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Pelvic Pain

National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) Symptom Evaluation in Multinational Cohorts of Patients with Chronic Prostatitis/Chronic Pelvic Pain Syndrome

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Abstract

Background: The assessment of patients with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) in everyday practice and clinical studies relies on National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) scores for symptom appraisal, inclusion criteria for clinical trials, follow-up, and response evaluation.
Objective: We investigated multiple databases of CP/CPPS patients to determine the prevalence and impact of pain locations and types to improve our strategy of individualized phenotypically guided treatment.
Design, setting, and participants: Four major databases with CPSI scores for nonselected CP/CPPS clinic patients from Canada, Germany, Italy, and the United States.
Outcome measurements and statistical analysis: Individual question scores and subtotal and total scores of CPSI were described and correlated with each other. Ordinal regression analysis was performed to define pain severity categories.
Results and limitations: A total of 1563 CP/CPPS patients were included. Perineal pain/discomfort was the most prevalent pain symptom (63%) followed by testicular pain (58%), pain in the pubic area (42%) and penis (32%); reports of pain during ejaculation and voiding were 45% and 43%, respectively. European patients had a significantly higher number of pain localizations and symptoms compared with North American patients ($p < 0.001$). Severity of pain correlated well with frequency of pain ($r = 0.645$). No specific pain localization/type was associated with more severe pain. Correlation of pain domain with quality of life (QoL) ($r = 0.678$) was higher than the urinary domain ($r = 0.320$). Individually, pain severity ($r = 0.627$) and pain frequency ($r = 0.594$) correlated better with QoL than pain localization ($r = 0.354$). Pain severity categories results for NIH-CPSI item 4 (0–10 numerical rating scale for average pain) were mild, 0–3; moderate, 4–6; severe, 7–10; CPSI pain domain (0–21): mild, 0–7; moderate, 8–13; and severe, 14–21.
Conclusions: Pain has more impact on QoL than urinary symptoms. Pain severity and frequency are more important than pain localization/type. Cut-off levels for disease severity categories have been identified that will prove valuable in symptom assessment and the development of therapeutic strategies.

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1. Introduction

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a frequently occurring disease [1,2] with a complex and heterogeneous etiology. The syndrome is characterized by pelvic pain, voiding symptoms, and additional phenotypic signs that are still poorly defined. Specific biomarkers for diagnosis and disease severity assessment are not available. The current diagnosis and clinical monitoring of CP/CPPS patients is based on multiple investigations including structured symptom assessment and the exclusion of obvious etiologic causes such as bacterial pathogens. To structure the assessment of CP/CPPS patients, the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) was developed in 1999 [3]. The NIH-CPSI is a formally developed and psychometrically validated instrument for the evaluation of CP/CPPS symptoms. It contains 13 items that are scored in three discrete domains: pain, urinary symptoms, and the impact on quality of life (QoL). In early studies, the NIH-CPSI was shown to be reliable and valid [4]. The NIH-CPSI total score and pain and QoL subscores are responsive to change [5]. A re-scored questionnaire was also evaluated, and although the re-scored NIH-CPSI provided better face validity than the standard score, additional calculation efforts were required that yielded only marginal improvements in performance [6]. The original NIH-CPSI therefore currently provides a valid assessment tool and outcome measure in the management of men with CP/CPPS, which is also commonly used in clinical trials [7–12], as well as in the evidence-based evaluation of treatment effects [13–15]. However, patient cohorts included in clinical trials are often highly selected populations and do not necessarily reflect the clinical situation.

Treatment strategies currently follow a more individualized, phenotypically based approach, where symptom quality assessment and the impact on health are drivers of patient management [16–19].

In this study we assessed the symptom characteristics of a multinational unbiased, nonselected population of CP/CPPS patients by NIH-CPSI; investigated the prevalence and impact of symptoms on QoL in this cross-sectional clinical population of CP/CPPS patients; and established cut-off values for pain severity categories.

2. Materials and methods

Four major databases with CPSI scores for nonselected CP/CPPS clinic patients from Canada, Germany, Italy, and the United States/Canada were included in this investigator-initiated nonprofit study. Of 1638 patients, 1563 patients (95.4%) with complete data from the NIH-CPSI score were selected for further analysis.

The individual question (Q) scores, subdomain scores, and total scores of the NIH-CPSI questionnaire are described. The pain localization (Q1A, Q1B, Q1C, Q1D), pain symptom (Q2A, Q2B), and pain quality questions (Q3 [pain frequency], Q4 [pain severity]) were related to each other. The impact of pain and voiding symptoms was calculated by correlating the individual question scores and subdomain scores with the QoL questions and subdomain. Validated NIH-CPSI translations in German or Italian were administered to European patients [20,21].

2.1. Statistical methods

Averages of these ordinal scores are shown as means (standard deviation [SD]) to allow for comparison with literature, but also as median (interquartile range [IQR]). For a comparison of independent samples, the nonparametric Mann-Whitney *U* test was used (a two-sided *p* value <0.05 was considered statistically significant). The chi-square test was calculated to test the null hypothesis for independence of pain symptoms versus urinary symptoms or QoL, and the nonparametric Spearman rank correlation (ρ) coefficient was used to investigate the relationship between two ordered categorical variables. The closer the value of ρ to either +1 or -1, the stronger the correlation.

The method for determining the optimal cut-off values of pain severity for mild, moderate, and severe pain in CP/CPPS was adapted from Serlin et al. [22] and Jensen et al. [23]. The subject's pain intensity was rated as mild, moderate, or severe using the numerical rating scale (NRS) (Q4; range: 0–10) and the pain domain score (Q1–4; range: 0–21) of the NIH-CPSI and calculating its pain interference. The NIH-CPSI total scores were not examined because the measure for pain interference would be part of the NIH-CPSI total score. Pain interference is the extent to which pain interfered with daily activities and QoL as represented by the QoL/impact domain of the NIH-CPSI (Q7–9), ranging from 0 to 12. Traditionally, on a 0–10 NRS, pain severity of 3 or 4 has been the upper boundary for mild pain, 4 or 5 the lower boundary for moderate pain, 6 or 7 the upper boundary for moderate pain, and 7 or 8 the lower boundary for severe pain. Thus there are four commonly used combinations of these boundary points [22]:

- CP (cut-off point upper limit of mild/moderate) 3/6: mild 1–3, moderate 4–6, severe 7–10
- CP3/7: mild 1–3, moderate 4–7, severe 8–10
- CP4/7: mild 1–4, moderate 5–7, severe 8–10
- CP4/6: mild 1–4, moderate 5–6, severe 7–10

A series of four analyses were performed using ordinal regression with classification group (mild, moderate, severe) as the grouping variable and pain interference as the dependent variable to determine which cut-offs were most able to distinguish mild from moderate and moderate from severe pain.

A similar analysis was performed to identify severity categories of the NIH-CPSI pain domain. Nickel et al. suggested a pain domain score ≥ 8 is moderate/severe [1]. The cut-off value between moderate and severe has never been identified. Cut-off point combinations to identify severity categories of the pain domain were set around both tertiles: cut-off points for mild/moderate were analyzed at 6, 7, or 8, and cut-off points for moderate/severe at 13, 14, and 15. Thus nine possible cut-off combinations were analyzed.

The chi-square test was applied as an indicator of the degree of relation between the scores in the pain categories and the pain interference. The chi-square statistic indicated the degree of relation between the scores in the pain categories and the pain interference using various cut-off values of pain severity. The most optimal classification strategy (the one that uses cut-offs where the greatest difference in pain interference occurs) could therefore be identified as that classification strategy associated with the largest chi-square value.

3. Results

The mean (SD) total NIH-CPSI of the whole group was 20.4 (7.8) and the median (IQR) 21 (15–26) (Fig. 1; Table 1). The differences between North American ($n = 379$) and European ($n = 1184$) groups in total CPSI, pain domain (due to a higher number of pain localizations and symptoms in the European patients), and QoL domain scores were