Use of the UPOINT Classification in Turkish Chronic Prostatitis or Chronic Pelvic Pain Syndrome Patients

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OBJECTIVE To determine the positive subdomain numbers and distribution of the UPOINT classification in chronic prostatitis and to compare the erectile dysfunction (ED) pattern.

MATERIALS AND METHODS From 2008 to 2013, 839 patients with symptomatic chronic prostatitis or chronic pelvic pain syndrome were included in this study. The correlation between UPOINT domains and National Institutes of Health chronic prostatitis symptom index (NIH-CPSI) total score, subscores, and the 5-item International Index of Erectile Function scores were evaluated retrospectively.

RESULTS The mean patient age was calculated as 37.7 ± 7.4 (range 21-65). The average total NIH-CPSI score was determined as 9.07 (range 1-40) and the average positive UPOINT subdomain number was determined as 2.87 ± 0.32 (range 1-6). Subdomain patient numbers and rates were calculated as 529 urinary (63%), 462 psychosocial (55%), 382 organ specific (45%), 290 infection (34%), 288 neurological or systemic (34%), and 418 tenderness (skeletal muscle) (50%), respectively. It was determined that ED, determining the subdomain of sexual dysfunction in patients, was positive in a total of 326 (39.9%) patients, with 220 patients having mild (26.2%), 76 mild to moderate (9.1%), 19 moderate (2.3%), and 5 with severe (0.6%) ED. A statistically significant correlation was not determined between the 5-item International Index of Erectile Function score and UPOINT subdomain number and NIH-CPSI score.

CONCLUSION It has been determined that although there is a strong and significant correlation between UPOINT classification and NIH-CPSI score in Turkish patients with chronic prostatitis or chronic pelvic pain syndrome, the inclusion of ED as an independent subdomain to the UPOINT classification is not statistically significant. UROLOGY 97: 227–231, 2016. © 2016 Elsevier Inc.

While the prevalence of chronic prostatitis (CP) is estimated to be around 10% worldwide, its etiology is not completely understood, and it has a significant impact on quality of life (QoL).[1] The National Institutes of Health (NIH) classification of prostatitis syndromes divides them into 4 distinct types; type I: acute bacterial prostatitis, type 2: chronic bacterial prostatitis, type 3: chronic nonbacterial prostatitis or chronic pelvic pain syndrome (CNP/CPPS), and type 4: asymptomatic inflammatory prostatitis.[2]

Chronic prostatitis category 3 or chronic pelvic pain syndrome (CP/CPPS) can have a variety of symptoms and is a disease characterized most commonly by genital pain and accompanying urinary problems, erectile and ejaculatory dysfunction, and psychological problems.[3,4] It is also known to have a close relationship with sexual dysfunction. Erectile dysfunction (ED), defined as the inability to develop and/or maintain an erection, is reported as the most common sexual dysfunction.[5,6]

Despite being common among urological diseases in men under the age of 50,[7] due to the variable clinical progression, a disease-specific treatment has not yet been clearly defined.[8] Although the existing treatment models were reported to be beneficial in some studies, due to the multifactorial etiology of the disease, the lack of a specific marker to be used in the monitoring of the treatment and the appearing with different symptoms in each patient, a satisfactory result cannot be obtained.[9]

Due to the complexity in the nature of this disease, a new strategy was developed by Shoskes et al in 2009 for the diagnosis and treatment of patients with CP/CPPS. Accordingly, a UPOINT classification consisting of 6 sub domains of urinary, psychosocial, organ specific, infection,

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neurological or systemic abnormalities, and muscle or skeletal tenderness was developed.[9]

We planned a retrospective study in our own clinic to provide a high number of patient participation from a single center in the UPOINT classification, to increase international validation and compliance and provide validation with Turkish society.

MATERIALS AND METHODS

Eight hundred thirty-nine patients with a diagnosis of CP/CPPS presenting to our clinic between 2008 and 2013 were studied retrospectively. To localize lower urinary tract infections, the traditional 4-glass test was administered to each patient who likely had CP/CPPS. The 4-glass test samples were obtained in the following way: (1) VB1, approximately the first 10 mL was used to give information about urethral colonization; (2) VB2, middle and late urine for sampling; (3) EPS, express prostate secretion; (4) VB3, the first 10 mL of urine was taken after a prostate massage is given to stimulate secretion. The 4 cup samples were analyzed with direct microscopes and standard microbiological methods (blood agar and MacConkey agar). All of the microbiological studies were performed under the care of a single expert in the same laboratory. This microbiologist was not given any information about the study. The symptom scores of all patients were calculated according to the NIH chronic prostatitis symptom index (NIH-CPSI) according to pain (0-21 points), QoL (0-12 points), and urinary (0-10 points) subdomains, for a total score of 0-43 points.

In all patients, there was at least 1UPOINT subdomain positivity present. Patients were separated into 3 domains as severe dysfunction (>29), moderate dysfunction (16-29), and mild dysfunction (0-15) according to their symptom degrees on the NIH-CPSI score. The presence and severity of ED in patients were determined using the 5-item International Index of Erectile Function (IIEF-5) survey form in 5 classes as follows: no dysfunction (25-30 points), mild dysfunction (19-24 points), mild to moderate dysfunction (13-18 points), moderate dysfunction (7-12 points), and severe dysfunction (0-6 points), respectively.

In the evaluation of the patients, medical history, physical examination, prostate examination by rectal palpation, and examination of urine and prostatic fluid following prostate massage were considered, and the subdomain positivity according to the UPOINT classification detailed below was determined.

Urinary subdomain was positive in presence of high postvoid residual volume, nocturia, urgency, and frequent urination. Psychosocial subdomain, despite patients not being specifically assessed using the survey form, was positive in those who have stated they are depressive and hopeless and helpless due to the disease. Organ-specific positivity was in prostate tension upon rectal palpation, leukocytes in the prostatic fluid, or the observation of intensive prostatic calcification. Infection subdomain was positive in patients other than category 1 and 2 CP, with the presence of Gram-negative bacilli or enterococci in the prostatic fluid. Neurological or systemic subdomain positivity was considered with pain in the pelvis or outside of the abdomen or newly diagnosed fibromyalgia or irritable bowel disease. Finally, tenderness subdomain was determined as positive for existence of palpable muscle spasm or abdominopelvic trigger points.

In addition, all patients' urine culture results, urinary system ultrasound, and postvoid residual measurements and the pelvic floor muscle examination results were considered; however, in depression or catastrophizing (helplessness, hopelessness), distinct examination was not carried out. Emotional mood drop related to the disease was considered, thus a lower-than-expected result being reached has been predicted in the psychosocial subdomain.

Among the patients included in the study were primary patients presenting for the first time, a small number of secondary patients generally treated previously with antibiotics, as well as tertiary patients who have been given different treatments many times (eg, alpha blocker, antibiotic therapy, analgesics) but without success.

Exclusion criteria for the study were the following: acute and/or chronic bacterial prostatitis, active history of genitourinary cancer, history of recent prostate surgery, and diagnosis of neurological diseases affecting the bladder.

Statistical Evaluation

Data were analyzed using the SPSS 14.0 statistics program (SPSS, Chicago, IL). The UPOINT, NIH-CPSI, and IIEF-5 scores of patients are not normally distributed with respect to Shapiro-Wilk's normality test, except urinary subdomain. The means of UPOINT groups are compared with Kruskal-Wallis test and then post hoc tests are employed to make pairwise comparisons by using Mann-Whitney *U* test followed by manual adjustment for *P* value by Bonferroni method. The correlations between the scores of CP patients were tested by Spearman correlation analyses. Data are summarized by mean and standard deviation values. A value of $P < .05$ was considered statistically significant.

RESULTS

The NIH-CPSI, IIEF-5, and UPOINT subdomain data of 839 patients with CP/CPPS meeting the study criteria determined by scanning the clinic database are given in Table 1. The mean patient age was calculated as 37.7 ± 7.4

Table 1. Positive UPOINT domains, NIH-CPSI scores, and IIEF-5 scores in patients with chronic prostatitis

Positive UPOINT Domain		NIH-CPSI		IIEF-5 Scores	
Subgroup	**n (%)**	**Classification**	**n (%)**	**ED Severity**	**n (%)**
Urinary	529 (63)	Mild	725 (86.4)	No ED	513 (61.1)
Psychosocial	462 (55)	Moderate	112 (13.3)	Mild	220 (26.2)
Organ specific	382 (45)	Severe	2 (0.2)	Mild to moderate	76 (9.1)
Infections	290 (34)			Moderate	19 (2.3)
Neurological systemic	288 (34)			Severe	5 (0.6)
Tenderness (skeletal muscle)	418 (50)				

ED, erectile dysfunction; IIEF-5, 5-item International Index of Erectile Function; NIH-CPSI, National Institutes of Health chronic prostatitis symptom index.

Table 2. NIH-CPSI, urinary, pain, and QoL values of UPOINT groups in patients with chronic prostatitis

UPOINT Groups	NIH-CPSI	Urinary	Pain	QoL
1	4.11 ± 3.60	2.55 ± 2.39	0.83 ± 2.22	0.76 ± 1.08
2	6.70 ± 5.04	3.10 ± 2.46	2.10 ± 3.74	1.52 ± 1.48
3	9.59 ± 5.64	3.20 ± 2.43	4.25 ± 4.21	2.21 ± 1.63
4	12.36 ± 6.31	3.70 ± 2.41	5.77 ± 4.36	2.98 ± 1.80
5	13.47 ± 5.64	3.35 ± 2.27	7.00 ± 3.89	3.13 ± 1.90
6	18.43 ± 7.22	4.31 ± 2.41	9.87 ± 4.22	4.25 ± 1.87

QoL, quality of life; other abbreviation as in Table 1.
The UPOINT groups have a significant difference in mean scores in terms of NIH-CPSI with respect to Kruskal-Wallis test ($P < .01$). The post hoc tests are employed to make pairwise comparisons by using Mann-Whitney test followed by manual adjustment for *P* value by Bonferroni method. The results show that there is a significant difference between each UPOINT group.

Table 3. The correlations between the data of patients with chronic prostatitis

Data	Correlation (r Coefficient)	(*P* Value)	Significance*
UPOINT-NIH	0.548	.000	<0.001
UPOINT-ED	–0.047	.147	>0.05
EDSCORE-NIH	0.055	.111	>0.05
UPOINT-URINARY	–0.153	0.000	<.001
UPOINT-PAIN	0.536	.000	<0.001
UPOINT-QoL	0.509	.000	<0.001

Abbreviations as in Tables 1 and 2.
The Spearman correlation coefficients are given in this table. The coefficients of skewness of ED, NIH, URINARY, PAIN, and QoL score, respectively, are –9.2, 11.8, 0.5, 8.9, and 16.8.
* Correlation is significant at the 0.05 level (Spearman correlation, 2-tailed).

Table 4. Urinary, pain, and QoL subgroup values of NIH-CPSI groups in patients with chronic prostatitis

NIH-CPSI Scores	**Urinary**	**Pain**	**QoL**
Mild dysfunction	3.02 ± 2.33	2.64 ± 3.03	1.59 ± 1.22
Moderate dysfunction	4.29 ± 2.72	11.37 ± 3.83	5.07 ± 1.77
Severe dysfunction	6.00 ± 5.67	20.00 ± 0.00	10.50 ± 0.70

Abbreviations as in Tables 1 and 2.
NIH-CPSI severity: mild dysfunction (0-15), moderate dysfunction (16-29), severe dysfunction (>29).

(range 21-65). The average total NIH-CPSI score was determined as 9.07 ± 0.63 (range 1-40) and the average positive UPOINT subdomain number was determined as 2.87 ± 0.32 (range 1-6). Subdomain patient numbers and rates were calculated as 529 urinary (63%), 462 psychosocial (55%), 382 organ specific (45%), 290 infection (34%), 288 neurological or systemic (34%), and 418 tenderness (skeletal muscle) (50%), respectively.

For the validation of the original article[6] by Shoskes et al, we calculated the correlation between positive UPOINT subdomain number and NIH-CPSI total score and subdomain pain (0-21 points), QoL (0-12 points), and urinary (0-10 points) scores in the Turkish population (Table 2). A statistically significant and strong correlation was determined between UPOINT subdomain positivity and NIH-CSPI total score. Even the subdomains urinary, pain, and QoL were considered separately, a statistically significant correlation with UPOINT subdomain positivity was observed. In addition, it has also been determined that as the UPOINT subdomain number increases, there is a gradual increase in the NIH-CPSI score, but no statistically significant correlation was determined between ED scores and UPOINT or NIH-CPSI scores (Table 3).

In our study, we also examined the correlation between the presence of UPOINT phenotype positivity and the presence and severity of ED (Table 4). ED, determining the sexual dysfunction subdomain, was found to be positive in 326 (39.9%) patients, with 220 patients determined to be in the mild (26.2%), 76 patients in the mild to moderate (9.1%), 19 patients in the moderate (2.3%), and 5 patients in the severe (0.6%) ED subdomains. Our results showed that there was no statistically significant correlation between IIEF-5 score and UPOINT subdomain number and NIH-CPSI score. As a result, it has been determined that ED has no impact on these parameters.

DISCUSSION

CP/CPPS emerges as a widely seen disease that has a serious impact on QoL of the affected individuals. The effectiveness of treatment applied without classification has been shown to be low[10,11] or controversial in prior multicentric monotherapy studies.[12,13] In their own study, Wagenlehner et al has shown that a classification to be made, considering the clinical symptoms of patients, may aid in the determination of effective treatment.[14]

The confusion in the etiology and the inadequacy in the treatment, despite the prevalence of the disease, led Shoskes et al to develop a new and alternative strategy in 2009, creating the UPOINT classification.[9] The disease was

reduced to 6 subclasses or phenotypes according to symptoms and findings, with the aim of effective targeted treatment and thus an increase in patient QoL. One of the most important findings achieved with this first retrospective study of 90 patients showing equivalence with our study is the increase in NIH-CPSI score, with a gradual increase in the number of positive subdomains in the UPOINT classification.[9]

In the prospective study carried out in 2010 again by Shoskes et al on 100 patients with 26 weeks follow-up, it has been shown that 84% of patients on a multimodal treatment protocol where the UPOINT subdomains were targeted showed 6 points or overimprovement according to the NIH-CPSI questionnaire.[15] The findings obtained were later verified and supported by many studies carried out with CP/CPPS patients in America and Europe.[16-18]

Although the average age of our patients differs from other studies, with an average age of 43-47[9,15,17,18] being younger, a statistically significant and strong correlation supporting previous studies[9,16-18] between UPOINT classification subdomain positivity and NIH-CPSI total score was observed. However, when studies are compared with subdomains individually examined, although positivity by phenotype does show some similarity, it has been shown that exact correlation is not provided. The possible causes for the differences have been considered to be the arrangement of the studies, the differences in number of patients, and differences in the survey of methods used in the subdomains.

The aims of this study were to determine positive subdomain number and distribution of the UPOINT classification in CP/CPPS patients and to compare these patients' ED pattern results, which was added as a subclass, with international data. When the studies carried out regarding UPOINT classification are reviewed, the most important matter with differences of opinion, where discussions were continuing, is whether sexual dysfunction should be added to this classification or not.

It is widely known that there is a close relationship between CP/CPPS and sexual dysfunction. ED, defined as the inability to develop and/or maintain an erection, is known to be the most common sexual dysfunction.[6,7] In addition, there are also studies showing that patients with CP/CPPS show a higher rate of anxiety, depression, sexual dissatisfaction, and lower QoL when compared to healthy individuals in the same age domain,[19-21] but it has not been clearly determined whether these symptoms indicate the disease or are a result of the disease.

In a 50-patient prospective study carried out by Hedelin including the sexual dysfunction component, a weak and inverse correlation was observed between ED and positive UPOINT phenotype number, despite using the same questioning method (IIEF-5) as our study.[17]

In a 100-patient prospective study carried out by Samplaski et al with an equivalent proportion of ED patients (28%) as our study, it has been reported that there is no statistically significant correlation between NIH-CPSI total score and subdomain scores and ED. Despite the difference of the IIEF-5 form not being used in the querying of ED, the values obtained are consistent with our own results and support our results.[18]

In a 2-center retrospective study from Germany (290 patients) and Italy (937 patients), a change and correlation between the NIH-CPSI scoring, with the addition of sexual dysfunction as a subclass to the UPOINT classification, were examined. In this study, when all patients are considered together (primary, secondary, and tertiary) or only the Italian domain with primary and secondary patients are considered, it was observed that ED did not change the correlation, in line with our own study including all patient domains. The addition of the ED component to the German domain with only tertiary patients was reported to create a significant and strong correlation between total NIH-CPSI score and subdomain scores.[22]

In another prospective study of 162 patients with CP/CPPS where changes to QoL were examined, despite correlation results of UPOINT classification with NIH-CPSI scoring being consistent with our study, the weak correlation reported when comparing QoL examination has been considered to be close due to possible different querying methods used (non-CPSI): SF-36 and male sexual health questionnaire.[23]

In a study of 389 patients carried out in China in 2013, a serious correlation between the severity of ED and positive UPOINT subdomain number and the addition of ED as a subcomponent to the UPOINT classification and NIH-CPSI score was determined.[24] When we examined the data presented in this study, despite the approximately 8-year difference in average age, patients without ED were found to be 70% consistent with our study; however, when considering the rate of patients with moderate ED, an almost 3-fold elevation was observed and this has been considered to cause the observed statistical difference.

Finally, in a study by Shoskes and Nickel where 100 patients were evaluated and 28% were determined to have significant ED, as a result of sexual dysfunction component being added as a subdomain, it has been determined that the correlation between symptom severity and clinic phenotyping system has been reduced. The Total NIH-CSPI score, QoL, and pain scores have been stated not to have been affected by ED, and thus it has been proposed that sexual dysfunction is not required to be added as a subdomain.[25] When considering the results of our study examining 839 patients, a statistically significant correlation between ED and UPOINT classification and NIH-CPSI score has not been detected, and findings supporting the results of Shoskes et al have been observed.

When the studies are considered, although the differences that emerge are primarily thought to be related to different querying methods, study design, and patient numbers, the true reason is thought to be the diversity in the etiology of ED[26,27] and ethnic or cultural differences.

There were some limitations to our study. Due to the functioning of the health system in Turkey, a mixed group of patients(primary, secondary, and tertiary) can present

to our clinic directly, different from Europe and America. It has been considered that this case may change the average values in the calculation of scores and may have impact on the findings. In addition, we also report that there may be limitations to our study due to the retrospective nature of the study and the high number of patients coming to our clinic from outside of the province.

CONCLUSION

The strong and significant correlation between the NIH-CPSI scoring used in the determination of CP/CPPS patients and UPOINT classification has been demonstrated in the Turkish population as it has in previous studies. Despite ED being common in CP/CPPS patients, being added as a seventh subdomain to the UPOINT classification has not been beneficial to our patients.

Nevertheless, we believe that to present clearer information regarding this issue, the standardization of study inclusion criteria and study design is required due to the aforementioned differences.

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