

### RELATIONSHIP BETWEEN THE NATIONAL INSTITUTES OF HEALTH CHRONIC PROSTATITIS SYMPTOM INDEX AND THE INTERNATIONAL PROSTATE SYMPTOM SCORE IN MIDDLE-AGED MEN ACCORDING TO THE PRESENCE OF CHRONIC PROSTATITIS-LIKE SYMPTOMS

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#### ABSTRACT

##### Background and objective

The characteristic symptom of chronic prostatitis (CP) is pain. Patients with CP often complain of lower urinary tract symptoms (LUTS); however, the voiding domain of the Chronic Prostatitis Symptom Index of the National Institutes of Health (NIH-CPSI) is not sufficient to evaluate LUTS. Therefore, we studied the relationship between the International Prostate Symptom Score (IPSS) and NIH-CPSI scores in men.

##### Materials and methods

We reviewed 870 men who visited our health care center for a general health check-up and completed IPSS and NIH-CPSI questionnaires between January 2014 and January 2019. An NIH-CPSI pain score  $\geq 4$  was defined as the presence of a prostatitis-like symptom (Group 1), and an NIH-CPSI pain score less than  $< 4$  was defined as the absence of a prostatitis-like symptom (Group 2). The relationship between IPSS and NIH-CPSI sub-scores was investigated. The associations between the IPSS total score and NIH-CPSI sub-scores were assessed using multiple linear regression analysis.

## Results

The mean IPSS total, voiding, storage, and quality-of-life (QOL) scores were higher in Group 1 than in Group 2. Group 1 had fewer subjects in the mild group and more in the moderate and severe groups than did Group 2. Among NIH-CPSI sub-scores, pain score showed the highest correlation between IPSS total ( $r=0.283$ ), voiding ( $r=0.266$ ), storage ( $r=0.237$ ), and QOL score ( $r=0.263$ ). In regression analysis, only the NIH-CPSI pain score was associated with the IPSS total score ( $B=0.962$ ,  $p<0.001$ ).

## Conclusions

The NIH-CPSI pain score showed a weak but statistically significant correlation with the IPSS, but the NIH-CPSI voiding score did not. This finding suggests that patients with CP-like symptoms need to be surveyed using the IPSS questionnaire. It will also be helpful to screen for comorbidities of benign prostatic hyperplasia and CP.

**Key Words:** *prostatitis; lower urinary tract symptoms; questionnaires; prostatic hyperplasia*

## INTRODUCTION

Lower urinary tract symptoms (LUTS) in aged men are often caused by prostate disorders, and of these, benign prostatic hyperplasia (BPH) is the most common.<sup>1,2</sup> To ideally assess LUTS, tools need to be noninvasive, inexpensive, simple, and reproducible with high diagnostic accuracy.<sup>3</sup> The International Prostate Symptom Score (IPSS) is a globally validated questionnaire that evaluates initial severity and treatment effects in men with BPH.<sup>4,5</sup>

Prostatitis is classified into four categories according to the National Institutes of Health: acute (I) or chronic (II) bacterial prostatitis; chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) (III); inflammatory (IIIa) or noninflammatory (IIIb); and asymptomatic inflammation of the prostate gland (IV).<sup>6,7</sup> Similar to BPH, the prevalence of CP is globally increasing and is estimated at about 5–9%. Additionally, its prevalence is 15–25% in primary medical institutes in Korea.<sup>8</sup>

The Chronic Prostatitis Symptom Index of the National Institutes of Health (NIH-CPSI) has been accepted as a basic screening questionnaire in patients with CP/CPPS.<sup>9</sup> NIH-CPSI consists of three domains (pain, voiding, and quality of life [QOL]) with nine items. Each sub-score and

total score are summed. Generally, the characteristic symptoms of CP are related to pain, and a summed total pain score  $\geq 4$  is defined as the presence of CP-like symptoms.<sup>10,11</sup> In a clinical setting, CP patients often complain of LUTS but they are commonly required to fill in the NIH-CPSI not IPSS. However, this is not sufficient to evaluate the severity of LUTS or to predict BPH using NIH-CPSI questionnaire alone in CP patients. Although the IPSS and NIH-CPSI are not diagnostic tools, they are useful for screening of BPH and CP in primary clinical fields. Therefore, in this study, we investigated the relationship between IPSS and NIH-CPSI scores including sub-group analysis according to the NIH-CPSI pain score.

## METHODS

### *Study Population*

We reviewed data from 1121 men who visited our health-care center for a general health check-up between January 2014 and January 2019. The inclusion criteria were as follows: (1) participants who were older than 40 years of age and (2) those who completed the questionnaires because individuals who are older than 40 years of age can undergo a health check-up including urologic function tests in our country.

The exclusion criteria were as follows: (1) participants who did not complete the questionnaires and (2) those who had been diagnosed and received ongoing medications for a psychogenic disease and/or those who had already been treated for urologic malignancy, CP/CPPS, and BPH with surgical treatment were not included in the study. Among those older than 70 years of age, only 22 men completed the questionnaires, and this sample was too small to perform analysis by age. Therefore, these participants were excluded, and 870 participants (40–69 years of age) were enrolled.

### **Ethics Statement**

The study protocol was reviewed and approved by the Institutional Review Board (IRB) (IRB number 2019-06-015). The requirement for informed consent was waived based on the study's retrospective design.

### **Questionnaire**

All participants completed the IPSS and NIH-CPSI questionnaires that had been validated in Korean versions after sufficient explanation of each item. The collected questionnaires were analyzed. An NIH-CPSI pain score  $\geq 4$  was defined as the presence of a prostatitis-like symptom (Group 1); an NIH-CPSI pain score  $< 4$  was defined as the absence of a prostatitis-like symptom (Group 2). We classified NIH-CPSI scores as mild (total  $\leq 14$ ), moderate (total  $> 14$ , total  $\leq 29$ ), or severe (total  $> 29$ ). The IPSS was classified as mild (total  $\leq 7$ ), moderate (total  $> 7$ , total  $\leq 19$ ), and severe (total  $> 19$ ).

### **Statistical Analysis**

Continuous variables were evaluated using the Student's *t*-test, and categorical variables were evaluated using the chi-squared test for inter-group comparisons. The correlations between IPSS questionnaire sub-scores (total, voiding, storage, and QOL) and NIH-CPSI questionnaire sub-scores (total, pain, voiding, and QOL) were

assessed. The associations between the IPSS total score and NIH-CPSI sub-scores were assessed using multiple linear regression analysis. Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY). All tests were two-sided and significant differences were set at  $p < 0.05$ .

## **RESULTS**

Table 1 shows the characteristics of the 870 participants and those of Group 1 (NIH-CPSI pain score  $\geq 4$ ) and Group 2 (NIH-CPSI pain score  $< 4$ ). The mean age was  $52.3 \pm 6.7$  years; 324 participants were in their 40s, 420 participants were in their 50s, and 126 participants were in their 60s. Proportions of the age groups did not differ significantly between Groups 1 and 2. Mean body weight, BMI, prostate size, and max flow rate showed similar results. Means of the IPSS total, voiding, storage, and QOL scores were  $10.4 \pm 6.8$ ,  $6.5 \pm 4.7$ ,  $3.9 \pm 2.8$ , and  $2.7 \pm 1.3$  in all subjects, respectively. All scores were significantly higher in Group 1 than in Group 2 ( $p < 0.001$ ). Means of the NIH-CPSI total, pain, voiding, and QOL scores also showed significant differences between the groups ( $p < 0.001$ ).

Table 2 shows the subclassification of the IPSS and NIH-CPSI total scores in total subjects and the difference between the groups. In Groups 1 and 2, IPSS total scores of mild, moderate, and severe subjects were 35 (26.9%) versus 369 (49.9%), 73 (56.2%) versus 299 (40.4%), and 22 (16.9%) versus 72 (9.7%), respectively. Group 1 showed fewer subjects in the mild group and more subjects in the moderate and severe groups than did those in Group 2 ( $p < 0.001$ ).

NIH-CPSI pain scores showed the statistically highest correlations between IPSS total ( $r = 0.283$ ), voiding ( $r = 0.266$ ), storage ( $r = 0.237$ ), and QOL scores ( $r = 0.263$ ) ( $p < 0.001$ ). The results between the NIH-CPSI total score and IPSS total ( $r = 0.072$ ,  $p = 0.033$ ) and voiding ( $r = 0.080$ ,  $p = 0.019$ ) scores showed statistically weak positive correlations.

**TABLE 1** Baseline Characteristics of All Participants

Variable	Total (N=870)	Group 1 (N=130) NIH-CPSI pain score $\geq 4$	Group 2 (N=740) NIH-CPSI pain score $< 4$	p-value
Mean $\pm$ SD				
Age, years	52.3 $\pm$ 6.7	52.8 $\pm$ 6.8	52.2 $\pm$ 6.2	0.346
Age group (%)				0.094
40–49 years	324 (37.2)	39 (30.0)	285 (38.5)	
50–59 years	420 (48.3)	66 (50.8)	354 (47.8)	
60–69 years	126 (14.5)	25 (19.2)	101 (13.6)	
Body weight, kg	72.2 $\pm$ 9.6	72.0 $\pm$ 9.5	72.3 $\pm$ 9.6	0.694
BMI, kg/m <sup>2</sup>	24.6 $\pm$ 2.9	24.8 $\pm$ 2.6	24.6 $\pm$ 2.9	0.529
Prostate size, g	27.1 $\pm$ 8.2	28.0 $\pm$ 7.1	27.0 $\pm$ 8.4	0.213
Qmax, ml/s	18.4 $\pm$ 9.4	17.7 $\pm$ 8.7	18.5 $\pm$ 9.5	0.395
IPSS score				<0.001
Total	10.4 $\pm$ 6.8	13.5 $\pm$ 7.0	9.8 $\pm$ 6.6	
Voiding	6.5 $\pm$ 4.7	8.7 $\pm$ 4.9	6.1 $\pm$ 4.6	
Storage	3.9 $\pm$ 2.8	4.8 $\pm$ 3.1	3.8 $\pm$ 2.7	
QOL	2.7 $\pm$ 1.3	3.2 $\pm$ 1.2	2.6 $\pm$ 1.3	
NIH-CPSI score				<0.001
Total	7.9 $\pm$ 5.3	15.1 $\pm$ 5.0	6.7 $\pm$ 4.3	
Pain	1.4 $\pm$ 2.4	6.2 $\pm$ 2.2	0.5 $\pm$ 0.9	
Voiding	2.6 $\pm$ 2.3	3.6 $\pm$ 2.6	2.4 $\pm$ 2.2	
QOL	4.0 $\pm$ 2.4	5.3 $\pm$ 2.3	3.7 $\pm$ 2.3	

SD = standard deviation; Qmax = maximum flow rate; IPSS = International Prostate Symptom Score; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QOL = Quality of Life.

**TABLE 2** Stratification of IPSS and NIH-CPSI Questionnaire Scores According to NIH-CPSI Pain Score

Variable	Total (N=870)	Group 1 (N=130) NIH-CPSI pain score $\geq 4$	Group 2 (N=740) NIH-CPSI pain score $< 4$	p-value
IPSS, N (%)				<0.001
Mild ( $\leq 7$ )	404 (46.4)	35 (26.9)	369 (49.9)	
Moderate (8–19)	372 (42.8)	73 (56.2)	299 (40.4)	
Severe ( $\geq 20$ )	94 (10.8)	22 (16.9)	72 (9.7)	
NIH-CPSI, N (%)				<0.001
Mild ( $\leq 14$ )	763 (87.7)	67 (51.5)	696 (94.1)	
Moderate (15–29)	105 (12.1)	61 (46.9)	44 (5.9)	
Severe ( $\geq 30$ )	2 (0.2)	2 (1.5)	0 (0)	

IPSS = International Prostate Symptom Score; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index.

**TABLE 3** Spearman’s Rank Correlation between IPSS and NIH-CPSI Sub-scores among Total Participants

NIH-CPSI	Total		Pain		Voiding		QOL	
	r	p-value	r	p-value	r	p-value	r	p-value
Total	0.072	0.033	0.283	<0.001	0.003	0.928	0.023	0.491
Voiding	0.080	0.019	0.266	<0.001	0.011	0.745	0.011	0.743
Storage	0.033	0.325	0.237	<0.001	0.016	0.632	0.047	0.164
QOL	0.053	0.117	0.263	<0.001	0.026	0.443	0.029	0.398

IPSS = International Prostate Symptom Score; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QOL = Quality of Life.

**TABLE 4** Multiple Linear Regression Analysis with IPSS Total Score and NIH-CPSI Sub-scores among Total Participants

	Pain score	Voiding score	Total score
IPSS total score	B=0.962	B=0.193	B=0.218
(r <sup>2</sup> =0.064)	t=5.751	t=0.866	t=1.770
	p<0.001	p=0.387	p=0.077

IPSS = International Prostate Symptom Score; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QOL = Quality of Life.

However, the NIH-CPSI voiding score showed no significant correlation between the IPSS total (r=0.003, p=0.928), voiding (r=0.011, p=0.745), storage (r=0.016, p=0.632), and QOL score (r=0.026, p=0.443) (Table 3).

The multiple linear regression model with NIH-CPSI scores showed that only the NIH-CPSI pain score was significantly associated with the IPSS total score (B=0.962, p<0.001). The NIH-CPSI voiding score was not associated with the IPSS total score in this model (B=0.193, p=0.387) (Table 4).

### DISCUSSION

In general, the most common symptoms of CP are perineal or low abdominal pain and discomfort. CP patients often complain of LUTS or erectile dysfunction (ED). Several studies reported correlations between CP and ED using

the NIH-CPSI and IIEF-5 questionnaires.<sup>12–15</sup> Nevertheless, it is unclear whether the voiding score of NIH-CPSI accurately reflects the severity of LUTS in patients with CP.<sup>16,17</sup> To our knowledge, this study is the first to examine the relationship between sub-scores of NIH-CPSI and IPSS. We propose that the IPSS would be helpful in the screening of LUTS in men, especially those with CP-like symptoms. Cho et al. studied the relationship between CP/CPPS and LUTS, and the prevalence of prostatitis-like symptoms. The patients like those in Group 1 in our study were aged 40–59 years and Korean (6.9%).<sup>18</sup> Marszalek et al. reported that the prevalence of prostatitis-like symptoms was 2.7% in 20–79-year-old men in Austria.<sup>19</sup> However, in our study, this proportion was 14.9%. The discrepancy might be explained by the age of participants. We enrolled 40–69-year-old participants because of the general health check-up policy of our country and poor compliance with questionnaire completion in older individuals. In this study, 60-year-old participants accounted for 14.5% of study participants. On the other hand, 20–30-year-old participants (33.4%) were enrolled in Marszalek et al.’s study. The NIH-CPSI score increased with age in men, and the IPSS revealed a similar pattern to that of the NIH-CPSI.

A few studies identified the relationship between histological prostate inflammation degree and severity of LUTS. Urkmez et al.

reported that there was a significant difference in the IPSS total score between the histological CP group and the BPH group.<sup>20</sup> Another study also reported that IPSSs were lower in patients with lower degrees of inflammation than those with higher degrees of inflammation.<sup>21</sup> A review of 30 studies reported that BPH patients with concomitant CP inflammation had more severe LUTS and were at increased risk of acute urinary retention.<sup>22</sup>

Nickel reported that the patients with chronic inflammation at biopsy had higher volumes than those of inflammation-negative patients.<sup>23</sup> In our study, prostate size showed no differences between the groups. The differences in examiners and the age of participants might explain the discrepancy. Nickel also stated that older age and higher degree of inflammation were significantly correlated with higher IPSS (8.8 vs. 8.2,  $p < 0.001$ ). Patients with chronic inflammation had higher storage IPSS sub-scores (4.3 vs. 4.1,  $p < 0.001$ ).<sup>23</sup> In our study, the mean IPSS storage scores in Groups 1 and 2 were  $4.8 \pm 3.1$  and  $3.8 \pm 2.7$  ( $p < 0.001$ ), respectively. Nevertheless, there was no significant correlation between the IPSS sub-scores and voiding scores of NIH-CPSI. In the correlation analysis, pain scores of NIH-CPSI showed the highest positive correlation with IPSS sub-scores, especially for total score ( $r = 0.241$ ,  $p < 0.001$ ). Unexpectedly, the voiding score of NIH-CPSI showed no significant correlation with any domain of IPSS, including total score (all  $p > 0.2$ ). This result supports the conclusion of our study. The questions for the domain of voiding symptoms were equivalent to Questions 1 and 2 in the IPSS. Mizuno et al. reported that Quick scores showed significant correlation with IPSS Questions 1 and 2.<sup>6</sup> In this study, we did not analyze the correlation between each question of the IPSS and NIH-CPSI. We will study this question presently. Although Questions 5 and 6 in the NIH-CPSI

are similar to Questions 1 and 2 in the IPSS, if a new questionnaire regarding voiding symptoms in patients with CP is developed, this point should be considered, as it will strengthen the accuracy of the questionnaire.

This study has some limitations. First, the IPSS and NIH-CPSI are not diagnostic tools for BPH and CP; they are just screening tools, and they do not dictate treatment. However, we focused on determining a meaningful association between IPSS and NIH-CPSI scores in participants with CP-like symptoms, not those with CP/CPPS. As aforementioned, the voiding domain of the NIH-CPSI is not sufficient to screen for LUTS compared to the IPSS. Second, the retrospective design and the cross-sectional nature make inferences problematic. Third, data were collected from a single institution, giving rise to potential selection bias. Thus, we plan to perform a multicenter study in the near future. Lastly, the protocol of the study involved a self-reported questionnaire, creating another limitation. Self-reported pain scores less accurately reflect the screening of CP than does histologic diagnosis using prostate biopsy. The pathology department of our center plans to collaborate on a study about this topic.

## CONCLUSIONS

Higher IPSS total, voiding, storage, and QOL scores were found in the NIH-CPSI pain score  $\geq 4$  group. NIH-CPSI pain scores showed the strongest correlation between IPSSs; however, the voiding scores showed no significant correlation with the IPSS. This suggests that patients with CP-like symptoms need to be assessed concurrently with the IPSS questionnaire.

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## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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