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ORIGINAL ARTICLE

A Novel Predictive Model of Detrusor Overactivity Based on Clinical Symptoms and Non-invasive Test Parameters in Female Patients with Lower Urinary Tract Symptoms

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Abstract

Introduction and Hypothesis This study was aimed at investigating non-invasive indicators correlated with detrusor overactivity (DO) and at developing a prediction model for DO by reviewing clinical and urodynamic data of female patients.

Methods We retrospectively enrolled 1,084 female patients who underwent a urodynamic study (UDS) at Tongji Hospital between September 2011 and April 2021. Associated factors and the independent prediction factors of DO were demonstrated by univariate and multivariate analysis. A non-invasive prediction model of DO was developed and validated by applying these data.

Results A total of 194 patients (17.9%) were classified as having DO. A logistic regression of a multivariate nature showed that DO risk factors were independent of age, nocturia, urgency, urgency urinary incontinence (UUI), and the lack of stress urinary incontinence (SUI). The DO prediction model had good performance, with an area under the curve of 0.880 (95% CI 0.826–0.933), which was verified by urodynamic data of patients in Tongji Hospital to be 0.818 (95% CI 0.783–0.853). An outstanding correspondence between the anticipated probability and the observed frequency was revealed by the calibration curve. Decision curve analysis demonstrated that clinical net benefit can be obtained by applying the DO prediction model when the DO risk probability was between 8 and 97%.

Conclusions A non-invasive prediction model of DO was developed and validated using clinical and urodynamic data. Five independent factors associated with DO were identified: age, nocturia, urgency, UUI, and SUI. This prediction model can contribute to assessing the risk of female DO without the need for invasive urodynamic studies.

Keywords Detrusor overactivity · Urodynamic study · Predictive model · Lower urinary tract symptoms · Non-invasive

Introduction

The prevalence of lower urinary tract symptoms (LUTS) was documented as being 66.6% in women in larger epidemiological studies [1], significantly impacts the quality of life, and are frequently linked to considerable economic burdens [2, 3]. In daily practice, LUTS are initially evaluated by history taking, physical examination, urinalysis, uroflowmetry and post-void residual (PVR). However, these tests are usually insufficient to distinguish the specific pathophysiological status of LUTS.

Detrusor overactivity (DO) is a common pathology underlying overactive bladder (OAB), which was usually diagnosed by urodynamic study (UDS) and can have significant effect on the treatment choice and results. It has been suggested that the occurrence of preoperative DO is the sole urodynamic finding, with a detrimental impact on

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the success of urinary incontinence surgery [4], and interventions such as botulinum toxin A or nerve stimulation are currently available, but they can only be recommended for patients with a diagnosis of DO [5]. Up to now, UDS remains the gold standard for diagnosing DO. Nevertheless, urodynamic examination is an invasive examination in urology, which can be painful and expensive, and current evidence only supports its use in the management of urinary incontinence. International professional organizations discourage their regular use [6, 7]. Second, it requires dedicated equipment and specific expertise. Third, UDS necessitate transurethral intubation and may induce urinary symptoms, including urinary tract infections and hematuria. These factors limit use and implementation in routine practice and prevent greater awareness and diagnosis of DO.

Several studies have examined the relationship between clinical and urodynamic diagnoses in women [8, 9] and some researchers have endeavored to pinpoint clinical indicators of DO. Factors such as the highest urgency rating on the urgency scale [10], the initial bladder volume during urodynamics [11], and the thickness of the bladder wall [12] have been suggested as potential predictive elements. Some prediction instruments have been formulated to assist in the non-invasive determination of DO. However, the utilization of these instruments in clinical practice has been constrained and subject to controversy, primarily because of the intricate calculations that they necessitate and the limited number of studies or sample size [13–15]. The objective of this research was to create a simple predictive model by incorporating both clinical symptoms and non-invasive test parameters. This model is aimed at, in a sizable cohort of female patients with LUTS, assessing the probability of DO.

Materials and Methods

Study Design and Patients

A retrospective analysis of clinical data was conducted on the female patients with LUTS who underwent UDS between September 2011 and April 2021 at a single institution, Tongji Hospital. The patients underwent evaluation through standard clinical assessments, including medical history review, completion of a symptom assessment form, urine examination, and transabdominal or transrectal ultrasound. A symptom assessment questionnaire designed to capture data on urinary frequency, urgency, nocturia, dysuria, and feelings of incomplete bladder emptying. The criteria for undergoing UDS were either severe LUTS that did not respond to medication or a complex condition suspected by expert urologists.

We included individuals aged 18 years and above and excluded individuals with conditions that may impact the function of the lower urinary tract, such as neurogenic bladder, interstitial cystitis and radical pelvic surgery history. Patients without available full UDS data and certain data including free uroflowmetry and PVR were excluded from the study. The included patients were stratified into two groups: to develop a predictive model for assessing the risk of DO, 70% of the patient population was included in the analysis, whereas 30% were reserved for model validation. Patients were randomly allocated to one of the two groups.

This study was performed in accordance with the ethical standards of the Declaration of Helsinki and approved by the Tongji Hospital Research Ethics Committee and the Institutional Review Board.

Urodynamic Study

In addition to conducting filling cystometry and pressure uroflow studies, we assessed both subjective symptoms reported by patients and quantifiable non-intrusive testing parameters. These parameters included free uroflow rate and PVR. Free uroflow rate analysis encompassed Q_{max}, Q_{ave}, voided time, flow time, time to Q_{max}, voided volume, and acceleration. PVR was evaluated using abdominal ultrasound following free uroflow rate. We also calculated bladder volume, which is equal to voided volume plus PVR. The urodynamic study was performed according to the good urodynamic practice of the International Society for Urinary Control (ICS), including filling cystometry and pressure-flow study [16]. The occurrence of involuntary detrusor muscle contractions characterized DO, either while the bladder was filling (phasic DO) or uncontrolled detrusor contraction results in voiding (terminal DO) throughout the assessment [17]. Information obtained from each item of urodynamic data was carefully reviewed for any artifacts and then manually inputted into the database. This process was employed to prevent errors that might arise from automated data extraction.

Statistical Analysis

The data on patient characteristics were displayed by presenting the mean ± standard deviation for continuous variables and by employing numbers (n) and percentages (%) for categorical variables. We evaluated the correlation between each potential predictive factor and DO using both single-variable and multiple-variable models. A backward stepwise approach was employed to include all variables in a multivariate logistic regression analysis to identify independent risk factors associated with the occurrence of DO. A risk model for DO was then constructed by integrating the independent risk factors that were identified, and it was developed using the corresponding weights assigned to the significant variables.

A DO nomogram was plotted by incorporating the independent risk factors, and a receiver operating characteristic (ROC) curve was generated to evaluate the predictive performance of the model. A higher value of the area under the curve (AUC), closer to 1, signifies a stronger predictive power. A calibration curve, constructed by plotting actual occurrences against projected probabilities, was employed to evaluate the calibration of the DO nomogram [18]. The 45° line represents the best calibration (the model's prediction perfectly matches the patient's actual risk). Deviations above and below the 45° line indicate under-predicted and over-predicted respectively. A review of the decision curve analysis (DCA) was performed to evaluate the practical usefulness of the model. We further validated the predictive ability of the DO model by applying another independent dataset. Statistical computations were conducted utilizing R software version 4.0.5 (R Project for Statistical Computing, Vienna, Austria). Statistical significance was defined as $p < 0.05$.

Results

Patient Characteristics

A final sample comprising 1,084 female patients was collected and then divided randomly into two sets in a proportion of 7:3. The initial cohort, encompassing 758 patients, was employed in crafting the predictive model, whereas the subsequent cohort, comprising 326 patients, was set aside for the validation of the model. The difference between the population used to construct the model and the population used to validate the model was not statistically significant. The model development group showed a mean age of 48 ± 15 years, among whom 136 patients (17.9%) were identified as having DO. In contrast, the model validation group exhibited a mean age of 49 ± 15 years, with 58 patients (17.8%) identified with DO.

Univariate and Multivariate Logistic Analyses

Significant factors identified through univariate analysis included age, Q_{max}, Q_{ave}, voided time, acceleration, voided volume, PVR, bladder volume, nocturia, urgency, dysuria, urgency urinary incontinence (UUI), stress urinary incontinence (SUI), and hypertension. A comparison of potential risk factors between patients with and without DO in the development and validation groups is presented in Table 1. Independent predictive factors for DO were identified through multivariate logistic analyses, revealing that age (OR = 1.04, 95% CI 1.02–1.05, $p < 0.001$) (it means the risk of DO increases by 0.04-fold per year), nocturia (OR = 2.03, 95% CI 1.37–3.01, $p < 0.001$), urgency (OR = 2.84, 95% CI 1.92–4.21, $p < 0.001$), UUI (OR = 3.85, 95% CI 1.96–7.69, $p < 0.001$), and SUI (OR = 0.11, 95% CI 0.04–0.26, $p < 0.001$) are presented in Table 2. These data were included to develop a predictive model for diagnosing DO.

Model Development and Model Validation

As shown in Fig. 1, a nomogram based on the predictive model incorporating age, nocturia, urgency, UUI and SUI was developed. An older age, presence of nocturia, urgency and UUI, and an absence of SUI suggested a higher risk of DO. For each independent risk factor, each value is associated with a corresponding point (Points line); by adding these five individual points the total points were obtained (Total Points line). Similarly, each total point corresponds to a risk of DO (Risk line). The formula to calculate an exact risk of the nomogram was displayed in Table 2. The individual probability of DO for each independent risk factor was calculated by using its regression coefficient. In the model development group, the ROC curve demonstrated a robust predictive value, with the AUC being 0.880 (95% CI 0.826–0.933; Fig. 2) and AUC was confirmed to be 0.818 (95% CI 0.783–0.853) in the validation group (see Fig. 5A). In both the model development group (Fig. 3) and the validation group (see Fig. 5B), the calibration curve demonstrated a close fit between the gray solid line "Bias-corrected" (representing the model's performance) and the diagonal dotted line (representing the ideal model). An excellent correspondence between the predicted probability and observed frequency is indicated by this close fit. Figure 4 presents the decision curve analysis for the DO predictive model. DCA revealed that utilizing the DO nomogram to predict DO risk adds more benefit than the treat-all or treat-none strategy when the threshold probability of DO falls between 8 and 97%. Similarly, within the predicted risk range of 7% and 93% in the validation group (Fig. 5C), the DCA results showed that the model showed more significant clinical application value than treat-all or treat-none, which provided support for its wider practical application.

Discussion

In this article, we investigated the clinical symptoms and urodynamic related non-invasive examination parameters associated with DO among 1,084 female patients experiencing non-neurogenic LUTS who underwent UDS. Nocturia, urgency, UUI, and SUI were identified, along with age, as predictors of DO among the identified factors. Using these five selected factors, we developed a predictive model for DO.

Table 1 Comparison of potential risk factors between the development and validation groups for patients with and without detrusor overactivity (DO)

	Development group			Validation group		
	DO		p	DO		p
	Yes (n = 136)	No (n = 622)		Yes (n = 58)	No (n = 268)	
Continuous variables						
Age	55.75 (17.68)	46.27 (13.62)	< 0.001	60.21 (14.44)	46.69 (14.58)	< 0.001
Q_{max}	13.03 (9.13)	18.26 (10.51)	< 0.001	11.30 (8.10)	17.94 (11.16)	< 0.001
Q_{ave}	6.97 (4.57)	10.11 (5.68)	< 0.001	6.26 (4.20)	9.86 (5.98)	< 0.001
VT	67.47 (106.09)	49.87 (42.17)	0.002	67.44 (97.54)	51.68 (46.16)	0.064
FT	39.13 (19.67)	38.30 (21.75)	0.684	35.74 (18.20)	40.50 (23.90)	0.154
TQ_{max}	13.19 (13.28)	13.92 (17.77)	0.647	18.81 (63.86)	15.45 (29.39)	0.54
Acceleration	1.71 (1.81)	2.12 (1.96)	0.027	1.38 (1.24)	2.25 (2.35)	0.007
VV	230.84 (121.78)	315.44 (132.11)	< 0.001	189.16 (105.14)	316.10 (132.62)	< 0.001
PVR	44.71 (62.30)	26.38 (89.93)	0.024	59.05 (95.45)	22.72 (55.02)	< 0.001
BV	275.54 (115.33)	341.82 (141.82)	< 0.001	248.21 (123.79)	338.82 (135.75)	< 0.001
Categorical variables						
Frequency	87 (64.0)	378 (60.8)	0.551	40 (69.0)	162 (60.4)	0.288
Nocturia	41 (30.1)	93 (15.0)	< 0.001	24 (41.4)	67 (25.0)	0.018
Urgency	60 (44.1)	117 (18.8)	< 0.001	32 (55.2)	52 (19.4)	< 0.001
Dysuria	54 (39.7)	136 (21.9)	< 0.001	28 (48.3)	58 (21.6)	< 0.001
Incomplete emptying	21 (15.4)	94 (15.1)	1	9 (15.5)	45 (16.8)	0.967
POP	5 (3.7)	39 (6.3)	0.332	2 (3.4)	11 (4.1)	1
UUI	40 (29.4)	91 (14.6)	< 0.001	20 (34.5)	37 (13.8)	< 0.001
SUI	9 (6.6)	147 (23.6)	< 0.001	4 (6.9)	57 (21.3)	0.018
Diabetes	7 (5.1)	16 (2.6)	0.19	5 (8.6)	10 (3.7)	0.206
Hypertension	11 (8.1)	21 (3.4)	0.025	5 (8.6)	9 (3.4)	0.151

Continuous variables are expressed as average and standard deviation

Categorical variables were defined based on their presence (yes/no)

Values are expressed as numbers (n) and percentages (%)

Differences between groups were compared using Student's t test with continuous variables and the Chi-squared test with categorical variables

Statistical significance was established at $p < 0.05$

Q_{max} maximum urinary flow rate, Q_{ave} average urinary flow rate, *VT* voiding time, *FT* flow time, *TQmax* time to Q_{max}, *VV* voided volume, *BV* bladder volume, *PVR* post-void residual, *POP* pelvic organs prolapse, *UUI* urgency urinary incontinence, *SUI* stress urinary incontinence

Table 2 Independent risk factors for the presence of detrusor overactivity (DO) resulting from the stepwise backward multivariate logistic regression analysis in the model development cohort and the formula of total points for the model

Risk factors	OR	95% CI	p	Points	
Age	1.04	1.02–1.05	< 0.001	1.25*Age-12.5	
Nocturia	2.03	1.37–3.01	< 0.001	Yes (24)	No (0)
Urgency	2.84	1.92–4.21	< 0.001	Yes (35)	No (0)
UUI	3.85	1.96–7.69	< 0.001	Yes (45)	No (0)
SUI	0.11	0.04–0.26	< 0.001	Yes (0)	No (73)

Total points = Age + Nocturia + Urgency + UUI + SUI

Risk = −0.00000035*Total points3 + 0.0002*Total points2-0.03*Total points + 1.4

DO detrusor overactivity, *OR* odds ratio, *CI* confidence interval, *UUI* urgency urinary incontinence, *SUI* stress urinary incontinence

The prevalence of DO in our study was 194/1,084 (17.9%). In a previous study, 4,184 female patients undergoing UDS for LUTS revealed that 399 patients (9.5%) were identified as having DO [19]. In another two studies, DO was found in 374 patients out of 1,006 (37.2%) and 259 out of 1,140 female patients (22.7%) [15, 20]. All of these patients underwent UDS for LUTS. Indeed, the broad range of prevalence observed in DO may be attributed to variations in characteristics within the study population. Factors such as age, gender, medical history, comorbid diseases, diagnostic criteria, and methods of UDS could contribute to this variability.

In our study, DO was found to be significantly predicted by older age (OR = 1.04, 95% CI: 1.02–1.05). This finding aligns with a prior study that similarly revealed a significant association between older age and DO in female

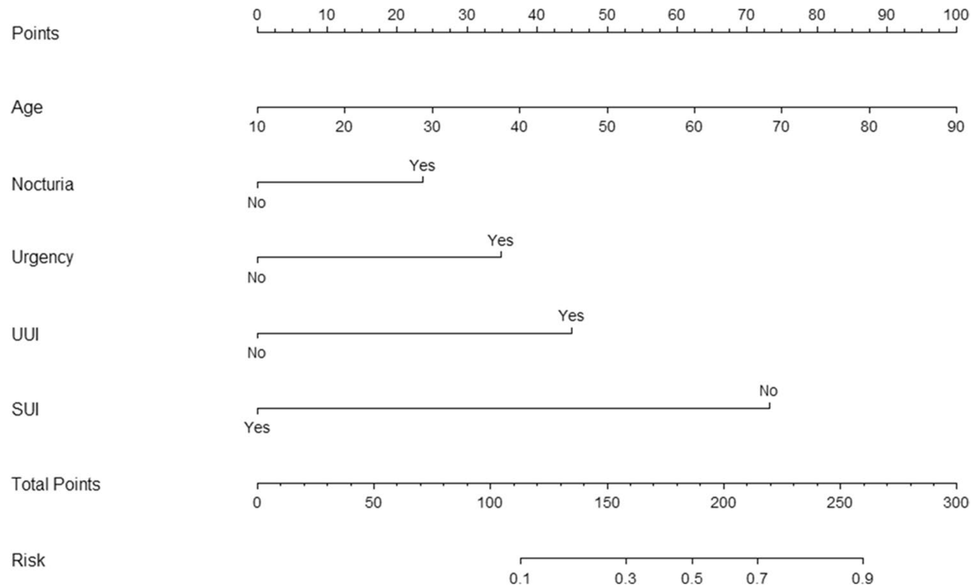

Fig. 1 Nomogram based on the final multivariable logistic regression model to predict the probability of DO in patients with LUTS. *UUI* urgency urinary incontinence, *SUI* stress urinary incontinence, *DO* detrusor overactivity, *LUTS* lower urinary tract symptoms. Note: for each independent risk factor, each value corresponds to a point (Points line), the total points were obtained by adding these five individual points (Total Points line). Similarly, each total point corresponds to a risk of obstruction (Risk line)

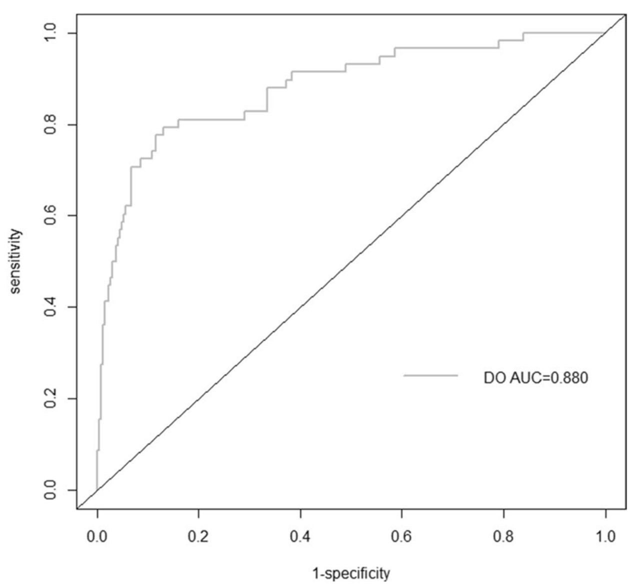

Fig. 2 Receiver operating characteristic curve of the proposed predictive model in assessing detrusor activity (DO): AUC = 0.880 (95% CI: 0.826–0.933). *AUC* area under the curve, *CI* confidence interval

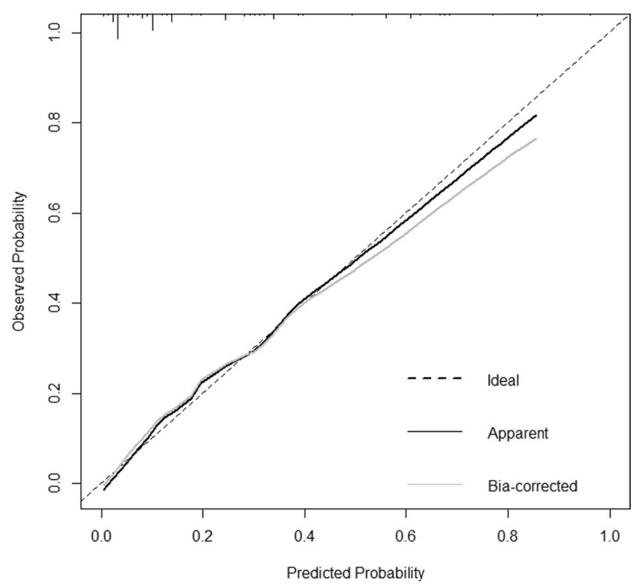

Fig. 3 Calibration curves of the detrusor activity (DO) predictive model. Notes: The x-axis represents the predicted risk of DO. The y-axis represents the actual probability of DO. The diagonal *dotted line* represents a perfect prediction by an ideal model. The *gray solid line* "Bia-corrected" represents the performance of the model of which a close fit to the diagonal *dotted line* represents a good prediction

patients through multiple logistic regression analysis (OR = 1.06) [19]. Another study focused on the incidence of DO with impaired bladder contractile function as well as the urodynamic characteristics of older adults with non-neurogenic LUTS in the community, the study revealed a significant increase in the prevalence rate of DO with impaired contractility with advancing age [21]. Microcellular variations and ischemia may lead to a condition wherein the detrusor muscle exhibits both overactivity and poor contractility, as has been observed in patients with DO with impaired contractile function. Age-related increases in DO may contribute to these histological changes.

Our findings revealed that nocturia emerged as a significant predictive factor for DO. An odds ratio (OR) of 2.03 was observed in patients experiencing nocturia compared with those without nocturia (Table 2). Consistent with prior findings, this result indicates that patients with a higher percentage of nocturia had a greater prevalence of DO than

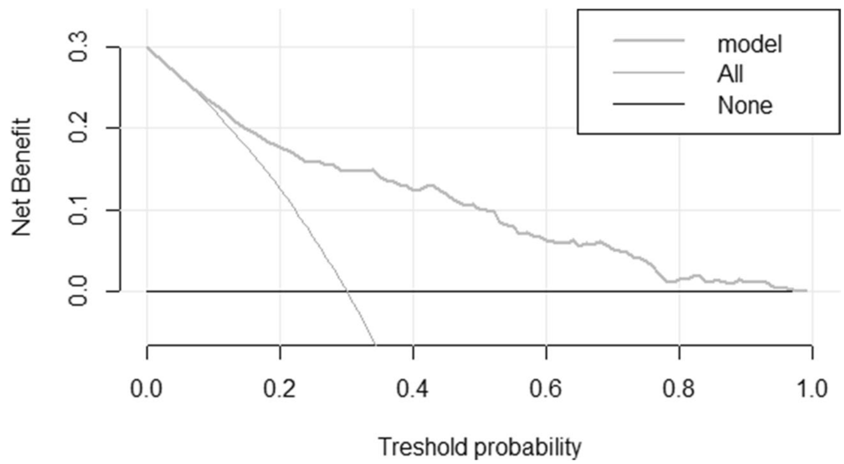

Fig. 4 Decision curve analysis for the predictive model. The y-axis measures the net benefit. The *thick gray line* represents patients treated using the model. The *thin gray line* represents all patients treated. The *black line* represents the net benefit of treating no patients. The decision curve showed that if the threshold probability is between 8 and 97%, using this predictive model in the current study to assess the risk of detrusor overactivity (DO) adds more benefit than the intervention-in-all-patients scheme or the intervention-in-none scheme

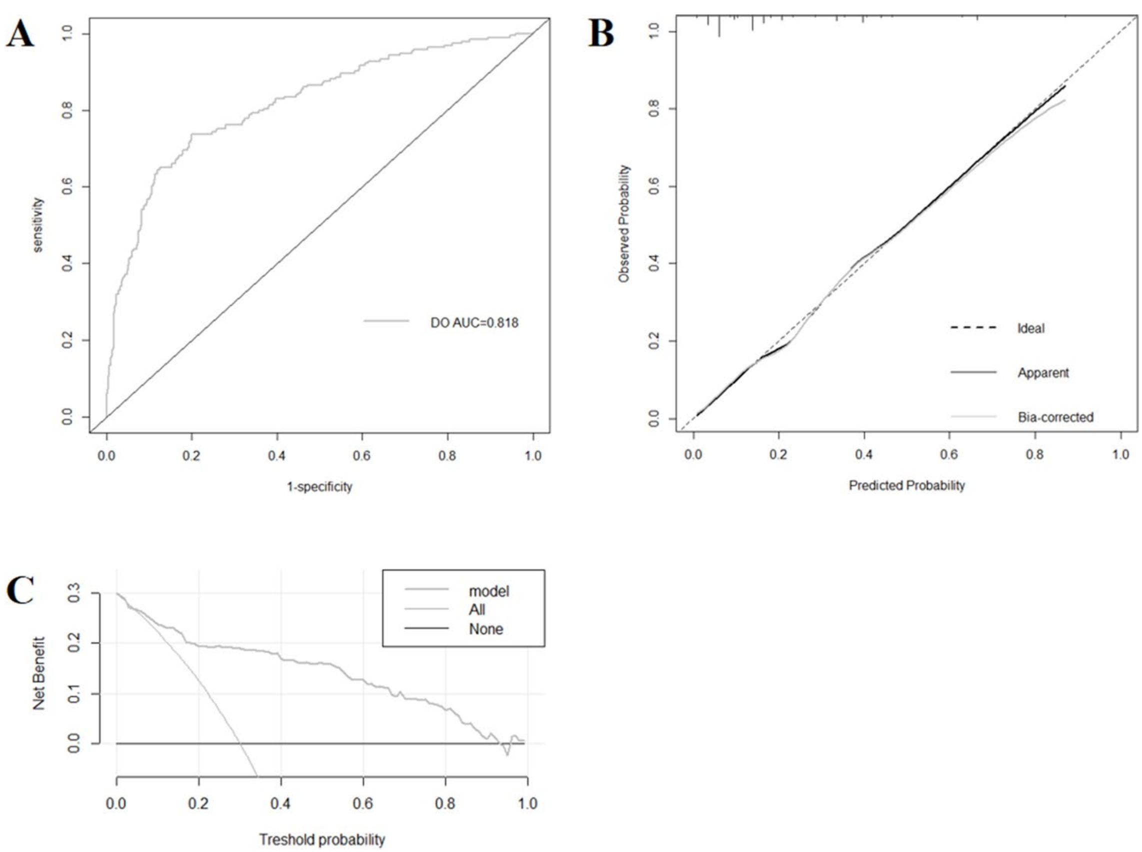

Fig. 5 The predictive ability of this model was validated by plotting the receiver operating characteristic (ROC) curve, calibration curve, and decision curve analysis (DCA) curve of the model validation group. **A** The ROC curve showed good diagnostic ability of the predictive model. **B** Calibration curve indicated an excellent correspondence between the predicted probability and the observed frequency of the predictive model. **C** The DCA curve presented greater clinical usefulness of the model than the treat-all or treat-none strategy within the predicted risk range of 7% and 93%. *DO* detrusor overactivity, *AUC* area under the curve

those without nocturia (50.7% vs 34.1%). Identified as a significant predictor variable for DO in female patients, nocturia stands out [22]. Furthermore, the study by Matharu et al. explored the relationship between LUTS reported on self-completed questionnaires and urodynamic diagnoses [23]. Nocturia was a positive predictor in their multivariate model of DO.

In our study, urgency was identified as another significant symptom distinguishing patients with DO from those without (OR = 2.84, 95% CI: 1.92–4.21). Patients with DO exhibited a significantly higher incidence of urgency, which is consistent with findings from a previous study involving 1,006 women with LUTS (OR = 2.82) [15]. DO is characterized by the involuntary occurrence of detrusor contraction during filling, which is its urodynamic feature, and can occur spontaneously or be provoked. Hashim and Abrams reported a significantly higher percentage of individuals with urgency having DO than of those without urgency (58.2% vs 8.2%). Their findings underscored the significance of urgency as a predictor variable for DO, particularly in female patients [22]. Also, many other studies demonstrated that urgency was a significant positive indicator for the prediction of DO in their own multivariable logistic regression models [20, 23]. The main symptom of overactive bladder (also known as urgency syndrome or urgent-frequency syndrome) is urgency to urinate. This condition is characterized by a sudden and urgent need to urinate that is difficult to delay. The presence of these symptoms strongly suggests the urodynamic demonstration of DO. Virtually all treatments for overactive bladder syndrome operate under the assumption of this causation.

The presence of UUI was proved to be a positive predictor of DO whereas SUI was a negative predictor of DO. This result was consistent with those of other studies. Haylen et al. found a significant association between the presence of UUI and the absence of stress SUI with DO [20]. Matharu et al. stated that UUI was a positive indicator and that SUI was a negative indicator for the presence of DO [23]. Giarenis et al. discovered that UUI was identified as being the most influential positive predictor (OR = 4.10), whereas SUI emerged as the most potent negative predictor (OR = 0.45) for DO [15]. The result was similar to that of our study. In another study involving female patients who underwent ambulatory urodynamics for urinary incontinence, it was reported that UUI showed a positive association with DO. Additionally, an inverse relationship between the occurrence of postural urinary incontinence and involuntary urine loss and patients with DO was found in the same study [24]. This accumulated evidence strongly demonstrated that UUI was a stable positive factor for the prediction of DO and that SUI was a stable negative predictor of DO.

Some prediction models have been created in the literature to forecast DO in women who are suffering from LUTS, aiming to assess the need for urodynamic evaluation. Giarenis et al. evaluated more than 1,000 women with LUTS and introduced a specific scoring system with six variables (KIDOS). The ROC analysis for the overall cut-off points indicated an AUC of 0.748 [15]. Haylen et al. constructed a model by including urgency, UUI, nocturia, lower parity, and absence of SUI, and obtained an AUC of 0.73 [20]. Matharu et al. reported a model with a moderate accuracy of sensitivity of 63.1% and specificity of 65.1% [23]. Arribillaga et al. developed a clinical model that uses an Overactive Bladder (OAB) score, incorporating seven variables, to predict the probability of DO in UDS. The AUC of the OAB score was 0.784 [25]. Seval et al. introduced a prediction model for DO in women with urinary incontinence during ambulatory urodynamics, with the AUC of this model being 0.72 [24]. The results indicated a moderate ability of the previous non-invasive model in predicting DO in female patients with LUTS. In addition, using these predictive models to diagnose DO cannot obtain a specific probability of DO. In our study, we developed a novel predictive model of DO by including age, nocturia, urgency, UUI and SUI. The model achieved an AUC of 0.880 (95% CI: 0.826–0.933), which was the highest when compared to previous models, revealing a good predictive value. In addition, the probability of DO can be obtained quickly and easily through the nomogram (Fig. 1) of the predictive model in daily clinical practice. A specific probability of DO can be calculated by applying the total points formula (Table 3). Therefore, predicting the risk of DO enables us to make suitable treatment decisions for patients experiencing LUTS and we can also assess the possible outcomes with the patients by referring to this easy-to-use predictive nomogram.

Our study has several limitations:.

1. The data were collected from a single center and all were retrospectively analyzed; there is a lack of external validation from other centers.
2. Unavoidable selection and attribution bias were present in our study owing to the inclusion of only those patients who underwent UDS. As a result this patient group may not accurately represent the broader urological patient population or the general population.
3. Owing to the complexity of this group of patients, there could be other variables (additional information regarding participant demographics and medical comorbidities) that are also important but have not been considered.

Despite the limitations, we maintain the significance of the outcomes of our study. We performed an easy-to-use predictive model of DO with the highest AUC compared with previous models by applying clinical symptoms and non-invasive parameters. It would be helpful to diagnose DO without a UDS and by a simple clinical examination.

Conclusions

Our predictive model included five variables, patient age, nocturia, urgency, UUI, and SUI, to assess the risk of DO in female patients with LUTS, which was conducted based on a large database of UDS. It is a quick and easy tool for predicting the probability of DO, making a treatment decision, and assessing the possible outcomes with the patients for urologists in clinical practice.

Authors' Contributions Shengfei Xu and Yu Cheng performed the research and wrote the paper. Xiaoyu Wu, Taicheng Li, and Guanghui Du collected and analyzed the data.

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Data Availability If requested, the corresponding author will provide data or will cooperate fully in obtaining and providing the data on which the manuscript is based for examination by the editors or their assignees.

Declarations

Ethics of Approval Statement This study was performed in accordance with the ethical standards of the Declaration of Helsinki and approved by the Tongji Hospital Research Ethics Committee and the Institutional Review Board.

Patient Consent Statement This study was exempt from patient informed consent.

Permission to Reproduce Material from Other Sources Not applicable.

Conflicts of Interest None.

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