



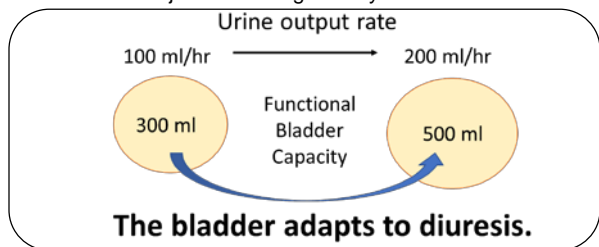
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Introduction

The vesical adaptation response to diuresis (VARD)

When urine output rate increases, voided volume at each voiding also increases in normal subjects. This is generally understood as the VARD.



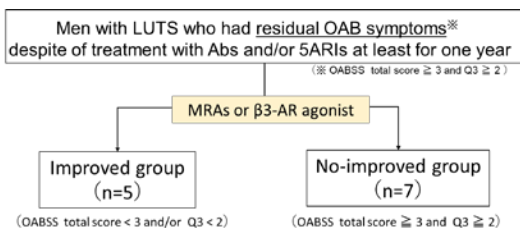
Aim of Study

Recently, attention has focused on VARD. It has been indicated that the VARD is lacking in overactive bladder (OAB). On the other hand, male lower urinary tract symptoms (male LUTS) secondary to bladder outlet obstruction (BOO) are common and interfere with the quality of life (QOL) of elderly men. Current oral therapies for male LUTS recommended by guidelines include α -adrenoceptor antagonists (α -blockers, Abs) and 5 α -reductase inhibitors (5ARIs). Some studies reported that AB and/or 5ARI monotherapy did not improve OAB symptoms of male LUTS patients sufficiently. It was suggested that muscarinic receptor antagonists (MRAs) or β 3-adrenoceptor (β 3-AR) agonist add-on therapy to the drug was effective for some patients with residual OAB symptoms. However, useful predictors of add-on therapy improving OAB symptoms in male LUTS patients remain unclear. **The aim of this study was to determine whether the VARD can be used to predict the efficacy of add-on therapy for OAB symptoms in men treated for LUTS.**

Patients and methods

Study design

Men with LUTS who had residual OAB symptoms despite treatment with ABs or 5ARIs for one year and received add-on therapy (MRAs or β 3-AR agonist) were included in this study. OAB was evaluated using the Overactive Bladder Symptom Score (OABSS). Residual OAB was defined as an OABSS total score greater than 3 and an urgency score greater than 2 before add-on therapy. Uroflowmetry, ultrasonography to measure the prostate volume, and 24-h frequency-volume charts (FVCs) were evaluated before and after add-on therapy.



Method of determining VARD

The 24-h frequency-volume chart (FVC) recorded the degree of urgency, as well as the volumes voided and the time of each micturition. The urine output rate was calculated by dividing the volume voided by the interval between 2 successive micturitions. Since the functional bladder capacity at night was demonstrated to be different from the daytime capacity, we use daily urination only.

24h Frequency-volume chart (sample)
Date: / / Name (Taro Fukushima)

Time	Degree of urgency	U	L	Voiding volume (ml)
7:00	1	2	3	400 ml
7:10	1	2	3	80 ml
12:00	1	2	3	300 ml
14:00	1	2	3	200 ml
18:30	1	2	3	300 ml
19:30	1	2	3	ml
21:00	1	2	3	100 ml
23:00	1	2	3	100 ml
1:30	1	2	3	150 ml
00:00	1	2	3	ml
Total				1630 ml

Bed time: am - pm 23:00
Wake up time the next morning: am - pm 7:00

Dairy Urination Only

0-U-L of Urgency were excluded.

[Urine output rate]

200 ml / 2 hr
→ 100 ml/hr

Statistical analysis

The association between the urine output rate and voided volume at each voiding was analyzed in each group. P-values <0.05 were considered significant.

Results

Result 1. Patient background

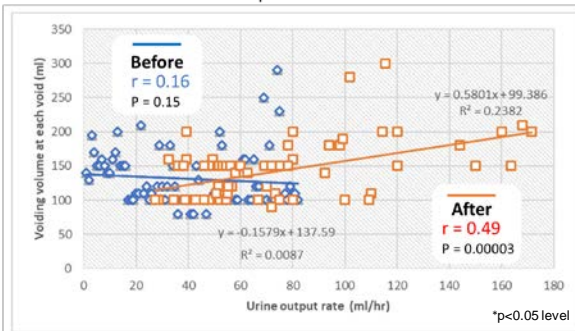
Before and After add-on therapy, age, prostate volume, PSA, voiding volume each void, maximum urinary flow rate, and residual urine volume were not significantly different between the two groups.

OAB improved group	Before	After
Age (years)	76.3 ± 1.9	77.5 ± 1.8
Prostate Volume (ml)	42.1 ± 4.3	46.1 ± 3.9
PSA (ng/ml)	3.4 ± 1.7	2.7 ± 1.7
Voiding Volume each void (ml)	131.0 ± 6.3	133.0 ± 6.3
Maximum flow rate (ml/s)	7.1 ± 1.6	7.1 ± 1.5
Residual urinary volume (ml)	31 ± 4.2	35.4 ± 4.7
OAB Non-improved group	Before	After
Age (years)	77.8 ± 1.7	79.3 ± 2.1
Prostate Volume (ml)	33.4 ± 4.2	33.6 ± 3.2
PSA (ng/ml)	2.7 ± 1.2	1.8 ± 0.7
Voiding Volume each void (ml)	133.3 ± 6.2	127.9 ± 5.9
Maximum flow rate (ml/s)	7.2 ± 2.1	10.5 ± 2.1
Residual urinary volume (ml)	24.8 ± 3.6	38.5 ± 4.9

Values are mean ± SEM

Result 2. OAB improved group

Correlation between diuretic adaptation before and after the add-on therapy

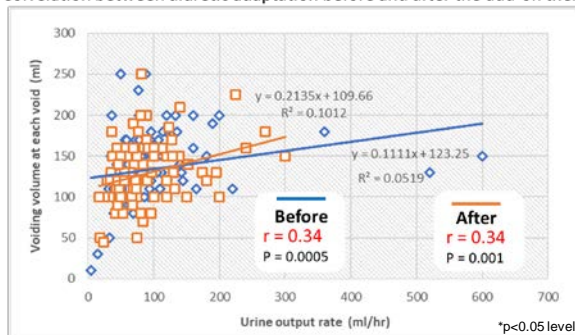


Before add-on therapy, there was **no significant correlation** between the urine output rate and voided volume at each voiding.

After add-on therapy, there was **a significant association** between the urine output rate and voided volume.

Result 3. OAB Non-improved group

Correlation between diuretic adaptation before and after the add-on therapy



Before add-on therapy, the urine output rate was associated with each voided volume.

After add-on therapy, the urine output rate and each voided volume remained correlated.

Interpretation of Result

These results suggest that the add-on therapy ameliorates residual OAB symptoms of male LUTS patients by improving the VARD.

Conclusions

The lack of VARD may contribute to maintaining OAB symptoms of male LUTS patients despite treatment with ABs or 5ARIs. The VARD may be a useful predictor of the efficacy of add-on therapy for OAB symptoms in men treated for LUTS.

Limitation

This study is a retrospective and small group study, thus it requires a prospective approach to more patients.

References

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- Haga N et al. The effect of the vesical adaptation response to diuresis on lower urinary tract symptoms after robot-assisted laparoscopic radical prostatectomy, PLOS ONE. 2016;11(7):e0159514