Who are suitable for low-dose tamsulosin monotherapy as initial treatment strategy in male patients with lower urinary tract symptoms?

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Abstract

This study aims to investigate the real indications for low-dose tamsulosin monotherapy for initial treatment.

A cross-sectional study was conducted in a total of 1643 patients with lower urinary tract symptoms (LUTS) and with initial low-dose tamsulosin. Initial pretreatment data including the International Prostate Symptoms Score (IPSS), prostate volume, and uroflowmetry data were reviewed. After 8 weeks of treatment, post-treatment IPSS and satisfaction was assessed. Logistic regression analysis was conducted to investigate the pretreatment factors influencing post-treatment satisfaction.

Overall satisfaction rate with low-dose tamsulosin as an initial treatment medication was 88.7%. Multivariate analysis revealed that symptom durations, IPSS voiding score, IPSS storage score, and quality of life (QoL) were determinant factors for patient satisfaction. ROC analysis revealed that a urinary score > 10 and symptom duration > 3 years showed satisfaction with a sensitivity of 85.8% and 90.6%, respectively, and specificity of 43.5% and 39.8%, respectively. Whereas, ROC analysis revealed that a storage score > 5 and QoL > 3 showed nonsatisfaction with sensitivity of 84.2% and 39.5%, respectively, and specificity of 43.5% and 45.7%, respectively. Multivariate regression analysis demonstrated that voiding score and storage score had a significant relationship with QoL (unstandardized coefficients: 0.073, 0.145, respectively; P-value: < .001, < .001, respectively).

The patient with higher storage scores and higher QoL before treatment could have a higher change of non-satisfaction. Combining treatment with anticholinergics could be considered in these patients.

Abbreviations: AUA = American Urological Association, BMI = body mass index, BPH = benign prostatic hyperplasia, IPSS = International Prostate Symptom Score, LUTS = lower urinary tract symptoms, QoL = quality of life, ROC = receiver operating characteristic, TRUS = transrectal ultrasonography.

Keywords: alpha-blocker, lower urinary tract symptoms, prostatic hyperplasia, tamsulosin

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1. Introduction

Benign prostatic hyperplasia (BPH) with lower urinary tract symptoms (LUTS) is common among older men. Medical treatment is the first recommended option for patients with BPH/LUTS [1]. The first-line therapy is typically alpha blockers, which improve LUTS by relaxing the prostatic urethra and bladder neck through alpha-adrenergic blockade [2].

As a result of its prostate selectivity, tamsulosin may improve LUTS with fewer side effects. Many studies have shown that tamsulosin is effective and tolerable at doses of 0.2 to 0.8 mg once daily in patients with symptomatic BPH.[3–7] In Asian populations, low-dose tamsulosin has been widely used [3,5,7] due to their low body mass index.

Patient perceptions and preferences are of increasing importance when making treatment decisions for BPH.[8–10] Treatment satisfaction has significant implications on patient compliance [8]. The initial treatment strategy is extremely important as the degree of improvement is limited after 2 or 3 months of initial treatment [11].

Although tamsulosin is one of the favored alpha blockers due to good efficacy fewer side effects, it also has some adverse events including retrograde ejaculation and anejaculation. If low-dose tamsulosin is suitable as an initial treatment strategy for male patients with LUTS, it has great merit, as the side effects of retrograde ejaculation or anejaculation are dependent on dosage [12].

Our previous study showed an initial successful experience of low-dose tamsulosin as an early treatment strategy. Although, more than two-thirds of the patients showed a satisfactory response with initial low-dose tamsulosin, some patients still had

a nonsatisfactory response. The suspected reasons for this nonsatisfactory response are due to the lack of limited response to voiding or storage score. The aim of this study is to find reasonable indications for initial low-dose tamsulosin treatment.

2. Methods

2.1. Study population and data collection

This study was a multicenter, cross-sectional survey from September 2010 to September 2011, which included 1643 patients with symptomatic BPH and treated with 0.2 mg of tamsulosin monotherapy from the outpatient clinics of 20 medical centers. Informed consent was obtained from each subject, and the study was approved by the Institutional Review Board at each center.

No patients had any life-threatening conditions, such as acute cardiovascular disease, neurologic disease, uncontrolled hypertension, or diabetes mellitus. The decision to enter the patient into the study was made after the following inclusion criteria were met: patient age ≥ 50 years, good overall mental and physical health, and complaint of LUTS.

Exclusion criteria included: patient age < 50 years, patients judged to be inappropriate for clinical survey, and patients with neurogenic bladder, urethral stricture, pelvic surgery, prostate surgery, or history of prostate or bladder cancer. Baseline data, including IPSS, transrectal ultrasonography (TRUS), and uroflowmetry were reviewed in detail and all patients completed a questionnaire, including IPSS and treatment satisfaction. A summary of patients deposition is provided in Figure 1.

2.2. Methodology

This was a cross-sectional study in which experienced investigators conducted face-to-face interviews of all study participants using a structured questionnaire.

2.3. IPSS questionnaire

The severity of LUTS was measured using the IPSS. The IPSS is based on the American Urological Association (AUA) symptom index with one additional question on quality of life (QOL), and is the most widely used measure to objectively assess LUTS. The Korean version of the IPSS has also been verified in terms of relevance and reliability, and is the most common diagnostic instrument for LUTS.

2.4. Treatment satisfaction

The treatment satisfaction questionnaire included 5 subscales: "very satisfied," "satisfied," "so so," "not satisfied," and "totally not satisfied." These 5 subscales were divided into 2 groups: "Satisfactory" which included "much satisfied," and "satisfied," and "Not Satisfactory" which included "so so," "not satisfied" and "totally not satisfied."

3. Data analyses

Data were analyzed using SAS version 9.1 (SAS Institute, Cary, NC). The Kolmogorov–Smirnov test was used to verify the normality of distributions of continuous variables. To analyze patient characteristics and satisfaction degree, a goodness-of-fit test was conducted. To analyze the factors affecting treatment

satisfaction, univariate and multivariate logistic regression were used. All statistics were two-tailed and P-values < .05 were considered significant.

4. Results

4.1. Patients characteristics

The overall satisfactory rate with low-dose tamsulosin as an initial treatment medication was 88.7% (1458 patients). In the comparative analysis of the satisfactory and not satisfactory patients, age, symptom duration, IPSS Q1, IPSS voiding score, and voiding subscore showed higher values in satisfactory patients. However, IPSS storage score and IPSS QoL were lower in satisfactory patients (Table 1). In an analysis of the frequency of adverse events, a total of 37 patients complained of retroejaculation or anejaculation after low dose tamsulosin therapy, but no patients discontinued medication due to side effects.

4.1.1. Univariate analysis between pretreatment variables and satisfaction. Age, symptom duration, total IPSS, IPSS voiding score, and voiding subscore showed a positive relationship with satisfaction (Table 2) (estimates: −0.0197, −0.3049, −0.0235, −0.070, −0.4318, respectively; P-value: .002, < .001, .027, < .001, < .001, respectively).

IPSS storage score and QoL showed negative relationships with satisfaction (Table 2) (estimates: 0.0742, 0.1705, respectively; P-value: .0005, .011, respectively).

4.2. Multivariate analysis between pretreatment variables and satisfaction

Multivariate analysis was conducted using both a full model and a stepwise model. Symptom duration, total IPSS, and IPSS voiding score showed a positive relationship with satisfaction (Table 3) (estimates: −0.1194, −0.4829, −0.3355, respectively; P-value: .0476, < .0001, 0.0003, respectively). IPSS storage score and QoL showed a negative relationship with satisfaction (Table 3) (estimate: 0.5703, 0.2401, respectively; P-value: < .001, .0444, respectively).

The stepwise model showed similar results, with the exception of total IPSS. Only symptom duration and IPSS voiding score demonstrated a positive relationship with satisfaction, and IPSS storage score and QoL showed a negative relationship with satisfaction (Table 4).

4.3. ROC analysis

ROC analysis revealed that a urinary score of more than 10 and symptom duration more than 3 years showed satisfaction with a sensitivity of 85.8% and 90.6%, respectively, and a specificity of 43.5% and 39.8%, respectively (Fig. 2). Whereas, the ROC analysis revealed that a storage score of > 5 and a QoL > 3 showed nonsatisfaction with a sensitivity of 84.2% and 39.5%, respectively, and specificity of 43.5% and 45.7%, respectively (Fig. 3).

4.4. Degree of improvement according to IPSS

Correlation analysis after age adjustment showed a positive correlation between IPSS and the degree of improvement (coefficient: 0.549; P-value: < .001) (Fig. 3).
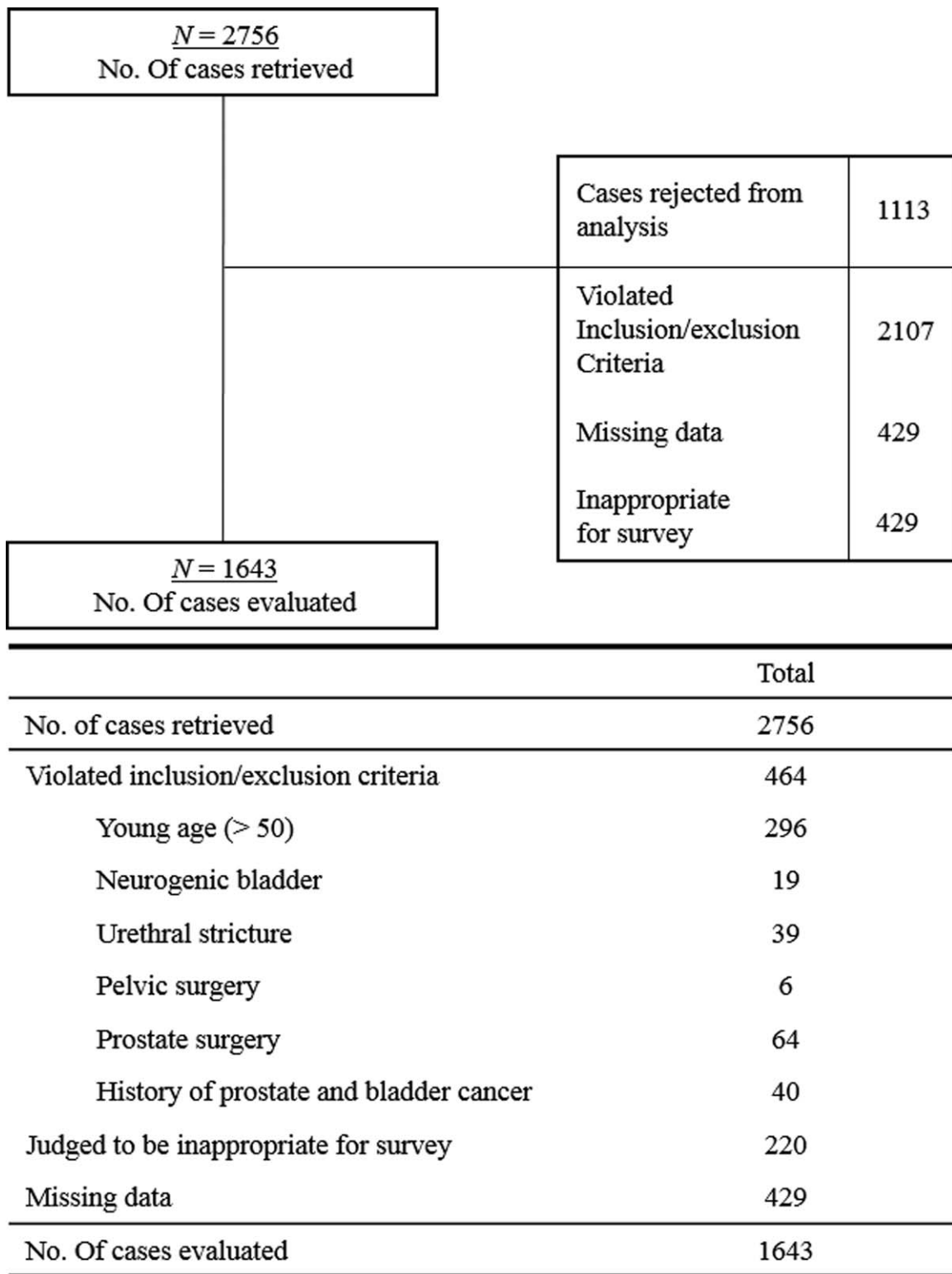
Cases rejected from analysis		1113
Violated Inclusion/exclusion Criteria		2107
Missing data		429
Inappropriate for survey		429

N = 2756
No. Of cases retrieved

N = 1643
No. Of cases evaluated

	Total
No. of cases retrieved	2756
Violated inclusion/exclusion criteria	464
Young age (> 50)	296
Neurogenic bladder	19
Urethral stricture	39
Pelvic surgery	6
Prostate surgery	64
History of prostate and bladder cancer	40
Judged to be inappropriate for survey	220
Missing data	429
No. Of cases evaluated	1643

Figure 1. Patients deposition.

5. Discussion

Traditionally, physicians prefer a biological and objective improvement after treating a disease, and this has been also true in the treatment of BPH/LUTS. Physicians have placed too much emphasis on IPSS, prostate volume, and urodynamic parameters. However, recently, patient satisfaction has come into focus to increase overall treatment satisfaction. Subjective outcome measures such as BPH impact index or KHQ are now widely used to assess treatment outcomes for LUTS and BPH. However, the relationship between the degree of change in

Table 1

Patient demographics.

Pretreatment variables	Satisfied (n=1458)	Nonsatisfied (n=183)	P-value
Age	66.51±10.68	64.17±10.36	.001
Symptom duration, years	3.82±3.76	2.06±1.90	<.001
Total IPSS	17.48±7.60	16.24±4.84	.902
IPSS Q1	1.66±1.45	1.84±1.11	.001
IPSS Q2	1.78±1.34	1.77±1.00	.376
IPSS Q3	1.65±1.47	1.50±1.08	.628
IPSS Q4	1.46±1.39	1.31±1.03	.767
IPSS Q5	2.21±1.55	1.86±1.14	.008
IPSS Q6	1.49±1.44	1.29±1.03	.559
IPSS Q7	1.78±1.15	1.71±0.96	.890
IPSS QoL	3.61±1.18	3.84±0.95	.001
IPSS Voiding Score	10.18±5.18	8.46±3.58	<.001
IPSS Storage Score	6.91±3.66	7.89±2.77	<.001
Voiding subscore	1.90±1.80	1.30±1.23	<.001
Prostate size	35.59±16.40	33.23±12.06	.215
Pre treatment maximal urinary flow rate, mL/min	14.48±6.54	14.08±5.96	.453
Post treatment maximal urinary flow rate	14.83±6.91	14.37±8.13	.623
Voiding volume , mL	238.40±107.28	239.60±99.43	.479
Residual volume, mL	35.41±35.21	40.23±40.33	.318

IPSS=International Prostate Symptom Score, QoL=quality of life.
P-value was analyzed with t-test.

Table 2

Univariate logistic regression analysis for satisfaction with initial low-dose treatment.

Pretreatment variables	Estimate	SE	OR 95% CI	P-value
Age	−0.0197	0.006	0.98 (0.968–0.993)	.002
Symptom duration	−0.3049	0.053	0.73 (0.663–0.819)	<.001
Total IPSS	−0.0235	0.010	0.97 (0.957–0.997)	.027
IPSS voiding Score	−0.070	0.016	0.93 (0.902–0.962)	<.001
IPSS storage Score	0.0742	0.021	1.07 (1.033–1.123)	.0005
Voiding subscore	−0.4318	0.092	0.64 (0.541–0.779)	<.001
QoL	0.1705	0.067	1.18 (1.040–1.353)	.011

IPSS=International Prostate Symptom Score, QoL=quality of life, SE=standard error.

Table 3

Multivariate logistic regression analysis for satisfaction with initial low dose treatment by full model.

| Pretreatment variables	Estimate	SE	Wald Chi-Sqaure	P-value
Symptom duration	−0.1194	0.0603	3.9238	.0476
Total IPSS	−0.4829	0.0928	27.0802	<.0001
IPSS voiding Score	−0.3355	0.0926	13.1326	.0003
IPSS storage Score	0.5703	0.11	26.8675	<.0001
QoL	0.2401	0.1194	4.0423	.0444

IPSS=International Prostate Symptom Score, QoL=quality of life, SE=standard error.

Table 4

Multivariate logistic regression analysis for satisfaction with initial low-dose treatment by stepwise method.

Pretreatment variables	Estimate	SE	Wald Chi-Square	P-value
Symptom duration	−0.1217	0.0579	4.4123	.0357
IPSS voiding Score	-0.1103	0.0252	19.2173	<.0001
IPSS storage Score	0.3703	0.0982	21.3571	<.0001
QoL	0.2857	0.1062	7.2348	.0072

IPSS=International Prostate Symptom Score, QoL=quality of life, SE=standard error.
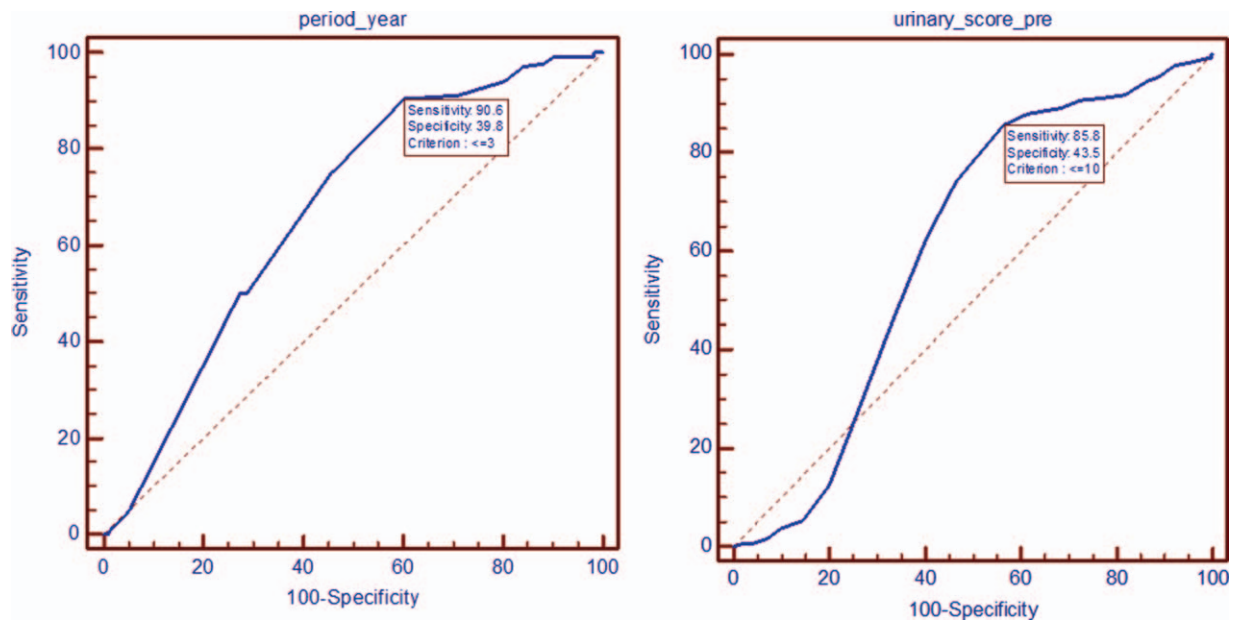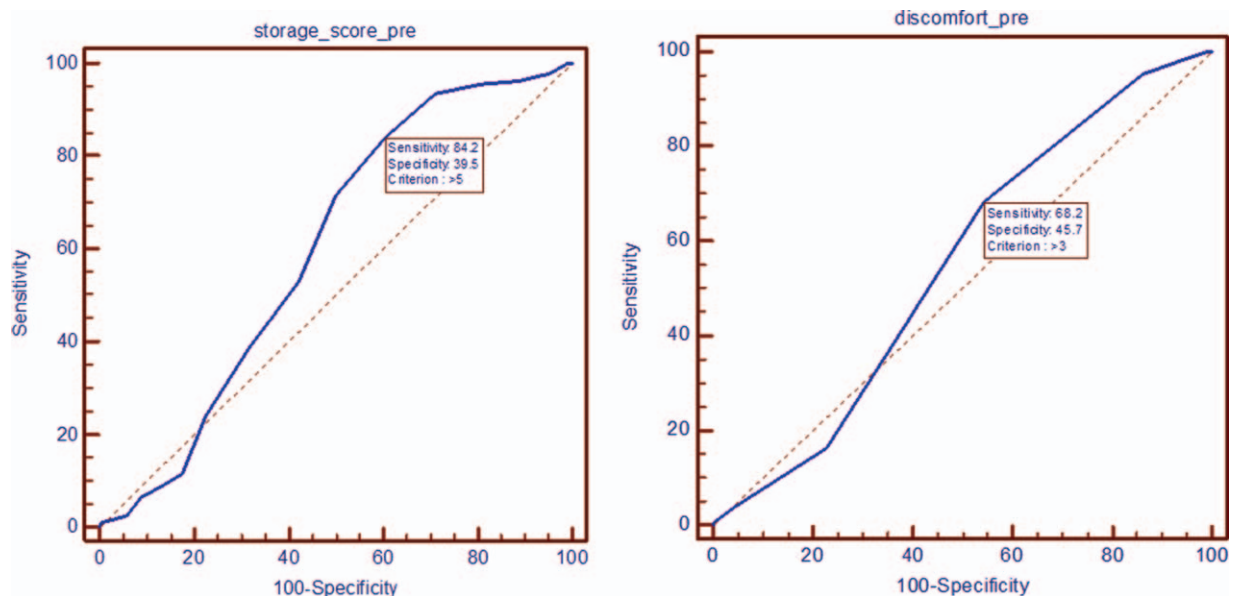
Figure 2. ROC analysis showed a positive relationship between symptom duration and IPSS voiding score, and satisfaction. IPSS = International Prostate Symptom Score, ROC = receiver operating characteristic.

these scores, and patient perception and satisfaction with change is not well understood. Moreover, low-dose tamsulosin has never been widely studied to investigate the treatment satisfaction except in our previously conducted study [13]. Establishing the initial treatment strategy is extremely important as the degree of improvement is limited after 2 or 3 months of initial treatment [11].

The intention of this investigation was to find a real clinical indication for low-dose tamsulosin as an initial treatment. Although we have judged the indication by patient satisfaction, we have also shown objective evidence for the indication criteria with various statistical analyses.

Among the current available alpha1 adrenergic blockers (i.e., terazosin, doxazosin, alfuzosin and tamsulosin), tamsulosin is one of the most commonly recommended option because of its tolerability, efficacy, and safety [14]. Tamsulosin has minimal effects on blood pressure and can be safely combined with other cardiovascular drugs [15,16].

An initial study by Abrams et al[17] demonstrated the efficacy and safety of tamsulosin, as well as its optimum dosage, which resulted in the establishment of 0.4 mg tamsulosin as the standard initial treatment dose. The treatment dosages of tamsulosin in clinical practice of Western countries range from 0.4 to 0.8 mg/day. However, low-dose tamsulosin (0.2 mg) as an initial

Figure 3. ROC analysis showed a negative relationship between IPSS storage score QoL, and satisfaction. IPSS = International Prostate Symptom Score, QoL = quality of life.

treatment has also been effective in several studies in Asian countries [3,5,7]. East Asian, especially Korean, Japanese, and Chinese men, have lower body mass indexes (BMIs) than Western men, and the initial low-dose tamsulosin was set because of expected adverse effects if the same dose as Western men was used.

This study has several important implications. First, if low-dose tamsulosin is effective, LUTS patients could maintain this medication without the need of dose enhancement or combination treatment. Second, low-dose tamsulosin could decrease the potential side effects of retroejcaculation or anejaculation.

The severity of IPSS is associated with higher baseline scores.[11,18,19] Originally, Barry et al[19] found that men with more severe symptoms at baseline required a greater magnitude of symptom reduction to perceive improvement.

Roehrborn et al. reported that to achieve a response of "satisfied" or "very satisfied" a man with very severe symptoms (baseline I-PSS 30) would require an improvement of almost 18 points, while a man with moderate symptoms (baseline I-PSS 12) would require an improvement of 4 points [11]. The seminal study by Barry et al[19] is the only other published report of the relevance to patients of changes in I-PSS scores. They evaluated changes in the AUA symptom index score by conducting patient global assessments of the degree of change. Patient assessment of marked, moderate, slight, and no improvement was associated with an AUA symptom index change of −8.8, −5.1, −3.0, and −0.7 points, respectively, while worse was associated with a 2.7

increase in score. These reports are pioneering work to assess the magnitude of IPSS to achieve patient satisfaction. However, it is a common phenomenon in many clinical studies that greater changes in IPSS were associated with higher baseline scores. Higher baseline IPSS scores reported greater improvement than those with lower baseline scores [11]. Our study also showed similar tendencies (Fig. 4). This finding suggests that initial treatment of LUTS should be more focused on combined treatment. It is well known that storage symptoms are more bothersome and more negatively related with QoL. In our study, storage symptoms showed the greatest association with QoL. To date, many studies have focused on the improvement of IPSS itself; however, physicians should consider earlier combination treatment with anticholinergics as an alternative initial treatment option.

Although we have demonstrated the real indications for low-dose tamsulosin, this study does not guarantee that combination treatment with anticholinergics and low-dose tamsulosin is effective in non-satisfactory indicated patients. Further studies are needed to determine this.

Our study has several limitations. First, this study has a short follow-up period, and more longitudinal studies are required to confirm our findings. Second, our definition of satisfaction was relatively simple. Satisfaction is likely to be a much broader issue than simply a response of LUTS. It might include the quality of physician interaction, treatment expectations, partner involvement, side effects, and many other variables. Third, a complex
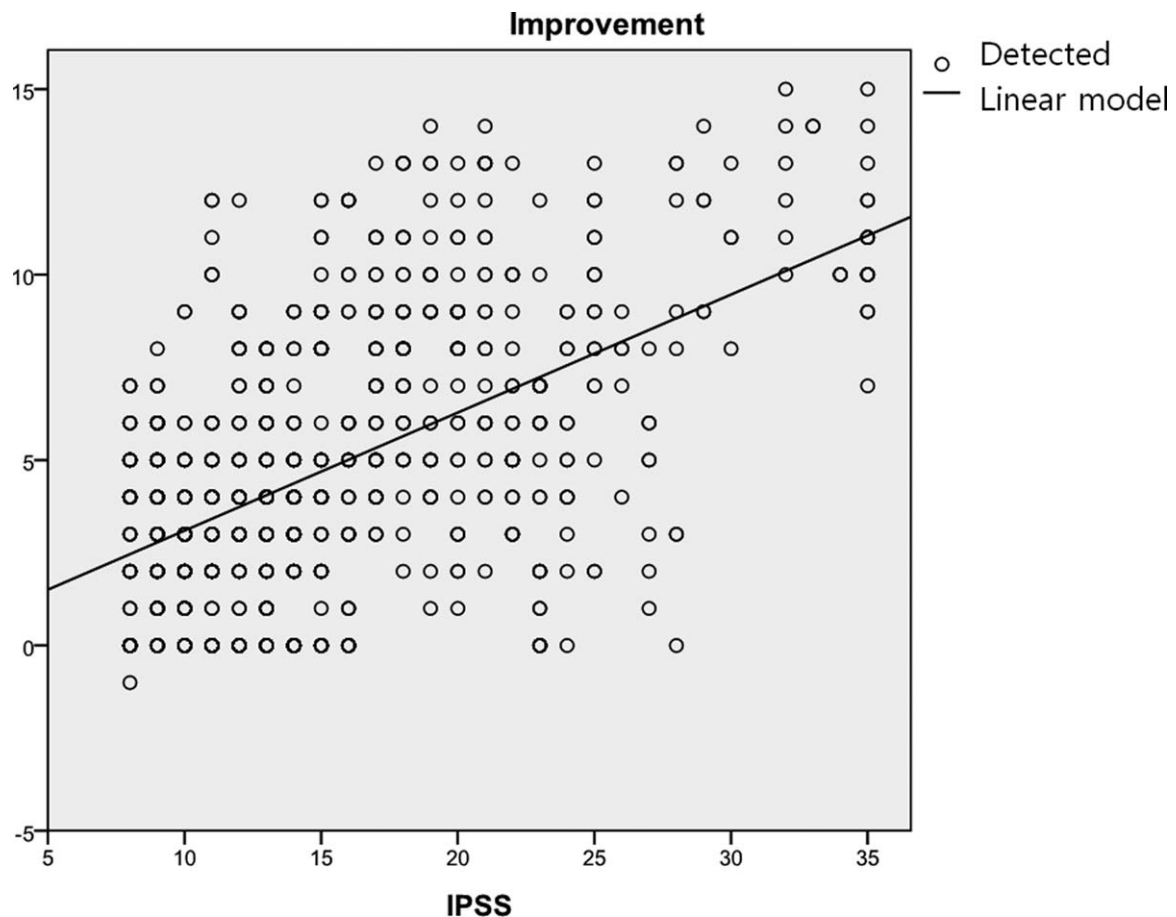
Figure 4. Correlation analysis showed the positive relationship between IPSS and the degree of improvement under age adjusted. IPSS = International Prostate Symptom Score.

relationship exists between bladder outlet obstruction index improvement and variations of both maximum urinary flow and detrusor pressure. Therefore it will be helpful for identifying specific satisfaction factor after medication. However, there were not many patients who underwent a urodynamic study, making it difficult to obtain adequate number of detrusor pressure values. Another limitation of the present study was that there were no considering sexual performances in terms of erection or ejaculation due to lack of data. Finally, our study requires additional analyses to confirm our results (including high sensitivity and low specificity) with longer follow-up. Considering the importance of the impact of patient satisfaction with treatment on patient compliance and long-term success of medical treatment, further prospective longitudinal studies have to be performed.

6. Conclusions

Treating patients with LUTS with low-dose tamsulosin is clinically effective, but a significant proportion of patients may not be satisfied with their symptom improvement. The patient with higher storage scores and higher QoL before treatment could have a higher change of non-satisfaction. In conclusion, our study has demonstrated the therapeutic indication of low-dose tamsulosin as an initial treatment strategy for patients with LUTS.

Author contributions

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Supervision: Soon Sun Kwon.
Writing – review & editing: Jae Hyun Bae.

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