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Primary investigation of negative impact on sexual function in patients with chronic prostatitis

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Summary

Background: Chronic pain conditions can have a pronounced negative impact on sexual function. Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), in particular, can cause severe pelvic pain, which can interfere with numerous functions such as urination, sexuality, and overall quality of life. This study aims to determine the impact of CP/CPPS on sexual function and its association with the patient's symptom burden, the full version of the International Index of Erectile Function (IIEF) and Sexual Function Index (SFI) questionnaires and the UPOINT(S) classification.

Methods: 174 patients with CP/CPPS and predominantly type IIIB prostatitis (87.4%) were prospectively enrolled and received a comprehensive andrological work-up. In addition to laboratory chemical analyses, microbiological processing and semen analysis, a detailed assessment of sexual function and symptom burden was carried out using the International Prostate Symptom Score (IPSS), National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), IIEF and SFI questionnaires.

Results: The NIH-CPSI total score showed a moderate symptom burden with a median of 28 points, while the median IIEF score of 26 points was within the normal range, and the SFI score of 28 points indicated slightly impaired sexual function. In addition, 62.6% of the subjects showed an affected sexual domain in the UPOINT(S) classification. Univariate analysis revealed a significant association ($p < 0.05$) between IIEF scores and (i) CPSI total score, (ii) the SFI score, (iii) the number of affected UPOINT(S) domains – particularly (iv) the sexual domain (S), and (v) marital status. Multivariate analysis revealed significant associations between IIEF scores and (i) the SFI score, (ii) the UPOINTS total score and (iii) the UPOINTS sexual domain. However, the results of microbiology and inflammatory seminal parameters showed no association with items of sexual function in respective questionnaires.

Conclusions: The prevalence of sexual problems was high in CP/CPPS patients in our cohort and it was shown a statistically significant association with (i) the IIEF scores, (ii) the SFI score, (iii) and the NIH-CPSI total score, so routine assessment of sexual function in patients with CP/CPPS seems reasonable.

KEY WORDS: Chronic prostatitis; CPPS; Sexual function; Erectile dysfunction; Pelvic pain.

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INTRODUCTION

With lifetime prevalences ranging from 1.8 to 8.2%, chronic prostatitis is a rather common disorder (1, 2).

Risk factors include conditions that increase the patient's vulnerability to urinary tract infections and illnesses that can result in neuropathic pain (3). Chronic prostatitis is thought to be more likely to occur in patients with a history of urethritis caused by sexually transmitted infections (STIs) and in those with conditions that permit retrograde ascension of bacteria into the urethra and prostate (3-5). When discussing prostatitis, it is crucial to differentiate the condition from other causes of pelvic pain like benign prostatic hyperplasia, interstitial cystitis, and other forms of dysuria (6, 7). Acute bacterial prostatitis (category I), chronic bacterial prostatitis (category II), chronic nonbacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (category III), and asymptomatic inflammatory prostatitis (category IV) are the four categories into which the National Institutes of Health (NIH) has classified the manifestations of prostatitis (7). Category III is further divided into type IIIA, which exhibits inflammatory characteristics in the ejaculate, and type IIIB, which does not (7). The CP/CPPS category encompasses more than 90% of chronic prostatitis cases and is regarded as a primary pain syndrome (7). A prerequisite for the diagnosis of CP/CPPS is that the prostatic symptoms have been present for at least 3 months and that a urinary tract infection has been ruled out as the cause of the symptoms (1, 6-9). Since type II requires antibiotic therapy and type III requires non-antibiotic symptom-oriented treatment, it is clinically important to distinguish between the two conditions (7).

Chronic pain syndromes generally have a strong negative impact on quality of life, psychological well-being, and sexual function (10). Meta-analyses on chronic bladder pain syndrome showed significantly worse sexual function compared to non-sufferers, with significant improvement after reduction of the symptom burden within the framework of symptom-oriented therapy (11). A negative influence on the relationship and sexual function has also been demonstrated for musculoskeletal pain syndromes and female genital pain syndromes (10, 12). In light of this background, sexual and urinary dysfunction, as well as emotional disorders including anxiety, depression, or catastrophizing, are commonly linked to CP/CPPS (13). Sexual dysfunction was found in 62% of CP/CPPS patients, resulting in greater impairment of quality of life compared to CP/CPPS patients without sexual problems (14). However, only a few studies with small case numbers are available to date that address sexual function in

the context of chronic prostatitis (14-17). The *European Association of Urology* (EAU) has classified the CP/CPPS into subgroups based on the system that is largely affected, such as musculoskeletal, neurologic, or psychologic, in accordance with the clinical diversity of chronic pelvic pain (18). The UPOINT(S) approach, which traditionally comprises six domains, has shown promise for this phenotypic classification: U: urinary symptoms or micturition-related symptoms; P: psychosocial dysfunction; O: findings specific to the prostate; I: recurrent infections; N: systemic or neurological disease; T: tenderness in the muscles (18, 19). The category of sexual dysfunction (S: erectile or ejaculatory dysfunction, post-orgasmic pain) has been included in the UPOINT scheme, but research has not yet verified its added value (20, 21). For domains with positive findings, there are corresponding recommendations for targeted treatment (19, 22).

The aim of this prospective study is to assess the influence of CP/CPPS on sexual function using the UPOINTS classification system in association with IIEF and SFI questionnaires.

MATERIALS AND METHODS

Study population

This was a prospective, single-center, single-cohort observational study conducted in our urology department at the University of Giessen. As part of our special outpatient clinic for CP/CPPS all patients who were referred to our tertiary university department between January 2023 and March 2025 for suspected CP/CPPS were invited for this study (Ethical permission number 55/13). A total of 223 patients agreed and provided written informed consent.

Inclusion criteria for study participation were the presence of chronic prostatitis/CPPS and willingness to complete sexual health questionnaires. Exclusion criteria included the presence of acute prostatitis (NIH type I). Furthermore, only patients who had discontinued their medication with antibiotics, alpha-blockers, and PDE-5 inhibitors at least 14 days prior to their appointment were included. Participants were informed of this beforehand via a cover letter.

Clinical Investigations

All patients underwent a comprehensive andrological examination that comprised a structured review of their medical history by validated questionnaires for erectile dysfunction (full version of the *International Index of Erectile Function*, IIEF), lower urinary tract symptoms (*International Prostate Symptom Score*, IPSS), and chronic prostatitis (*National Institutes of Health Chronic Prostatitis Symptom Index*, NIH-CPSI), a physical examination, sex hormone analysis, a 2-glass urine test, and additional semen analysis (23-25). Since the IIEF primarily assesses erectile function but does not represent the entirety of all male sexual dysfunctions, the *Sexual Function Index* (SFI) was additionally assessed in each patient, which also includes sexual desire, ejaculation disorders, and general sexual satisfaction (23). Phenotyping was accomplished by using the categories of the UPOINT(S) system (20, 22). Ultrasonography was uti-

lized to measure the prostate and testicular volumes in accordance with clinical guidelines (26, 27). Additionally, any sonographic anomalies were carefully recorded.

Laboratory methods

Routine blood samples were taken from each patient to determine serum levels of *C-reactive protein* (CRP), testosterone, estradiol, and *prostate-specific antigen* (PSA) and measured via the central laboratory of the *Giessen University Hospital* (ADVIA and ADVIA Centaur, Siemens Health Care) using standard laboratory procedures. In case of low serum testosterone, a repeat measurement was performed at a second appointment to rule out hypogonadism.

Routine microbiological tests and semen analysis

Urine (first void urine, post-prostatic massage urine) and semen were tested for *sexually transmitted infections* (STIs) (*Mycoplasma genitalium*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Ureaplasma parvum*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis*) with *polymerase chain reaction* (PCR), and bacterial cultures were provided to rule out the presence of infections, as previously described (24, 28). For bacteriospermia, a bacterial count of more than 1000 *colony-forming units* (CFU) per milliliter of ejaculate was deemed significant (24,29). A bacterial count of 1000 colony-forming units per milliliter was considered significant for the urine samples (30).

According to WHO 2021 recommendations, a blind analysis of the semen was carried out within an hour of collection (31).

As part of standard processing, the concentration of seminal leukocytes that tested positive for peroxidase was determined (*Leucoscreen*, *FertiPro*) (31).

Additionally, an enzyme-linked immunoassay was used in each semen sample to assess *polymorphonuclear* (PMN) elastase, a marker of local inflammation, in cell-free seminal plasma (*Demeditec Diagnostics GmbH*). The *enzyme-linked immunosorbent assay* (ELI-SA) (*BD Biosciences*, San Diego, CA, USA) was used to measure the quantities of the inflammatory cytokine interleukin-8 (IL-8). The quantities of neutral α -glucosidase and fructose (total enzymatic activity) were measured using spectrophotometric techniques (29).

Statistical analysis

The statistical analysis was conducted using SPSS 29 for Windows (*IBM GmbH, Ehningen, Germany*).

Univariate and multivariate regression modeling was used to examine the association between the results of the SFI score and various clinical parameters. Only non-missing data were included in the linear regression model using a forward stepwise process. A value of $p < 0.05$ was considered statistically significant.

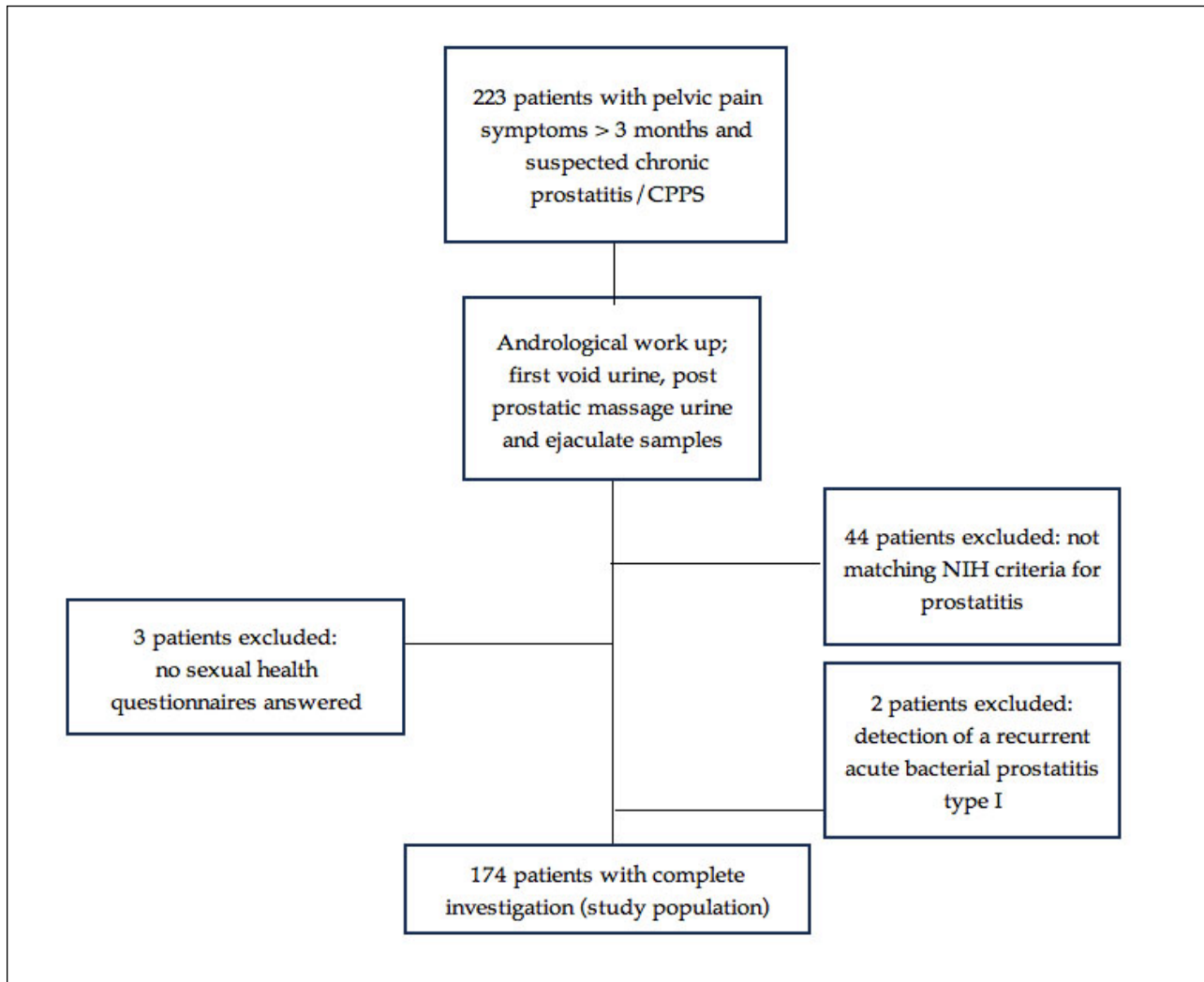
RESULTS

Demographics

The study population excluded males who did not fit the diagnosis criteria for chronic prostatitis/CPPS ($n = 44$) and men who did not wish to have their sexual history taken

Figure 1.

Composition of the study population.



or to complete questionnaires on sexual health ($n = 3$). Furthermore, two additional males with sub-vesical obstruction and recurrent acute bacterial prostatitis type I were not included. Consequently, 174 CP/CPSP patients made up the study group (Figure 1).

The full clinical and demographic outcomes are shown in Table 1.

The median age of the patients was 37, and their ages ranged from 20 to 84. While 12.6% of the study group exhibited type IIIA chronic prostatitis, the majority of patients (87.4%) had type IIIB chronic prostatitis. The study group had a medium degree of lower urinary tract symptoms, as shown by the median score of 12 points on the *International Prostate Symptom Score* (IPSS) (32). The *National Health Institute's Chronic Prostatitis Symptom Index* (NIH-CPSI) showed a moderate symptom burden from chronic prostatitis, with median scores of 12 points for pain (CPSI-I), 3 points for urinary tract symptoms (CPSI-II), and 9 points for impact on quality of life (CPSI-III) (33). However, not all patients were able to complete the questionnaires because of language barriers ($n = 3$ for the CPSI questionnaire and $n = 7$ for the IPSS questionnaire).

Table 1.

Demographic and andrological findings of the study population.

Parameter	Median (IQR) or n (%)	Number of patients
Age (years)	37 (29-50)	174
Type of prostatitis		174
· Type IIIA	12.6%	
· Type IIIB	87.4%	
IPSS (points)	12 (8-14)	167
CPSI-I (points)	12 (8-14)	171
CPSI-II (points)	3 (2-6)	171
CPSI-III (points)	9 (7-11)	171
CPSI total score (points)	24 (18-28)	171
Total testosterone (ng/dL)	480 (367-582)	173
Estradiol (pg/mL)	33 (26-39)	172
PSA (ng/mL)	0.71 (0.44-1.04)	172
CRP (mg/L)	0.5 (0.5-1.5)	172
Median testicular volume (mL)	15.0 (13-18)	173
Median Prostate volume (mL)	20.0 (15-25)	174

IQR: interquartile range.

Sexual parameters and UPOINT(S) classification

The results of the collected parameters on sexuality and UPOINT(S) classification are shown in Table 2. The *International Index of Erectile Function* (IIEF) had a median score of 26 points, which was within the normal range (34). Of the 171 surveyed patients, 86 (50.3%) had normal erectile function with scores between 26-30, 23 (13.5%) had mild erectile dysfunction, 19 (11.1%) had mild to moderate erectile dysfunction, 21 (12.3%) had moderate erectile dysfunction, and 22 (12.9%) complained of severe erectile dysfunction. The *Sexual Function Index* (SFI) had a median score of 28 points, indicating a slightly impaired sexual function (35). The majority of our participants were heterosexually oriented (95.4%). The majority were married or in a stable relationship (61.5%), and 40.2% of participants had at least one child. Only a small proportion (17.2%) of patients experienced a negative impact on their relationship due to CP/CPPS-associated symptoms. Based on the UPOINT(S) classification, the most frequently affected domains were organ-specific (97.7%), urinary (75.9%), and sexual function (62.6%). The median number of affected domains was three.

Andrological results

With an average of 15.0 mL, the median testicular volume was within the reference range (26, 36). Additionally, the median prostate volume, 20.0 mL, was also within normal bounds (27, 36). With median levels of *C-reactive protein* (CRP) at 0.5 mg/L, total testosterone at 480 ng/dL, estradiol at 33 pg/mL, and PSA at 0.71 ng/mL, the lab findings were within the normal range.

The WHO lower reference limits for the basic semen variables are included in Table 3, along with the patients' semen parameters. Seminal parameters indicating inflammation (elastase, peroxidase-positive leukocytes, and interleukin-8) were all within normal limits, excluding inflam-

Table 2.

Sexuality and UPOINT(S) classification of the study population.

Parameter	Median (IQR) or n (%)	Number of patients
IIEF	26 (16-30)	171
SFI	28 (21-35)	171
Sexual orientation		
· Heterosexual	166 (95.4)	
· Homosexual	7 (4.0)	
· Bisexual	1 (0.6)	
Marital status		
· Single	62 (35.6)	
· Married/partnership	107 (61.5)	
· Changing partnerships	5 (2.9)	
Number of children		
· No children	104 (59.8)	
· One child	23 (13.2)	
· Two children	33 (19.0)	
· Three or more children	14 (8.0)	
Impact on relationship		
· No relationship	62 (35.6)	
· No impact	18 (10.3)	
· Slight impact	64 (36.8)	
· Heavy impact	30 (17.2)	
UPOINT(S)		174
· Urinary	132 (75.9)	
· Psychosocial	75 (43.1)	
· Organ specific	170 (97.7)	
· Infection	20 (11.5)	
· Neurological	44 (25.3)	
· Tenderness	42 (24.1)	
· Sexual	109 (62.6)	
· Number of positive domains	3 (2.4)	

IQR: interquartile range.

Parameter	Patients with chronic prostatitis/CPPS (n = 174) Median (IQR)	WHO 2021 reference values	Number of patients
Volume	2.5 (1.5-3.5)	1.41	153
pH value	7.9 (7.6-8.3)	≥7.22	153
Sperm concentration (10 ⁶ /ml)	54.4 (22.1-132.8)	161	153
Total sperm count (10 ⁶ /ejaculate)	126.3 (55.0-299.5)	391	153
Progressive motility (%)	49 (40-57)	301	152
Sperm vitality (%)	68 (50-77)	581	37
Normal forms (%)	11 (7-16)	41	144
α-glucosidase (mU/ejaculate)	37.9 (31.1-65.6)	≥ 20/ejaculate ²	150
Fructose (μmol/ejaculate)	25.9 (10.6-45.7)	≥ 13/ejaculate ²	150
Peroxidase-positive leukocytes (10 ⁶ /ml)	0.4 (0.1-0.9)	< 1 ²	152
Elastase (ng/ml)	62.0 (17-191)	< 250 ³	151
Interleukin-8 (pg/ml)	4132.0 (2058-7550)	< 10000 ³	149

¹ Lower reference limit based on 5th percentile.

² Consensus-based reference values.

³ Threshold levels established in the Giessen Andrology laboratory.

IQR: interquartile range.

Table 3.

Semen parameters of the study population compared with WHO 2021 reference values (30).

matory/infectious conditions. Due to the low number of participants with type IIIA chronic prostatitis in our study population, no increase in inflammatory parameters was observed in the overall group. However, semen analysis was not possible in all cases due to insufficient ejaculate volume, the inability of the patient to provide a sample on site, or the patient's postoperative condition following prostate surgery. As a result, 21 patients were unable to provide a processable ejaculate sample.

Microbiology

For each sample type (first void urine, post-prostatic massage urine, ejaculate), we performed a conventional bacterial culture, an STI-PCR, and, in the case of a previously missing bacterial detection, an additional 16S rRNA analysis.

There were only $n = 2$ patients with a positive STI test result in our study population with *Ureaplasma ure-*

Table S1.

A. Microbiological findings of the first void urine samples, patients with negative culture and negative STI-PCR received additional 16S rRNA analysis.

Pathogen	Conventional bacterial culture, n (%) (n = 170)	STI-PCR, n (%) (n = 170)	16S rRNA Analysis, n (%) (n = 139)
No pathogen detected	139 (82)	168 (99)	128 (92)
Mixed flora	15 (9)		
<i>Streptococcus mitis</i>	10 (6)		1 (0.5)
<i>Escherichia coli</i>	2 (1)		
<i>Enterococcus faecalis</i>	2 (1)		
<i>Streptococcus agalactiae</i>	2 (1)		
<i>Ureaplasma urealyticum</i>			1 (0.5)
<i>Mycoplasma hominis</i>			1 (0.5)
<i>Fusobacterium nucleatum</i>			7 (5)
<i>Bacteroidaceae</i> spp.			2 (1)
<i>Finnegoldia magna</i>			1 (0.5)

Table S1.

B. Microbiological findings of the post-prostatic massage urine samples, patients with negative culture and negative STI-PCR received additional 16S rRNA analysis.

Pathogen	Conventional bacterial culture, n (%) (n = 173)	STI-PCR, n (%) (n = 173)	16S rRNA Analysis, n (%) (n = 160)
No pathogen detected	161 (93)	172 (99.5)	151 (94)
Mixed flora	3 (2)		
<i>Streptococcus mitis</i>	4 (2)		
<i>Escherichia coli</i>	3 (2)		
<i>Enterococcus faecalis</i>	2 (1)		
<i>Ureaplasma urealyticum</i>		1 (0.5)	
<i>Fusobacterium nucleatum</i>			4 (2.5)
<i>Bacteroidaceae</i> spp.			2 (1)
<i>Corynebacterium striatum</i>			1 (0.5)
<i>Lactobacillus iners</i>			2 (1)

Table S1.

C. Microbiological findings of the ejaculate samples, patients with negative culture and negative STI-PCR received additional 16S rRNA analysis.

Pathogen	Conventional bacterial culture, n (%) (n = 153)	STI-PCR, n (%) (n = 153)	16S rRNA Analysis, n (%) (n = 1259)
No pathogen detected	126 (82)	152 (99.5)	115 (92)
Mixed flora	5 (3.5)		
<i>Streptococcus mitis</i>	5 (3.5)		1 (0.5)
<i>Escherichia coli</i>	4 (2.5)		
<i>Enterococcus faecalis</i>	6 (4)		1 (0.5)
<i>Staphylococcus epidermidis</i>	6 (4)		2 (1)
<i>Aerococcus urinae</i>	1 (0.5)		
<i>Ureaplasma urealyticum</i>		1 (0.5)	
<i>Fusobacterium nucleatum</i>			2 (1)
<i>Finnegoldia magna</i>			1 (0.5)
<i>Corynebacterium striatum</i>			1 (0.5)
<i>Lactobacillus iners</i>			2 (1)

alyticum (detectable in all the three patient's samples) and *Mycoplasma hominis* being detected. Both patients received antibiotic therapy with pathogen eradication verified by repeated STI-PCR. Persistent pelvic pain symptoms during a follow-up visit 6 to 12 months after initial presentation and continued negative microbiology results led to classification as type III prostatitis.

The detailed microbiological findings for the first void urine are presented in Supplement Table S1A.

Because our study cohort had a history of extensive treatment with antibiotics, the conventional culture yielded positive results in only 31 patients. The majority of the pathogens found were contaminants or components of the typical flora, exhibiting a bacterial count that was largely low, ranging from 100 to 1,000 CFU per milliliter. In 92% of cases, the 16S rRNA analysis performed on negative bacterial cultures and STI-PCR did not identify any pathogen. In the 8% of cases where a positive detection occurred, bacteria from the normal flora were identified. If two or more species were detected, the microbiologists classified the results as mixed flora.

Supplement Table S1B displays the microbiological findings of the urine collected after prostatic massage. Urethral mucosal flora was detected in the majority of cases when a positive result was obtained in culture ($n = 12$) and 16S rRNA analysis ($n = 9$). Furthermore, the STI-PCR detection of *Ureaplasma urealyticum* was limited to a single patient, which is consistent with the results of the first void urine samples.

No detectable pathogen was observed in the vast majority of the analyses (151 of 173 patients, 87%).

The microbiological results for the ejaculate samples are presented in Supplement Table 1C. Again, only very few pathogens were identified by culture ($n = 27$), STI-PCR ($n = 1$), and 16S rRNA analysis ($n = 10$). The results are comparable with the previous analyses of the urine samples.

	Correlation coefficient <i>r</i>	<i>p</i> (univariate)	Correlation coefficient β	<i>p</i> (multivariate)
CPSI total score	-0.210	0.018*	-0.104	0.018
SFI score	0.619	0.001*	0.441	0.001*
Microbiology results	0.100	0.388	-0.085	0.460
Number of positive UPOINT(S) domains	-0.255	0.008*	-0.233	0.021*
Number of positive UPOINT domains	-0.155	0.242	-0.017	0.882
Urinary (U)	-0.152	0.119	-0.078	0.493
Psychosocial (P)	-0.165	0.090	-0.173	0.075
Organ specific (O)	0.169	0.084	0.131	0.177
Infection (I)	-0.114	0.245	-0.107	0.279
Neurological (N)	0.094	0.338	0.115	0.247
Tenderness (T)	0.099	0.311	0.116	0.206
Sexual (S)	-0.369	0.001*	-0.371	0.001*
Marital status	0.213	0.017*	0.111	0.277
Impact on relationship	0.092	0.313	0.189	0.070
Sperm concentration	-0.081	0.394	-0.180	0.061
Leukocytes in ejaculate	-0.142	0.141	-0.130	0.174
Seminal plasma elastase	-0.118	0.218	0.032	0.747
Seminal plasma IL-8	0.104	0.211	-0.147	0.135

Multivariate analysis: univariate and multivariate regression analysis between IIEF score and the listed parameters.
A value of $p < 0.05$ was considered statistically significant, * marks significant results.

Table 4.

A. Association of IIEF score with CPSI total score, SFI score, a positive result in any microbiology, marital status, impact on relationship, sperm concentration and inflammatory seminal parameters.

	Correlation coefficient <i>r</i>	<i>p</i> (univariate)	Correlation coefficient β	<i>p</i> (multivariate)
CPSI total score	-0.205	0.008*	-0.093	0.414
Microbiology results	-0.062	0.581	-0.145	0.204
Number of positive UPOINT(S) domains	-0.295	0.001*	-0.280	0.001*
Number of positive UPOINT domains	-0.133	0.119	-0.164	0.096
Urinary (U)	0.020	0.816	0.091	0.354
Psychosocial (P)	-0.179	0.034*	-0.167	0.049*
Organ specific (O)	-0.039	0.647	-0.035	0.678
Infection (I)	-0.198	0.019*	-0.182	0.034*
Neurological (N)	-0.060	0.478	-0.028	0.745
Tenderness (T)	0.071	0.401	0.121	0.124
Sexual (S)	-0.410	0.001*	-0.434	0.001*
Marital status	0.134	0.081	0.081	0.389
Impact on relationship	-0.058	0.462	-0.048	0.608
Sperm concentration	-0.061	0.459	-0.135	0.108
Leukocytes in ejaculate	0.010	0.908	0.015	0.857
Seminal plasma elastase	0.022	0.792	0.161	0.057
Seminal plasma IL-8	-0.080	0.355	-0.135	0.110

Multivariate analysis: Multivariate analysis: univariate and multivariate regression analysis between SFI score and the listed parameters.
A value of $p < 0.05$ was considered statistically significant, * marks significant results.

Table 4.

B. Association of SFI score with CPSI total score, IIEF score, a positive result in any microbiology, marital status, impact on relationship, sperm concentration and inflammatory seminal parameters.

Association between sexual function questionnaires and other CP/CPPS parameters

Table 4A shows a univariate and multivariate analysis between the IIEF score and various other parameters. For the analysis with the microbiological findings, the presence of bacterial detection was taken as a parameter. The univariate analysis revealed a significant association between IIEF and CPSI total score, the SFI score, the num-

ber of affected UPOINT(S) domains and especially the sexual domain (S), and the marital status. The multivariate analysis revealed a significant association with the SFI score, the UPOINTS total score and the sexual domain. Univariate and multivariate analyses of the association between SFI score and various other parameters assessed in this study are shown in Table 4B. There was a significant association with the IIEF score and the number of

affected UPOINT(S) domains, especially the psychosocial, infection, and sexual domains, as shown by the univariate analysis. The multivariate analysis showed a significant association between the IIEF score and the UPOINT(S) score and, notably, the psychosocial, infection, and sexual domains.

Discussion

As a continuation of our previous work (24, 37) our study focused on sexual function in CP/CPPS patients and showed a significant association between sexual dysfunction, measured by the SFI and the full version of the IIEF scores, and the symptom burden measured by the NHI-CPSI questionnaire. Regarding erectile function, the cohort we examined was very heterogeneous. Although the median erectile function score on the IIEF questionnaire was 26 points, 43 participants (25.2%) had severe to moderate erectile dysfunction. Mild to moderate or mild erectile dysfunction was also found in 19 (11.1%) and 23 (13.5%) participants, respectively, while 86 participants (50.3%) had no erectile dysfunction. Despite a minimally impaired sexual function according to the SFI questionnaire results of 28 points in the median, an affected sexual domain was found in 62.6% of the subjects in the UPOINT(S) classification. One possible cause for this could be the aforementioned distribution of erectile dysfunction.

However, in addition to erectile dysfunction, sexual dysfunction also includes premature ejaculation, delayed or absent orgasm, dyspareunia, postcoital discomfort, and genital sensory disturbances such as glandular numbness. This could also explain the significant association found between the result of the UPOINT(S) categorization and the scores of the IIEF and SFI questionnaires in the univariate and multivariate analysis. Additionally, the univariate analysis showed a significant association between the NIH-CPSI score and the two sexual function questionnaires.

The clinical benefit of adding sexual function as a further UPOINT(S) category has been controversially discussed in the past (13, 20, 21); for example, Samplaski et al found no association between erectile function and symptom severity in 100 CP/CPPS patients (21). In their study, an affected sexual domain was found in only 28 percent of subjects, and without statistical significance for symptom severity measured using the NIH-CPSI score. One reason for this may be the small sample size of 100 patients, which could not demonstrate such a relationship. Furthermore, an affected sexual domain was only assumed in cases of erectile dysfunction and loss of libido; other forms of sexual dysfunction, such as premature ejaculation, were not recorded. Moreover, there was no systematic assessment of erectile function using validated questionnaires such as the IIEF, but rather based solely on patient information during the medical history. In general, determining sexual function solely using self-reported erectile quality or the IIEF score seems insufficient, as it only assesses erectile function as part of male sexuality. Furthermore, the IIEF is heteronormative and focuses only on vaginal intercourse, thus poorly reflecting other sexual orientations, as well as patients without pen-

etrative intercourse. As mentioned, some patients also report other sexual complaints like premature ejaculation and post-orgasmic pain as leading sexual complaints, which cannot be determined by examining erectile quality alone (20).

In our analysis, no correlation was found between the symptom burden of the IIEF and SFI questionnaires and the results of microbiology and inflammatory seminal parameters. In general, our population showed a predominantly unremarkable microbiology as measured by the results of conventional bacterial culture and STI-PCR of first void urine, post-prostatic massage urine and ejaculate. If bacteria were found in the culture, they were mostly contaminations; even in the rare case of pathogens such as *Escherichia coli*, these were also considered contamination if the number of bacteria was low and leukocytes were not detected. The STI-PCR also remained negative in most cases, with *Ureaplasma urealyticum* and *Mycoplasma hominis* being detected only in a few cases. To detect pathogens that are difficult to cultivate, an additional 16S rRNA analysis was performed in cases of negative bacterial culture and STI-PCR. This analysis also failed to detect any pathogens in the majority of cases (92-94%) and, in cases of positive results, almost exclusively detected components of the normal genital flora. Despite the postulated association between urogenital infection and sexually transmitted diseases with CP/CPPS, we were unable to detect any such infection in the vast majority of subjects. This is likely due to the strong antibiotic pretreatment in these patients. Since most patients were referred to our university-based special consultation by urologists in private practice, general practitioners, or peripheral hospitals, the referring physician had already prescribed medication in the vast majority of cases. Due to symptoms typical of urinary tract infections, such as dysuria or bladder and pelvic pain, or in cases of suspected bacterial prostatitis, antibiotics, particularly fluoroquinolones, were prescribed in many instances. We inquired about this with each patient during the medical history interview, but it was not systematically recorded within the study. A challenge here was that while most patients could confirm taking an antibiotic, they could not always specify which one or for how long. However, all patients were generally informed when scheduling their appointment that at least 14 days had to have passed since their last course of antibiotics at the time of their visit. In contrast, multiple studies demonstrated a strong association between chronic prostatitis and STDs (38-39). In the population of Bielecki et al., 24.6% of subjects had an active or recent genital infection with *C. trachomatis* (40). At least our study did not reveal any evidence of an infection-related impairment of sexual function measured by the results of the microbiology. Furthermore, our study population found no evidence of hypogonadism as a cause of sexual dysfunction: the testosterone levels measured were all within the normal range, with a median of 480 ng/dL. However, we did not systematically assess other endocrine causes such as hypothyroidism or hyperprolactinemia.

No correlation could be demonstrated between the two sexual questionnaires and the impact of the illness on the relationship. Although 17.2% of participants ($n = 30$)

reported a strong negative influence, no significant correlation was found for either the IIEF or the SFI. This is surprising; a possible reason could be the small number of participants in this subgroup and the fact that one-third of our population (35.6%) was not in a committed relationship. A significant association with relationship status was also found only for the IIEF questionnaire in the univariate analysis; the SFI did not demonstrate such an association. One explanation for this could again be that the IIEF can only be completed to a limited extent outside of regular heterosexual penetrative intercourse.

There are study limitations to mention. Our study was conducted at a single-center, tertiary clinic, so the vast majority of patients had already received prior treatment from their external referring urologist that could have had an impact on sexual function. This includes, in particular, drug therapies such as alpha-blockers and antidepressants, which have a potentially negative impact, as well as previous treatment of erectile dysfunction with a PDE-5 inhibitor. Other negative factors influencing sexual function besides CP/CPPS, such as pre-existing couple conflicts or mental illness, were also not separately recorded. Furthermore, no systematic classification into the various identified sexual dysfunctions was carried out as part of the data collection. Our study population was also limited to 174 prospectively enrolled patients, which particularly hindered a detailed subgroup analysis. Similarly, the impact on the psychosocial domain was not assessed using a standardized depression/anxiety questionnaire, but only during the patient interview. To further validate the results,

a prospective multicenter study would be advisable in the future. This study could also include the measurement of additional parameters related to inflammation or hormone levels, such as prolactin or thyroid hormones.

CONCLUSIONS

In clinical practice, assessing sexual function in the evaluation of CP/CPPS patients appears to be useful. Our study showed a clear association between the two questionnaires used and the symptom burden of the NIH-CPSI questionnaire, with a concurrent high prevalence of an affected sexual UPOINT(S) domain. Expanding the classic UPOINT categorization to include the sexual domain also appears reasonable based on our data. Through systematic recording of sexual problems, symptom-oriented, multimodal therapy can also be carried out in this domain in order to effectively reduce the symptom burden caused by chronic prostatitis.

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DECLARATIONS

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Ethics Committee of Justus-Liebig-University Giessen (protocol code 55/13, date of approval: 4 November 2013).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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