


# The Lifetime Risk and Prognosis of Chronic Prostatitis/Chronic Pelvic Pain Syndrome in the Middle-Aged Chinese Males

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## Abstract

Knowledge is limited about the lifetime risk of chronic pelvic pain syndrome (CPPS) occurrence in Chinese middle-aged males and the prognosis of CPPS patients with and without treatment. Noninstitutionalized Chinese males aged 40 to 81 years were enrolled in this study from a total of 76 local communities across 30 provinces of China. Information about the occurrence of CPPS, symptom relief, and previous treatment was collected. Based on completed answers to specific questions about self-reported and physician-diagnosed CPPS, the lifetime risk of CPPS occurrence was 25.3% (1,091 out of 4,315) in Chinese males aged 40 to 81 years. Over 77% of patients with CPPS had received treatment. The symptom relief rate was not significantly different between the treatment (57.3%, 142/248) and nontreatment (50.1%, 422/843) groups. Regardless of whether patients had received medical treatment, engagement in sedentary work and regular alcohol consumption had a significant negative influence, while marriage had a positive influence, on the prognosis of CPPS. A good prognosis could be achieved without treatment for some cases of CPPS, while others required a timely symptom-orientated treatment using adequate medications combined with lifestyle adjustment and follow-up.

## Keywords

lifetime risk of occurrence, prognosis, chronic pelvic pain syndrome, symptom relief, lifestyle adjustment

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According to the definition and classification of the latest version of National Institutes of Health (NIH) consensus, chronic pelvic pain syndrome (CPPS) is a pelvic pain condition in men where there is no proven infection or obvious local pathological change causing the pain (Krieger, Nyberg, & Nickel, 1999). CPPS can be further categorized into inflammatory or noninflammatory CPPS, depending on laboratory confirmation of the presence and levels of leukocytes in expressed prostatic secretion (EPS) (Pontari, 2002). Various causes and conditions have been assumed to be associated with CPPS, including prostatitis, sexual dysfunction, spicy food ingestion, alcohol consumption, cold weather, pessimistic personality, abnormalities in the central nervous system, and hormone imbalance (Sandhu & Tu, 2017; Sant, Kempuraj, Marchand, & Theoharides, 2007). The lack of clear etiology and understanding of pathogenesis has made clinical diagnosis of CPPS very challenging. In most circumstances, a tentative diagnosis of CPPS is largely based on medical history and a cluster of symptoms described by patients, in addition to limited or no pathological evidence. Since initial diagnosis of CPPS is typically vague with no supporting laboratory

evidence, clinical management of CPPS is usually targeted to symptoms described by individual patients. Many drugs and procedures are available to alleviate symptoms: for example,  $\alpha$ -blockers, anti-inflammatory drugs, phytotherapy, antidepressants, physiotherapy, acupuncture, and extracorporeal shock wave therapy (Anderson, Wise, & Nathanson, 2018; Doiron, Tripp, Tolls, & Nickel, 2018; Morgia et al., 2017; Zhang, Zhang, Yu, & Ma, 2019; Zhou, Liu, Li, & Liu, 2018). Results of these treatments remain

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controversial and require further evaluation. One or two antibiotics are typically included in a prescription as combined therapy for patients with CPPS, especially in those cases where leukocytes are present in EPS. Inconsistent outcomes have further obscured the efficacy of antibiotics use in treatment of CPPS, and there is a potential risk of creating antibiotic-resistant strains of bacteria (Liang et al., 2009a; Magri, Marras, Restelli, Wagenlehner, & Perletti, 2015; Nickel, 2017). It has been reported that the lack of clear evidence of consistent symptom relief by the most commonly prescribed abovementioned drugs suggests that there is no universal protocol that works for all patients with symptomatic CPPS (Magistro et al., 2016).

A critical question has been raised based on accumulated evidence from clinical practice: Do drug and/or other treatments have a significant impact on the prognosis of patients with CPPS? The argument was recently put forward that CPPS should be considered as a cluster of associated symptoms rather than a disease entity (Doiron, Shoskes, & Nickel, 2019). If this idea is proven to be true, it may influence clinical diagnosis and management of CPPS. As a part of a nationwide epidemiological survey on erectile dysfunction in Chinese adult males (Zhang, Yang, Li, & Li, 2017), this study was to estimate the lifetime risk of CPPS occurrence in Chinese middle-aged males, and investigate the prognosis of CPPS patients with and without treatment. The influence of other factors and conditions of daily life on the prognosis of CPPS in adulthood was also investigated. The results from this study will further the understanding of the relationship between the prognosis of CPPS and medical treatments, and help to develop a new module for clinical management of patients with CPPS.

## Materials and Methods

### *Study Design and Specific Questions About CPPS*

The survey used in this study was aimed at noninstitutionalized Chinese males at least 40 years old. A total of 4,315 participants from 76 local communities across 30 provinces of China (except for Xinjiang autonomies, Qinghai Province, Tibet, and Hong Kong) were enrolled in this study. Study participants ranged in age from 40 to 81 years, and consented in writing to provide their associated medical histories. Men with severe disease (such as malignant tumors) or psychological disorders, and men requiring assisted living, were not included in the study. As an attachment to the larger study questionnaire, the following four specific questions regarding CPPS were asked: (a) Have you ever been diagnosed with chronic pelvic pain syndrome by a doctor or other health professional at some point in your life (Yes/No)? (b) If Yes, did you receive any medical treatment after you were diagnosed with chronic

pelvic pain syndrome (Yes/No)? (c) If Yes, did the treatment you received help to resolve the symptoms associated with your complaint (Yes. Helped/No. No help)? (d) If No, the treatment did not help your symptoms, have you continued with or given up the treatment (Yes. Continued/No. Stopped)? Surveyed individuals were diagnosed by physicians (urologists and andrologists) at clinics or hospitals. Symptom relief, and symptoms unchanged or worse were reported by the patients themselves based on their perception of existing symptoms. Written informed consent was obtained from all participants before the survey. The study was approved by the Medical Ethics Committee of Peking Union Medical College Hospital (Study No. S-214). All participants attended education sessions where they received detailed instructions before completing the questionnaire. The questionnaire can be seen in the published paper of the larger study (Zhang et al., 2017).

### *Data Collection and Analysis*

Information about age, occupation, smoking and drinking habits, marital status, and medical history of diabetes and benign prostatic hyperplasia (BPH) were collected from the questionnaire and medical histories. Response percentages were calculated from the questionnaire. The lifetime risk of CPPS occurrence, and the rates of symptom relief, unchanged, or worse, in those who had and had not received treatment were calculated and analyzed. The prognosis of CPPS associated with the abovementioned factors and conditions was also assessed. The chi-square test was utilized to compare the categorical data in order to determine potential significant impacts of these factors and conditions on the prognosis of CPPS. SPSS 13.0 software was used for statistical analysis (SPSS, Inc., Chicago, IL, USA). The significance level was set at  $p < .05$ .

## Results

### *The Lifetime Risk and Prognosis of CPPS in Treated and Nontreated Patients*

A total of 5,210 completed questionnaires were counted as valid responses to the erectile questionnaire survey (Zhang et al., 2017). Of those, 4,315 participants completed the additional CPPS questions that were attached to the questionnaire, a response rate of 82.82% (4,315/5,210). Participants age ranged from 40 to 81 years, with the average age being  $55.79 \pm 9.41$  years (Table 1). Of the 4,315 Chinese males enrolled in this study, 1,091 (25.3%) had been diagnosed with CPPS at some point, including 843 (77.3%) who had received treatment for their associated symptoms, and 248 (22.7%) who had received no treatment. Of those who had received treatment, 422 (50.1%, 422/843) reported that

**Table 1.** Influence of Ages, Job Types, Drinking/Smoking, Marriage, and Chronic Diseases on Prognosis of CP/CPPS in Patients With and Without Treatment.

Prognosis Factors	Symptom relief		Symptom unchanged/worse		Total	
	Treatment, N (%)	Nontreatment, N (%)	Treatment, N (%)	Nontreatment, N (%)	Treatment, N	Nontreatment, N
<b>Ages</b>						
40–49	122(53.28)	53(55.21)	107(46.72)	43(44.79)	229	96
50–59	147(51.94)	47(66.20)	136(48.06)	24(33.80)	283	71
60–69	123(47.13)	35(53.85)	138(52.87)	30(46.15)	261	65
70 and above	30(42.86)	7(43.75)	40(57.14)	9(56.25)	70	16
<b>Types of job</b>						
Sedentary work	75(42.37)*	12(40.00)*	102(57.63)	18(60.00)	177	30
Nonsedentary work	347(52.10)	130(59.63)	319(47.90)	88(40.37)	666	218
<b>Smoking</b>						
No	204(46.68)*	49(45.37)*	233(53.32)	59(54.63)	437	108
Yes	218(53.69)	93(66.43)	188(46.31)	47(33.57)	406	140
<b>Drinking</b>						
No or occasionally drink	310(52.24)*	125(60.68)*	280(47.46)	81(39.32)	590	206
Daily or regularly drink	112(44.27)	17(40.48)	141(55.73)	25(59.52)	253	42
<b>Marriage status</b>						
Married	405(51.72)*	136(59.13)*	378(48.28)	94(40.87)	783	230
Unmarried or widowed	17(28.33)	6(33.33)	43(71.67)	12(66.67)	60	18
<b>Diabetes</b>						
No	380(51.49)*	134(57.51)	358(48.51)	99(42.49)	738	233
Yes	42(40.00)	8(53.33)	63(60.00)	7(46.67)	105	15
<b>BPH</b>						
No	351(55.19)*	117(63.24)	285(44.81)	68(36.76)	636	185
Yes	71(34.30)	25(55.56)	136(65.70)	20(44.44)	207	45

Note. BPH = benign prostatic hyperplasia; CP = chronic prostatitis; CPPS = chronic pelvic pain syndrome.

\*Statistically significant difference at  $p < .05$  (chi-square test).

their symptoms had been relieved, and 421 (49.9%, 421/843) reported that their symptoms had either worsened or not changed. Of those who had not received treatment, 142 (57.3%, 142/248) reported spontaneous symptom resolution, while 106 (42.7%, 106/248) reported that their symptoms were unchanged or worse. A chi-square test was performed, revealing that the symptom relief experienced by patients without medical intervention was slightly higher than those who had received medical treatment ( $p < .05$ ).

### *Influence of Different Factors and Conditions on Prognosis of CPPS*

Rates of symptom relief, unchanged, and worse associated with CPPS were analyzed in patients with and without medical treatment (Table 1). The purpose of this analysis was to determine whether other factors could have had an impact on the prognosis of CPPS, and whether these conditions interacted with medical intervention. Regardless of whether patients had received treatment or not, those engaged in sedentary work

experienced a significantly lower symptom relief rate (SRR) than those engaged in nonsedentary work ( $p < .01$ , chi-square). SRR was also significantly higher in patients who had no or occasional alcohol consumption compared to those who drank alcohol daily or more often, especially in cases where there was no medical treatment ( $p < .001$ ). Patients age had no significant influence on SRR; however, the percentage of patients with unchanged or worse symptoms was higher in all age groups with treatment compared to those with no treatment ( $p < .02$ ). A better SRR was observed in patients with a history of smoking compared to those with no history of smoking ( $p < .01$ ). A better SRR was also observed in the treatment groups in patients who had not had comorbidities of diabetes and/or BPH compared to those with the comorbidities. The differences were statistically significant ( $p < .01$ ). The percentage of symptoms unchanged or worse in the patients with diabetes and/or BPH was higher than in those without diabetes and/or BPH. It seems that marriage has a positive influence on the prognosis of CPPS, as SRR was higher ( $p < .01$ ), and the percentage of symptoms unchanged or worse was lower, in married

patients compared to unmarried or widowed patients, regardless of whether they had received treatment or not.

## Discussion

It has been reported that 35% to 50% of the male population is likely to be affected by symptoms associated with CPPS during their lifetime (Krieger et al., 2008; McNaughton Collins et al., 2001). The risk of having or having had CPPS increases with age, being 1.7 times greater in men aged 40 to 49 years, and 3.1 times greater in those aged 50 to 59 years, compared to those aged 20 to 39 years (Mehik, Hellstrom, Lukkarinen, Sarpola, & Jarvelin, 2000). As part of a nationwide epidemiological survey of erectile dysfunction in noninstitutionalized Chinese males (Zhang et al., 2017), this study demonstrated that the lifetime risk of CPPS occurrence was 25.3% in Chinese males over 40 years of age. This lifetime risk of CPPS was estimated based on answers to the specific questions included in the questionnaire completed by 4,315 surveyed individuals who were aware of their prostate-related disorders and CPPS, as diagnosed at some point in their lives by physicians. Prevalence estimates of CPPS reported from different countries, such as the United States, Canada, Singapore, and China, ranged from 2.7% to 16% (Habermacher, Chason, & Schaeffer, 2006; Krieger et al., 2008; Liang et al., 2009a; 2009b), all lower than the cumulative incidence of CPPS found in this study. The prevalence estimates of CPPS were mostly derived from epidemiological surveys, while the lifetime risk of CPPS was calculated as the cumulative proportion of CPPS appearing at some point in the lives of individuals within a population. Some patients with CPPS in this study had or had had CPPS, but it was completely resolved during the study. In the Finnish study (Mehik et al., 2000), the overall lifetime risk of prostatitis occurrence was 14.2% based on a population of men aged 20 to 59 years. Of those with prostatitis, 27% had suffered from symptoms at least once a year, and 16% suffered from persistent symptoms. The average participant age in this study was  $55.79 \pm 9.41$  years (age ranged from 40 to 81 years). The lifetime risk of CPPS seems much greater in the population aged 20 to 59 years in the Finnish study and other studies (Bartoletti et al., 2007; Mehik et al., 2000). In a prospective cohort study of older men recruited from six clinical centers in the Boston area, Daniels et al. demonstrated that the self-reported incidence of prostatitis and associated symptoms was 25% in 5,821 men over 65 years old (Daniels, Ewing, Zmuda, Wilt, & Bauer, 2005).

Among the 1,091 individuals who reported to suffer from associated symptoms of CPPS in this study, 77.3% had received medical intervention (specific treatment methods and types or doses of drugs were not the interest

of this study, and details of therapy received by patients with CPPS were not collected). Although a wide variety of treatment is available for CPPS, treatment efficacy is still controversial, as indicated in numerous clinical reports (Anderson et al., 2018; Daniels, Ewing, Zmuda, Wilt, & Bauer, 2005; Morgia et al., 2017; Zhou et al., 2018, 2019). There is no single medication or procedure that can completely resolve associated symptoms of CPPS and achieve satisfactory results for patients. Lack of knowledge about the pathogenesis and definitive etiology of CPPS is a major obstacle to cost-effective clinical patient management. Some recent studies indicate that lifestyle adjustment combined with a timely symptom-orientated treatment is preferable to an extended course of multiple drugs and varied instrumental therapies (Gallo, 2014; Zhang et al., 2015). The results from the current study indicate that 57.3% of patients with CPPS achieved symptom relief spontaneously without treatment. It is likely that this group of patients included those with a newly occurring episode of CPPS or less severe symptoms. In a 1-year follow-up cohort study, Nickel et al. observed that about one third of patients (those who usually had less severe symptoms of shorter duration) had experienced resolution of prostatitis-like symptoms after 1 year (Nickel, Downey, Nickel, & Clark, 2002). This observation also supports the idea that associated symptoms of CPPS are likely self-limited, and that such cases of CPPS may respond well to lifestyle changes, such as less sedentary work and lower alcohol consumption. Due to individual perceptions toward associated symptoms of CPPS, the patients who had received medical treatment in this study might have reported either severe and/or recurrent symptoms or mild symptoms with relatively high sensitivity, which might explain the lower rate of symptom relief (50.1%) in the treatment group. It has been reported that patients with persistent or recurrent episodes and more severe symptoms of chronic prostatitis were insensible to the treatment and prone to develop chronic pelvic pain (Turner, Ciol, Von Korff, & Berger, 2004). In this questionnaire-based study, the severity of symptoms could not be measured using the National Institutes of Health Chronic Prostatitis Symptom Index (Litwin et al., 1999). As a result, the SRRs could not be adjusted in the treatment group. Information about CPPS symptoms experienced, and whether they were relieved, unchanged, or worse, was collected from the questionnaire, and therefore self-reported by the participants. No objective measures were included. CPPS diagnoses made by urologists and andrologists in different hospitals followed the national guideline, and were not considered to have a large variation. Chart reviews and laboratory examinations (including EPS) were not conducted. The abovementioned were all limits in this study. Nevertheless, overall better SRRs



in the nontreatment group imply that the prognosis for some cases of CPPS can be improved without medical intervention.

Some of the risk factors commonly predisposing to CPPS were analyzed to understand the influence of lifestyle and other factors on the prognosis of CPPS (Zhang et al., 2015). Patients engaged in nonsedentary work and low or no alcohol consumption had significantly increased SRRs in both treated and nontreated groups, implying that increased daily activity and limited alcohol consumption could lead to a better resolution of CPPS. Sedentary jobs may not cause CPPS, but could intensify the severity of pain and discomfort associated with CPPS because of increased pelvic congestion while in a sitting position (Chen et al., 2016). Regular alcohol consumption was obviously associated with an increased percentage of patients with symptoms unchanged or worse in both the treated and untreated groups, which was consistent with previous studies (Collins et al., 2002; Herati et al., 2013; Krieger et al., 2008). One possible explanation is that the ethanol level in circulation could result in prostate congestion (Liu et al., 2019), aggravating local pain and discomfort. Although smoking is usually considered to be a harmful factor for CPPS (Chen et al., 2016), the adverse effect of smoking on the prognosis of CPPS was not obviously observed in this study. Instead, a better SRR was observed in patients with a smoking history in both treatment and nontreatment groups. Possible reasons are: (a) coincidentally, there were more smokers than nonsmokers in the symptom relief group, and (b) there was no distinction made between men who had smoked in the past but stopped before the survey and those who were current smokers when they completed the survey. Married men seemed to achieve a higher percentage of symptom relief and lower percentage of symptoms unchanged or worse than unmarried or widowed men: however, the number of patients in the latter group was relatively small. Moreover, the same trend was observed in patients without diabetes and/or BPH but not in patients with those comorbidities. It has been reported that a history of CPPS was associated with an eightfold increased risk for BPH (95% CI [6.8, 9.5]) and vice versa (Nickel et al., 2002). Definitive influence of diabetes and BPH on the prognosis of CPPS will be further studied with a large number of patients with these comorbidities.

## Conclusions

This nationwide survey data from 1,091 patients with CPPS from 4,315 valid questionnaires identify that the lifetime risk of CPPS occurrence is about 25% in Chinese males over 40 years old. A good prognosis could be achieved without treatment for some cases of CPPS,

while others required a timely symptom-orientated treatment using adequate medications combined with lifestyle adjustment and follow-up. Lifestyle adjustment, especially less sedentary work and lower alcohol consumption, could play an important role in symptom relief in patients with CPPS, whether or not they receive treatment.

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