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Research Article

Association between predictors of progression of benign prostatic hyperplasia and moderate-to-severe prostatitis-like symptoms: A propensity score–matched analysis

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ABSTRACT

Background: We investigated the association between moderate-to-severe prostatitis-like symptoms and the predictors of benign prostatic hyperplasia (BPH) progression.
Methods: Men who underwent health checkups were analyzed. We classified symptoms as "moderate to severe" if the pain score according to the National Institutes of Health-Chronic Prostatitis Symptoms Index was ≥8 and predictors of the progression of BPH were defined as having a prostate-specific antigen (PSA) ≥1.6 ng/mL, total prostate volume (TPV) ≥31 mL, international prostate symptom score (IPSS) ≥20, and maximal flow rate (Q_{max}) <10.6 mL/s. A total of 8368 patients formed the cohort for propensity score matching, including 445 men with moderate-to-severe prostatitis-like symptoms and 5390 men with no symptoms; ultimately, however, the propensity score of these groups matched at a 1:2 ratio.
Results: After propensity matching, the two groups were evenly distributed with respect to age, International Index of Erectile Function-5 score, metabolic syndrome, and testosterone. The percentage of participants with ≥1 predictor for the progression of BPH, a TPV of ≥31 cm^3, PSA levels of ≥1.6 ng/mL, Q_{max} <10.6 mL/s, and IPSS ≥20 were all greater in men with moderate-to-severe prostatitis-like symptoms. There were significant differences in the percentage of participants with ≥1 predictor for the progression of BPH (30.6% vs. 58.0%; $p < 0.001$), Q_{max} <10.6 mL/s (3.9% vs. 7.0%, $p = 0.023$), and IPSS ≥20 (9.6% vs. 44.7%, $p < 0.001$).
Conclusion: Moderate-to-severe prostatitis-like symptoms are significantly and independently associated with predictors of BPH progression.

1. Introduction

Benign prostatic hyperplasia (BPH) is clinically progressive.[1-3] Urinary tract infection, urinary incontinence, renal insufficiency, acute urinary retention, and lower urinary tract symptoms are known to worsen as a result of BPH progression.[1-3]

Baseline prostate-specific antigen (PSA), maximal flow rate (Q_{max}), total prostate volume (TPV), International Prostate Symptom Score (IPSS), and age were predictors of BPH progression in a previous study.[1] These predictors are clinically important because the progression of BPH leads to increased medical costs as well as a deterioration in the quality of life of men with BPH.

It has recently been suggested that chronic intraprostatic inflammation induces BPH progression.[4] It can be reasonably speculated that the symptoms of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) could predict BPH progression; however, this has not yet been elucidated. Therefore, we investigated the association of CP/CPPS symptoms with known predictors of BPH progression using propensity score–matched analysis.

2. Materials and methods

2.1. Subjects

From 2011 to 2013, 8727 men in their 40s and 50s underwent urological health checkups.[5] The participants applied to be part of the study. Anthropometric measurements (weight, height, waist circumference, and blood pressure measurements), serum

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testosterone levels, PSA levels, and basic blood chemistry analyses were included in the health screening. Serum was drawn between 7:00 AM and 9:00 AM after overnight fasting.

Medical histories were collected by trained nurses. Participants were asked to complete questionnaires, including the National Institutes of Health-Chronic Prostatitis Symptoms Index (NIH-CPSI), the International Index of Erectile Function-5 (IIEF), and IPSS. All participants provided written informed consent, and data concerning the participants were prospectively collected.

Transrectal ultrasonography and uroflowmetry were used to measure TPV and Qmax.

The institutional review board reviewed and approved the study protocol (approval number:11100176-202202-HR-003).

2.2. CP/CPPS symptoms classification

We classified symptoms as "no prostatitis-like symptoms" if respondents did not report perineal or ejaculatory pain and had an NIH-CPSI pain score of <4. We classified symptoms as "moderate to severe" if the pain score was ≥8.[6]

2.3. Predictors for BPH progression

The predictors of the progression of BPH were defined as PSA ≥1.6 ng/mL, TPV ≥31 mL, IPSS ≥20 points, and Q_{max} <10.6 mL/s according to previous data.[3,7]

2.4. Metabolic syndrome

Metabolic syndrome[8] was diagnosed when ≥3 of the following National Cholesterol Education Panel-Adult Treatment Panel III criteria were met: blood pressure ≥130/85 mm Hg or antihypertensive medication; fasting blood glucose ≥110 mg/dL or antidiabetic medication; waist circumference ≥90 cm; high-density lipoprotein cholesterol <40 mg/dL or antihypercholesterolemic medication; and triglycerides ≥150 mg/dL or antihypercholesterolemic medication.

2.5. Comorbid conditions

Age [3] erectile dysfunction [9], and metabolic syndrome [10] are well-known risk factors for BPH. Testosterone is essential for BPH development. Age[11], erectile dysfunction[12], and testosterone levels[13] are also associated with CP/CPPS. Therefore, age, erectile dysfunction assessed by IIEF, testosterone, and metabolic syndrome were adjusted to elucidate the relationship between predictors of progression of BPH and moderate-to-severe prostatitis-like symptoms.

2.6. Statistical analysis

We excluded men with a history of cancer ($n = 22$), men with data missing on their IPSS, IIEF, or NIH-CPSI questionnaires ($n = 159$), men with an NIH-CPSI pain score of ≥4, <8 ($n = 2412$), men with missing testosterone ($n = 5$), and men with missing data relating to metabolic syndrome ($n = 294$).

Demographics were assessed using descriptive statistics. The significance of the differences was analyzed using the *t*-test or χ^2 tests. The propensity score was established using a multivariable logistic regression model considering age, IIEF, testosterone, and metabolic syndrome status. Propensity score matching was considered for 445 men with moderate-to-severe prostatitis-like symptoms and 5390 men with no prostatitis-like symptoms. We matched subjects by propensity at a 2:1 ratio of controls to men with moderate-to-severe prostatitis-like symptoms ($n = 890$ and 445, respectively). The MatchIt package in the R statistical package was used to perform this process.

After matching, each of the predictors of BPH progression and the presence of ≥1 predictor for BPH progression were compared using a χ^2 test.

All tests were two sided, with statistical significance set at $p < 0.05$. Analyses were conducted with the R statistical package v.2.13.1 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

The characteristics before and after matching for men with moderate-to-severe prostatitis-like symptoms and men with no prostatitis-like symptoms are shown in Tables 1 and 2, respectively. Overall, 445 men with moderate-to-severe prostatitis-like symptoms and 5390 with no prostatitis-like symptoms were included. After propensity score matching, 890 men with no prostatitis-like symptoms were included.

Table 1
Characteristics of participants before propensity score matching

Variables	Prostatitis-like symptom		p[a]
	No ($N = 5390$)	Moderate to severe ($N = 445$)	
Age, years (mean ± SD)	50.5 ± 5.3	50.9 ± 5.3	0.114
No. metabolic syndrome (%)	2038 (37.8%)	161 (36.2%)	0.528
IIEF (mean ± SD)	18.4 ± 5.2	15.0 ± 5.3	<0.001
Testosterone, ng/mL (mean ± SD)	5.3 ± 1.6	5.3 ± 1.6	0.818

IIEF, International Index of Erectile Function-5; SD, standard deviation.
[a] *T*-test or χ^2 test.

Table 2
Characteristics of participants after propensity score matching

Variables	Prostatitis-like symptom		p[a]
	No ($N = 890$)	Moderate to severe ($N = 445$)	
Age, years (mean ± SD)	51.1 ± 5.3	50.9 ± 5.3	0.486
No. metabolic syndrome (%)	291 (32.7%)	161 (36.2%)	0.228
IIEF (mean ± SD)	15.0 ± 5.3	15.0 ± 5.3	0.985
Testosterone, ng/mL (mean ± SD)	5.3 ± 1.6	5.3 ± 1.6	0.701

IIEF, International Index of Erectile Function-5; SD, standard deviation.
[a] *T*-test or χ^2 test.

Before matching (Table 1), the mean age, metabolic syndrome, and mean testosterone levels were not significantly different between the two groups, although mean IIEF was significantly lower in men with moderate-to-severe prostatitis-like symptoms.

After matching (Table 2), age, testosterone, metabolic syndrome status, and IIEF were evenly dispersed and did not differ significantly between the groups, thus validating the propensity score matching model.

Table 3 shows the frequency of each of the predictors of BPH progression and the presence of ≥1 predictor for BPH progression between men with no and moderate-to-severe prostatitis-like symptoms.

The percentage of participants with ≥1 predictor for the progression of BPH, percentage of participants with a TPV ≥31 cm^3, percentage of PSA level ≥1.6 ng/mL, percentage of Qmax <10.6 mL/s, and percentage of IPSS ≥20 were all greater in men with moderate-to-severe prostatitis-like symptoms. There was a significant difference in the percentage of participants with ≥1 predictor for the progression of BPH, percentage of Qmax <10.6 mL/s, and percentage of IPSS ≥20.

The relative risk of the presence of ≥1 predictor for the progression of BPH in men with moderate-to-severe prostatitis-like symptoms was 1.9 compared with men with no prostatitis-like symptoms ([258/445]/[272/890]).

4. Discussion

In our propensity score–matched analysis, moderate-to-severe prostatitis-like symptoms were significantly related to predictors of BPH progression, specifically, Q_{max} <10.6 mL/s, and IPSS ≥20.

Prostatitis was classified into four categories: acute bacterial prostatitis (category I), chronic bacterial prostatitis (category II), CP/CPPS (category III prostatitis), and asymptomatic inflammatory prostatitis (category IV). Among these categories, CP/CPPS is the most common type of prostatitis in daily practice.[14] CP/CPPS is characterized by chronic pelvic pain, which is often associated with lower urinary tract symptoms (LUTS). Pain may be felt in the pelvis, lower abdomen, lower back, and/or genitals.

Previous reports have shown a clinical overlap between CP/CPPS and BPH. The combination rate of CP/CPPS and BPH ranges from 18.6% to 38.7% across studies.[15,16] The prevalence of CP/CPPS increases with the severity of LUTS.[17,18] A longitudinal study found that a history of physician-diagnosed prostatitis was related to future BPH development requiring treatment;[19] however, scant data are available concerning the association of CP/CPPS with BPH progression.

To our knowledge, this is the first study to show the association of prostatitis-like symptoms with predictors of BPH progression, which is indirect clinical evidence that symptoms of CP/CPPS are predictors of clinical progression of BPH. Our results could be a catalyst for further longitudinal observational studies to elucidate the usefulness of CP/CPPS symptoms as predictors of BPH progression. Positive results would be very helpful in treating and counseling BPH patients because simply asking whether a patient is experiencing chronic pelvic pain is simple, noninvasive, not time-consuming, and has no associated costs; this would be advantageous over the traditional predictors for clinical progression of BPH.

Pathologically, prostate inflammation is related to the progression of BPH. Acute urinary retention was only observed in men with baseline inflammation on prostate biopsy, and symptomatic progression of BPH was increased in men with acute or chronic inflammation compared with those without, although this is not statistically significant.[20] Moreover, acute or chronic intraprostatic inflammation was higher in men who underwent transurethral resection of the prostate (TURP) for urinary retention than in men who underwent TURP for LUTS only (70% vs. 45%, $p < 0.001$).[21] These data could explain the association of prostatitis-like symptoms with the predictors of BPH progression because intraprostatic inflammation is the basic pathophysiology of CP/CPPS.

BPH progression was defined as IPSS worsening of ≥4 points from baseline, acute urinary retention, renal insufficiency, recurrent urinary tract infection or urinary incontinence and PSA ≥1.6 ng/mL, TPV ≥31 mL, IPSS ≥20 points, and Qmax <10.6 mL/s are independent predictors for BPH progression in a previous study.[3] Our study showed the percentage of Qmax <10.6 mL/s and the percentage of IPSS ≥20 were significantly greater in men with moderate-to-severe prostatitis-like symptoms. Although this study failed to show the significance, the percentage of participants with a TPV ≥31 cm^3 and the percentage of PSA level ≥1.6 ng/mL were greater in men with moderate-to-severe prostatitis-like symptoms. Therefore, the sum of a number of each predictor of progression of BPH, all of which was greater in men with moderate-to-severe prostatitis-like symptoms, made significant results in the relationship between moderate-to-severe prostatitis-like symptoms and ≥1 predictor of BPH progression.

In Korea, the diagnosis rate of BPH was steadily increasing during the study period. Overall surgical treatment gradually decreased compared with an increase in medical treatment among all treatments for BPH.[22,23] We believe our results would be very helpful in treating and counseling BPH patients.

The limitation of our study is that it is difficult to make causal inferences because of the nature of our data set. Nevertheless, our study is meaningful because the data set was the result of a propensity score–matched case-control study, which mimics some of the particular characteristics of randomized controlled trials.[24]

In conclusion, moderate-to-severe prostatitis-like symptoms are significantly and independently related to the predictors of BPH progression. Our data suggest a possible role of CP/CPPS symptoms in predicting BPH progression. Further longitudinal studies are needed to confirm our results.

Table 3
Association between predictors for benign prostatic hyperplasia progression and prostatitis-like symptom

Variables	Prostatitis-like symptom		p[a]
	No ($N = 890$)	Moderate to severe ($N = 445$)	
≥1 Predictor of BPH progression, n (%)	272 (30.6)	258 (58.0)	<0.001
TPV of ≥31 cm^3, n (%)	141 (15.8)	73 (16.4)	0.854
PSA level of ≥1.6 ng/mL, n (%)	88 (9.9)	45 (10.1)	0.974
Qmax <10.6 mL/s, n (%)	35 (3.9)	31 (7.0)	0.023
IPSS ≥20, n (%)	85 (9.6)	199 (44.7)	<0.001

BPH, benign prostatic hyperplasia; IPSS, international prostate symptoms score; PSA, prostate-specific antigen; Q_{max}, maximal flow rate; TPV, total prostate volume.
[a] χ^2 test.

Conflicts of interest

The authors have no potential or financial conflicts of interests to declare.

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