Tadalafil is sufficiently effective for severe chronic prostatitis/chronic pelvic pain syndrome in patients with benign prostatic hyperplasia

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Abstract

Objectives: To investigate the efficacy of tadalafil for patients with benign prostatic hyperplasia and especially with chronic prostatitis/chronic pelvic pain syndrome.

Methods: Tadalafil 5 mg was given each morning for 12 weeks to patients diagnosed as having either moderate or severe lower urinary tract symptoms. Voiding symptoms were compared between patients with a high (≥4; high group) and low (<4; low group) pain subscore of the National Institutes of Health Chronic Prostatitis Symptom Index before and after tadalafil administration. Correlation between changes in the Chronic Prostatitis Symptom Index and the International Prostate Symptom Score during treatment was also investigated.

Results: At the pretreatment baseline, the pain subscore of the Chronic Prostatitis Symptom Index was high (≥4) in 24 of 74 (32.4%) patients. The International Prostate Symptom Score in the group with high pain subscore was significantly higher than that in the group with low pain subscore. As an indicator of the efficacy of tadalafil, the International Prostate Symptom Score and National Institutes of Health Chronic Prostatitis Symptom Index total score and pain subscore were significantly improved. The change in the Chronic Prostatitis Symptom Index total score correlated positively with the change in the International Prostate Symptom Score. The decrease in the

International Prostate Symptom Score was significantly greater in the group with high versus low pain subscore.

Conclusion: Tadalafil was sufficiently effective in the treatment of patients with benign prostatic hyperplasia and severe chronic prostatitis/chronic pelvic pain syndrome.

Key words: benign prostatic hyperplasia, chronic prostatitis/chronic pelvic pain syndrome, National Institutes of Health chronic prostatitis symptom index, tadalafil, lower urinary tract symptom

Abbreviations & Acronyms

BPH = benign prostatic hyperplasia

CP/CPPS = chronic prostatitis/chronic pelvic pain syndrome

IPSS = International Prostate Symptom Score

LUTS = lower urinary tract symptoms

NIH-CPSI = the National Institutes of Health Chronic Prostatitis Symptom Index

OABSS = Overactive Bladder Symptom Score

PDE5 = phosphodiesterase type 5

QOL = quality of life

TNF-α = tumor necrosis factor alpha

Introduction

Patients with benign prostatic hyperplasia (BPH) often complain not only of lower urinary tract symptoms (LUTS) but also lower abdominal pain and/or perineal discomfort recognized as chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).[1] In fact, several clinical studies have reported that CP/CPPS is strongly associated with BPH.[2] Although it is naturally accepted that a histological inflammatory process in the prostate gland causes CP/CPPS, this process is usually taken to be one of the mechanisms for inducing BPH through the effect of several cytokines associated with inflammation. Indeed, the degree of histological prostatic inflammation is positively correlated with the severity of LUTS as evaluated by the International Prostate Symptom Score (IPSS).[3] Recently, immunohistological staining by anti-CD45 antibody, which is one of the markers for inflammation, was reported to be useful for the evaluation of inflammatory change in the prostate gland.[4] We also reported that a positive rate of immunohistological staining by anti-CD45 antibody was significantly related with the severity of CP/CPPS evaluated by the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI),[5] which is a commonly used 13-item questionnaire for the assessment of symptom severity in men with CP/CPPS.[6] Thus, the degree of histological prostatic inflammation in CP/CPPS may be predicted by the score

of NIH-CPSI. However, it is also well known that patients without inflammatory signs such as pyuria are also bothered by CP/CPPS, and this may cause confusion in the understanding and treatment of CP/CPPS. NIH-CPSI has been used even for these patients as a reliable and valuable tool for the diagnosis of CP/CPPS in the clinical setting. Because CP/CPPS is basically diagnosed only by symptoms without histological confirmation at present, NIH-CPSI is of increasing significance.

Until recently, α1-antagonists and 5α-reductase inhibitors were the primary medications prescribed for BPH in Japan. However, these treatments are not effective in all patients, especially those with CP/CPPS.[7] Furthermore, an effective therapeutic approach for CP/CPPS remains unclear. The phosphodiesterase type 5 (PDE5) inhibitor tadalafil was approved to treat men with BPH with or without erectile dysfunction in Japan in 2014. The effectiveness and tolerability of tadalafil for this indication has been established in placebo-controlled clinical studies in Asian populations with BPH.[8] In addition, it was shown that PDE-5 inhibitors exert an anti-inflammatory effect on endothelial cells to blunt reactions to inflammatory cytokines.[9] Thus, the basic clinical question has arisen of whether tadalafil can resolve CP/CPPS symptoms, especially pain, and LUTS in patients with BPH.

In the present study, we focused on whether tadalafil is more effective for patients

with severe CP/CPPS than others after confirming its efficacy in patients with BPH/LUTS. We also investigated the relation between pain among CP/CPPS symptoms as evaluated by NIH-CPSI and LUTS as evaluated by several questionnaires including the IPSS, quality of life (QOL) index and the Overactive Bladder Symptom Score (OABSS).

Methods

In evaluating CP/CPPS, its symptoms were assessed by NIH-CPSI although not all patients complained of CP/CPPS. Patients with NIH-CPSI pain subscore ≥4 were defined as a group having prostatitis and were regarded as having a high NIH-CPSI pain subscore. This study included 74 men (mean age, 68.2 ± 9.2 years) diagnosed as having either moderate or severe BPH, as indicated by a total score of >8 on the IPSS. LUTS were assessed by the QOL index and OABSS together with the IPSS. As one objective finding, maximum flow rate by uroflowmetry was evaluated at the same time as the questionnaire. Patients were excluded if they had taken tadalafil for <12 weeks, been diagnosed as having prostate cancer, undergone surgical treatment of the prostate gland, had a urinary tract infection, experienced acute urinary retention within 4 weeks of the screening visit, or had a history or evidence of urethral stricture or renal dysfunction.

Although urinary tract infection was not indicated in the intermediate urine sample, the initial urine sample obtained after prostate massage had not been examined for the presence of infection. All patients were instructed to take tadalafil 5 mg orally each morning for 12 weeks.

First, the IPSS was compared between patients with a high (≥4; high group) and low (<4; low group) NIH-CPSI pain subscore at the pretreatment baseline to clarify whether pain among CP/CPPS symptoms is associated with the severity of LUTS. Second, LUTS and CP/CPPS symptoms were compared before and after treatment to evaluate the efficacy of tadalafil. Third, in patients with high NIH-CPSI pain subscore, the presence of a correlation between the changes in the NIH-CPSI and the IPSS during treatment was investigated. Finally, improvement of the IPSS was compared between the group with high versus that with low NIH-CPSI pain subscore.

This study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines, and written informed consent was obtained from all patients. The procedures were approved by the Regional Ethics Committee of Juntendo Urayasu Hospital, Urayasu, Japan (approval number: 29-041).

Statistical analysis

Data are presented as the mean ± standard error. A comparison of the IPSS at the baseline and the change of IPSS during the treatment between the groups with high and low NIH-CPSI pain subscore were performed by Mann-Whitney's U test. The change of score on several questionnaires and maximum flow rate were evaluated by paired *t*-test. The relation between the changes of NIH-CPSI and IPSS was determined using the Pearson correlation coefficient. A *P*-value of less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 24.0 (SPSS Inc., Chicago, IL, USA).

Results

Patients' characteristics are summarized in **Table 1**. At the pretreatment baseline, the NIH-CPSI pain subscore was high (≥4) in 24 of the 74 (32.4%) patients. IPSS in the group with high NIH-CPSI pain subscore was significantly higher (19.6 ± 5.3) than that in the group with low pain subscore (16.6 ± 5.3; $P < 0.05$) (**Table 2**). Regarding the efficacy of tadalafil, IPSS was significantly improved after the treatment as expected (17.6 ± 5.5 vs 12.3 ± 6.7; $P < 0.001$). The QOL index (4.7 ± 0.9 vs 3.1 ± 1.7; $P < 0.001$) and OABSS (5.3 ± 2.5 vs 4.3 ± 2.2; $P < 0.001$) were also significantly improved. However, maximum urinary flow rate did not show a significant improvement. NIH-

CPSI total score was significantly improved (14.6 ± 6.2 vs 9.3 ± 5.4; $P < 0.001$). A significant improvement was also found in the pain subscore (2.6 ± 3.6 vs 1.2 ± 2.0; $P < 0.01$) (**Table 3**). The change of NIH-CPSI correlated positively with the change of IPSS in patients with high NIH-CPSI pain subscore (Pearson's correlation 0.624, $P < 0.001$) (**Fig. 1**). The decrease in IPSS in the group with high NIH-CPSI pain subscore (-8.5 ± 7.1) was significantly greater than that in the group with low pain subscore (-3.0 ± 5.6; $P < 0.05$) (**Table 4**).

Discussion

This study investigated the efficacy of tadalafil for patients with BPH/LUTS, and especially CP/CPPS, as evaluated by several questionnaires. It is common that treatment of CP/CPPS is usually difficult because the causes and etiology of this disease have not been established, and current treatments are basically empirical and mostly untested. BPH is often associated with histological inflammation that sometimes induces CP/CPPS. It was reported that chronic prostatic inflammation can develop and progress to BPH.[10] Several studies showed that inflammation was identified in prostate tissue of more than half of patients with BPH who underwent transurethral resection of the prostate.[11,12] The 4-year Reduction by Dutasteride of Prostate Cancer Events study in

men randomized to placebo reported prostate inflammation with BPH was associated with the severity of LUTS.[13] The degree of prostate inflammation on histological examination in patients with BPH was significantly and positively correlated with the severity of the IPSS.[3] In addition, CP/CPPS was also significantly correlated with the severity of the IPSS.[14] Expressed prostatic secretions and semen in men with CP/CPPS included a higher level of tumor necrosis factor alpha (TNF-α), which is one of the markers for inflammation, than in men without CP/CPPS.[15,16] However, CP/CPPS is usually diagnosed in the clinical setting only by symptoms with no subsequent histological confirmation. Thus, we place high importance on NIH-CPSI in the present study because we already found that NIH-CPSI score was closely correlated with the degree of histological inflammation in the prostatic gland in patients with BPH.[5] NIH-CPSI provided by Nickel et al. for the assessment especially of CP/CPPS in LUTS is a 13-item index with a point range of 0 to 43 points that includes a pain subscore (NIH-CPSI questions 1a, b, c, d, 2a, b, 3 and 4), urinary symptoms subscore (NIH-CPSI questions 5 and 6), and QOL impact subscore (NIH-CPSI questions 7, 8 and 9) (**Fig. S1**). Usually, a pain subscore ≥4 is regarded as being indicative of prostatitis.[17]

In the present study, the first question is whether LUTS of patients with BPH complaining of pain among their CP/CPPS symptoms are worse than those of patients

without pain. Our study provides the valuable finding that the IPSS in the group with high NIH-CPSI pain subscore was significantly higher than that in the group with low pain subscore. This means that patients complaining of severe pain are more bothered by LUTS than those without it. The second question relates to the efficacy of tadalafil for patients with BPH/LUTS and CP/CPPS. Tadalafil increases nitric oxide/cyclic guanosine monophosphate and reduces RhoA/Rho-kinase signaling, thus affecting several pathways for LUTS. In the present study, we clearly showed the efficacy of tadalafil for LUTS as indicated by the improvement of the IPSS, QOL index and OABSS. CP/CPPS, however, is usually refractory to medications. Historically, the standard medical treatments for BPH including α1-antagonists, 5α-reductase inhibitors and phytotherapy have been tried for CP/CPPS. However, it was already reported that the efficacy of α1-antagonists and 5α-reductase inhibitors in patients with high-grade inflammation of the prostate tissue is poorer than that in patients with low-grade inflammation.[7] Symptom improvement with antibiotics including levofloxacin and ciprofloxacin was not significantly different from placebo.[18,19] Only phytotherapy with pollen extract in herbal therapies for CP/CPPS significantly improved NIH-CPSI total score and the pain and QOL subscores compared to placebo in a randomized control study.[20] Thus, in the clinical setting, we usually use phytotherapy with pollen extract in

herbal therapy for patients with CP/CPPS according to the findings of this randomized control study. However, even phytotherapy with pollen extract offered no statistical improvement in IPSS in patients with BPH/LUTS and CP/CPPS in a previous randomized control study.[20] In other words, there is no standardized treatment for LUTS with CP/CPPS.[21] Tadalafil as a PDE5 inhibitor is now the first-line treatment for BPH/LUTS. Recently, a double-blind control study showed a significantly lower level of CD45 in human prostate tissue in the PDE5 inhibitor arm (vardenafil 10 mg/day for 12 weeks) versus the placebo arm.[4] In addition, tadalafil was expected to positively affect various aspects such as oxidation, blood flow, inflammation and endothelial function. In an in vitro experiment with PDE5 inhibitors, only tadalafil, and not sildenafil or vardenafil, decreased the inflammatory response on endothelial cells stimulated by the oxidation of low-density lipoproteins by myeloperoxidase or TNF-α.[9] Further, tadalafil administered to investigate vascular endothelial function in patients with erectile dysfunction and at cardiovascular risk showed significant improvement in brachial artery blood flow-mediated dilation and nitrite/nitrate and endothelin-1 plasma levels.[22] Tadalafil also improved endothelial function by reducing serum levels of oxidative stress.[23] Nitric oxide increased by PDE5 inhibitors has the effect of relaxing the prostatic duct smooth muscles and increasing wash-out of prostatic reflux

products.[24] Furthermore, prostate blood flow and oxygenation were increased by tadalafil.[25] These actions can significantly reduce prostatic inflammation. Thus, tadalafil has been expected to cure CP/CPPS to decrease the inflammatory response in the prostate gland. Our present finding showing the improvement of NIH-CPSI, especially the pain subscore, clearly indicates the efficacy of tadalafil for CP/CPPS. Although it is already interesting that tadalafil was shown to be effective for CP/CPPS, the more interesting finding is that the change of NIH-CPSI correlated positively with the change of the IPSS. Furthermore, we also showed that the change of the pain subscore correlated positively with the change of the IPSS. These findings may indicate that reducing the symptoms of CP/CPPS including pain is essential in the treatment of LUTS.

Finally, the most interesting finding in the present study was that the decrease in the IPSS in the group with high NIH-CPSI pain subscore at the pretreatment baseline was significantly greater than that in the group with low pain subscore. Soluble cyclic guanosine monophosphate was reported to have a key role in the nitric oxide-mediated inhibition of leukocyte rolling, and PDE5 inhibition may reduce atherosclerotic damage and overall inflammation by reducing leukocyte recruitment. Tadalafil was shown in vitro to attenuate the expression of the inflammatory cytokines TNF-α and IL-1β in

pulmonary arteries and that of TNF-α and IL-8 in endothelial cells.[4] On the basis of these previous reports and our present findings, we conclude that tadalafil is sufficiently effective for patients with BPH and severe CP/CPPS.

Some limitations of the present study need to be mentioned. First, this study was a retrospective single-arm study based on routine medical care. Controlled randomized clinical trials with a placebo arm are needed. Second, the number of patients in the present study was small, and not all patients complained of CP/CPPS. It would be better to construct a large-scale study with many patients having only CP/CPPS. Third, although there were no additions or changes of medications during the study period, information on previous treatments and concomitant medication for BPH was unclear. Fourth, there was a potential for selection bias in this study. CP/CPPS was compared between patients with low-grade LUTS and those with high-grade LUTS, but the background of the two groups might not match. Finally, the voided volume measured by uroflowmetry before the treatment (224.7 ± 92.8 mL) was significantly higher that after treatment (172.7 ± 98.4 mL; $P < 0.001$). We could not elucidate a reason for the treatment to decrease the voided volume at uroflowmetry. However, we speculate that this may be misleading and due to our study protocol. Basically, the process to enroll patients in the study took a long time because of the time needed to explain the study

protocol and obtain patient agreement. Thus, there was enough time for urine to pool in the patient's bladder. However, after the initial treatment, most patients who wanted to continue treatment did not have to stay at the clinic or the hospital for a long time. We speculate that this situational difference may be associated with the decrease in voided volume after the treatment, even though the patients were adequately instructed to have a full bladder at the reexamination performed at the final visit. Although these limitations may have some influence on the results, we believe that our findings are adequately informative and valuable for practitioners in the fields of urology and public health.

In conclusion, tadalafil was sufficiently effective in treating patients with BPH and severe CP/CPPS. When patients with BPH complain of perineal discomfort and/or pain, tadalafil may be considered the first choice for medical treatment.

Conflict of interest

None declared.

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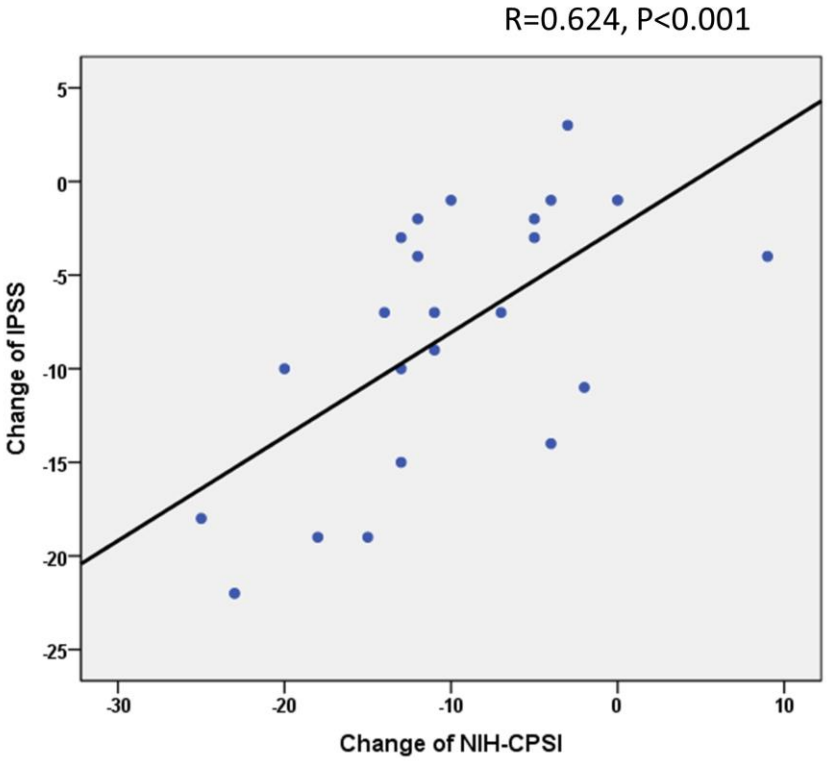
Figure legends

Fig. 1 Correlation between the change of the National Institutes of Health Chronic Prostatitis Symptom Index and the change of the International Prostate Symptom Score in patients in the high pain group.

Fig. S1 The National Institutes of Health Chronic Prostatitis Symptom Index.

Figure 1


R=0.624, P<0.001
Change of IPSS
5
0
-5
-10
-15
-20
-25
-30
-20
-10
0
10
Change of NIH-CPSI

the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI)

Pain or Discomfort

1. In the last week, have you experienced any pain or discomfort in the following areas?

		Yes	No
a.	Area between rectum and testicles (perineum)	❑1	❑0
b.	Testicles	❑1	❑0
c.	Tip of the penis (not related to urination)	❑1	❑0
d.	Below your waist, in your pubic or bladder area	❑1	❑0

2. In the last week, have you experienced:

		Yes	No
a.	Pain or burning during urination?	❑1	❑0
b.	Pain or discomfort during or after sexual climax (ejaculation)?	❑1	❑0

3. How often have you had pain or discomfort in any of these areas over the last week?

❑0 Never
❑1 Rarely
❑2 Sometimes
❑3 Often
❑4 Usually
❑5 Always

4. Which number best describes your AVERAGE pain or discomfort on the days that you had it, over the last week?

❑0 ❑1 ❑2 ❑3 ❑4 ❑5 ❑6 ❑7 ❑8 ❑9 ❑10

NO PAIN — PAIN AS BAD AS YOU CAN IMAGINE

Urination

5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?

❑0 Not at all
❑1 Less than 1 time in 5
❑2 Less than half the time
❑3 About half the time
❑4 More than half the time
❑5 Almost always

6. How often have you had to urinate again less than two hours after you finished urinating, over the last week?

❑0 Not at all
❑1 Less than 1 time in 5
❑2 Less than half the time
❑3 About half the time
❑4 More than half the time
❑5 Almost always

Impact of Symptoms

7. How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?

❑0 None
❑1 Only a little
❑2 Some
❑3 A lot

8. How much did you think about your symptoms, over the last week?

❑0 None
❑1 Only a little
❑2 Some
❑3 A lot

Quality of Life

9. If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?

❑0 Delighted
❑1 Pleased
❑2 Mostly satisfied
❑3 Mixed (about equally satisfied and dissatisfied)
❑4 Mostly dissatisfied
❑5 Unhappy
❑6 Terrible

Scoring the NIH-Chronic Prostatitis Symptom Index Domains

Pain: Total of items 1a, 1b, 1c,1d, 2a, 2b, 3, and 4 =

Urinary Symptoms: Total of items 5 and 6 =

Quality of Life Impact: Total of items 7, 8, and 9 =

Table 1 Patient background

Age (y)	68.2 ± 9.2	(42-85)
Prostate volume (mL)	39.7 ± 23.2	(14.0-143.0)
NIH-CPSI total	14.8 ± 6.4	(2-32)
Pain	2.7 ± 3.7	(0-16)
Urinary	5.5 ± 2.4	(0-10)
QOL	6.6 ± 2.3	(0-11)
IPSS total	17.5 ± 5.6	(8-32)
Voiding	10.4 ± 4.5	(0-20)
Storage	7.1 ± 2.4	(2-14)
QOL index	4.7 ± 0.9	(2-6)
OABSS	5.3 ± 2.5	(0-12)
Flow time (seconds)	41.8 ± 20.3	(12.7-116.0)
Maximum flow rate (mL/second)	13.2 ± 5.0	(4.8-26.0)
Voided volume (mL)	228.4 ± 95.8	(106.0-515.0)
Residual urine volume (mL)	44.3 ± 38.3	(0-153.0)

NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; IPSS = International Prostate Symptom Score; OABSS = Overactive Bladder Symptom Score.
Values are expressed as mean ± SE.

Table 2 High and low pain subscores of the NIH-CPSI at the pretreatment baseline

	Pain subscore of NIH-CPSI		
	<4	≥4	*P*
Case (n)	50	24	
Age (y)	69.5 ± 7.8	65.4 ± 11.4	0.371
Prostate volume (mL)	37.4± 19.1	44.2± 29.9	0.689
NIH-CPSI total	11.7 ± 4.2	20.7 ± 5.2	<0.001
Pain	0.6 ± 1.0	6.9 ± 3.3	<0.001
Urinary	4.9 ± 2.1	6.5 ± 2.5	0.004
QOL	6.2 ± 2.4	7.4 ± 1.7	0.027
IPSS total	16.6 ± 5.3	19.6 ± 5.3	0.041
Voiding	9.8 ± 4.5	12.0 ± 4.0	0.058
Storage	6.8 ± 2.4	7.6 ± 2.6	0.094
QOL index	4.6 ± 1.0	5.0 ± 0.8	0.044
OABSS	5.2 ± 2.4	5.6 ± 2.7	0.615
Flow time (seconds)	39.2 ± 20.0	47.1 ± 19.4	0.119
Maximum flow rate (mL/second)	13.3 ± 5.1	13.0 ± 5.0	0.793
Voided volume (mL)	215.4 ± 95.0	244.2 ± 87.4	0.067
Residual urine volume (mL)	43.3 ± 35.8	47.0 ± 45.1	0.962

NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; IPSS = International Prostate Symptom Score; OABSS = Overactive Bladder Symptom Score.
Values are expressed as mean ± SE.

Table 3 Questionnaire and uroflowmeter results before and after treatment with tadalafil

	Before	After	*P*
NIH-CPSI total	14.6 ± 6.2	9.3 ± 5.4	<0.001
Pain	2.6 ± 3.6	1.2 ± 2.0	0.001
Urinary	5.4 ± 2.3	3.8 ± 2.3	<0.001
QOL	6.5 ± 2.3	4.3 ± 2.5	<0.001
IPSS total	17.6 ± 5.5	12.3 ± 6.7	<0.001
Voiding	10.5 ± 4.4	7.1 ± 5.1	<0.001
Storage	7.1 ± 2.5	5.2 ± 2.5	<0.001
QOL index	4.7 ± 0.9	3.1 ± 1.7	<0.001
OABSS	5.3 ± 2.5	4.3 ± 2.2	<0.001
Flow time (seconds)	41.6 ± 20.0	35.0± 16.8	0.011
Maximum flow rate (mL/second)	13.2 ± 5.0	12.0 ± 5.7	0.074
Voided volume (mL)	224.7 ± 92.8	172.7 ± 98.4	<0.001
Residual urine volume (mL)	44.5 ± 38.6	34.0 ± 28.1	0.055

NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; IPSS = International Prostate Symptom Score; OABSS = Overactive Bladder Symptom Score.
Values are expressed as mean ± SE.

Table 4 Change in questionnaire scores between groups with low and high pain subscores of the NIH-CPSI

	Pain subscore of NIH-CPSI		
	<4	≥4	*P*
Case (n)	50	24	
NIH-CPSI total	-3.0 ± 5.0	-10.0 ± 7.8	<0.001
Pain	0.1 ± 1.5	-4.4 ± 4.5	<0.001
Urinary	-1.2 ± 2.2	-2.5 ± 3.0	0.038
QOL	-1.8 ± 2.8	-3.1 ± 2.7	0.048
IPSS total	-3.0 ± 5.6	-8.5 ± 7.1	0.021
Voiding	-1.8 ± 4.5	-5.5 ± 5.7	0.045
Storage	-1.2 ± 2.1	-3.0 ± 2.9	0.029
QOL index	-1.3 ± 1.9	-1.9 ± 1.9	0.313
OABSS	-0.8 ± 2.0	-1.8 ± 2.3	0.098

NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; IPSS = International Prostate Symptom Score; OABSS = Overactive Bladder Symptom Score. Values are expressed as mean ± SE.