR (202 vs 73 mL; $P < 0.001$). Before surgery, the large capacity bladder had a significantly elevated PVR (202 vs 73 mL, $P < 0.001$) and significantly lower VE (74 vs 82%, $P < 0.05$). With regard to surgical characteristics, there was no difference in prolapse stage or type of repair for large- vs normal-capacity bladders. Following prolapse repair, there was ongoing incomplete bladder emptying with elevated PVR noted in patients with large capacity bladder (101 vs 49 mL, $P < 0.05$), meanwhile postoperative VE appears to be similar after surgery regardless of bladder capacity (87 vs 88%, $P = 0.772$).

To look at the effect of duration of follow-up of on longest follow-up PVR, patient characteristics were stratified for women who were followed for at least 1 year after prolapse repair (Table 4). There were 69 women identified with at least 12 months of follow-up (mean, 1249 days) who had a mean 3.3 PVRs checked after surgery vs 1.7 for follow-up less than 1 year. Despite this difference in the number of PVRs after surgery, there was no statistically significant difference in age, comorbid medical conditions (with the exception of urinary tract infection), prolapse stage, preoperative UDS, type of prolapse repair, mean PVR, or VE after surgery. The only statistical difference between patient characteristics was the presence of a diagnosis code for any diagnosis of urinary tract infection (follow-up <12 months [n = 70/170, 41%] vs ≥12 months [n = 45/69, 65%], $P < 0.01$).

To look at the time association between any diagnosis of urinary tract infection and longest follow-up PVR greater than 200 mL, we applied the Kaplan-Meier cumulative incidence methods (event = longest follow-up PVR > 200 mL), as utilized by other investigators.[11,12] Using this approach, any diagnosis of urinary tract infection appeared to be nonsignificantly associated with a higher proportion of patients with a PVR greater than 200 mL at most recent follow-up, as the HR and CI include the null association (HR, 1.81; CI, 0.69-4.75). The Kaplan-Meier methods were also used to look at the time association between preoperative bladder capacity and longest follow-up PVR greater than 200 mL. Using this approach, bladder capacity greater than 600 mL was found to be significantly associated with a higher proportion of patients with PVR greater than 200 mL at most recent follow-up (HR, 3.60; CI, 1.50-8.63). From this

TABLE 3 Patient characteristics stratified by preoperative bladder capacity (n = 239)

	Mean ± SD/n (%)		
	Capacity ≤600 mL(n = 160)	**Capacity >600 mL(n = 79)**	***P* value**
Age, y	62.6 ± 10.5	57.2 ± 12.8	<0.01
Comorbid medical conditions			
Urinary tract infection	74 (46)	41 (52)	0.411
Hyperlipidemia	60 (38)	25 (32)	0.374
Obesity	26 (16)	15 (19)	0.597
Diabetes	20 (13)	14 (18)	0.277
Neuropathy	9 (6)	8 (10)	0.203
Overall POP-Q prolapse stage			
Stage I	3 (2)	1 (1)	0.730
Stage II	61 (38)	26 (33)	0.431
Stage III	85 (53)	48 (61)	0.264
Stage IV	11 (7)	4 (5)	0.587
Preoperative UDS			
Bladder capacity, mL	413 ± 119	766 ± 142	<0.001
*P*det@*Q*max, cm H_2O	22 ± 14	21 ± 14	0.717
*Q*max, mL/s	17 ± 11	19 ± 11	0.148
Preoperative PVR, mL	73 ± 99	202 ± 233	<0.001
Preoperative PVR > 200 mL	17 (11)	30 (38)	<0.001
Preoperative VE, %	82 ± 24	74 ± 28	<0.05
BCI (*P*det@Qmax + 5 × *Q*max)	108 ± 50	118 ± 54	0.166
BOOI (*P*det@Qmax − 2 × *Q*max)	−13 ± 28	−18 ± 27	0.200
Prolapse repair			
Anterior only	72 (45)	32 (41)	0.510
Anterior and apical repair	66 (41)	33 (42)	0.939
Apical only	22 (14)	14 (18)	0.419
Sling placement	94 (59)	43 (54)	0.525
Sling removal	8 (5)	4 (5)	0.983
Follow-up			
Longest follow-up, d	392 ± 638	404 ± 703	0.900
Number of PVRs (per patient)	2.1 ± 1.6	2.3 ± 1.6	0.521
PVR at longest follow-up, mL	49 ± 77	101 ± 173	<0.05
PVR > 200 mL at longest follow-up	8 (5)	13 (16)	<0.01
VE at longest follow-up, %	88 ± 19	87 ± 24	0.772

Abbreviations: BCI, bladder contractility index; BOOI, bladder outlet obstruction index; *P*det@Qmax, detrusor pressure at maximal flow; POP-Q pelvic organ prolapse quantification-staging vaginal examination; PVR, postvoid residual; *Q*max maximal flow; SD, standard deviation; UDS, urodynamics; VE, voiding efficiency.

analysis, the cumulative incidence lines are noted to diverge, with separation of the lines noted at all follow-up time points without crossing (figure not shown). Taking into account the assumptions made by grouping patients according to the longest follow-up PVR in our logistic regression model, the separation of the cumulative incidence lines at all time points provides further confirmation of the validity of using longest follow-up PVR in our logistic regression model.

4 | DISCUSSION

We propose that a female bladder capacity greater than 600 mL may be a clinically applicable cutpoint and could be incorporated into the preoperative decision making for women considering anterior and/or apical prolapse repair. Additionally, we present in our results the predicted probability of longest follow-up PVR greater than 200 mL at all bladder capacities, presented as a

TABLE 4 Patient characteristics stratified by duration of follow-up (n = 239)

	Mean ± SD/n (%)		
	Follow-up <12 mo (n = 170)	**Follow-up ≥12 mo (n = 69)**	***P* value**
Age, y	60.2 ± 11.5	62.4 ± 11.5	0.184
Comorbid medical conditions			
Urinary tract infection	70 (41)	45 (65)	<0.01
Hyperlipidemia	60 (35)	25 (36)	0.891
Obesity	24 (14)	17 (25)	0.051
Diabetes	25 (15)	9 (13)	0.739
Neuropathy	12 (7)	5 (7)	0.959
Overall POP-Q prolapse stage			
Stage I	3 (2)	1 (1)	0.863
Stage II	65 (38)	22 (32)	0.355
Stage III	89 (52)	44 (64)	0.107
Stage IV	13 (8)	2 (3)	0.170
Preoperative UDS			
Bladder capacity, mL	534 ± 209	518 ± 208	0.577
*P*det@Qmax, cm H_2O	22 ± 14	21 ± 14	0.596
*Q*max, mL/s	18 ± 10	19 ± 11	0.202
Preoperative PVR, mL	117 ± 174	113 ± 152	0.887
Preoperative PVR > 200 mL	32 (19)	15 (22)	0.607
Preoperative VE, %	79 ± 26	79 ± 24	0.966
BCI (*P*det@Qmax + 5 × *Q*max)	109 ± 52	118 ± 52	0.244
BOOI (*P*det@Qmax − 2 × *Q*max)	−13 ± 27	−18 ± 30	0.217
Prolapse repair			
Anterior only	70 (41)	34 (49)	0.252
Anterior and apical repair	71 (42)	28 (41)	0.866
Apical only	29 (17)	7 (10)	0.176
Sling placement	97 (57)	40 (58)	0.897
Sling removal	7 (4)	5 (7)	0.316
Follow-up			
Longest follow-up, d	50 ± 80	1249 ± 684	<0.001
Number of PVRs (per patient)	1.7 ± 1.2	3.3 ± 1.8	<0.001
PVR at longest follow-up, mL	66 ± 130	66 ± 90	0.992
PVR > 200 mL at longest follow-up	13 (8)	8 (12)	0.329
VE at longest follow-up, %	88 ± 21	86 ± 18	0.667

Abbreviations: BCI, bladder contractility index; BOOI, bladder outlet obstruction index; *P*det@Qmax, detrusor pressure at maximal flow; POP-Q, pelvic organ prolapse quantification-staging vaginal examination; PVR, postvoid residual; *Q*max, maximal flow; SD, standard deviation; UDS, urodynamics; VE, voiding efficiency.

continuous variable including a 95% confidence interval envelope (Figure 1D). These results, along with the percent of women with elevated PVR after surgery presented as a histogram stratified by bladder capacity (Figure 1B), are both useful figures for counseling an individual woman considering prolapse repair based on her preoperative bladder capacity. In the context of our findings, postoperative VE appears to be similar after surgery regardless of bladder capacity, however, a large capacity bladder should raise the clinician's index of suspicion for ongoing incomplete emptying following surgery (Table 3).

There are several important points that should be acknowledged when interpreting and generalizing the findings of our results. First and foremost is the patient selection in our study design. We identified 592 sequential patient records at our institution from 2009 to 2015 which contained anterior and/or apical prolapse repair CPT codes. We acknowledge the long timeframe over which UDS and surgical repairs were performed, by a heterogeneous group of multiple providers according to their standard practice, before surgical repair of prolapse. From this group, there were 266 women with chart reviewed and verified preoperative UDS. The strength of our approach is the large sample size and the granularity of detail which was systematically assessed from chart review. Additionally, charts were directly reviewed for accuracy and the recording of repeated PVR measures on many women, with a mean follow-up of over 1 year.

Limitations of our approach include an acknowledgment of the difficulty of systematically quantifying follow-up PVR after surgery in a retrospective fashion. Our approach is subject to selection bias since not all patients were followed up at equal intervals and for equal durations of time after surgery. However in our series of 266 patients, only 27 patients were missing the longest follow-up PVR value, and there were 239 women who had at least one follow-up PVR available for analysis. Additional limitations include the method of assessing PVR. Since PVR is not a static measure, there may be variability in the measurement of PVR based on technique, since both bladder scanner and catheterization were used to quantify residual urine after surgery. Theisen et al[13] recently reported the accuracy of ultrasound bladder scanner in women with stage II or greater prolapse and concluded that the bladder scanner accurately measures residual, and only underestimated maximum bladder capacity by a mean of 21 mL compared to catheterization. Given the exchangeability of these two techniques in real-world practice, in our study to minimize the effect that the technique used to obtain PVR could play on our outcome, we treated longest follow-up PVR as a categorical variable in our analysis, with a PVR greater than 200 mL used to define elevated PVR after surgery. There is still debate on what is a clinically relevant PVR after prolapse repair surgery. We selected a PVR greater than 200 mL to define incomplete emptying after surgery, which is consistent with the clinical relevance of the 100 to 200 mL threshold for PVR reported in the literature.[11,14-16] While there is not one single PVR threshold which should prompt intervention, our findings offer insight into the effect that prolapse repair has on incomplete bladder emptying for the large capacity bladder after surgery.

Much of the reported literature on urodynamic nomograms assessing bladder contractility (BCI) and the implications of capacity on outcomes have been reported in men.[17-21] There are only a handful of publications which have identified the importance of a large capacity bladder and elevated PVR in women undergoing anterior and/or apical POP repair. In a retrospective study by Lo et al on urodynamic improvements in detrusor underactivity following prolapse repair ($n = 49$), the authors found a reduction in cystometric capacity from 449 to 377 ($P < 0.001$) after prolapse repair, and advocate early surgical intervention since the duration of obstruction may adversely increase capacity and result in a state of detrusor decompensation.[20] What is not defined by these authors is the actionable PVR threshold upon which mandatory intervention is needed to prevent irreversible bladder decompensation after prolapse repair. In one of the few other published studies in women, a recent study by Ulrich et al aimed to identify risk factors for incomplete emptying after prolapse repair (control group: preoperative PVR < 100 mL [n=50] vs elevated: preoperative PVR > 100 mL [n=50]), the authors found no significant difference in PVR resolution after prolapse repair.[10] While this study was not specifically designed to look at the effect of bladder capacity on outcomes after surgery, there was no significant difference in preoperative capacity between groups. The study by Ulrich suggests that volumes below a 100 mL preoperative PVR threshold may be inconsequential, and when interpreted in the context of our present investigation ($n = 266$), a PVR greater than 200 mL is likely to be more clinically relevant.

Interestingly, comorbid conditions identified by ICD code (age, diabetes, cardiovascular disease, and neurologic impairment) which have been implicated in the pathogenesis of underactive bladder and/or detrusor underactivity,[22] were not significantly associated with either large-bladder capacity greater than 600 mL or elevated PVR after surgery. Possible explanations of this null association for these comorbid conditions could include nondifferential misclassification bias, which would tend to bias our findings towards the null. Additional limitations should also acknowledge our inability to quantify the magnitude or duration of each comorbid condition using ICD diagnosis code alone in a retrospective study design.

With regard to urodynamic findings stratified by bladder capacity greater than 600 mL (Table 3), neither BCI nor bladder outlet obstruction index was significantly associated with the large capacity bladder. While these indices are quantifiable in women using Qmax and Pdet@Qmax, they were originally described in male patients with varying grades of bladder outlet obstruction. Our findings are consistent with what has been previously reported in the literature,[23-25] and thus corroborate the poor applicability of these indices to female lower urinary tract physiology.

In our series, we found that the third tertile cutpoint for the large capacity bladder (>600 mL) was associated with a two- to three-fold increase in the risk of elevated

PVR (>200 mL) after surgery. Women with a large capacity bladder greater than 600 mL had a 14.3% (600-799 mL) to 20.3% (>800 mL) rate of incomplete bladder emptying after prolapse repair. Our findings suggest that the large capacity bladder may be important to acknowledge for women considering prolapse repair who are concerned about the possibility of ongoing incomplete emptying after prolapse repair.

5 | CONCLUSIONS

In a woman considering prolapse repair, a large capacity bladder should raise the clinician's index of suspicion for incomplete emptying following surgery. While postoperative VE appears to be similar after surgery regardless of capacity, the decision to pursue prolapse repair should be individualized and based on the symptoms attributed to incomplete bladder emptying along with goals for PVR improvement after surgery.

ACKNOWLEDGMENTS

The project described herein was conducted with author (ADD) support from the KL2 component of the Stanford Clinical and Translational Science Award to Spectrum (NIH KL2TR001083) and REDCap data collection (NIH/NCRR UL1TR001085). ADD (NIH 5KL2TR001083-05 and 1L30DK115056-01; SUFU Foundation), RKS (Stanford Medical Scholars Program), BC (CIRM DISC1-08731 and TRAN1-10958), and SNG (NIH 5UL1RR025742).

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ORCID

Amy D. Dobberfuhl http://orcid.org/0000-0003-3451-3878

REFERENCES

1. Dobberfuhl AD, De EJB. Female stress urinary incontinence and the mid-urethral sling: is obstruction necessary to achieve dryness? *World J Urol*. 2015;33(9):1243-1250. https://doi.org/10.1007/s00345-015-1600-x
2. Wein AJ. Classification of neurogenic voiding dysfunction. *J Urol*. 1981;125(5):605-609.
3. Lo T-S, Chua S, Uy-Patrimonio MC, Kao CC, Lin CH. Clinical outcomes of detrusor underactivity in female with advanced pelvic organ prolapse following vaginal pelvic reconstructive surgery. *Neurourol Urodyn*. 2018;37:2242-2248. https://doi.org/10.1002/nau.23576
4. Blaivas JG, Groutz A. Bladder outlet obstruction nomogram for women with lower urinary tract symptomatology. *Neurourol Urodyn*. 2000;19(5):553-564. https://doi.org/10.1002/1520-6777(2000)19:5<553::AID-NAU2>3.0.CO;2-B
5. Chassagne S, Bernier PA, Haab F, Roehrborn CG, Reisch JS, Zimmern PE. Proposed cutoff values to define bladder outlet obstruction in women. *Urology*. 1998;51(3):408-411.
6. Nitti VW, Tu LM, Gitlin J. Diagnosing bladder outlet obstruction in women. *J Urol*. 1999;161(5):1535-1540.
7. Lemack GE, Zimmern PE. Pressure flow analysis may aid in identifying women with outflow obstruction. *J Urol*. 2000;163(6):1823-1828.
8. Defreitas GA, Zimmern PE, Lemack GE, Shariat SF. Refining diagnosis of anatomic female bladder outlet obstruction: comparison of pressure-flow study parameters in clinically obstructed women with those of normal controls. *Urology*. 2004;64(4):675-679. discussion 679-681. https://doi.org/10.1016/j.urology.2004.04.089
9. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. https://doi.org/10.1016/j.jbi.2008.08.010
10. Ulrich A, Davis P, Propst K, O'Sullivan DM, Tulikangas P. Elevated postvoid residual urine volume: identifying risk factors and predicting resolution in women with pelvic organ prolapse. *Female Pelvic Med Reconstr Surg*. 2018;24(6):444-448. https://doi.org/10.1097/SPV.0000000000000471
11. Hsiao S-M, Lin H-H, Kuo H-C. Urodynamic prognostic factors for large post-void residual urine volume after intravesical injection of onabotulinumtoxin A for overactive bladder. *Sci Rep*. 2017;7:1-7. https://doi.org/10.1038/srep43753
12. Liao C-H, Kuo H-C. Increased risk of large post-void residual urine and decreased long-term success rate after intravesical onabotulinumtoxin A injection for refractory idiopathic detrusor overactivity. *J Urol*. 2013;189(5):1804-1810. https://doi.org/10.1016/j.juro.2012.11.089
13. Theisen JG, Deveneau NE, Agrawal A, et al. The accuracy of portable ultrasound bladder scanner measurements of postvoid residual volume in women with pelvic organ prolapse. *Female Pelvic Med Reconstr Surg*. 2018. [Epub ahead of print]. https://doi.org/10.1097/SPV.0000000000000565
14. Lee K-S, Han DH, Lee Y-S, et al. Efficacy and safety of tamsulosin for the treatment of non-neurogenic voiding dysfunction in females: a 8-week prospective study. *J Korean Med Sci*. 2010;25(1):117-122. https://doi.org/10.3346/jkms.2010.25.1.117
15. Schulz JA, Nager CW, Stanton SL, Baessler K. Bulking agents for stress urinary incontinence: short-term results and complications in a randomized comparison of periurethral and transurethral injections. *Int Urogynecol J Pelvic Floor Dysfunct*. 2004;15(4):261-265.
16. Cho S-T, Song H-C, Song H-J, Lee Y-G, Kim K-K. Predictors of postoperative voiding dysfunction following transobsturator sling procedures in patients with stress urinary incontinence. *Int Neurourol J*. 2010;14(1):26-33. https://doi.org/10.5213/inj.2010.14.1.26

17. Oelke M, Rademakers KLJ, van Koeveringe GA, FORCE Research Group, Maastricht & Hannover. Unravelling detrusor underactivity: development of a bladder outlet resistance-bladder contractility nomogram for adult male patients with lower urinary tract symptoms. *Neurourol Urodyn*. 2016;35(8): 980-986. https://doi.org/10.1002/nau.22841
18. Rom M, Waldert M, Klingler HC, Klatte T. Bladder outlet obstruction in men with acute urinary retention: an urodynamic study. *World J Urol*. 2013;31(5):1045-1050. https://doi.org/10.1007/s00345-013-1027-1
19. Rademakers KLJ, van Koeveringe GA, Oelke M, FORCE Research Group, Maastricht and Hannover. Ultrasound detrusor wall thickness measurement in combination with bladder capacity can safely detect detrusor underactivity in adult men. *World J Urol*. 2017;35(1):153-159. https://doi.org/10.1007/s00345-016-1902-7
20. Lo T-S, Chua S, Uy-Patrimonio MC, Kao CC, Lin CH. Clinical outcomes of detrusor underactivity in female with advanced pelvic organ prolapse following vaginal pelvic reconstructive surgery. *Neurourol Urodyn*. 2018;37(7):2242-2248. https://doi.org/10.1002/nau.23576
21. Warner JN, Grimsby GM, Tyson MD, Wolter CE. Bladder capacity on preoperative urodynamics may impact outcomes on transobturator male slings. *Neurourol Urodyn*. 2012;31(7): 1124-1127. https://doi.org/10.1002/nau.22233
22. Van Koeveringe GA, Rademakers KLJ. Factors impacting bladder underactivity and clinical implications. *Minerva Urol Nefrol*. 2015;67(2):139-148.
23. Dybowski B, Bres-Niewada E, Radziszewski P. Pressure-flow nomogram for women with lower urinary tract symptoms. *Arch Med Sci*. 2014;10(4):752-756. https://doi.org/10.5114/aoms.2014.44867
24. Ahmed A, Farhan B, Vernez S, Ghoniem GM. The challenges in the diagnosis of detrusor underactivity in clinical practice: a mini-review. *Arab J Urol*. 2016;14(3):223-227. https://doi.org/10.1016/j.aju.2016.06.005
25. Gammie A, Kaper M, Dorrepaal C, Kos T, Abrams P. Signs and symptoms of detrusor underactivity: an analysis of clinical presentation and urodynamic tests from a large group of patients undergoing pressure flow studies. *Eur Urol*. 2016;69(2):361-369. https://doi.org/10.1016/j.eururo.2015.08.014

How to cite this article: Dobberfuhl AD, Shaffer RK, Goodman SN, Chen BH. Urodynamic factors associated with the large capacity bladder and incomplete emptying after prolapse repair (2009-2015). *Neurourology and Urodynamics*. 2019;1-10. https://doi.org/10.1002/nau.23982