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Factors associated with low-compliance bladder in end-stage renal disease patients and development of a clinical prediction model for urodynamic evaluation: the DUDi score

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Abstract

Objectives To investigate factors associated with low-compliance bladders (LCB) in pretransplant patients with end-stage renal disease (ESRD) and develop a clinical prediction model for urodynamic studies.

Methods This study was a prospective cohort study. Patients with ESRD on the renal transplantation waiting list were recruited and underwent the urodynamic study. Demographics data, predictor factors related to the bladder compliance such as underlying disease of the lower urinary tract disease (LUTD), duration of urine < 250 mL/day, type and duration of renal replacement therapy (RRT), urine volume per day and urodynamic study information were collected. Univariable and multivariable logistic regression models were used to assess the independence of explanatory factors, then we developed the clinical prediction model.

Results One hundred fifty-two patients participated in the study: 94 patients in the normal bladder group and 58 patients in LCB group. Demographic data were not significantly different between the two groups, except diabetes. Cystometric capacity, detrusor pressure, compliance were significantly different. From the univariate analysis, DM status, duration of RRT, and passing < 100 mL of urine per day were related to LCB. We named the prediction model, the DUDi score based on the predictors (**D**uration of RRT, **U**rine volume/day, **Di**abetes). Higher scores predicted a higher risk of low-compliance bladder [*P* value = 0.464 according to the Hosmer–Lemeshow test, and the AUC was 0.87 (95% CI 0.81–0.92)].

Conclusions Our clinical prediction model is easy to use and provides a high predictive value that is appropriate for patients who have no known LUTD to identify low-compliance bladder.

Trial registration number and date of registration for prospectively registered trials This study was approved by the Thai Clinical Trials Registry Committee on 09 February 2021. The TCTR identification number is TCTR20210209006.

Keywords Low-compliance bladder · End-stage renal disease · Prerenal transplantation · Clinical prediction model

Introduction

The bladder is one of the most important organs and has a critical role in the success of renal transplantation. A good bladder reservoir is essential to prevent transplant related complications and failure of the transplantation. It has recently become routine to perform at least a Voiding Cystourethrography (VCUG) and/or cystoscopy as part of the pre-renal transplantation evaluation to ensure the bladder has a good functional reservoir and can empty properly.

Patients with chronic oliguria may develop bladder dysfunction, characterized by low volume capacity and low compliance [1] and most patients with low capacity bladders have low-compliance bladders (LCB). Moreover, some patients may have other functional bladder abnormalities, like a neurogenic bladder, or dysfunctional voiding that cannot be diagnosed by VCUG or cystoscopy. These abnormalities may result in renal damage and if a renal transplantation were performed in these patients, complications would occur that might lead to allograft damage.

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Although several studies report that bladder capacity and storage pressure may improve within 24 weeks of renal transplantation [1, 2], high storage pressure may still cause complications while waiting for bladder function to improve, such as urinary reflux into the allograft, urinary tract infection, or anastomosis leakage. Moreover, some patients with LCB or very low capacity bladder may not improve post-transplant and might require augmentation or diversion before or after transplantation [2, 3]. Several studies support pretransplant bladder evaluation and pretransplant correction of LCB, especially in patients whose bladder dysfunction results from urological etiologies [4–6]. Moreover, a study report that LCB in kidney transplant patients leads to decrease graft survival and increase risk of complications such as urinary tract infection [7].

A urodynamic study can identify LCB and lower urinary tract dysfunction, however, there is still no consensus, and there are no guidelines, regarding optimal pretransplant urodynamic evaluation, notably in asymptomatic patients and those who have unknown lower urinary tract diseases (LUTD). Remarkably, some 30–50% of patients with no lower urinary tract symptoms (LUTS) have lower urinary tract (LUT) abnormalities revealed by urodynamic evaluation [8, 9]. These patients should be managed before transplantation.

Given the continuing lack of standard guidelines for LUT evaluation and the need for more data [6, 8, 9], we undertook this study to investigate factors associated with low-compliance bladders in pretransplant patients with end-stage renal disease (ESRD) and to develop a clinical prediction model for urodynamic studies. The prediction model aims to identify high risk of LCB and lower urinary tract dysfunction in patients with ESRD prior to transplantation. These patients would benefit from urodynamic evaluation, to identify LCB or lower urinary tract dysfunction, for proper management prior to or after transplantation, which would help increase graft survival and reduce complications from lower urinary tract dysfunction.

Methods

Study design, setting and participants

This study was a prospective cohort study conducted between February 2021 and March 2022 at Thammasat University Hospital (TUH), Pathum Thani, Thailand. We recruited patients with ESRD on the renal transplantation waiting list who were attending the TUH Nephrology and Urology clinic if they were aged more than 18 years old and gave consent to undergo the urodynamic study. We excluded patients who were physically unable to undergo a urodynamic study, for example; patient who could not insert the urethral catheter, patients who refused to perform urodynamic study.

Variables and data measurement

Data were collected on a standardised case record form, including demographics, age, sex, body mass index (BMI), underlying diseases, cause of their renal failure, history of surgery, trauma, previous urological disease, bowel history, medications (beta-blockers, calcium channel blockers), and menstruation. Constipation was defined using the ROME IV criteria and the Bristol stool criteria. Women with normal menstrual periods were defined as normal hormonal status, while those with abnormal or absent menstrual periods were defined as abnormal hormonal status.

To analyze factors related to bladder compliance, we collected data on underlying disease of the LUTD: neurogenic bladder, posterior urethral valve, tuberculosis, benign prostatic hypertrophy (BPH), dysfunctional voiding, overactive bladder, urethral stricture, vesicoureteral reflux, chronic cystitis, interstitial cystitis, duration of very low (< 250 mL/day) urine output, type and duration of renal replacement therapy (RRT), and urine volume per day [1, 10, 11]. We used a three-day bladder diary to measure the functional capacity and the volume of urine output/day.

The data collected from the VUDS were cystometric capacity, bladder compliance, vesicoureteral reflux, maximal flow rate, maximal detrusor pressure at the maximal flow rate, and post-void residual urine.

Urodynamic evaluation

All VUDS procedures were performed, according to good urodynamic practice (International Continence Society guidelines). All patients underwent a rectal enema the night before the study. We used a computerized urodynamic study machine (MMS, solar intelligent) and water-filled catheters with external transducers at the reference level of the upper edge of the symphysis pubis concomitantly with fluoroscopy. Intravesical pressure was measured using a 6Fr, side-holed, water-filled transurethral, double-lumen catheter. The bladders were filled with normal saline mixed with contrast media at a ratio of 1:4 at a rate of 12 mL/min. Zero pressure corresponded to the surrounding atmospheric pressure. Patients were examined in the sitting position for women and standing position for men. All patients were prescribed antibiotic to prevent urinary tract infection after performing urodynamics.

The cystometric capacity was defined as the volume that patient's desired to void [12]. Bladder compliance was calculated from the detrusor pressure and volume of the two standard points of the tracing, that is, at the start of bladder filling with volume zero and at cystometric capacity without

detrusor contraction [13]. The maximum flow rate (Qmax) was recorded while voiding and the maximal detrusor pressure at the maximum flow (PdetQmax) rate was also noted. Low-compliance bladder (LCB) was defined as a < 12.5 mL/cm H_2O [14].

Sample size calculation

To analyze the factors associated with the LCB using multivariable logistic regression model, this study needs 10 samples per variable [15]. Based on previous research, there were five interesting factors that could affect the compliance of the bladder; underlying diseases that can affect lower urinary tract function, constipation, medications (beta-blockers, calcium channel blockers), duration of renal replacement therapy, and urine volume/day. Also, the prevalence of low-compliance bladder in patients with ESRD is about 30–50% [8, 9]. Therefore, we calculated that we would need a total of at least 125 samples with 50 index cases to analyze in this cohort study.

Data analysis and development of a prediction model

We classified patients into two groups, those with a normal bladder and those with LCB, and compared the data between the two groups. We used the student's t test for normally distributed continuous data [expressed as mean and standard deviation, (SD)] and the Wilcoxon Rank Sum test for skewed data [expressed as median and interquartile range (IQR)]. We used the Fisher's exact test for categorical data. Univariable and multivariable logistic regression models were used to assess the independence of explanatory factors by backward elimination. The selection criterion of $p < 0.2$ was used for the elimination of a variable in univariable analysis that was not statistically significant. Some variables were initially excluded from the multivariable model to avoid multicollinearity. Then the β coefficients of each predictor factor was calculated. Finally, to determine the score of each factor, its β coefficient was divided by the lowest β coefficient. As a result, we were able to develop an integer score-based prediction model. Data were analyzed using STATA version 15.0 (Stata Corp., College Station, TX, USA). The statistical significance of the Hosmer–Lemeshow test was set at $p > 0.05$. We assessed the diagnostic ability of a derived score, the DUDi score (see below) for predicting the presence of an LCB.

Result

Patients' characteristic

A total of 152 patients participated in the study: 94 patients in the normal bladder group and 58 patients in LCB group. Age, sex, BMI, underlying diseases, cause of ESRD, constipation and hormonal status in women were not significantly different between the two groups and their mean ages were 42 years (Table 1). Only DM was significantly more common in the normal bladder group. It is interesting to note that there were only 3 patients in each group who had a history of LUTD and none of the patients in this study reported LUTS. The use of beta-blockers and calcium channel blockers were similar between the two groups as were the types of RRT but RRT duration was significantly longer in the LCB group. Urine volume/day, duration of passing < 250 mL/d and maximal functional capacity were significantly different.

The video urodynamic result of normal bladder and bladder dysfunction groups

In the filling phase, six variables were highly significantly different between the two groups: cystometric capacity, volume at first desire to void, volume at strong desire to void, detrusor pressure, compliance and bladder shape as shown in Table 2. There were no significant variables in the void phase but there were trends for detrusor pressure and postvoid urine volume.

Development of the clinical prediction model

We examined a number of factors for bladder compliance in the univariate analysis and found only three significant factors, DM status, duration of RRT, and passing < 100 mL of urine per day (Table 3). When assessed in the multivariable model, there was collinearity between the duration of having a urine output < 250 mL/day and the duration of RRT; therefore, we opted to use the duration of RRT because this is an objective measure. Previous studies, and also statistical analysis of this study, demonstrated that duration of RRT longer than 24 months and 48 months was significantly associated with decreased detrusor compliance and capacity; therefore, we used cut off durations of RRT at less than 24 months, 24–48 months and more than 48 months for analysis in this study [2, 8, 9]. Long-term dialysis patients will develop decreased urine output over time and nephrologists define low urine output at < 100 mL/day. Therefore, we also chose this cut off [16]. DM status, RRT duration and passing < 100 mL/day of urine were the only three independent variables in the multivariable analysis.

Tables 4 and 5 show the developed clinical prediction model called the DUDi score: **D**uration of RRT, **U**rine volume per day, and **Di**abetes. The lowest score was 0 and the highest score was 7 points. Higher scores predicted a higher risk of low-compliance bladder.

Table 1 Clinical characteristics of normal bladder vs low-compliance bladder in ESRD patients, evidence of difference (p value) and 95% confidence interval

Variables	Normal bladder ($n=94$)	Low-compliance bladder$^{\theta}$ ($n=58$)	p value
Age, years, mean (SD)	42.8 (9.8)	42.0 (9.8)	0.648
Sex			
Male, *n* (%)	55 (58.51)	38 (65.52)	
Female, *n* (%)	39 (41.49)	20 (34.48)	0.741
BMI, kg/m^2 (SD)	23.69 (4.70)	23.45 (4.11)	0.742
Underlying disease			
Cardiovascular disease, *n* (%)	13 (13.83)	10 (17.24)	0.325
Neurological disease, *n* (%)	5 (5.32)	2 (3.45)	0.286
Psychological disease, *n* (%)	0	0	
DM, *n* (%)	29 (30.85)	8 (13.79)	0.020
HT, *n* (%)	76 (80.85)	44 (75.86)	0.54
Dyslipidemia, *n* (%)	20 (21.28)	9 (15.52)	0.406
Others, *n* (%)$^{\alpha}$	21 (22.34)	12 (20.69)	0.843
Cause of ESRD			
Glomerular/tubular, *n* (%)	19 (20.21)	8 (13.79)	0.385
Drug induce, *n* (%)	9 (9.57)	6 (10.34)	1.000
DM, *n* (%)	28 (29.79)	6 (10.34)	0.005
HT, *n* (%)	15 (15.96)	12 (20.69)	0.515
LUTD, *n* (%)	0	0	
Others, *n* (%)$^{\mu}$	9 (9.57)	9 (15.52)	0.307
Trauma and surgical history			
Head, *n* (%)	1 (1.06)	0	1.000
Spine, *n* (%)	0	0	
Pelvic, *n* (%)$^{\epsilon}$	1 (1.06)	0	1.000
LUT diseases history			
Neurogenic bladder	0	0	
BPH	0	0	
Dysfunctional voiding	0	0	
OAB	0	0	
Urethral stricture	1 (1.06)	0	1.000
TB bladder	0	0	
VUR	0	0	
PUV	0	0	
Chronic cystitis	0	0	
Interstitial cystitis	0	0	
Others$^{£}$	2 (2.13)	3 (5.17)	0.370
Constipation			
Yes	7 (7.45)	7 (12.07)	
No	87 (92.55)	51 (87.93)	0.392
IPSS, median (IQR)	5 (3–10)	5.5 (3–10)	0.832
LUT drug used$^{\infty}$			
Yes	0	0	
No			
Previous LUT surgery			
Yes, *n* (%)$^{¥}$	3 (3.19)	1 (1.72)	
No, *n* (%)	91 (96.81)	57 (98.28)	1.000
Drug affected bladder used¶			
Yes, *n* (%)	32 (34.04)	28 (48.28)	
No, *n* (%)	62 (65.96)	30 (51.72)	0.090
Hormonal status (female)$^{\Sigma}$, *n*%	39 (100)	20 (100)	

Table 1 (continued)

Variables	Normal bladder ($n=94$)	Low-compliance bladder[θ] ($n=58$)	p value
Normal	19 (48.72)	8 (40.00)	
Abnormal	5 (12.82)	1 (5.00)	0.446
Renal replacement therapy			
Type			
HD, *n* (%)	72 (77.42)	45 (77.59)	
PD, *n* (%)	19 (20.43)	7 (12.07)	1.000
Duration, months, median (IQR)	24.4 (16.3–34.8)	60.8 (34.1–89.6)	< 0.001
Urine volume/day at present, mL, median (IQR)	200 (100–500)	50 (0–75)	< 0.001
Duration of Urine volume < 250 mL/day, months, median (IQR)	12.9 (7.9–32.9)	34.1 (12.7–49.1)	0.007
Maximal functional capacity, mL, mean (SD)	208 (104)	103 (49)	< 0.001

SD standard deviation, n number, *BMI* body mass index, *DM* diabetes mellitus, *HT* hypertension, *LUTD* lower urinary tract diseases, *BPH* benign prostatic hyperplasia, *OAB* overactive bladder, *TB* tuberculosis, *PUV* posterior urethral valve, *VUR* vesicoureteral reflux, *LUT* lower urinary tract, *HD* hemodialysis, *PD* peritoneal dialysis, *IQR* interquartile range, *IPSS* the International Prostate Symptom Score

[Θ]Low-compliance bladder defined as a cut-point of < 12.5 cm/H_2O

[A]Other underlying diseases were gouty arthritis, allergic rhinitis and dyspepsia

[µ]Other underlying diseases were an unknown cause of ESRD

[€]Patient was performed hysterectomy from myoma uteri

[£]Three patients were performed surgery since they were a child and they did not know what type of surgery they was performed. Other 2 patients had frequency voiding with unknown specific cause

[∞]Medication that used to treat lower urinary tract diseases

[¥]One patient was performed dilate urethra and three patients were performed surgery since they were a child and they did not know what type of surgery they were performed

[¶]Alpha-blocker, beta-blocker, and calcium channel blocker

[Σ]Women who have normal menstrual period were defined as normal hormonal status. Women who have abnormal menstrual period or absence from menstruation were defined as abnormal hormonal status

Model performance

The statistical significance of the DUDi score was $p=0.464$ according to the Hosmer–Lemeshow test, and the AUC was 0.87 (95% CI 0.81–0.92) (Fig. 1). The relationship between the DUDi score and the predicted probability of bladder dysfunction is shown in Tables 4 and 5 and Figs. 1 and 2.

A score ≥ 6 is associated significantly with LCB (LHR 4.25 [2.65–6.83], $p<0.001$) and a score ≤ 3 has a low probability of bladder dysfunction (LHR 0.15, [0.07–0.32], $p<0.001$). When translating into absolute risks, the DUDi score predicts an increase risk with increasing score and this has a curvilinear relationship (Fig. 2).

Internal validation of the clinical prediction model

To internally validate our clinical prediction model, we retrospectively categorized risk of low-compliance bladder in patients with ESRD who underwent renal transplantation using the DUDi score, and we reviewed the urological complications which occurred within the first year following transplantation. There were 67 patients with ESRD who underwent renal transplantation between January 2014 and December 2021. Of these, 31 patients were classified as low probability of low-compliance bladder, 9 patients as moderate probability, and 27 patients as high probability. In the high probability group, nine patients had recurrent urinary tract infection, six patients developed allograft hydronephrosis, which urodynamic study revealed to be associated with low-compliance bladder, one patient had overactive bladder, and three patients had dysfunctional voiding. These patients were treated by antimuscarinic. One patient was treated by intravesical Botox injection due to failed antimuscarinic, and biofeedback was used in the dysfunctional voiding patients. Two patients in the moderate group had urinary tract infection and allograft hydronephrosis; they were treated by antimuscarinic. None of patients in low probability group developed urinary tract complications (Table 6).

Table 2 Video urodynamic study result of normal bladder group vs low compliance group

Variable	Normal bladder ($n=94$)	Low compliance ($n=58$)	p value
Filling phase			
Cystometric capacity, mL, mean (SD)	207(104)	103 (49)	< 0.001
Volume at first desire to void, mL, mean (SD)	129(65)	67 (28)	< 0.001
Volume at strong desire to void, mL, mean (SD)	200 (100)	93 (37)	< 0.001
Pdet at 50 ml, cmH_2O, median (IQR)	0 (0–2)	6 (3–10)	< 0.001
Pdet at 100 mL, cmH_2O, median (IQR)	1 (0–4)	14 (8–20)	< 0.001
Pdet at 150 mL, cmH2O, median (IQR)	2 (0–5)	18.5 (14–25)	< 0.001
DO			
Positive	6 (6.38)	4 (6.90)	
Negative	88 (93.62)	54 (93.10)	1.00
Incontinence			
Yes	1 (1.06)	0	
No	93 (98.94)	58 (100)	1.000
Compliance, mL/cm H_2O, median (IQR)	61.3 (25.33–150)	5.3 (3.2–8.5)	< 0.001
Reflux			
Yes	2 (2.13)	3 (5.17)	
No	92 (97.87)	55 (94.83)	0.370
Bladder shape from imaging			
Spherical	92 (97.87)	50 (86.21)	
Elongate	2 (2.13)	8 (13.79)	
Pine	0	0	0.007
Diverticulum			
Yes	2 (2.13)	1 (1.72)	
No	92 (97.87)	57 (98.28)	1.000
Voiding phase			
PdetQmax, cmH_2O, median (IQR)	42.5 (29–60)	49.5 (35.5–72)	0.052
Qmax, mL/s, median (IQR)	9 (6–12)	7.5 (5–10)	0.162
Post-void residual urine, mL, median (IQR)	0 (0–5)	0 (0)	0.072
Obstruction from imaging			
Yes BPH Dysfunctional voiding	4 (4.26) 1 (1.06) 3 (3.19)	0	
No	90 (95.74)	57 (100)	0.297

Pdet detrusor pressure, *DO* detrusor overactivity, *PdetQmax* maximal detrusor pressure at maximal flow rate, *Qmax* maximal flow rate

Discussion

Patients with ESRD may have a dysfunctional bladder characterized by a reduced capacity, LCB and detrusor overactivity [8, 17, 18]. Anuria and oliguria in patients with ESRD can lead to a dysfunctional bladder because of long-term disuse [19], which, in turn, may result in bladder fibrosis, and reduced bladder compliance and capacity [20]. In addition, a low urine output may conceal the symptoms of bladder dysfunction. Patients with LUTD like neurogenic bladder and posterior urethral valves, or those with LUTS, should be investigated. By contrast, a decision to conduct a urodynamic study in asymptomatic patients is more challenging.

Even though many patients with a dysfunctional bladder that is neurologically intact show spontaneous resolution in bladder function 6–12 months post-transplantation [3, 5], they are still at an increased risk of developing complicated urinary tract infections and other complications like high pressure of vesicoureteral reflux to allograft during the period of LCB. Therefore, it would be better to identify LCB patients before transplantation to plan for proper post-transplant management. Bladder cycling has been suggested as a treatment option prior to transplantation for a small, dysfunctional bladder [1], but others suggest that this procedure is not necessary [21]. One advantage of bladder recycling is that it can predict which defunctionalized bladders would improve after resuming normal cycling [22]. It

Table 3 Univariable and multivariable analysis of interesting factors

Predictors	OR (95% CI)	*p* value	Adjusted OR (95% CI)	*p* value
Age < 42 years	1.195 (0.618–2.312)	0.596		
Male gender	1.347 (0.682–2.657)	0.390		
BMI (kg/m^2)	0.988 (0.917–1.063)	0.741		
Non-diabetic	2.788 (1.173–6.624)	0.020	2.175 (0.741–6.385)	0.157
Constipation	1.706 (0.566–5.141)	0.343		
Drug affected bladder used	1.808 (0.926–3.530)	0.083		
Hemodialysis	1.009 (0.460–2.215)	0.981		
Duration of RRT				
24–48 months	4.739 (1.589–14.135)	0.005	4.718 (1.433–15.532)	0.011
> 48 months	22.08 (7.334–66.471)	< 0.001	12.174 (3.726–39.771)	< 0.001
Duration of urine volume < 250 mL/day				
24–48 months	1.62 (0.67–3.92)	0.285		
> 48 months	4 (1.28–12.53)	0.017		
Urine volume/day < 100 mL	11.065 (4.821–25.393)	< 0.001	8.18 (3.260–20.527)	< 0.001

Table 4 Best multivariable clinical predictors, odds ratio (OR), 95% confidence interval (CI), logistic regression beta coefficient (β) and assigned item scores

Predictors	OR	95% CI	*P* value	β	score
DM					
DM	1	Ref			0
Non-DM	2.175	0.741–6.385	0.157	0.777	1
Duration of RRT (months)					
< 24 months	1	Ref			0
24–48 months	4.718	1.433–15.532	0.011	1.551	2
> 48 months	12.174	3.726–39.771	< 0.001	2.499	3
Present urine volume per day(ml)					
≥ 100	0	Ref	< 0.001	2.101	0
< 100	8.18	3.260–20.527			3

is safer to transplant into a normal bladder, but if the bladder is abnormal, the risk of a poor outcome can be minimised by conducting appropriate pretransplant investigations and planning optimal management [7].

From our study, we developed a new clinical prediction model, called the DUDi score. This prediction model is based on the sum score of the 3 clinical predictors that clinicians can understand and use easily. The DUDi score had an AUC > 0.85, which is classified as high accuracy [23, 24], and so should be a good tool for identifying patients who require a pretransplant urodynamic study.

The DUDi score also has good discriminating power to predict the probability of LCB in patients with ESRD. A score ≤ 3 points predicts a low (10%) probability of LCB and we would not recommend a urodynamic study. If the score is between 4 and 5, the probability is equivocal and decision to perform a urodynamic study should be individualized. If the score is ≥ 6, we recommend performing a urodynamic study because of the high probability of LCB as shown in Fig. 3. Patients who had low-compliance bladder were managed by bladder recycling prior to renal transplantation to estimate the ability to improve compliance of the bladder. Four patients did not improve their compliance after daily self-cycling for 3 months. These patients will be closely monitored after transplantation and reconstruction will be planned for if needed. We cannot perform reconstruction prior transplantation because these patients are waiting for a deceased donor; therefore, we cannot plan the exact time of transplantation. Three patients had prostatic obstruction and were treated by alpha-blocker.

Table 5 Categorized low, moderate and high probability scores associated with Low-compliance bladder in ESRD patients and the likelihood ratio of a positive association (LHR+) and 95% confidence intervals (CI)

Probability categories	Score	Low-compliance bladder *n* = 58	Normal *n* = 94	LHR +	95% CI	*p* value
Low	0–3	6 (10.34)	65 (69.15)	0.15	0.07–0.32	< 0.001
Moderate	4–5	10 (17.24)	13 (13.83)	1.25	0.58–2.66	0.643
High	6–7	42 (72.41)	16 (17.02)	4.25	2.65–6.83	< 0.001
Mean (SD)		5.8 (1.5)	2.7 (2.1)			< 0.001

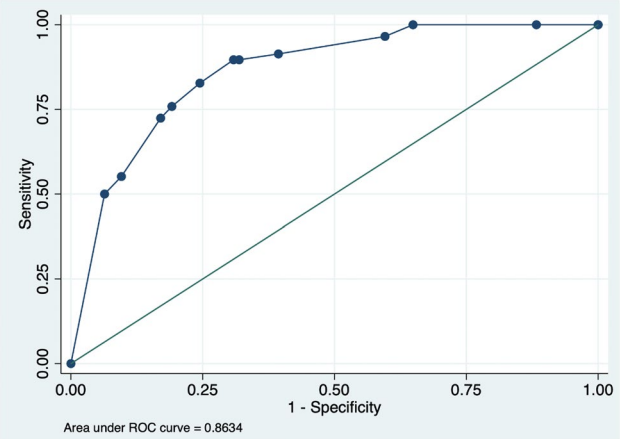

Fig. 1 Area under receiver operating characteristic curve of DUDi score on prediction of low-compliance bladder in ESRD patients

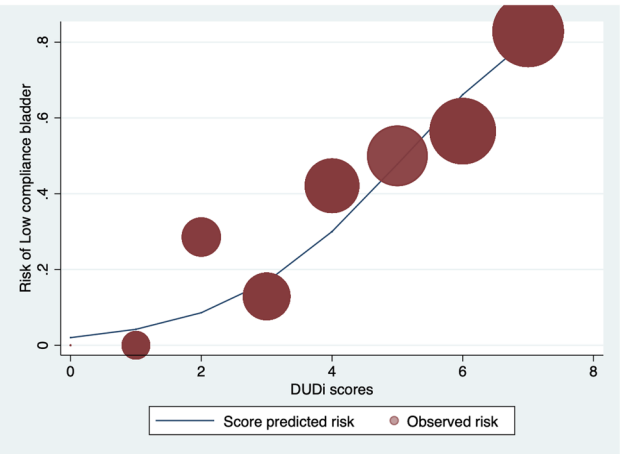

Fig. 2 Observed risk (circle) vs score predicted risk (solid line) of low-compliance bladder, size of circle represented frequency of low-compliance bladder patients in each score

From this study, it was interesting to note that DM patients were more common in patients with bladders of normal compliance. This might be because patients with diabetes, who were poor control hyperglycemia, are at risk of developing diabetic cystopathy over time, characterized by hypocontractility, atonia and overdistension from detrusor muscle underactivity and neuronal impairment [25]. Our study demonstrated that patients with diabetes had a lower number of LCB. These patients have post-renal transplantation complications from LCB may low in these cases. However, these patients may have a risk of developing detrusor underactivity or diabetic cystopathy. Therefore, we recommend urodynamic studies in all patients with known or suspected of diabetic cystopathy and plan for monitoring post-transplant bladder function. For DM patients who are not suspected to have bladder dysfunction, we suggest using the DUDi score for planning further investigations.

The limitation of our study was that it was a single-center study that might not have included the full spectrum of LCB patients; more research should be conducted to validate the DUDi score and include a greater number and spectrum of patients. There were only six patients in our study who had a history of LUTD; therefore, we cannot generalize our DUDi score findings to such patients. Nevertheless, we still recommend performing a complete urinary tract evaluation, including a urodynamic study, in patients with known or suspected LUTD.

We prospectively collected data on post-renal transplant bladder status in only 11 patients (follow-up range from 5 to 8 months), because most of the patients have not yet undergone a renal transplant due to the pandemic of COVID-19. Five patients had high DUDi scores and were managed with bladder re-cycling before transplantation. They did not have urological complication after transplantation. A prospective cohort study documenting the complications related to bladder dysfunction and the improvement of bladder function in a large-scale external validation of post-renal transplantation patients would add further information about the benefits of the DUDi prediction score. Patients with neurogenic bladders whose compliance does not normalize after transplantation may benefit from intravesical botulinum toxin. If not, surgical reconstruction, bladder augmentation or ileal conduit in well-selected patients [26, 27].

Low compliance does not directly impact the decision to be a candidate for renal transplantation, but it impacts the pre and post-transplant monitoring and preparation to increase graft survival and reduce the complications from

Table 6 Internal-validate the clinical prediction model

Post-KT complications	Score 0–3 ($n=31$)	Score 4–5 ($n=9$)	Score 6–7 ($n=27$)	p value
Dysfunctional voiding, n (%)	0	0	3 (11.1)	0.106
UTI, n (%)	0	1 (11.1)	9 (33.3)	0.001
Hydronephrosis, n (%)	0	2 (22.2)	6 (22.2)	0.007
Treatments related to LCB (cycling, antimuscarinic or Intravesical BOTOX), n (%)	0	0	5 (18.5)	0.024

KT kidney transplant, *UTI* urinary tract infection, *LCB* low-compliance bladder

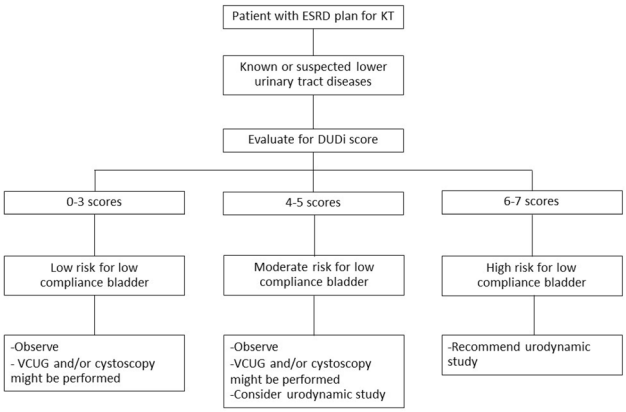

Fig. 3 Flow of management according to the DUDi score

low-compliance bladder. Based on previous studies and our research, we suggest informing the transplantation team about the importance of evaluating bladder function prior to transplantation. Due to the shortage of kidney donor grafts, transplantation teams need to prepare patients properly. Bladder dysfunction is associated with intra and post-operative urological complications, including anastomosis leakage, post-operative LUTS symptoms, UTI, and might impact graft function. Our study helps the transplant team decide which patients on the waiting list need to be evaluated prior to transplant to decrease the risk of urological complications and prolonged graft function.

Conclusion

This study demonstrated that the factors associated with LCB in patients with ESRD are the duration of the RRT, urine volume per day, and not having DM. We used these factors to develop a clinical prediction score, the DUDi Score, to identify patients for pretransplant urodynamic studies. Our clinical prediction model is easy to use and provides a high predictive value that is appropriate for patients who have no known lower urinary tract diseases. More research is needed to validate the score and to assess its usefulness in post-transplant patients to see if its generalizability can be broadened.

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Author contributions TT: conceptualization, research design, methodology, research summary and recommendation, writing—review and editing (equal); formal analysis (lead). VS: conceptualization, research design, methodology, data-analysis, research summary and recommendation (equal); investigation, writing—original draft preparation and editing (lead).

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Declarations

Conflict of interest Both authors have no conflict of interest.

Animal studies N/A.

Ethical consideration Both authors have no conflict of interest. The study is approved by The Human Research Ethics Committee of Thammasat University (Faculty of Medicine). The date of approval is April 23, 2020. The approval number is MTU-EC-SU-6-043/63. All patients were informed and signed consent forms before participating in the study. This study is approved by the Thai Clinical Trials Registry Committee on 09 February 2021. The TCTR identification number is TCTR20210209006.

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