



## Original Article

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# Relationship Between Chronic Periodontitis and Lower Urinary Tract Symptoms/Benign Prostatic Hyperplasia

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**Purpose:** We investigated the relationship between lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH) and chronic periodontitis (CP).

**Methods:** A total of 103 middle-aged men who had received a health checkup were included. All participant data were prospectively collected. CP was defined as a 30% increase in the number of probed sites with a clinical attachment level of  $\geq 4$  mm among all probed sites. LUTS/BPH were assessed using transrectal ultrasonography, the International Prostate Symptom Score (IPSS), uroflowmetry, and postvoiding residual urine volume.

**Results:** The median age, IPSS, prostate volume, and maximal flow rate were 55.0 years, 9.0, 29.0 mL, and 20.0 mL/sec, respectively. In addition, the prevalence of CP was 27.2%. The IPSS total, IPSS voiding, IPSS storage, and quality of life (QoL) scores were significantly higher in patients with CP (median [interquartile range, IQR]–IPSS total: 8.0 [5.0–13.5] vs. 12.0 [7.5–20.5],  $P=0.004$ ; IPSS voiding: 5.0 [2.0–9.0] vs. 8.5 [4.0–15.0],  $P=0.002$ ; IPSS storage: 3.0 [2.0–5.0] vs. 4.0 [3.0–6.0],  $P=0.021$ ; QoL: 2.0 [1.0–3.0] vs. 3.0 [2.0–4.0],  $P=0.015$ ). Additionally, the average flow rate was significantly lower in patients with CP (median [IQR] (mL/sec): 9.0 [8.0–13.0] vs. 8.0 [6.0–11.0],  $P=0.047$ ). After adjustment for age, testosterone level, prostate volume, glucose level, cholesterol level, and waist circumference, the IPSS total and voiding scores were significantly and positively related to CP (IPSS total: odds ratio [OR], 1.141; 95% confidence interval [CI], 1.045–1.245;  $P=0.003$ ; IPSS voiding: OR, 1.243; 95% CI, 1.092–1.415;  $P=0.001$ ).

**Conclusions:** Our data suggest that LUTS/BPH is significantly related to CP.


**Keywords:** Lower urinary tract symptoms; Benign prostatic hyperplasia; Chronic periodontitis

- **Research Ethics:** This study was approved by the Institutional Review Board (IRB) of the National Police Hospital (IRB No. 11100176-201909-HR-009).
- **Conflict of Interest:** No potential conflict of interest relevant to this article was reported.

## INTRODUCTION

Chronic periodontitis (CP) is an infectious disease resulting in inflammation within the supporting tissue of the teeth, progressive attachment, and bone loss [1]. CP is a highly prevalent dis-

ease, and a nationwide cohort study in Korea reported that among a total of 1,025,340 samples, 31.3% of the associated patients were diagnosed with periodontitis [2]. Recently, a relationship between CP and systemic diseases including cardiovascular disease [3], metabolic syndrome [4,5], and endothelial

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dysfunction [6] has been reported.

Benign prostatic hyperplasia (BPH) refers to voiding dysfunction resulting from prostate enlargement and bladder outlet obstruction [7]. BPH is caused by nonmalignant, unregulated growth of the prostate gland, and it is a major cause of lower urinary tract symptoms (LUTS) [8]. BPH is highly prevalent in older men, and the prevalence was 27.7% according to a community-based study [9]. Interestingly, recent data showed that LUTS/BPH was related to CP. However, scant data are currently available, and these data are limited by the definition of both CP and LUTS/BPH by using only a simple questionnaire or the absence of adjustment for potential confounding factors such as age, obesity, and metabolic factors. The relationship between CP and LUTS/BPH might be an important issue because both CP and LUTS/BPH are highly prevalent diseases. Therefore, we conducted this study to investigate the relationship between CP and LUTS/BPH in order to gain a better understanding of the pathophysiology of both CP and LUTS/BPH.

## MATERIALS AND METHODS

### Subjects

From September 2017 to August 2019, 108 men in their 40s or 50s received LUTS/BPH and CP health check-ups. We collected all participant data prospectively.

### Periodontal Examination

According to the clinical criteria proposed by the World Workshop on Periodontics in 1999, CP was defined as a 30% increase in the number of probed sites with a clinical attachment level (CAL) of  $\geq 4$  mm among all probed sites [10].

Each patient underwent periodontal examinations. We measured the plaque index, bleeding upon probing, probing depth, and CAL. Bleeding upon probing was assessed by using the bleeding point index. The probing depth was defined as the distance between the gingival margin and the deepest aspect of the pocket. The CAL was defined as the distance between the cemento-enamel junction of the tooth and the deepest aspect of the pocket. A periodontal measurement was made on 6 surfaces per tooth (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual) of all teeth except the third molars using a Willams probe (PCP-15, Hu-Friedy, Chicago, IL, USA). A single periodontist and 2 well-trained dentists who were blinded to the urological data performed all periodontal examination. Before the start of the study, the periodontal ex-

aminer was trained on the periodontal examination standard. In this study, we used only the CAL parameter to investigate the relationship between CP and LUTS/BPH because other parameters were not significantly related to LUTS/BPH in our pilot study.

### Assessment of LUTS/BPH

The urinary flow rate was assessed by uroflowmetry (Medtronic Inc., Minneapolis, MN, USA) and postvoid residual urine volume was measured using transabdominal ultrasonography (UltraView 800, BK Medical, Amsterdam, The Netherlands). We discarded the uroflowmetry data when the voided was less than 150 mL [11]. We also used the validated Korean version of the International Prostate Symptom Score (IPSS). We measured the total prostate volume using transrectal ultrasonography (UltraView 800, BK Medical, Herlev, Denmark). All total prostate volume measurements were made by the same sonographer. We calculated the total prostate volume according to previous methods [12].

BPH was defined as IPSS  $\geq 8$  [13], maximal flow rate  $< 15$  mL/sec [14], and prostate gland volume  $\geq 30$  mL [13].

### Anthropometry and Biochemical/Hormonal Assay

The waist circumference (cm) was measured to the nearest 0.1 cm midway between the lowest rib and the iliac crest. Serum was drawn between 7:00 AM and 9:00 AM after an overnight fasting. The biochemical analysis measurements included prostate-specific antigen, fasting serum glucose level, and total cholesterol level. Serum testosterone was measured via radioimmunoassay by using a kit from Cisbio Bioassays, Inc. (Parc Marcel Boiteux, Codolet, France). The intra-assay coefficients of variation for all assays were less than 9%, and the interassay coefficients of variation were less than 12%. For each assay, all samples from each subject were used in the same assay run.

### Potential Confounders

Age [15], diabetes mellitus (DM) [15], hyperlipidemia [16], and obesity [15] are known to be risk factors for CP. Additionally, some reports demonstrated that low testosterone levels were associated with CP [17]. Age, DM, hyperlipidemia, hormonal imbalance, and obesity are also known as risk factors for LUTS/BPH [18]. Therefore, we adjusted these confounders when elucidating the relationship between LUTS/BPH and CP.

Obesity was assessed by waist circumference. DM was defined as fasting blood glucose  $\geq 126$  mg/dL, or use of antidia-

betic medication, or insulin [19]. Hyperlipidemia was defined as total cholesterol >240 mg/dL or use of antihypercholesterolaemic medication [19].

### Statistical Analysis

We excluded the following subjects from the study: (1) those who were administered certain drugs, including antipsychotics, alpha blockers, 5-alpha reductase inhibitors, or phosphodiesterase-5 inhibitors; (2) those who underwent surgery or were hospitalized in the last 3 months; and (3) those with pyuria. Finally, 103 subjects were included in this study.

First, we evaluated whether there were any differences in the prostate volume, maximal flow rate, average flow rate, residual urine volume, IPSS total score, IPSS voiding subscore, IPSS storage score, IPSS QoL score, CAL measurements and the percentage of cases of prostate volume  $\geq 30$  mL, maximal flow rate <15 mL/sec, maximal flow rate <10 mL/sec, IPSS total  $\geq 8$ , IPSS total  $\geq 20$ , and BPH or CP according to the presence of CP or BPH using the Mann-Whitney U-test or Fisher exact test. Finally, we tested whether there was a relationship between CP and the prostate volume, maximal flow rate, average flow rate, residual urine volume, IPSS total score, IPSS voiding score, IPSS storage score, or IPSS QoL score after adjusting for confounding factors using logistic regression analysis.

All tests were 2-sided, with statistical significance set at  $P < 0.05$ . Analyses were conducted using R ver. 2.13.1 (R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

### Patient Characteristics

The characteristics of the study subjects are shown in Table 1. The median age, total prostate volume, IPSS total score, and maximal flow rate were 55.0 years, 29.0 mL, 9.0, and 20.0 mL/sec, respectively. In addition, the prevalence of CP was 27.2% (Table 1).

### Relationships Between CP and LUTS/BPH

In subjects with CP, the age, prostate volume, residual urine volume, IPSS total score, IPSS voiding score, IPSS storage score, and IPSS quality of life (QoL) score were higher, while maximal flow rate and average flow rate were lower.

In addition, the percentage of cases of prostate volume  $\geq 30$  mL, maximal flow rate <15 mL/sec, maximal flow rate <10 mL/sec, IPSS total  $\geq 8$ , IPSS total  $\geq 20$ , and BPH (IPSS  $\geq 8$ ,

maximal flow rate <5 mL/sec, and prostate gland volume  $\geq 30$  mL) were significantly greater in the subjects with CP.

Moreover, there were significant differences in the age, average flow rate, IPSS total score, IPSS voiding score, IPSS storage score, IPSS QoL score, and the percentage of cases of IPSS total  $\geq 20$  and BPH (IPSS  $\geq 8$ , maximal flow rate <15 mL/sec, and prostate gland volume  $\geq 30$  mL) between the 2 groups, which suggests that men with CP have more severe LUTS/BPH (Table 1).

In the subjects with BPH, CAL mean and the percentage of cases of CAL  $\geq 4$  mm and CP were significantly greater, which suggests that men with BPH had more chance of CP (Table 1). After adjusting for confounding factors, the IPSS total score, IPSS voiding score, and IPSS QoL were significantly, positively, and independently related to CP, which means that the presence of CP is significantly, positively, and independently related to severe LUTS/BPH (Table 2).

## DISCUSSION

In this study, we found that the IPSS and the percentage of cases of IPSS total  $\geq 20$  or BPH were significantly higher and the average flow rate was significantly lower in men with CP and that the IPSS total, voiding, and QoL score were significantly, positively, and independently related to CP, all of which suggest that LUTS/BPH severity is increased in men with CP.

The severity of LUTS is best measured using subjective symptom indices such as the IPSS questionnaire and objective diagnostic tools such as uroflowmetry, postvoid residual urine volume, and prostate size assessed by transrectal ultrasound [20]. In this study, we evaluated LUTS/BPH using all of these methods, which are widely used in urological clinical practice based on clinical guidelines [11].

In terms of IPSS questionnaires, Matsumoto et al. [21] reported the positive relevance of CP to urgency and a weak stream in their subanalysis of IPSS. However, there was no significant association of CP with the IPSS voiding score or IPSS storage score. In our study, we found significant associations of CP with the IPSS voiding score and IPSS storage score. Furthermore, there were significant associations of CP with the IPSS voiding score after adjustment for confounding factors. These discrepancies might be attributable to the limited number of subjects in the study of Matsumoto et al. (data from 88 male participants) and relatively young age of their participants compared to our participants (50.9 years vs. 55.0 years). Additional-

**Table 1.** Patients' characteristics

Variable	Total (n = 103)	CP (-) (n = 75)	CP (+) (n = 28)	P-value	BPH (-) (n = 93)	BPH (+) (n = 10)	P-value
Age (yr)	55.0 (52.5–58.0)	55.0 (52.0–56.0)	56.5 (54.0–58.0)	0.028*	55.0 (52.0–58.0)	55.0 (53.0–57.0)	0.727
Waist circumference (cm)	89.5 (85.0–93.0)	89.0 (85.0–93.0)	90.0 (86.0–92.0)	0.944	90.0 (85.0–94.0)	88.5 (87.5–90.5)	0.701
Hyperlipidemia	11 (10.7)	9 (12.0)	2 (7.1)	0.725	11 (11.8)	0 (0)	0.541
DM	19 (18.4)	15 (20.0)	4 (14.3)	0.704	17 (18.3)	2 (20.0)	1.000
Testosterone (ng/mL)	4.4 (3.3–5.6)	4.3 (3.3–5.7)	4.7 (3.3–5.5)	0.979	4.4 (3.3–5.6)	4.4 (3.1–5.8)	0.844
PSA (ng/mL)	0.8 (0.5–1.0)	0.8 (0.5–1.0)	0.8 (0.6–1.0)	0.299	0.8 (0.5–1.0)	1.8 (1.0–2.8)	<0.001*
Prostate volume (mL)	29.0 (24.5–34.0)	28.0 (23.5–32.5)	31.0 (26.5–37.5)	0.051	28.0 (24.0–33.0)	36.5 (32.0–45.0)	<0.001*
Prostate volume ≥ 30 mL	45 (43.7)	30 (40.0)	15 (53.6)	0.311	35 (37.6)	10 (100.0)	0.001*
Voiding volume (mL)	329.0 (244.0–467.0)	314.0 (249.5–512.5)	357.0 (213.0–432.0)	0.512	353.0 (257.0–487.0)	209.5 (132.0–250.0)	0.001*
Maximal flow rate (mL/sec)	20.0 (15.0–27.5)	21.0 (16.0–28.0)	18.0 (13.0–24.0)	0.085	21.0 (17.0–28.0)	11.5 (7.0–13.0)	<0.001*
Maximal flow rate < 15 mL/sec	22 (21.4)	12 (16.0)	10 (35.7)	0.057	12 (12.9)	10 (100)	<0.001*
Maximal flow rate < 10 mL/sec	7 (6.8)	4 (5.3)	3 (10.7)	0.599	3 (3.2)	4 (40.0)	<0.001*
Average flow rate (mL/sec)	9.0 (7.0–13.0)	9.0 (8.0–13.0)	8.0 (6.0–11.0)	0.047*	9.0 (8.0–13.0)	5.0 (2.0–5.0)	<0.001*
Residual urine volume (mL)	0.0 (0.0–40.0)	0.0 (0.0–40.0)	30.0 (0.0–40.0)	0.077	0.0 (0.0–40.0)	0.0 (0.0–40.0)	0.772
IPSS total	9.0 (6.0–15.5)	8.0 (5.0–13.5)	12.0 (7.5–20.5)	0.004*	8.0 (5.0–15.0)	19.5 (11.0–24.0)	0.002*
IPSS voiding	5.0 (3.0–10.5)	5.0 (2.0–9.0)	8.5 (4.0–15.0)	0.002*	5.0 (2.0–10.0)	11.5 (7.0–18.0)	0.003*
IPSS storage	4.0 (2.0–5.0)	3.0 (2.0–5.0)	4.0 (3.0–6.0)	0.021*	4.0 (2.0–5.0)	6.0 (3.0–10.0)	0.010*
IPSS QoL	3.0 (1.0–4.0)	2.0 (1.0–3.0)	3.0 (2.0–4.0)	0.015*	2.0 (1.0–4.0)	3.0 (3.0–4.0)	0.018*
IPSS total ≥ 8	66 (64.1)	45 (60.0)	21 (75.0)	0.238	56 (60.2)	10 (100.0)	0.032*
IPSS total ≥ 20	16 (15.5)	7 (9.3)	9 (32.1)	0.011*	11 (11.8)	5 (50.0)	0.007*
BPH	10 (9.7)	4 (5.3)	6 (21.4)	0.037	-	-	-
CAL mean	2.7 (2.5–3.2)	2.6 (2.4–2.8)	3.5 (3.3–3.7)	<0.001*	2.7 (2.5–3.1)	3.3 (3.0–3.7)	0.013*
CAL ≥ 4 mm (%)	15.9 (8.9–32.1)	11.1 (7.2–17.3)	43.2 (36.6–53.7)	<0.001*	14.8 (8.9–27.4)	38.1 (23.2–52.5)	0.008*
CP	28 (27.2)	-	-	-	22 (23.7)	6 (60.0)	0.037*

Values are presented as medians (interquartile range) or number (%).

DM, diabetes mellitus; PSA, prostate-specific antigen; IPSS, International Prostate Symptom Score; QoL, quality of life; BPH, benign prostatic hyperplasia (IPSS ≥ 8, maximal flow rate < 5 mL/sec, and prostate gland volume ≥ 30 mL); CAL, clinical attachment level; CP, chronic periodontitis.

Chronic periodontitis was defined as a 30% increase in the number of probed sites with a CAL of ≥ 4 mm among all probed sites. DM was defined as fasting blood glucose ≥ 126 mg/dL, or use of antidiabetic medication, or insulin. Hyperlipidemia was defined as total cholesterol > 240 mg/dL or use of antihypercholesterolaemic medication.

\*P < 0.05, statistically significant differences.

**Table 2.** Adjusted ORs of LUTS/BPH parameters for CP

Variable	OR (95% CI)	P-value <sup>†</sup>
Prostate volume (mL) <sup>a)</sup>	1.024 (0.960–1.093)	0.471
Maximal flow rate (mL/sec) <sup>b)</sup>	0.967 (0.899–1.040)	0.366
Average flow rate (mL/sec) <sup>b)</sup>	0.939 (0.793–1.113)	0.470
Residual urine volume (mL) <sup>b)</sup>	1.004 (0.995–1.012)	0.374
IPSS total <sup>c)</sup>	1.141 (1.045–1.245)	0.003*
IPSS voiding <sup>c)</sup>	1.243 (1.092–1.415)	0.001*
IPSS storage <sup>c)</sup>	1.219 (0.997–1.489)	0.054
IPSS QoL <sup>c)</sup>	1.676 (1.124–2.500)	0.011*

Chronic periodontitis was defined as a 30% increase in the number of probed sites with a CAL of  $\geq 4$  mm among all probed sites.

OR, odds ratio; LUTS, lower urinary tract symptoms; BPH, benign prostatic hyperplasia; CP, chronic periodontitis; IPSS, International Prostate Symptom Score; QoL, quality of life.

<sup>a)</sup>Adjusted for age, testosterone level, diabetes mellitus (DM), hyperlipidemia, and waist circumference. <sup>b)</sup>Adjusted for age, testosterone level, prostate volume, DM, hyperlipidemia, waist circumference, and voided volume during uroflowmetry. <sup>c)</sup>Adjusted for age, testosterone level, prostate volume, DM, hyperlipidemia, and waist circumference. <sup>†</sup>Logistic regression analysis.

\*P < 0.05, statistically significant differences.

ly, Matsumoto et al. [21] used a simple questionnaire, the chronic periodontal disease self-checklist, to define CP, which is a definite drawback to defining CP. Considering that the number of participants is related to the power of the data, that age is the most important factor for developing LUTS/BPH, and that the assessment of CP was more appropriate in our study, the aforementioned factors could explain the very different results between Matsumoto et al.'s and our data.

With regard to prostate volume, we first assessed the prostate volume in studies on the relationship between CP and LUTS/BPH. Boland et al. [22] reported an association between BPH and CP with the largest number of participants. However, they used International Classification of Diseases (ICD)-9 codes to represent medical conditions. It is well known that ICD-9 codes have low specificity [23]. Additionally, these data are limited by a lack of data on prostate size. Because the prostate volume is an important part of the diagnosis and pathogenesis of BPH, our data are valuable. In our study, the total prostate volume in men with CP was larger than that in men without CP, and the difference was nearly statistically significant. (28 mL vs. 31 mL, P=0.051). Further study is needed to investigate the relationship between CP and prostate volume.

In regard to uroflowmetry, we first used this method to examine the strength of the urinary stream as identified in reports about the relationship between CP and LUTS/BPH. Our findings demonstrated that the average flow rate was significantly lower in men with CP, which suggests that a weak urinary

stream is related to CP. Uroflowmetry is one of the most commonly used examinations for the objective measurement of voiding difficulty. Additionally, uroflowmetry is a time-consuming method to conduct, because participants need to hold their urine for approximately 2 to 3 hours. Therefore, our results have significant clinical implications. Our data showed that LUTS/BPH was significantly related to CP using objective assessment methods (uroflowmetry) as well as subjective methods (IPSS).

The reason that CP is related to LUTS/BPH is unclear. Additionally, in this clinical cross-sectional setting, it is difficult to determine the pathophysiology underlying these relationships. However, we can assume the reasons from previous data.

Metabolic syndrome refers to a cluster of cardiovascular risk factors, including atherogenic dyslipidemia, elevated blood pressure, obesity, hypertension, elevated glucose, a prothrombotic state, and a proinflammatory state [24]. Metabolic syndrome is a risk factor for both CP [25] and LUTS/BPH [26,27], which means that both CP and LUTS/BPH share metabolic syndrome as a risk factor. We believe that this similarity is an explanation of the relationship between CP and LUTS/BPH. The other possible explanation is the direct dissemination of oral pathogens to the prostate. There is a report that oral pathogens in subgingival plaque have simultaneously been detected in the prostate fluid of men [28]. In addition, it has been suggested that bacterial prostatitis is related to the development of BPH [29,30]. Therefore, prostatitis from oral pathogens might

be the cause of the association between CP and LUTS/BPH.

Systemic inflammation could be another explanation of the relationship. It has been reported that periodontal diseases are related to markers of systemic inflammation, such as interleukin (IL)-1, IL-2, tumor necrosis factor-alpha, and C-reactive protein. It has also been suggested that systemic inflammation affects voiding dysfunction [31]. Therefore, systemic inflammation induced by CP might exacerbate the voiding difficulties found in this study.

The present study has several limitations. First, this cross-sectional study could not be used to infer causality. Second, we could not adjust genetics and inflammations components as risk factors, both of which are one of important risk factors [8]. Additionally, this study might have a potential selection bias because we used a single institutional data. However, despite these limitations, we believe that the results of this study are highly relevant because among studies evaluating LUTS/BPH and CP, this study is the first to combine the use of transrectal ultrasound, uroflowmetry, and IPSS and the first to adjust for potential confounding factors including age and metabolic syndrome components.

The present results show that CP is closely related to LUTS/BPH in men in their 40s and 50s. Future investigations should explore the temporal relationship between CP and BPH/LUTS. To confirm this, a prospective, longitudinal data set would be needed.

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- Conceptualization: BKC, JHL
- Data curation: HH, YWP, YCK, JHL
- Formal analysis: JHL
- Funding acquisition: JHL
- Methodology: JHL
- Project administration: JHL
- Visualization: JHL
- Writing-original draft: HH, JHL

· Writing-review & editing: JHL

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