

## REVIEW

# Chronic prostatitis and related psychological problems. Which came first: The chicken or the egg?

## A systematic review

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### Summary

**Introduction/Aim:** A spectrum of psychological problems is commonly found in CP/CPPS patients, though it is not yet clear whether, a priori, psychological dysfunctions are the cause of these pain syndromes, or whether these pain conditions are themselves causing psychological disturbances. In this article we present the current perspective on the impact of psychological problems in chronic prostatitis syndromes and we discuss the implications thereof from a clinical perspective.

**Materials and Methods:** A database and a manual search were conducted in the MEDLINE database of the National Library of Medicine, EMBASE, and other libraries using the key words “prostatitis syndromes”, “chronic bacterial prostatitis”, “chronic pelvic pain”, in various combinations with the terms “psychological issues”, “depression”, “anxiety”, “stress”, “unhappiness”, “cognitive status” and “personality”. Two independent reviewers performed data extraction. We included clinical studies with available information on chronic prostatitis and related psychological conditions. We considered full-text written papers. We excluded reviews and case reports. In order to reduce the risk of bias we analyzed only studies including patients with confirmed CBP or CP/CPPS. Bibliographic information in the selected publications was checked for relevant records not included in the initial search.

**Results:** Database search allowed us to retrieve 638 studies to which we added to 16 additional studies retrieved by hand-searching. After screening, 34 relevant papers were identified for thorough review. Most studies included patients with chronic pelvic pain and prostatitis-like symptoms, whereas a smaller number of studies included patients with methodologically confirmed CP/CPPS including studies with a microbiologically confirmed diagnosis of CBP. The psychosocial factors examined in the selected studies include pain, catastrophizing, stress, personality factors and social aspects. Comorbid psychiatric disorders evidenced in the studies included depression, anxiety and trauma-related disorders, somatization disorders, and substance abuse. Some studies investigated the association of pain with each individual psychological disturbance, while others examined the impact of pain in association with the overall quality of life. Sample size, study design and diagnostic measures varied among studies.

**Conclusions:** Despite limitations and variations in sample size, study design and diagnostic measures in all included studies, a relation between chronic prostatitis and psychological problems

is a consistent finding. The existing evidence does not permit to definitely conclude whether psychological problems are a risk factor for CP/CPPS or whether they represent an array of symptoms that are associated with the exacerbation of this disease.

**KEY WORDS:** Prostatitis syndromes; Chronic bacterial prostatitis; Chronic pelvic pain; Psychological issues: Depression; Anxiety; Stress; Unhappiness; Cognitive status; Personality.

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### INTRODUCTION

The term *Chronic Prostatitis* (CP) Refers to a group of syndromes of various etiology characterized by subacute and persistent prostatic inflammation although a large proportion of patients with prostatic inflammation don't have any symptoms (category IV, asymptomatic inflammatory prostatitis). The remaining patients, affected by category II *chronic bacterial prostatitis* (CBP) or by category III *chronic prostatitis/chronic pelvic pain syndrome* (CP/CPPS) may experience pelvic pain, including suprapubic pain, pain in the penis, testicles or perineum, pain during sexual intercourse or during ejaculation, dysuria (painful urination), nocturia and/or urinary urgency.

The duration and severity of pain and discomfort varies among patients. Chronic pain may be accompanied by several voiding disturbances mainly urgency and nocturia sexual dysfunction as well (1). However pelvic pain is the most prominent symptom (as compared with patients with BPH and those with erectile dysfunction (2).

Stress and a spectrum of various psychological problems are commonly found in CP patients, but it is not yet clear whether, a priori, psychological dysfunctions are the cause of these pain syndromes, or whether these pain conditions are themselves causing psychological disturbances (3). Moreover, the exact incidence of individual psychological problems remains unspecified.

In this article we present the current perspective on the impact of psychological problems in chronic prostatitis syndromes and we discuss the implications thereof from a clinical perspective.

## MATERIALS AND METHODS

A database and a manual search were conducted in the MEDLINE database of the National Library of Medicine, EMBASE, and other libraries using the key words “prostatitis syndromes”, “chronic bacterial prostatitis”, “chronic pelvic pain”, “males” in various combinations with the terms “psychological issues”, “depression” “anxiety”, “stress”, “unhappiness”, “cognitive status”, “personality”. Two independent reviewers performed data extraction by using identical extraction tables.

The search was carried out in accordance with *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) methodology (4) and were extended from first records up to 15<sup>th</sup> December 2022.

Titles were screened and any duplicates removed before abstracts and finally full-text articles were assessed for relevance (Figure 1). Reference lists were also checked. Relevant studies were evaluated by all authors and included in the narrative data synthesis.

We included clinical studies with available information on chronic prostatitis and related psychological problems. We considered full-text written papers. We excluded reviews and case reports. In order to reduce the risk of bias we analyzed only studies including patients with confirmed CBP or CP/CPPS. Bibliographic information in the selected publications was checked for relevant records not included in the initial search.

The methodological quality of included studies was assessed independently by 2 authors. Case-control and cohort were evaluated using the *Newcastle-Ottawa Scale* (NOS) as bias assessment tool (5).

## RESULTS

The initial search of the databases retrieved 668 studies. Title/abstract screening led to select 60 papers after exclusion of 618 papers that were judged as not directly relevant to the research question. Out of these 60 papers, 19 duplicates were removed. Sixteen additional studies were retrieved by handsearching. Review of the abstracts led to exclusion of 23 papers due to several reasons (review papers, papers reporting the same series described in other selected papers, congress reports/abstracts with limited information).

Finally, 34 relevant papers were identified for systematic review (6-39).

Specifically, 15 records reported case series, 13 were case-control studies and 6 were cross-sectional cohort studies. According to the quality assessment of Newcastle-Ottawa Scale, 11 studies out 19 were characterized by high quality with scores ranging between 7 and 9 (**Supplementary Materials**).

### Data synthesis

Most studies included patients with chronic pelvic pain and prostatitis-like symptoms, whereas a smaller number of studies included patients with methodologically confirmed CP/CPPS including studies with a microbiologically confirmed diagnosis of CBP.

The psychosocial factors examined in the selected studies include pain, catastrophizing, stress, personality factors and social aspects. Comorbid psychiatric disorders evi-

denced in the studies included depression, anxiety and trauma-related disorders, somatization disorders, and substance abuse. Some studies investigated the association of pain with each individual psychological disturbance, while others examined the impact of pain in association with the overall quality of life. Sample size, study design and diagnostic measures varied among studies.

Several studies showed that this disease has a significant negative impact on mental and physical quality of life domains (6-9). Men with CP/CPPS have significantly more disturbances in their psychological profile compared to both healthy control patients (10-12) and patients with chronic pain of different etiology (13). In CP/CPPS patients, pain has an impact in different domains of life (viz., sexual relationships) compared with patients with chronic pain of different etiology (viz., work and professional activity) (13). Aubin and coworkers, compared self-report questionnaires measuring demographic, pain, and sexual function of men with CP/CPPS with those of men without any pain condition. According to their findings, patients affected by CP/CPPS differed from controls in the domains of sexual desire, frequency of sexual intercourse, and in the quality of erectile and orgasm functions (14). Erectile dysfunction and decreased libido were reported by 43% and 24% of men with CP/CPPS, respectively (15).

One key difference between the populations investigated was the presence of depression and anxiety. Smith et al. compared (a) the sexual and relationship functioning of 38 male patients with CP/CPPS with those of their female partners, and (b) the sexual and relationship functioning of both CP/CPPS men and their partners with the same items assessed in 37 control couples. Compared to control males, men with CP/CPPS reported significantly more sexual dysfunction and symptoms of depression. Furthermore, the symptoms of depression mediated the relationship between some aspects of sexual function and male participant status as a patient or control (16). Therefore, in CP/CPPS subjects, the frequency of sexual activity decreased with increasing depression, the orgasm function decreased with increasing depression, and the quality of erectile function decreased with increasing pain symptoms. In addition, overall sexual satisfaction decreased with increasing pain symptoms (14). Thus, from these data it appears that the psychological profile of patients can deteriorate in function of the kind and severity of symptoms of CP/CPPS.

The severity of erectile dysfunction also correlates significantly with anxiety. Moreover, both depression and anxiety are closely correlated with chronic pain and urinary symptoms and contribute to the recurrence, refractoriness, and outcome of the disease (17, 18).

The incidences of depression and anxiety in patients with CP/CPPS are estimated to be approximately 20-50% and 40-60%, respectively. Besides depression and anxiety, a variety of somatic and psychological conditions were detected among CP/CPPS patients, including disturbances of several personality traits, mental distress, psychological stress, somatization, obsessive-compulsive disorder and interpersonal sensitivity (12, 19).

A large population-based cross-sectional survey demonstrated a significantly high occurrence of mental distress

and psychological stress related to CP/CPPS in Finnish men: suicidal thinking and fear of undetected prostate cancer or of having a sexually transmitted disease was reported by 17% of patients (15). Psychological stress has a major impact on the sexuality of CP/CPPS patients. In fact, the frequency of sexual activity decreased with increasing depression, arousal/erectile function decreased with increasing pain symptoms and orgasm function decreased with increasing depression. Moreover, sexual satisfaction decreased with increasing pain symptoms, stress appraisal, and decreasing belief of a relationship between emotions and pain (14).

Male participants of the MAPP study (*National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, USA*) had a significant rate of non-urological associated somatic syndrome (31%) associated with longstanding disease, more severe urological symptoms and higher rates of depression and anxiety (20).

A Chinese study compared the demographics, character, leukocyte counts in EPS, disease course, *NIH chronic prostatitis syndrome index* (NIH-CPSI), *self-rating anxiety scale* (SAS) and *self-rating depression scale* (SDS) of 291 CP/CPPS patients and 100 normal controls, in order to establish the psychological factors related with CP/CPPS. All patients were treated with the same protocol and followed-up for 6 weeks. According to this study, the rate of introversion was significantly higher while that of extroversion was significantly lower in the CP/CPPS group compared to the control group. Univariate and multivariate analyses with Cox regression revealed that anxiety, depression and disease course were the definite factors that negatively affected the prognosis of CP/CPPS, while other factors such as age, NIH-CPSI, character and leukocyte counts in EPS had no influence (12).

A Korean study investigated the association of personality traits with the baseline clinical characteristics and treatment outcomes of patients with CP/CPPS. According to this study, although extraversion, agreeableness, and conscientiousness can influence the clinical characteristics of patients with CP/CPPS, they do not affect the overall symptoms or the treatment response in those patients. In contrast, neuroticism is associated with a significantly poorer treatment response and with higher levels of depression and somatization (21).

A small study conducted in the USA measured the perceived stress, pain intensity, and pain-related disability 1, 3, 6, and 12 months after a health care visit resulting in a new diagnosis of nonbacterial prostatitis/pelvic pain. According to this study, greater perceived stress during the 6 months after the health care visit was associated with greater pain intensity and disability at 12 months (22). Another Chinese study compared anxiety, depression, erectile function and the scores of the NIH-CPSI among refractory CPPS patients who had never received any psychotherapy and non-refractory CPPS patients. No significant differences were observed in the chronic prostatitis symptom scores between the two groups, while anxiety and depression scores were significantly higher and that on erectile function was significantly lower in the refractory than in the non-refractory CPPS patient group (23).

A study based on the *Taiwan Longitudinal Health Insurance Database*, compared 8,088 subjects with CP/CPPS with

24,264 randomly matched controls and found that CP/CPPS is consistently and significantly associated with prior anxiety disorder in all age groups. In particular, subjects aged 40-59 years had the highest rates of prior anxiety disorder among cases compared to controls (24). These results reflected those of a previous study which found that men who experienced severe stress were 1.2 and 1.5 times more likely to report prostatitis than those whose lives were relatively stress-free (25). Similarly, a cross-sectional study from Estonia revealed a familial predisposition to CP/CPPS that may be associated also with susceptibility to respiratory tract infections (26).

## DISCUSSION

Chronic prostatitis is a relatively common male chronic pain condition. It is characterized by recurrent symptomatic episodes, or flare-ups. Between flare-ups, some patients are asymptomatic, while others complain of mild symptoms. Patients usually have a long history of persistent symptoms. It isn't clear what causes chronic pain in CP/CPPS, and the etiology of this disease is still uncertain. Various theories have been hypothesized, such as autoimmunity, persistent inflammatory statuses, neuroinflammation oxidative stress, pathogen and host-specific factors, pelvic floor tension myalgia, and differences in systemic pressure sensitivity (40-42). In addition, there is evidence that CP/CPPS patients show alterations of the hypothalamic-pituitary adrenal axis function in response to acute stress (9). Moreover, it has been suggested that stress is a potent factor in the development of CP/CPPS; for this reason the term "stress prostatitis" was proposed as an appropriate label for this condition (43). Currently, psychological factors are considered to play an important role in CP/CPPS and the possible association between personality disorders and chronic pelvic pain development has garnered increasing attention. For example, the validated UPOINT diagnostic-therapeutic algorithm, in its original or modified version (i.e. UPOINTS, including a sexual function domain), acknowledges the importance of psychological factors in CP/CPPS and includes a domain specifically focusing on the psychosocial functioning of patients (44, 45). In the UPOINT/UPOINTS system, items such as a history of clinical depression, ongoing antidepressant therapy, a history of abuse, maladaptive coping mechanisms (for example, catastrophizing), anxiety, or a high score of a depression scale such as HADS qualifies a patient as having a positive psychosocial phenotype.

Stress can have a significant impact on CP/CPPS, as it can worsen the symptoms and significantly affect the emotional state of patients by causing extreme overwhelming or distress (36). On the other hand, it was shown that the development of stress in CP/CPPS is time-dependent and is associated with subsequent pain and disability (23, 25). The severity of stress has been reported to depend on individual perception or subjective interpretation of causative factors rather than on the contents or frequency of factors causing stress (37). In a such a case, pain and disability are causative factors of stress while stress is a potent factor in the prolongation and perpetuation of the symptoms. In fact, psychological stress can lead to the

worsening of symptoms, and particularly to pain and discomfort during sexual intercourse, thus making patients more anxious and irritated. In turn, these negative emotions can worsen CP/CPPS, thus triggering a vicious circle (14). As a consequence, the quality of life of men with CP/CPPS can decrease to levels comparable to patients with severe illnesses (38, 39).

Existing data suggest that the experience and perception of pain is complex, and is maintained by educational, psychosocial, and behavioral variables (46). For this reason, the rate of introversion is significantly higher than that of extroversion in CP/CPPS patients (21), and this evidence may also explain the association of CP/CPPS with lower educational levels, poor emotional health and a lack of social support (44). Therefore, several patients are more prone to develop persisting diseases, especially in the presence of exaggerated media-reported information, describing chronic prostatitis as a very serious condition. In addition, because of the lack of correct understanding about this disease, many patients can feel anxious and worried, fearing that the sexual function and fertility will be affected by CP/CPPS. Other patients may fear of having undetected prostate cancer or of having a sexually transmitted disease (15). In certain patients, persistent urinary symptoms may lead to weak masculine identity disorder (47). Given that depression and anxiety are closely correlated with chronic pain, urinary symptoms, sexual dysfunction and weak masculine identity (14, 37), it could be assumed that, in addition to stress perception, psychological problems, personality traits, educational and behavioral variables can be considered as factors causing or deteriorating symptoms in patients with CP/CPPS. This hypothesis explains the high incidence of anxiety and depression in treatment-resistant chronic bacterial prostatitis (24).

Given the familial predisposition to CP/CPPS, the high incidence of CP/CPPS among men who experience severe stress and the fact that CPPS is consistently and significantly associated with prior anxiety disorders (24, 26), several researchers suggested CP/CPPS patients to be psychologically seriously ill. In fact, studies on quality-of-life outcomes suggest that psychiatric disorders strongly coexist with CP/CPPS (48). However, in a study by de la Rosette and coworkers, it was shown that differences in scores of personality inventory (NVM), symptom checklist (SLC-90), and depression inventory (IDD) between CP/CPPS patients and controls were not of a great magnitude, and in any case of lesser extent compared with differences in scores from psychiatric patients (10). In addition, Fishbain *et al.* showed that some trait tests and inventories may not be pain state-independent, and therefore may interpret post-pain development personality profiles as being indicative of the true pre-pain personality structure (49).

## CONCLUSIONS

Despite limitations and variations in sample size, study design and diagnostic measures shown by the studies included in this review, the relation between chronic prostatitis and different psychological conditions is a consistent finding. The existing evidence does not permit to definite-

ly conclude whether psychological problems are a risk factor of CP/CPPS or whether they represent a complex of symptoms that characterize the exacerbation of this disease. However, it seems logical that patients living with chronic (persistent or long-term) physical conditions such as CBP and CP/CPPS are more likely to experience poor mental health, characterized by impaired emotional, psychological, and social well-being. In turn, individuals whose mental well-being is affected are at a higher risk of developing such physical conditions.

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