



OPEN Predictors of non-persistence in women with overactive bladder syndrome

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Persistence is important for the success in the treatment of women with overactive bladder syndrome (OAB). We aimed to identify the predictors of non-persistence in women with OAB after first-line medical treatment. All consecutive women with OAB ($n = 608$), who underwent urodynamic studies and received first-line medical treatment (5 mg of solifenacin or 25 mg of mirabegron per day) in a referral medical center, were reviewed. Mirabegron (hazard ratio [HR] = 0.711) was associated with a higher persistence rate, compared to solifenacin. Mirabegron treatment (HR = 0.269) was less likely to switch medication; however, a high Urogenital Distress Inventory score (HR = 1.082) was more likely to switch medication. Furthermore, old age (HR = 1.050, especially for ≥ 75 years) and high voided volume (dL, HR = 1.420, especially for voided volume ≥ 250 ml) were associated with added medication at follow-up. Additionally, women with low parity (HR = 0.653, especially for parity ≤ 3) and a low Incontinence Impact Questionnaire (IIQ-7) score (HR = 0.828, especially for IIQ-7 score ≤ 7) were associated with improvement without medication. In conclusion, mirabegron can be considered as the first frontline treatment to increase the persistence rate and decrease the rate of switched medications, compared to solifenacin. In addition, combination therapy or higher-dose monotherapy could be used as the first front-line treatment for women ≥ 75 years of age or with ≥ 250 ml of voided volume.

Keywords Medication adherence, Mirabegron, Solifenacin succinate, Urinary bladder, Overactive, Urodynamics

Overactive bladder syndrome (OAB) is characterized by urinary urgency, frequency, and nocturia. Both antimuscarinics and beta-3 agonists are considered first-line medical treatments for OAB. Several antimuscarinics (for example, solifenacin and tolterodine) are currently marketed for OAB treatment. Solifenacin has a moderate selectivity for the M3 receptor over the M2 receptor. Beta-3 agonists relax the detrusor muscle during the bladder storage phase and increase bladder capacity. Mirabegron is the first beta-3 agonist approved for OAB treatment. Mirabegron has been reported to have similar efficacy to antimuscarinics¹; however, the beta-3 agonist is associated with less bothersome adverse effects, such as dry mouth². However, the question of whether solifenacin and mirabegron have different persistence rates remains undetermined^{3–6}.

Persistence is generally referred to the overall duration of drug therapy. OAB typically requires long-term persistence with medical therapy⁷. Patients who persist in taking OAB medication have a significant improvement in OAB symptoms compared to non-persistent⁸. Discontinuation of medication or lost follow-up had been used as the definition of non-persistence⁹; switched medications and added medication were excluded as non-persistence¹⁰.

Lack of efficacy, improvement in symptoms, adverse effects, insurance limits, cost concerns, and inconvenience are considered causes of non-persistence^{5,10,11}. Knowledge of non-persistence is important to improve persistence and personal precision treatment.

In addition, urodynamic studies might be helpful in the treatment of complex storage diseases such as OAB¹². A Female Urgency, Trial of Urodynamics as Routine Evaluation (FUTURE) study was conducted to evaluate whether routine urodynamics improves treatment results in women with refractory OAB¹³.

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Due to the positive association between the persistence of OAB medication and therapeutic efficacy⁸, the issue of improving persistence is important. Therefore, this study aimed to analyze clinical and urodynamic predictors of non-persistence.

Results

Between July 2010 and December 2020, a total of 608 women were reviewed in this study. Except age, OAB-wet and pad weight, there were no differences between solifenacin and mirabegron (Table 1).

There was a statistical difference in the persistent curves between the mirabegron and solifenacin groups (log-rank test, $p = 0.008$, Fig. 1A). The multivariable Cox regression model also showed that mirabegron (hazard

Variables	Mirabegron (n = 212)	Solifenacin (n = 396)	P ^a
Age (years)	58.5 ± 14.0	53.4 ± 11.9	<0.001
Parity	2.4 ± 1.3	2.4 ± 1.3	0.306
BMI (kg/m ²)	19.8 ± 1.7	19.7 ± 1.6	0.489
SUI	72 (34)	154 (39)	0.231
OAB-wet	127 (60)	204 (52)	0.048
UDI-6	6.7 ± 3.6	6.2 ± 3.2	0.162
IIQ-7	7.2 ± 5.5	6.7 ± 5.1	0.481
Pad weight (g)	36.8 ± 65.2	17.9 ± 48.5	<0.001
Qmax (mL/s)	23.9 ± 13.0	22.3 ± 12.3	0.220
VV (dL)	2.76 ± 1.44	2.76 ± 1.38	0.769
PVR (dL)	0.97 ± 0.72	1.07 ± 0.86	0.299
SD (dL)	2.69 ± 1.20	2.66 ± 1.03	0.548
PdetQmax (cmH ₂ O)	43 ± 36	38 ± 24	0.385
MUCP (cmH ₂ O)	75 ± 37	80 ± 36	0.072
FPL (mm)	30 ± 11	31 ± 11	0.436
PTR (%)	82 ± 43	87 ± 40	0.352
Non-persistence	66 (31)	161 (41)	0.008 ^b
Switched medications	17 (8)	72 (18)	<0.001 ^b
Added medications	12 (6)	6 (2)	0.026 ^b
Improvement without medication	8 (4)	11 (3)	0.809 ^b

Table 1. Baseline data of women with overactive bladder syndrome (n = 608). Values were presented with mean ± standard deviation or number (percentage). *BMI* body mass index; *FPL* functional profile length; *IIQ-7* Incontinence Impact Questionnaire; *MUCP* maximum urethral closure pressure; *OAB* overactive bladder syndrome; *PdetQmax* detrusor pressure at maximum flow rate; *PTR* pressure transmission ratio at maximum urethral pressure; *PVR* postvoid residual volume; *Qmax* maximum flow rate; *SD* the volume at strong desire to void; *SUI* stress urinary incontinence; *UDI-6* short form of Urinary Distress Inventory; *VV* voided volume. ^aWilcoxon rank sum test, chi-square test or Fisher's exact test. ^bLog-rank test.

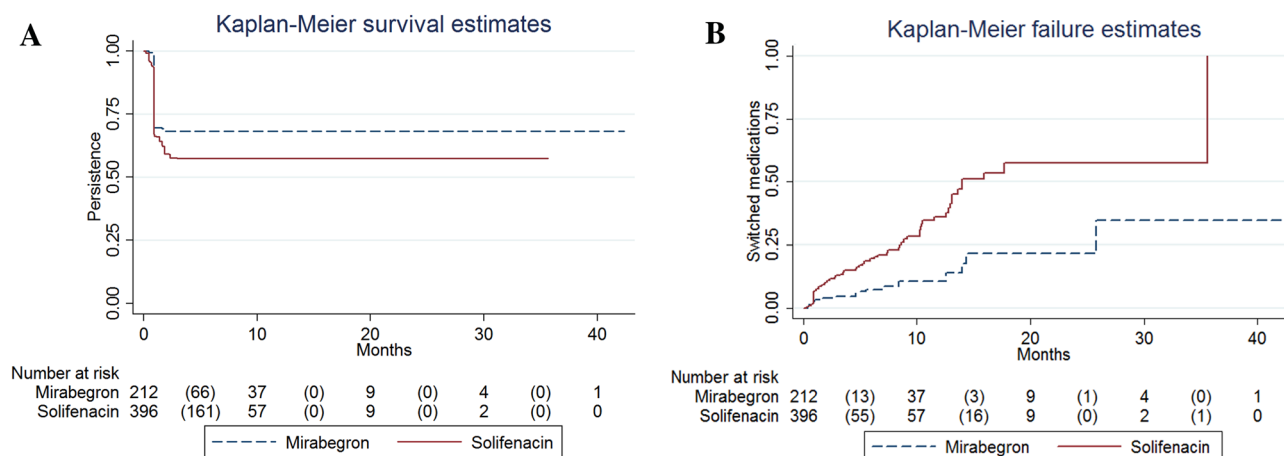


Figure 1. Comparison of (A) persistence and (B) switched medications probabilities between mirabegron and solifenacin.

ratio [HR] = 0.711, $p = 0.019$) was the only predictor of non-persistence (Table 2). OAB-wet was not a predictor of non-persistence (HR = 1.047, $p = 0.729$, Table 2).

Mirabegron (HR = 0.269, $p < 0.001$) was associated with a lower incidence of switched medications (Fig. 1B, Table 3). Furthermore, a higher baseline Urogenital Distress Inventory (UDI-6) score¹⁴ (HR = 1.082, $p = 0.029$) was associated with a higher incidence of switched medications (Table 3). The UDI-6 score ≥ 10 was the optimal

Variables	Univariate			Multivariable		
	HR	95% CI	P^a	HR	95% CI	P^b
Mirabegron	0.711	0.534–0.946	0.019	0.711	0.534–0.946	0.019
Age (years)	0.992	0.983–1.003	0.142	–	–	–
Parity	0.974	0.881–1.077	0.610	–	–	–
BMI (kg/m ²)	0.984	0.901–1.075	0.723	–	–	–
SUI	1.259	0.967–1.639	0.087	–	–	–
OAB-wet	1.047	0.806–1.360	0.729	–	–	–
UDI-6	1.012	0.963–1.063	0.644	–	–	–
IIQ-7	0.999	0.968–1.031	0.959	–	–	–
Pad weight (g)	1.000	0.998–1.002	1.000	–	–	–
Qmax (mL/s)	1.002	0.992–1.012	0.721	–	–	–
VV (dL)	1.000	0.913–1.096	0.998	–	–	–
PVR (dL)	0.974	0.823–1.152	0.756	–	–	–
SD (dL)	0.972	0.859–1.100	0.655	–	–	–
PdetQmax (cmH ₂ O)	1.000	0.995–1.006	0.945	–	–	–
MUCP (cmH ₂ O)	1.001	0.997–1.004	0.742	–	–	–
FPL (mm)	1.000	0.989–1.012	0.971	–	–	–
PTR (%)	1.000	0.997–1.004	0.852	–	–	–

Table 2. Univariate and multivariable Cox proportional hazards model to predict non-persistence in women with overactive bladder syndrome ($n = 608$). HR hazard ratio; CI confidence interval. The other abbreviations are the same as in Table 1. ^aUnivariate Cox proportional hazards model. ^bMultivariable backward stepwise Cox proportional hazards model was performed using all variables in the univariate analysis with $p < 0.10$ until all remaining variables with $p < 0.10$.

Variables	Univariate			Multivariable		
	HR	95% CI	P^a	HR	95% CI	P^b
Mirabegron	0.334	0.196–0.569	<0.001	0.269	0.152–0.477	<0.001
Age (years)	0.997	0.982–1.013	0.744	–	–	–
Parity	1.041	0.896–1.210	0.597	–	–	–
BMI (kg/m ²)	0.991	0.864–1.135	0.891	–	–	–
SUI	1.468	0.959–2.247	0.077	–	–	–
OAB-wet	1.311	0.850–2.021	0.221	–	–	–
UDI-6	1.061	0.989–1.138	0.097	1.082	1.008–1.162	0.029
IIQ-7	1.021	0.975–1.068	0.378	–	–	–
Pad weight (g)	0.997	0.993–1.002	0.252	–	–	–
Qmax (mL/s)	0.996	0.978–1.014	0.679	–	–	–
VV (dL)	0.976	0.843–1.129	0.743	–	–	–
PVR (dL)	1.031	0.767–1.386	0.838	–	–	–
SD (dL)	0.814	0.660–1.004	0.055	–	–	–
PdetQmax (cmH ₂ O)	1.002	0.996–1.010	0.430	–	–	–
MUCP (cmH ₂ O)	0.997	0.991–1.003	0.343	–	–	–
FPL (cm)	1.004	0.985–1.023	0.700	–	–	–
PTR (%)	0.999	0.994–1.005	0.782	–	–	–

Table 3. Univariate and multivariable Cox proportional hazards model to predict switched medications in women with overactive bladder syndrome ($n = 608$). The abbreviations are the same as in Tables 1 and 2. ^aUnivariate Cox proportional hazards model. ^bMultivariable backward stepwise Cox proportional hazards model was performed using all variables in the univariate analysis with $p < 0.10$ until all remaining variables with $p < 0.10$.

cutoff value for predicting switched medications, with an area under the receiver operating characteristic curve (AUC) of 0.534 (95% confidence interval [CI] = 0.452 to 0.616; sensitivity = 26.6%, specificity = 83.6%).

Old age (HR = 1.050, $p = 0.009$) and larger voided volume (dL, HR = 1.420, $p = 0.001$) were associated with a higher incidence of added medications (Table 4). Age ≥ 75 years was the optimal cut-off value for predicting added medications, with an AUC of 0.727 (95% CI = 0.611 to 0.842; sensitivity = 33.3%, specificity = 92.2%). Voided volume ≥ 2.50 dL (i.e., 250 mL) was the optimal cut-off value for predicting added medications, with an AUC of 0.657 (95% CI = 0.541 to 0.772; sensitivity = 76.5%, specificity = 50.0%).

Mirabegron was not associated with improvement without treatment (Table 5). However, low parity (HR = 0.653, $p = 0.020$) and low baseline Incontinence Impact Questionnaire (IIQ-7) score¹⁴ (HR = 0.828, $p = 0.007$) were associated with improvement without medication (Table 5). Parity ≤ 3 was the optimal cutoff value for predicting improvement without medication, with an AUC of 0.692 (95% CI = 0.587 to 0.797; sensitivity = 43.4%, specificity = 89.5%). The baseline IIQ-7 score ≤ 7 was the optimal cut-off value for predicting improvement without medication, with an AUC of 0.705 (95% CI = 0.602 to 0.808; sensitivity = 47.1%, specificity = 83.3%).

The details of the switched medications and the added medications are shown in Table 6.

Discussion

In this study, women who received mirabegron treatment tended to have a higher incidence of persistence (Fig. 1A, Table 2). Similarly, a study from the national cohort database of Korea found that mirabegron has a longer persistence than antimuscarinics⁴. The PERSPECTIVE (a Prospective Non-interventional Registry Study of Patients Initiating a Course of Drug Therapy for Overactive Bladder) study revealed that the persistence was longer for mirabegron compared with antimuscarinics⁵. Chapple et al. also reported that mirabegron had a higher persistence rate compared to antimuscarinics⁶. Nazir et al. and Yeowell et al. had similar findings on the superiority of mirabegron in persistence^{15,16}. However, Lee et al. reported that there is no difference in persistence between groups⁴. Sussman et al. reported that persistence rates were similar between solifenacin and mirabegron¹⁷.

In our study, mirabegron was associated with a lower incidence of switched medications (Fig. 1B, Table 3). The causes of switched medications could include cost consideration, lack of efficacy, or intolerable adverse effects. In Taiwan, the fee for solifenacin and mirabegron was covered by the National Health Insurance. In addition, the same efficacy between mirabegron and solifenacin has been reported¹. Furthermore, higher adverse effects were observed for antimuscarinic drugs². Thus, the lower adverse effects of mirabegron should contribute to its lower rate of switching medications.

The UDI-6 score (HR = 1.082) is a predictor of switched medications (Table 3). UDI-6 question 2 is the question for urgency incontinence severity. In this study, the UDI-6 score was strongly associated with UDI-6 question 2 (Spearman's rho = 0.62, $p < 0.001$); and this meant that higher severity of urgency incontinence was associated with higher rate of switched medications. Thus, a lower side effect of the medication (for example, mirabegron) or a higher dose (for example, 50 mg mirabegron) could be used as an initial first-line treatment for women with severe urgency incontinence to decrease the rate of switched medications.

Variables	Univariate			Multivariable		
	HR	95% CI	P^a	HR	95% CI	P^b
Mirabegron	2.894	1.083–7.732	0.034	2.592	0.861–7.808	0.090
Age (years)	1.053	1.018–1.090	0.003	1.050	1.012–1.089	0.009
Parity	1.277	0.949–1.718	0.107	–	–	–
BMI (kg/m ²)	1.136	0.864–1.493	0.362	–	–	–
SUI	0.639	0.210–1.948	0.431	–	–	–
OAB-wet	2.032	0.723–5.712	0.179	–	–	–
UDI-6	1.038	0.898–1.199	0.615	–	–	–
IIQ-7	0.913	0.818–1.019	0.104	–	–	–
Pad weight (g)	1.007	1.002–1.012	0.009	–	–	–
Qmax (mL/s)	1.002	0.964–1.042	0.915	–	–	–
VV (dL)	1.396	1.107–1.759	0.005	1.420	1.149–1.755	0.001
PVR (dL)	0.987	0.501–1.941	0.969	–	–	–
SD (dL)	1.350	0.963–1.892	0.082	–	–	–
PdetQmax (cmH ₂ O)	0.984	0.960–1.010	0.219	–	–	–
MUCP (cmH ₂ O)	0.999	0.986–1.011	0.843	–	–	–
FPL (cm)	0.973	0.922–1.026	0.311	–	–	–
PTR (%)	1.004	0.993–1.015	0.508	–	–	–

Table 4. Univariate and multivariable Cox proportional hazards model to predict added medications in women with overactive bladder syndrome (n = 608). The abbreviations are the same as in Tables 1 and 2.

^aUnivariate Cox proportional hazards model. ^bMultivariable backward stepwise Cox proportional hazards model was performed using all variables in the univariate analysis with $p < 0.10$ until all remaining variables with $p < 0.10$.

Variables	Univariate			Multivariable		
	HR	95% CI	P ^a	HR	95% CI	P ^b
Mirabegron	1.119	0.449–2.788	0.810	–	–	–
Age (years)	0.967	0.934–1.002	0.065	–	–	–
Parity	0.591	0.403–0.866	0.007	0.653	0.443–0.933	0.020
BMI (kg/m ²)	0.959	0.719–1.279	0.774	–	–	–
SUI	0.890	0.338–2.345	0.813	–	–	–
OAB-wet	0.771	0.313–1.898	0.571	–	–	–
UDI-6	0.885	0.746–1.050	0.162	–	–	–
IIQ-7	0.829	0.723–0.950	0.007	0.828	0.723–0.949	0.007
Pad weight (g)	0.978	0.947–1.010	0.181	–	–	–
Qmax (mL/s)	1.010	0.976–1.046	0.551	–	–	–
VV(dL)	0.918	0.652–1.292	0.622	–	–	–
PVR (dL)	1.062	0.596–1.891	0.838	–	–	–
SD (dL)	1.304	0.919–1.849	0.137	–	–	–
PdetQmax (cmH ₂ O)	1.002	0.988–1.016	0.763	–	–	–
MUCP (cmH ₂ O)	1.005	0.994–1.016	0.390	–	–	–
FPL (cm)	1.003	0.965–1.043	0.861	–	–	–
PTR (%)	1.004	0.993–1.015	0.457	–	–	–

Table 5. Univariate and multivariable Cox proportional hazards model to predict improvement without medication in women with overactive bladder syndrome (n = 608). The abbreviations are the same as in Tables 1 and 2. ^aUnivariate Cox proportional hazards model. ^bMultivariable backward stepwise Cox proportional hazards model was performed using all variables in the univariate analysis with $p < 0.10$ until all remaining variables with $p < 0.10$.

First frontline medication	Switched medications at follow-up (n = 89)	n	First frontline medication	Added medications at follow-up (n = 18)	n
Mirabegron	Solifenacin	12	Mirabegron	Oxybutynin ER	8
	Imipramine	3		Imipramine	4
	Oxybutynin ER	1			
	Bethanechol	1			
Solifenacin	Mirabegron + oxybutynin ER	7	Solifenacin	Oxybutynin ER	3
	Tolterodine + imipramine	2		Imipramine	2
	Mirabegron	36		Mirabegron	1
	Tolterodine	12			
	Oxybutynin ER	7			
	Bethanechol	4			
	Desmopressin	3			
	Imipramine	1			

Table 6. Switched/added medications in the mirabegron and solifenacin groups.

Age (HR = 1.050, especially for those ≥ 75 years) was a predictor of the added medications (Table 4). Similarly, Soda et al. found that old age was associated with continuous treatment, which included added medication⁹. In this study, old age was associated with a higher score on UDI-6 Question 2 (that is, the urgency incontinence, Spearman's rho = 0.27, $p < 0.001$), and this represents that women of old age had a greater severity of urgency incontinence. Therefore, the medication (5 mg solifenacin or 25 mg mirabegron) might be inadequate in some old women. Higher dose (for example, 50 mg mirabegron) or combination therapy could be used as a first line treatment for old age women.

In our study, high voided volume (HR = 1.420, especially for voided volume ≥ 2.50 dL) was a predictor of added medication (Table 4). High voided volume represents mild severity of OAB^{18,19}. Mild severity of OAB was reported to be associated with a poor response to solifenacin²⁰. That is, high voided volume might be associated with poor therapeutic response; and women with high voided volume might need higher dose medication or combination therapy to improve treatment response.

In this study, low parity (HR = 0.653, especially for parity ≤ 3) was a predictor of improvement without medication (Table 5). Low parity was associated with mild severity of OAB²¹. Similarly, high parity (HR = 1.81) has been reported to be a predictor of the retreat of OAB symptoms²².

In this study, a low IIQ-7 score (HR = 0.828, especially for IIQ-7 score ≤ 7) was a predictor of improvement without medication (Table 5). A low IIQ-7 score means a mild urgency incontinence severity (i.e., IIQ-7 score versus UDI-6 question 2 score (i.e., urgency incontinence score), Spearman's $\rho = 0.31$, $p = 0.001$). Thus, our data represent that women with mild OAB severity have a higher incidence of improvement in symptoms without treatment.

Limitations of this study include retrospective nature and non-randomized. Additionally, the sample size was not equal in both groups. Furthermore, this study covered a period of almost 10 years, and 25 mg of mirabegron was only available since 2016 in our hospital, leading to a significant difference in the median follow-up intervals between solifenacin and mirabegron; and the above might also bias our results. In addition, 50 mg mirabegron was not available in our hospital and our data could not be extrapolated to 50 mg mirabegron. In this study, women with improvement without medication were identified from the medical record. However, the true causes responsible for lost to follow-up include improvement of symptoms or no response to treatment. Therefore, in this study, the percentage of improvement without medication in Table 1 should be underestimated.

In conclusion, mirabegron can be considered as the first frontline treatment to increase the persistence rate and decrease the rate of switched medications, compared to solifenacin. In addition, combination therapy or higher-dose monotherapy could be used as the first front-line treatment for women ≥ 75 years of age or with ≥ 250 ml of voided volume.

Methods

Between July 2010 and December 2020, medical records of all consecutive OAB women who underwent pre-treatment urodynamic studies and then received first-line medication (5 mg of solifenacin or 25 mg of mirabegron per day) were reviewed. Women with coexistent stress urinary incontinence were also included. However, women who underwent a midurethral sling procedure or vaginal laser therapy for coexisting stress urinary incontinence were excluded. The hospital's Research Ethics Review Committee approved this study (Far Eastern Memorial Hospital, No.110053E, approval date: April 27, 2021). All methods were performed in accordance with relevant guidelines and regulations. The Research Ethics Review Committee agreed that informed consent was not required due to the retrospective nature of this study.

Urodynamic studies were performed on women in a seated position using a Life-Tech six-channel monitor with computer analysis and the Urolab/Urovision System V (Houston, Texas, USA). Urodynamic studies included uroflowmetry, filling cystometry with 35° C distilled water at a rate of 60 ml/s, a pressure flow study, and a stress urethral pressure profile with a strong desire volume of distilled water in the bladder. In addition, a 1 h pad test was performed²³.

All terminology used in this document is consistent with the standards recommended by the joint report of the International Urogynecological Association and the International Continence Society²⁴. All procedures were performed by an experienced technician and the data was interpreted by a single observer to avoid interobserver variability. OAB was defined as the presence of urinary urgency, with or without urgency incontinence, which is generally accompanied by urinary frequency and nocturia²⁴. OAB-wet was diagnosed in women who complained of at least one episode of urgency incontinence in the previous month; otherwise, OAB-dry was diagnosed¹⁹.

Non-persistence after first-line medication was defined as the presence of lost follow-up. The switch of medication was defined as the discontinuation of the first-line OAB medication and the switch to other medications. Improvement without medication was referred to spontaneous improvement of OAB symptoms after first-line medical treatment, and the patients did not need additional OAB medication. The persistence interval was calculated as the time interval from the date of the start of the prescribed medication to the date of loss of follow-up, improvement without medication, or the last follow-up for continuous prescription.

Stata version 11.0 (Stata Corp, College Station, TX) was used for statistical analyzes. Survival curves were generated using the Kaplan–Meier method and differences in survival curves were calculated with the log-rank test. A p -value less than 0.05 was considered statistically significant. The multivariable backward stepwise Cox proportional hazards model was used to identify independent predictors using all variables in the univariate analysis with $p < 0.10$ until all remaining variable with $p < 0.10$. A receiver operating characteristic (ROC) curve analysis was performed to identify the optimal cut-off value. The optimal cut-off value was determined by the point on the ROC curve that was closest to the upper left corner.

Ethical approval

This study was approved by the Research Ethics Committee (Far Eastern Memorial Hospital Research Ethics Review Committee, No.110053E, approval date: 27 April 2021) at Far Eastern Memorial Hospital.

Informed consent

The Research Ethics Review Committee of Far Eastern Memorial Hospital approved the informed consent waiver.

Data availability

The datasets generated and / or analysed during the current study are available from the corresponding author on reasonable request.

Received: 22 December 2023; Accepted: 25 March 2024

Published online: 29 March 2024

References

- Chapple, C. R. *et al.* Safety and efficacy of mirabegron: Analysis of a large integrated clinical trial database of patients with overactive bladder receiving mirabegron, antimuscarinics, or placebo. *Eur. Urol.* **77**, 119–128 (2020).
- Wagg, A. *et al.* Oral pharmacotherapy for overactive bladder in older patients: Mirabegron as a potential alternative to antimuscarinics. *Curr. Med. Res. Opin.* **32**, 621–638 (2016).
- Kinjo, M., Sekiguchi, Y., Yoshimura, Y. & Nutahara, K. Long-term persistence with mirabegron versus solifenacin in women with overactive bladder: Prospective, randomized trial. *Low. Urin. Tract. Symptoms* **10**, 148–152 (2018).
- Lee, K. S. *et al.* Mirabegron has longer treatment persistence than antimuscarinics: Real-world data from a Korean national cohort database. *Neurourol. Urodyn.* **40**, 1972–1980 (2021).
- Carlson, K. V. *et al.* Persistence with mirabegron or antimuscarinic treatment for overactive bladder syndrome: Findings from the PERSPECTIVE registry study. *Low. Urin. Tract. Symptoms* **13**, 425–434 (2021).
- Chapple, C. R. *et al.* Persistence and adherence with mirabegron versus antimuscarinic agents in patients with overactive bladder: A retrospective observational study in UK clinical practice. *Eur. Urol.* **72**, 389–399 (2017).
- Schabert, V. F. *et al.* Challenges for managing overactive bladder and guidance for patient support. *Am. J. Manag. Care.* **4**(Suppl), S118–122 (2009).
- Kim, T. H., Choo, M. S., Kim, Y. J., Koh, H. & Lee, K. S. Drug persistence and compliance affect patient-reported outcomes in overactive bladder syndrome. *Qual. Life. Res.* **25**, 2021–2029 (2016).
- Soda, T., Tashiro, Y., Koike, S., Ikeuchi, R. & Okada, T. Overactive bladder medication: Persistence, drug switching, and reinitiation. *Neurourol. Urodyn.* **39**, 2527–2534 (2020).
- Sexton, C. C. *et al.* Persistence and adherence in the treatment of overactive bladder syndrome with anticholinergic therapy: A systematic review of the literature. *Int. J. Clin. Pract.* **65**, 567–585 (2011).
- Illiano, E., Finazzi Agrò, E., Natale, F., Balsamo, R. & Costantini, E. Italian real-life clinical setting: The persistence and adherence with mirabegron in women with overactive bladder. *Int. Urol. Nephrol.* **52**, 1035–1042 (2020).
- Kim, S. J., Choo, H. J. & Yoon, H. Diagnostic value of the maximum urethral closing pressure in women with overactive bladder symptoms and functional bladder outlet obstruction. *Int. Neurourol. J.* **26**(Suppl 1), S1–7 (2022).
- Abdel-Fattah, M. *et al.* Female Urgency, Trial of Urodynamics as Routine Evaluation (FUTURE study): A superiority randomised clinical trial to evaluate the effectiveness and cost-effectiveness of invasive urodynamic investigations in management of women with refractory overactive bladder symptoms. *Trials.* **22**, 745 (2021).
- Uebersax, J. S., Wyman, J. F., Shumaker, S. A., McClish, D. K. & Fantl, J. A Short forms to assess life quality and symptom distress for urinary incontinence in women: The Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Continence Program for Women Research Group. *Neurourol. Urodyn.* **14**, 131–139 (1995).
- Nazir, J. *et al.* A retrospective study of treatment persistence and adherence to mirabegron versus antimuscarinics for the treatment of overactive bladder in Spain. *BMC. Urol.* **18**, 76 (2018).
- Yeowell, G. *et al.* Real-world persistence and adherence to oral antimuscarinics and mirabegron in patients with overactive bladder (OAB): A systematic literature review. *BMJ. Open.* **8**, e021889 (2018).
- Sussman, D. *et al.* Adherence and persistence of mirabegron and anticholinergic therapies in patients with overactive bladder: A real-world claims data analysis. *Int. J. Clin. Pract.* **71**, e12824 (2017).
- Hsiao, S. M., Chang, T. C., Chen, C. H., Wu, W. Y. & Lin, H. H. Frequent nocturia episodes, a suboptimal response to treatment, and small bladder capacity predict the need for persistent antimuscarinic therapy or retreatment after discontinuation of antimuscarinics in female overactive bladder. *Menopause* **24**, 100–104 (2017).
- Hsiao, S. M., Wu, P. C., Chang, T. C., Chen, C. H. & Lin, H. H. Urodynamic and bladder diary factors predict overactive bladder-wet in women: A comparison with overactive bladder-dry. *Int. Neurourol. J.* **23**, 69–74 (2019).
- Hsiao, S. M., Lin, H. H. & Kuo, H. C. Factors associated with a better therapeutic effect of solifenacin in patients with overactive bladder syndrome. *Neurourol. Urodyn.* **33**, 331–334 (2014).
- Palma, T. *et al.* Prospective study of prevalence of overactive bladder symptoms and child-bearing in women of reproductive age. *J. Obstet. Gynaecol. Res.* **39**, 1324–1329 (2013).
- Hsiao, S. M., Chang, T. C. & Lin, H. H. The probability of retreatment after discontinuation of a 3-month versus a 6-month course of solifenacin for female overactive bladder: A prospective randomized controlled study. *Maturitas* **126**, 11–17 (2019).
- Wu, W. Y., Sheu, B. C. & Lin, H. H. Comparison of 20-minute pad test versus 1-hour pad test in women with stress urinary incontinence. *Urology* **68**, 764–768 (2006).
- Haylen, B. T. *et al.* An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Int. Urogynecol. J.* **21**, 5–26 (2010).

Author contributions

S.-M.H. contributed to study design, data collection, statistical analysis, and manuscript writing.

Funding

This work was supported by Astellas Pharma, Inc. under a general research grant.

Competing interests

S-M H has received research support from Astella Pharma Ltd.

Additional information

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