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Psychological and sexological assessment of patients with chronic prostatitis

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Summary *Purpose: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is characterized by a multiform clinical presentation requiring a differentiated treatment based on different phenotypes including the psychosocial and sexual domains. The aim of this study was assessing the complex correlations between somatic, psychological, and sexual symptoms of CP/CPPS patients.*
Materials and methods: We performed a cross-sectional study on patients attending a Prostatitis Clinic. Patients were administered the following questionnaires: National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI), International Prostate Symptom Score (IPSS), International Index of Erectile Function (IIEF), Premature Ejaculation Diagnostic Tool (PEDT), Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder 7-item (GAD-7), Oxford Happiness Questionnaire (OHQ), and Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire (TEMPS-A).
Results: Linear regression analyses show highly significant correlations between scores of the NIH-CPSI and the scores of the GAD-7, PHQ-9 and OHQ psychometric questionnaires. IPSS scores correlate significantly with the psychometric scores only when a non-parametric analysis is performed. IIEF and PEDT sexual function scores did not correlate with any of the psychometric tests. NIH-CPSI scores correlate positively with most of the TEMPS-A profiles but the hyperthymic profile correlated negatively with the total and QoL NIH-CPSI and with PEDT scores.
Conclusions: Scores measuring anxiety, depression, and psychological well-being in patients with CP/CPPS are strictly correlated with prostatitis-like symptoms although they are poorly correlated with symptoms of prostatism, as measured by IPSS, and not correlated with scores of sexual dysfunctions, as measured by IIEF and PEDT. A hyperthymic temperament may temperament may increase resilience against the disease.

KEY WORDS: *Chronic prostatitis; chronic pelvic pain syndrome; Depression; Anxiety; Affective temperaments.*

INTRODUCTION

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a common clinical condition presenting with a variety of signs and symptoms including chronic pain, voiding symptoms, sexual and psychosocial disturbances (1). The importance of recognizing the psychological impact of CP/CPPS has been taken into primary consideration by the UPOINT phenotyping and therapeutic algorithm (2), which rates a specific "*Psychosocial*" domain in the frame of the work-up of *chronic prostatitis* (CP) patients. It is suggested to use self-administered questionnaires to assess depression and anxiety and to measure negative thoughts associated with pain.

The implementation of the UPOINT system with the evaluation of a sexual domain ("S") has further extended the evaluation of patients with CP/CPPS who frequently present with significant rates of erectile and orgasmic dysfunction (3).

The aim of this study was an in-depth assessment of the complex correlations between somatic, psychological, and sexual disorders in CP/CPPS patients.

METHODS

Study design and endpoints

We performed a cross-sectional study on a cohort of patients with CP-CP/CPPS, consecutively enrolled among patients attending two outpatient clinics. The study was ethically approved by the local *Ethics Committee of Tzaneio Hospital* (protocol 8295/05-05-2022) and complied with the requirements of the Helsinki declaration.

The primary endpoint of the study was the association between the total and subdomain scores (pain, voiding symptoms, quality of life) of the *National Institute of Health-Chronic Prostatitis Symptom Index* (NIH-CPSI) (4), and the total score of the *Patient Health Questionnaire-9* (PHQ-9), a self-administered tool focusing on the presence and severity of depression (5).

Secondary endpoints of the study included the assessment of an association between the scores (i) of the NIH-CPSI questionnaire, (ii) of the *International Prostate Symptom Score* (IPSS) (6), (iii) of the erectile function domain of the *International Index of Erectile Function* (IIEF) (7), and (iv) of the *Premature Ejaculation Diagnostic Tool* (PEDT) (8) (independent variables), and the scores of the following psychosocial tests: (i) the PHQ-9 questionnaire (5), (ii) the

Generalized Anxiety Disorder 7-item questionnaire (GAD-7) (9), (iii) the *Oxford Happiness Questionnaire* (OHQ) (10), and (iv) the *Temperament Evaluation of Memphis, Pisa, Paris* and *San Diego Autoquestionnaire* (TEMPS-A, 39-item short version), which includes 5 domains, focusing on the presence of cyclotimic, depressive, irritable, hyperactive and anxious personalities (11).

Patient selection criteria

We included adult patients (>/= 18 years) who agreed to participate in the study, referring for long-standing (at least 18 months) documented signs and symptoms of category II CP or category III CP/CPPS assessed according to NIH criteria (12) after a thorough work up including clinical and laboratory assessments.

Exclusion criteria were: signs and symptoms present for a period shorter than 6 months; recent (< 8 weeks) category I acute bacterial prostatitis; neoplasia, indwelling catheters; nephrostomy; any chronic and/or painful and/or disabling illness significantly affecting the quality of life, potentially generating anxiety or depression; recent events (< 3 months) that may have had a considerable impact on the psychological profile of patients, possibly acting as confounders in this study (e.g., the loss of a child or spouse, divorce, loss of a job, other traumatic events).

Data collection

At referral, patients were informed about the aim of the study and reassured about the anonymous handling of their data. After signing an informed consent, patients underwent a thorough urological examination after being interviewed about their clinical history. Patients were also asked to fill the questionnaires listed above.

Questionnaires were collected by the consulting urologist and uploaded in a study database. Personal data were rendered anonymous in such a manner that patients were no longer identifiable in the database. Data were analyzed by a member of the research group (GP) in a blinded fashion.

Statistical analysis

Median and *interquartile range* (IQR) or mean and standard deviation were used as measures of the central tendency and data dispersion of non-continuous and continuous variables, respectively.

Simple linear regression

Simple linear regression was performed to analyze the significance of associations between baseline scores of the NIH-CPSI, IPSS, IIEF (short version) and PEDT questionnaires (independent variables), and the scores of the PHQ-9, GAD-7, OHQ and TEMPS-A (39-item short version) questionnaires (dependent variables in the present prediction model).

Both nonparametric (Kendall's rank coefficient 'tau') and parametric (Pearson's product-moment 'rho') correlation coefficients were calculated, to take into account the existence of non-linear relationships between the bivariates.

Sample size calculation

To estimate the effect size for sample size calculation, we referred to the *Koh et al.* (13) trial, reporting a significant correlation between the NIH-CPSI and PHQ-9 scores (p = 0.009), resulting in a Spearman's coefficient (ρ) equal to 0.307. Sample size calculations was performed using the G*Power 3.1.3 software (14). We computed that a sample of 127 patients was required to analyze by simple linear regression (one predictor) the primary endpoint of the study, namely, the correlation between the NIH-CPSI total score and the PHQ-9 depression score, with 95% power, a 5% alpha error probability, a f^2 effect size of 0.104 and a f^2 coefficient equal to 0.0942.

Logistic regression analysis

Simple binary logistic regression analysis was performed to ascertain the goodness of fit of models whereby the increasing symptom scores of tests (e.g., the NIH-CPSI) showing significant linear correlation with psychometric scores, would be significant predictor of dichotomized psychometric outcomes (e.g., no depression vs. moderate-to-severe depression).

The null hypothesis for the logistic regression was the absence of an association between the symptom score predictor and the psychologic condition dichotomic outcome. The coefficients of the logistic functions, the intercepts, the odds ratios, and the confidence intervals related to the odds ratios (95%CI) were calculated. The statistical significance of the model was evaluated by means of the Wald test and the likelihood ratio test.

The Hosmer/Lemeshow test was performed to evaluate the goodness-of-fit of the models, and the Nagelkerke-R^2 value was be calculated. For the Hosmer and Lemeshow test, the null hypothesis was that the number of expected dichotomic psychological disturbances – when the entire patient cohort is divided into 10 groups of approximately similar size – is not significantly different from the same outcomes observed in the overall logistic model. Values > 0.05 of the probability associated with the zero hypothesis indicated an acceptable goodness-of-fit.

For statistical analysis only two-tailed tests were performed, 95% confidence intervals were calculated, and the conditional probability of a type I error, in the presence of a true null hypothesis, was set at < 0.05.

Statistical softwares

Statistical analysis of linear and logistic regressions was carried out in the "R" software environment for statistical computing and graphics (https://www.r-project.org/). Logistic regression analysis was performed using the *car* and *lmtest* packages.

The *Hosmer* and *Lemeshow* goodness-of-fit test was performed with the *Resource* Selection package, whereas the Nagelkerke pseudo (ψ)-R2 was calculated using the *rcompanion* package. Odds ratios and 95% CIs for the model were calculated using the *epiDisplay* package. Intergroup differences between questionnaire scores were analyzed with the two-tailed Mann-Whitney-Wilcoxon test, using the R platform.

RESULTS

One hundred and forty-one consecutive patients were prospectively enrolled for the study between January 1st and November 30th, 2022. The median age of patients

Table 1.
Baseline scores of clinical symptom tests and psychological questionnaires.

Test	Median score	Interquartile range
NIH-CPSI (total)	18	16
NIH-CPSI (pain domain)	9	9
NIH-CPSI (voiding domain)	3	4
NIH-CPSI (QoL impact domain)	6	5
IPSS	7	9
IIEF	26	8.5
PEDT	4	5.5
GAD-7	7	7.25
PHQ-9	6	5
	Mean score	**Standard deviation**
TEMPS-A Cyclothymic	0.38	0.29
TEMPS-A Depressive	0.32	0.30
TEMPS-A Irritable	0.21	0.24
TEMPS-A Hyperthymi	0.53	0.28
TEMPS-A Anxious	0.33	0.38
Oxford Happiness	3.68	0.54

NIH-CPSI: National Institutes of Health Chronic Prostatitis Symptom Score (QoL, impact of the disease on the quality of life).
IPSS: International Prostate Symptom Score.
IIEF (1-5,15), Short International Index of Erectile Function (sum of questions 1, 2, 3, 4, 5, 15).
PEDT: Premature Ejaculation Diagnostic Tool.
GAD-7: General Anxiety Disorder-7.
PHQ-9, Patient Health Questionnaire-9.
TEMPS-A: Temperament Evaluation of Memphis, Pisa, Paris and San Diego - Auto-questionnaire version.

was 48 (IQR, 18). The median year of first diagnosis of CP was 2018.
Baseline clinical and psychological symptoms are shown in Table 1.

Linear regression
Table 2 shows the results of linear regression analyses comparing the scores of the NIH-CPSI, IPSS, IIEF and PEDT questionnaires with the GAD-7, PHQ-9 and Oxford questionnaires.
The results show highly significant correlations between all domains (pain, voiding, quality of life impact and total scores) of the NIH-CPSI test and the scores of the GAD-7, PHQ-9 and Oxford psychometric questionnaires.
Conversely, the IPSS, IIEF and PEDT tests correlate poorly and, in most cases, not significantly with any of the psychometric tests, except for IPSS, whose scores correlate significantly with the scores of the GAD-7, PHQ-9 and Oxford tests only when a non-parametric analysis is performed (The *Kendall's Tau*).

Temperament profiling
Table 3 shows the results of linear regression analyses comparing the scores of the NIH-CPSI, IPSS, IIEF and PEDT questionnaires with the scores of basic patient temperament profile, measured with the TEMPS-A test.
Highly significant correlations were found between NIH-CPSI scores (total score and pain, voiding and QoL subscores) with most of the TEMPS-A profiles. An exception was the hyperthymic profile, which correlated significantly and negatively with the total and QoL NIH-CPSI scores. In other words, a less severe impact of prostatitis on total and QoL NIH-CPSI correlated with higher hyperthymic scores.
Conversely, the IPSS, IIEF and PEDT tests correlate poorly and in almost all cases not significantly with any of the TEMPS-A profile scores. Exceptions were the significant correlation of the IPSS scores with the TEMPS-A depressive profile and the significant negative correlation of PEDT scores with the hyperthymic TEMPS-A profile.

Logistic regression models
We tested the NIH-CPSI and the IPSS interval scores as predictors versus dichotomized outcomes of the GAD-7, PHQ-9 and Oxford happiness scores.
Dichotomization was as follows: for the GAD-7 test, a score equal or higher than 5 predicted mild to severe anxiety according to *Spitzer et al.* (2006) (9); for the PHQ-9 test a score equal or higher than 10 predicted moderate to severe depression according to *Kroenke et al.* (2001) (5), and for the Oxford happiness test a score equal to 3.5 was the cutoff to discriminate between happy or unhappy responses (*Hills & Argyle, 2002*)(15).

Table 2.
Psychological profiling of chronic prostatitis patients included in our study according to the GAD-7, PHQ-9 and Oxford Happiness questionnaires. Scores are analyzed by linear regression against the total or subdomain scores of the NIH_CPSI, IPSS, IIEF and PEDT tests. Correlation coefficients are shown. Statistically significant differences are shown in bold.

	NIH-CPSI, Total Score		NIH-CPSI, Pain domain		NIH-CPSI, Voiding domain		NIH-CPSI, QoL domain	
	Kendall's Tau (P)	Pearson's r (P)	Kendall's Tau (P)	Pearson's r (P)	Kendall's Tau (P)	Pearson's r (P)	Kendall's Tau (P)	Pearson's r (P)
GAD-7	**0.285 (< 0.0001)**	**0.413 (< 0.0001)**	**0.316 (< 0.0001)**	**0.439 (< 0.0001)**	**0.188 (0.0023)**	**0.271 (0.0011)**	**0.283 (< 0.0001)**	**0.407 (< 0.0001)**
PHQ-9	**0.365 (< 0.0001)**	**0.464 (< 0.0001)**	**0.392 (< 0.0001)**	**0.475 (< 0.0001)**	**0.218 (0.0004)**	**0.290 (0.0004)**	**0.375 (< 0.0001)**	**0.469 (< 0.0001)**
Oxford Happiness Score	**-0.230 (0.002)**	**-0.335 (0.001)**	**-0.229 (0.002)**	**-0.335 (0.001)**	-0.1 (0.20)	**-0.21 (0.043)**	**-0.21 (0.005)**	**-0.288 (0.006)**
	IPSS		IIEF (1-5,15)		PEDT			
GAD-7	**0.170 (0.026)**	0.191 (0.075)	-0.129 (0.094)	-0.119 (0.27)	0.09 (0.25)	0.179 (0.096)		
PHQ-9	**0.198 (0.009)**	**0.267 (0.012)**	-0.077 (0.32)	-0.052 (0.63)	0.085 (0.27)	0.114 (0.29)		
Oxford Happiness Score	**-0.168 (0.024)**	-0.17 (0.102)	0.138 (0.067)	0.189 (0.078)	-0.097 (0.20)	-0.131 (0.22)		

NIH-CPSI: National Institutes of Health Chronic Prostatitis Symptom Score.
IPSS: International Prostate Symptom Score.
IIEF (1-5,15): Short International Index of Erectile Function (sum of questions 1, 2, 3, 4, 5, 15).
PEDT: Premature Ejaculation Diagnostic Tool.
GAD-7: General Anxiety Disorder-7.
PHQ-9, Patient Health Questionnaire-9.

Table 3.
Temperament profiling of chronic prostatitis patients included in our study according to the Temperament Evaluation of Memphis, Pisa, Paris and San Diego auto-questionnaire (TEMPS-A). TEMPS-A scores are analyzed by linear regression against the total or subdomain scores of the NIH_CPSI, IPSS, IIEF and PEDT tests. Statistically significant differences are shown in bold.

		NIH-CPSI, Total		NIH-CPSI, Pain domain		NIH-CPSI, Voiding domain		NIH-CPSI, QoL domain	
		Kendall's Tau (P)	Pearson's r (P)	Kendall's Tau (P)	Pearson's r (P)	Kendall's Tau (P)	Pearson's r (P)	Kendall's Tau (P)	Pearson's r (P)
TEMPS-A	Cyclothymic	**0.411 (< 0.0001)**	**0.590 (< 0.0001)**	**0.433 (< 0.0001)**	**0.612 (< 0.0001)**	**0.206 (0.0009)**	**0.344 (< 0.0001)**	**0.369 (< 0.0001)**	**0.512 (< 0.0001)**
	Depressive	**0.367 (< 0.0001)**	**0.503 (< 0.0001)**	**0.362 (< 0.0001)**	**0.479 (< 0.0001)**	**0.257 (< 0.0001)**	**0.361 (< 0.0001)**	**0.355 (< 0.0001)**	**0.468 (< 0.0001)**
	Irritable	**0.366 (< 0.0001)**	**0.485 (< 0.0001)**	**0.402 (< 0.0001)**	**0.512 (< 0.0001)**	**0.216 (0.001)**	**0.296 (0.0003)**	**0.310 (< 0.0001)**	**0.390 (< 0.0001)**
	Hyperthymic	-0.115 (0.058)	**-0.172 (0.042)**	-0.944 (0.127)	-0.132 (0.12)	-0.051 (0.42)	-0.075 (0.37)	**-0.132 (0.03)**	**-0.186 (0.02)**
	Anxious	**0.288 (< 0.0001)**	**0.393 (< 0.0001)**	**0.326 (< 0.0001)**	**0.421 (< 0.0001)**	**0.184 (0.006)**	**0.237 (0.004)**	**0.222 (0.0008)**	**0.302 (0.0002)**
		IPSS		IIEF (1-5,15)		PEDT			
	Cyclothymic	0.126 (0.11)	0.147 (0.17)	-0.10 (0.20)	-0.166 (0.12)	-0.026 (0.74)	0.044 (0.68)		
	Depressive	**0.233 (0.004)**	**0.294 (0.005)**	-0.06 (0.45)	-0.006 (0.94)	0.076 (0.36)	0.126 (0.24)		
	Irritable	0.11 (0.24)	0.049 (0.65)	0.116 (0.18)	0.123 (0.25)	-0.032 (0.71)	-0.06 (0.55)		
	Hyperthymic	-0.051 (0.51)	-0.84 (0.44)	0.143 (0.071)	0.20 (0.059)	**-0.199 (0.012)**	**-0.263 (0.013)**		
	Anxious	0.067 (0.43)	0.11 (0.31)	-0.15 (0.078)	-0.138 (0.19)	-0.0042 (0.96)	-0.0065 (0.95)		

NIH-CPSI: National Institutes of Health Chronic Prostatitis Symptom Score.
IPSS: International Prostate Symptom Score.
IIEF (1-5,15): Short International Index of Erectile Function (sum of questions 1, 2, 3, 4, 5, 15).
PEDT: Premature Ejaculation Diagnostic Tool.
TEMPS-A: Temperament Evaluation of Memphis, Pisa, Paris and San Diego - Auto-questionnaire version.

Bivariate analysis comparing all NIH-CPSI scores (pain, micturition, impact on QoL and total scores) with GAD-7. PHQ-9 and Oxford Happiness resulted in significant prediction models (Table 4). The only exception was the model comparing the voiding NIH-CPSI domain with the Oxford test of happiness.

Analysis of the predictor significance and goodness-of-fit of all models showed statistical significance in all cases, apart from the comparison of the voiding NIH-CPSI domain with the Oxford test of happiness (Table 5).

Conversely, logistic regression models comparing IPSS predictor scores against dichotomized anxiety (GAD-7), depression (PHQ-9) or happiness (Oxford) outcomes were found to be not statistically significant (Table 4). This was confirmed by the predictor significance and goodness-of-fit parameters shown in Table 5.

Severity of CP symptoms in patients showing various degrees of happiness, depression and anxiety

We investigated whether any significant difference could be observed by dichotomizing our population into two cohorts. Cohorts included patients with moderate/severe

Table 4.
Logistic regression models for Generalized Anxiety Disorder (GAD-7 test), depression (PHQ-9 test), or degree of happiness (Oxford test) as function of the score of the NIH-CPSI test (total score and pain, voiding symptoms and impact on the quality of life subdomains) and of the IPSS test. Significant results are shown in bold.

Psychometric test (outcome)	Logistic Model Parameters	Prostatitis/Prostate Symptom Scores (predictor)				
		NIH-CPSI, Total Score	NIH-CPSI, Pain domain	NIH-CPSI, Voiding domain	NIH-CPSI, QoL domain	IPSS
GAD-7	Intercept ± SE	-0.356 ± 0.37	-0.435 ± 0.31	0.285 ± 0.29	-0.56 ± 0.39	0.101 ± 0.37
	Corfficient ± SE (P)	**0.073 ± 0.020 (0.0003)**	**0.142 ± 0.034 (< 0.0001)**	**0.141 ± 0.07 (0.05)**	**0.220 ± 0.059 (0.0002)**	0.045 ± 0.033 (0.183)
	Odds Ratio (96% CI)	**1.08 (1.03-1.12)**	**1.15 (1.08-1.23)**	**1.15 (1-1.33)**	**1.25 (1.11-1.4)**	1.05 (0.98-1.12)
	EL50	4.88	3.07	2.03	2.58	2.23
PHQ-9	Intercept ± SE	-2.93 ± 0.54	-2.717 ± 0.49	-1.96 ± 0.36	-2.79 ± 0.57	-1.131 ± 0.39
	Corfficient ± SE (P)	**0.093 ± 0.021 (< 0.0001)**	**0.159 ± 0.030 (< 0.0001)**	**0.218 ± 0.072 (0.002)**	**0.227 ± 0.067 (0.0007)**	0.014 ± 0.033 (0.668)
	Odds Ratio (96% CI)	**1.1 (1.05-1.15)**	**1.17 (1.09-1.27)**	**1.24 (1.08-1.43)**	**1.26 (1.1-1.43)**	1.01 (0.95 to 1.08)
	EL50	31.65	17.06	8.99	12.31	78.21
Oxford Happiness Score	Intercept ± SE	2.09 ± 0.52	2.29 ± 0.51	1.51 ± 0.42	1.92 ± 0.52	1.741 ± 0.51
	Corfficient ± SE (P)	**-0.075 ± 0.026 (0.0038)**	**-0.155 ± 0.05 (0.0023)**	-0.201 ± 0.11 (0.072)	**-0.177 ± 0.074 (0.014)**	-0.999 ± 0.051 (0.051)
	Odds Ratio (96% CI)	**0.93 (0.88-0.98)**	**0.86 (0.77-0.95)**	0.82 (0.66-1.02)	**0.84 (0.73-0.97)**	0.9 (0.82-1)
	EL_{50}	27.76	14.74	7.51	10.85	17.42

NIH-CPSI: National Institutes of Health Chronic Prostatitis Symptom Score (QoL, impact of the disease on the quality of life of patients).
IPSS: International Prostate Symptom Score.
IIEF (1-5,15): Short International Index of Erectile Function (sum of questions 1, 2, 3, 4, 5, 15).
GAD-7: General Anxiety Disorder-7.
PHQ-9: Patient Health Questionnaire-9.
SE: Standard Error.
96% CI: 95% Confidence Interval.
EL_{50}: median effective level, i.e., symptom score associated with 50% probability of the psychometric test outcome.

Table 5.
Predictor significance and goodness-of-fit parameters of the logistic regression models shown in Table 3.

Psychometric test (outcome)	Test	Prostatitis/Prostate Symptom Scores (predictor)				
		NIH-CPSI, Total Score	NIH-CPSI, Pain domain	NIH-CPSI, Voiding domain	NIH-CPSI, QoL domain	IPSS
GAD-7	Wald	χ^2 = 12.86, P = 0.00035	χ^2 = 17.11, P < 0.0001	χ^2 = 3.75, P = 0.05	χ^2 = 13.63, P = 0.00022	χ^2 = 1.77, P = 0.18
	Likelihood Ratio	χ^2 = 14.91, P = 0.0001	χ^2 = 20.16, P < 0.0001	χ^2 = 4.06, P = 0.043	χ^2 = 15.50, P < 0.0001	χ^2 = 1.87, P = 0.17
	Hosmer & Lemeshow	χ^2 = 19.24, P = 0.013	χ^2 = 4.22, P = 0.83	χ^2 = n.a.	χ^2 = 1.62, P = 0.99	χ^2 = 35.93, P < 0.0001
	Nagelkerke	ψR^2 = 0.364	ψR^2 = 0.652	ψR^2 = 0.318	ψR^2 = 0.701	ψR^2 = 0.078
PHQ-9	Wald	χ^2 = 17.76, P < 0.0001	χ^2 = 16,49, P < 0.0001	χ^2 = 9.20, P = 0.0024	χ^2 = 11.38, P = 0.00074	χ^2 = 0.18, P = 0.67
	Likelihood Ratio	χ^2 = 21.93, P < 0.0001	χ^2 = 20.02, P < 0.0001	χ^2 = 9.54, P = 0.002	χ^2 = 13.20, P = 0.00027	χ^2 = 0.18, P = 0.67
	Hosmer & Lemeshow	χ^2 = 5.87, P = 0.661	χ^2 = 1.66, P = 0.98	χ^2 = 0.85, P = 0.99	χ^2 = 1.87, P = 0.98	χ^2 = 5.01, P = 0.75
	Nagelkerke	ψR^2 = 0.469	ψR^2 = 0.648	ψR^2 = 0.591	ψR^2 = 0.645	ψR^2 = 0.0081
Oxford Happiness Score	Wald	χ^2 = 8.36, P = 0.038	χ^2 = 9.27, P = 0.023	χ^2 = 3.21, P = 0.072	χ^2 = 5.99, P = 0.014	χ^2 = 3.80, P = 0.051
	Likelihood Ratio	χ^2 = 9.34, P = 0.022	χ^2 = 10.73, P = 0.0011	χ^2 = 3.28, P = 0.069	χ^2 = 6.50, P = 0.011	χ^2 = 3.91, P = 0.047
	Hosmer & Lemeshow	χ^2 = 6.83, P = 0.55	χ^2 = 6.94, P = 0.54	χ^2 = 3.22, P = 0.919	χ^2 = 0.83, P = 0.999	χ^2 = 7.77, P = 0.45
	Nagelkerke	ψR^2 = 0.293	ψR^2 = 0.485	ψR^2 = 0.315	ψR^2 = 0.412	ψR^2 = 0.201

NIH-CPSI: National Institutes of Health Chronic Prostatitis Symptom Score (QoL, impact of the disease on the quality of life of patients).
IPSS: International Prostate Symptom Score.
IIEF (1-5,15): Short International Index of Erectile Function (sum of questions 1, 2, 3, 4, 5, 15).
GAD-7: General Anxiety Disorder-7.
PHQ-9: Patient Health Questionnaire-9.
SE: Standard Error.
96% CI: 95% Confidence Interval.
P: statistical probability of an alpha error.
EL_{50}: median effective level, i.e., symptom score associated with 50% probability of the psychometric test outcome.
n.a.: not available.

versus absent or very mild anxiety or depression. The Oxford score was also used to distinguish patients showing a happiness versus little or no happiness. Dichotomization thresholds are indicated in the previous paragraph.

Table 6 shows that the pain, quality of life impact, and total scores of the NIH-CPSI test are significantly higher in patients with moderate to severe depression or anxiety and in patients with a poor Oxford happiness score. A significantly higher NIH-CPSI voiding score was related to moderate to severe depression, but no difference was observed between patients with or without symptoms of anxiety and between patients reporting or not psychological well-being.

The IPSS score was significantly higher in patients showing a poor Oxford happiness score.

DISCUSSION

The bidirectional relationship between psychological disturbances and prostatitis is complex, with several factors interacting or interfering with each other (16).

Our findings can be divided into two sections, the first evaluating correlations between measures of anxiety, depression, and psychological well-being and the scores of symptoms associated with CP/CPPS as measured with NIH-CPSI and questionnaires evaluating sexual function (IIEF or

Table 6.
Severity of CP symptoms in patients showing various degrees of happiness, depression and anxiety.
Statistically significant differences are shown in bold.

	GAD-7 0-4 median (IQR)	GAD-7 5-21 median (IQR)	P (Mann-Whitney)	PHQ-9 1-9 median (IQR)	PHQ-9 10-27 median (IQR)	P (Mann-Whitney)	Oxford happiness >3.5 median (IQR)	Oxford happiness </=3.5 median (IQR)	P (Mann-Whitney)
NIH-CPSI Total score	15 (14)	21 (19)	**0.0003**	18 (14)	28 (15)	**0.0002**	12 (15)	19 (9)	**0.0074**
NIH-CPSI Pain score	7 (9)	11(9)	**0.0002**	8 (8)	13 (9.5)	**< 0.0001**	4.5 (10)	10 (5)	**0.0083**
NIH-CPSI Voiding score	2 (3)	3 (3.5)	0.073	2 (4)	4 (5)	**0.0024**	2 (3)	3 (3)	0.21
NIH-CPSI Quality of life impact score	5 (5)	7 (6)	**0.0003**	6 (4)	10 (5)	**0.0005**	5 (6)	7 (3)	**0.025**
IPSS score	6 (10)	8 (8)	0.27	7 (8.75)	8 (10)	0.15	6 (9)	8 (10)	**0.048**
IIEF score	27 (4.5)	25 (10)	0.123	25.5 (9)	26 (8)	0.88	26 (6.75)	27 (14)	0.41
PEDT score	4 (4.75)	5 (6)	0.37	4 (5.5)	2.5 (6.25)	0.34	4 (5)	4 (5)	0.63

NIH-CPSI: National Institutes of Health Chronic Prostatitis Symptom Score.
IPSS: International Prostate Symptom Score.
IIEF (1-5,15): Short International Index of Erectile Function (sum of questions 1, 2, 3, 4, 5, 15).
PEDT: Premature Ejaculation Diagnostic Tool.
GAD-7: General Anxiety Disorder-7.
PHQ-9, Patient Health Questionnaire-9.

PDT), the second studying the correlation of CP/CPPS symptom intensity and different personality traits.

Among patients with CP/CPPS, a higher rate of psychiatric disorders as diagnosed by a psychiatrist using a semi-structured interview was previously observed (17). The higher rate of patients with CP/CPPS on psychiatric drugs can also be considered a reliable measure of the association between an existing substrate of psychiatric conditions and the subsequent onset of chronic prostatitis (18, 19).

A recent metanalysis (20) found several case-control studies showing higher scores of psychological disturbances in CP/CPPS using a variety of diagnostic tools. Some of those series showed a correlation of symptoms measured with NIH-CPSI and the severity of psychological dysfunctions.

The results of our study confirm a good correlation between NIH-CPSI scores (total, pain, voiding symptoms and, QoL) and measures of depression, anxiety, and psychological well-being although median values of these measures are indicative of mild disturbances.

However, the question whether chronic prostate inflammation is the cause of anxiety or depression, or, on the contrary, a chronic depressive or anxious condition can generate or enhance the symptoms of chronic prostatitis remains still unsolved.

In our series, logistic regression analysis of increasing NIH-CPSI score as predictor of the dichotomized GAD-7 test outcome (absent versus mild-to-severe anxiety) showed that anxiety in at least 50% of cases (EL50) is predicted by very low levels of the NIH-CPSI total score (4.88), pain score (3.07), voiding score (2.03) and QoL score (2.58). This finding could suggest that an anxious profile may be a "*background*" feature independent from the prostatitis syndrome. In other words, it may be hypothesized that traits of preexisting anxiety may be part of the general psychological profile of an individual, and that this may precede the manifestation of chronic prostatitis and, when the syndrome presents, lead to an exaggerated perception of its symptoms.

On the contrary, poor correlation of IPSS scores with GAD-7, PHQ-9 and Oxford scores may be explained by the structure of the IPSS questionnaire that is designed to assess symptoms of prostatism including voiding symptoms related to bladder neck obstruction rather than filling or irritative symptoms that are typical of prostatitis.

When our CP/CPPS patients with and without psychological disorders were separately assessed, the total NIH-CPSI scores and the sub scores for pain and QoL were higher in patients with psychological dysfunction compared to those without. Conversely, voiding sub scores were different in patients with depression but not in those with anxiety or psychological distress. This finding suggests that pain symptoms are crucial in the comorbidity of CP/CPPS and depression or anxiety.

Although the prevalence of erectile dysfunction was high in our series (52% of patients showed an IIEF score ≤ 26), we did not find significant correlations between anxiety, depression and psychological well-being scores and the IIEF-5 and PEDT scores. This observation contrasts with the common knowledge that psychological disorders negatively impact sexual function (21-23). On the contrary, the lack of a relationship between psychological dysfunctions and sexual functioning in a CP/CPPS population could be explained by a prevalent impact of other factors in the pathogenesis of sexual dysfunction in CP/CPPS subjects (inflammatory cytokines, vascular dysfunction) (24).

Information on the impact of personality traits in CP/CPPS patients is scarce. In the present study, we administered TEMPS-A, which is an instrument suitable for measuring traits which could make subjects vulnerable to affective episodes. Affective temperaments (depressive, anxious, irritable, hyperthymic, and cyclothymic) are regarded as subclinical manifestations and high-risk states for various affective disorders and some somatic diseases (25).

In our series, scores for depressive, anxious, irritable, and cyclothymic characters were significantly and positively correlated with NIH-CPSI scores, showing that all these tracts may increase the clinical expression of the disease. On the contrary, a hyperthymic character was negatively correlated with the severity of total NIH-CPSI scores and NIH-CPSI QoL sub score.

Temperaments affected the *International Prostate Symptom Score* (IPSS) with a similar trend, although correlation was statistically significant only for depressive temperament. In fact, as above discussed, both IPSS and NIH-CPSI (voiding domain) score voiding dysfunctions, but IPSS focuses more on voiding symptoms related to bladder neck obstruction (incomplete emptying, intermittency, weak stream and straining) rather than to storage symptoms, that are mainly related to prostatitis.

Affective temperaments showed a limited influence on scores of sexual functions in our series, although PEDT scores were negatively correlated with hyperthymic scores. The negative correlation of PEDT scores with hyperthymic temperament scores confirms that this personality trait could be present in subjects who are able to better manage symptoms associated with prostatitis.

A limitation of this study was the lack of a cohort of healthy controls, that would have been useful to better define the clinical relevance of the levels of psychological dysfunction observed in our patients with CP/CPPS. In addition, the study design did not include measures of catastrophism and perceived stress for a more complete assessment of the psychological profile of patients.

Previous studies confirmed an association between catastrophizing and pain intensity and quality of life whereas data on the influence of stress are less consistent (16). Another aspect that would have deserved more attention is the interrelationship between patients and their spouses, that could have an impact on painful symptoms (26). All these aspects will be the goal of future studies.

CONCLUSIONS

Our results confirm the strict correlation between scores measuring anxiety, depression and well-being and scores of prostatitis-like symptoms. In particular, the presence on anxiety disorders is predicted at very low NIH-CPSI values. IPSS, an assessment tool for measuring symptoms of patients with prostatism is more focused on bladder neck obstruction symptoms and correlated poorly with measures of anxiety, depression and well-being.

No correlations were observed between scores measuring

psychological conditions and those measuring erectile and ejaculatory dysfunction.

Information on temperamental profiling of patients with prostatitis-like symptoms is limited, although depressive, anxious, irritable, and cyclothymic temperaments are associated to more severe prostatitis symptoms whereas hyperthymic temperament seems to be protective against symptoms of prostatitis and ejaculatory dysfunction.

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