Symptom Duration in Patients With Urologic Chronic Pelvic Pain Syndrome is not Associated With Pain Severity, Nonurologic Syndromes and Mental Health Symptoms: A Multidisciplinary Approach to the Study of Chronic Pelvic Pain Network Study

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OBJECTIVE To evaluate if patients with urologic chronic pelvic pain syndromes (UCPPS) with longer duration of symptoms experience more severe pain and urologic symptoms, higher rates of chronic overlapping pain conditions (COPC) and psychosocial comorbidities than those with a more recent onset of the condition. We evaluated cross-sectional associations between UCPPS symptom duration and (1) symptom severity, (2) presence of COPC, and (3) mental health comorbidities.

METHODS We analyzed baseline data from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain. Symptom severity, COPC, and mental health comorbidities were compared between patients with symptom duration of < 2 vs ≥ 2 years. Symptom severity was assessed by the Genitourinary Pain Index, the Interstitial Cystitis Symptom and Problem Index, and Likert scales for pelvic pain, urgency, and frequency. Depression and anxiety were evaluated with the Hospital Anxiety and Depression Scale and stress with the Perceived Stress Scale.

RESULTS Males (but not females) with UCPPS symptom duration ≥2 years had more severe symptoms than those with <2 years. Participants with short (<2 years) and longer (≥2 years) symptom duration were as likely to experience COPC.

CONCLUSION Longer UCPPS symptom duration was associated with more severe symptoms only in limited patient subpopulations. Symptom duration was not associated with risk for COPC or mental health comorbidities. Females with longer UCPPS duration had decreased distress, but the association was largely attributable to age. UROLOGY 124: 14–22, 2019. © 2018 Elsevier Inc.

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Urologic chronic pelvic pain syndromes are defined by the hallmark symptoms of chronic pain in the region of the pelvis often associated with urinary symptoms.[1-3] Symptom severity in patients with urologic chronic pelvic pain syndromes (UCPPS) has been suggested to be associated with symptom duration. It has also been hypothesized that the time-dependent progression of severity of symptoms may represent a phenotypic progression of disease from an organ specific (bladder) to a more systemic or centralized pain syndrome (involving the bladder and other organs outside the pelvis).[4-7] Nevertheless, there is a paucity of data documenting the natural history of the disease and little evidence to confirm that longer duration of symptoms leads

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to symptom progression or centralization. We hypothesize that longer UCPPS symptom duration is associated with more severe symptoms and higher risk of other somatic syndromes. The aim of the current study was to evaluate cross-sectional associations between UCPPS symptom duration and (1) symptom severity, and (2) presence of other chronic overlapping pain conditions (COPC) and mental health symptoms (depression, anxiety, and stress) in participants in the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network Epidemiology and Phenotyping Study, an NIH-sponsored multicenter observational study of 424 men and women with UCPPS.

MATERIALS AND METHODS

Overview of the MAPP

The MAPP Research network represents a systemic longitudinal approach to the study of UCPPS. It includes 6 discovery sites and 2 core sites that coordinate data collection and provide technical support. The MAPP central protocol, the MAPP Epidemiology, and Phenotyping Study, is a longitudinal observational study of the treated natural history of UCPPS. UCPPS participants in the trans-MAPP study provide comprehensive phenotyping data at baseline and then abridged assessments in-clinic at 6 months and 12 months.[2,3] This report examined baseline data for all UCPPS participants from the trans-MAPP case-control study. The study population was enriched to include similar number of participants with a recent onset of UCPPS (≤2 years) and longer onset of symptoms (>2 years).

Study Participants

The sample consisted of 233 female and 191 male UCPPS subjects. Recruitment was generally balanced across the 6 MAPP sites. Participants were 18 years of age or older, and provided self-report data in English. Subjects were required to score at least 1 on a pain, pressure or discomfort scale (0-10 scale) and also met specific criteria for a UCPPS diagnosis. Both men and women had to report an unpleasant sensation of pain, pressure or discomfort, perceived to be related to the bladder and/or pelvic region associated with lower urinary tract symptoms (IC/PBS) or pain or discomfort associated with urination or sex or located in the genital region (CP/CPPS) for most of the time during any 3 of the previous months. For detailed specific inclusion or exclusion criteria please see Landis et al.[3]

Measures

Urinary and bladder symptoms: The Genitourinary Pain Index (GUPI) assesses pain and urinary symptoms and quality of life as separate subscales, and overall as a total score, and has been validated for use in both males and females with UCPPS.[8] The Interstitial Cystitis Symptom Index (ICSI) and Problem Index were used to assess urinary and pain symptoms and bother associated with these symptoms.[9] Urinary symptoms were also assessed by the American Urological Association Symptom Index (AUASI).[10] In addition, a 12-item questionnaire developed specifically for this study, the Symptom and Health Care utilization Questionnaire containing items assessing pain, urinary symptoms, the presence of nonurologic symptoms, and mood.[3] Pain was further assessed by the brief pain inventory.[11]

Nonurologic and psychological measures: COPC were assessed using the Complex Multisymptom Inventory.[12] Other psychosocial measures included the Hospital Anxiety and Depression Scale,[13] the Perceived Stress Scale (PSS),[14] the Catastrophizing scale from the short form of the Coping Strategies Questionnaire (CSQ),[15] the Positive and Negative Affect Schedule (PANAS),[16] and the International Personality Item Pool.[17] For further justification and description of the chosen questionnaires and measures please see Landis et al.[3]

Covariates: Age, income (as a marker for socioeconomic status), race, ethnicity, highest level of education, employment status, age at which symptoms began, and presence of other COPC such as fibromyalgia (FM), irritable bladder syndrome (IBS), chronic fatigue syndrome (CFS) were collected and compared between patients with short (<2) vs long (≥2 years) UCPPS symptom duration.

Statistical Analysis

MAPP Research Network recruitment targets of 95 males and females with short and long duration were informed by 2-sided 2-group comparisons at the 0.05 level of significance and 80% power. Considering the testing of multiple urologic and psychosocial symptoms between short and long duration participants in this study, retrospective power analysis was conducted for the magnitude of association that could be detected within sex at the reduced type I error rate of 0.01 using the observed sample sizes of 89 short-duration 144 long-duration females and 90 and 101 short- and long-duration males. The magnitudes of association that could be detected with 80% power were effect size 0.5 for continuous variables and odds ratios of 1.3 and 2.1 for binary factors of prevalence 60% and 20%, respectively, among short duration participants.

Demographic and medical history data were compared between patients with short and long duration by *t* tests and chi-square tests for continuous and categorical variables, respectively, in unadjusted analyses, and linear regression and logistic regression in age-adjusted analyses. Multinomial logistic regression was used for categorical variables with >2 categories. The primary analysis evaluated the association of urologic and nonurologic symptoms with dichotomous (< and ≥ 2 years) duration of symptoms by multivariable linear regression adjusted for age for continuous symptom severity measures and logistic regression for binary variables. Unadjusted analyses by *t* test and chi-square tests are shown for comparison. All analyses were stratified by sex. Logistic regression was used to associate binary symptom measures with dichotomous duration. The threshold for statistical significance was set at $P < .01$ to reduce the likelihood of a false-positive result among multiple tests; uncorrected *P* values are presented. A secondary analysis looking at differences in coping ability and psychosocial differences between male and female and patients with short vs long symptom duration was similarly performed to test the hypothesis that longer UCPPS symptom duration is associated with increased mental health comorbidity. In exploratory analyses, nonparametric regression was used to examine the linearity of the association between continuous symptom duration and severity measures adjusting for age, and to evaluate alternative duration thresholds for increasing symptom severity. To flexibly assess the association of the prevalence of duration of symptoms with COPC continuous duration was categorized into an ordinal construct based on categories of 0 to <2 years, ≥2 to <5 years, ≥5 to <10 years, ≥10 years to <15 years and ≥15 years, and prevalence of COPC was calculated for each category. The association of ordinal duration with the presence of COPC was evaluated by the Chi-Square trend test.

RESULTS

Baseline demographic and covariate characteristics are presented stratified by sex in Table 1. For both males and females, patients with short symptom duration were younger at study enrollment than patients with long duration (Mean ± SD age at enrollment 42.2 ±15.3 short duration, 50.9 ±14.3 long duration males, $P < .001$; 38.0 ± 15.1 short duration, 42.1 ± 13.7 long duration females, $P < .001$) but older at the time of symptom onset (Age at symptom onset 40.5 ± 15.2 short duration, 37.7 ± 14.4 long duration males, $P < .001$; 36.1 ± 15.0 short duration, 28.4 ± 13.6 long duration females, $P < .001$). Among males, 90 (47%) and 101 (53%) had duration less than and greater than 2 years, respectively; in females, 89 (38%) and 144 (62%) had duration less than and greater than 2 years, respectively. When adjusted for age there were no significant differences in race, ethnicity, level of education, employment status or income levels in individuals with shorter vs longer symptom duration for either sex.

Table 2 depicts the baseline medical history for UCPPS participants. Overall, participants with recent vs ≥ 2 year symptom duration did not differ in the prevalence of COPC. There was a slight increase in the likelihood of females but not males in experiencing CFS (Adjusted OR 1.04 per year.) for each additional year of UCPPS symptoms ($P = .0095$) when duration was analyzed as a continuous variable. In males longer duration was not associated with concurrent CFS, FM, or IBS.

Men but not women had slightly more severe urinary symptoms with longer duration (Table 3). Men with ≥2 year duration had significantly worse ICSI and AUASI scores and voiding symptoms (ICSI Adj. Mean Diff. 2.0, $P = .004$; AUASI Adj. Mean Diff 3.4, $P = .006$; Voiding Adj. Mean Diff. 0.4, $P = .009$). Men who had symptoms for ≥ 2 years also had increased urgency, worse severity as indicated by the GUPI Urinary subscale, GUPI Total, and IC Problem index, and greater pain severity, but these differences were smaller than could be detected with high power (effect sizes 0.2-0.4). No significant difference in urologic or pain symptoms was observed for women by duration. In summary, the symptom differences between the early and late group were generally small and likely of minimal clinical significance.

Table 4 presents psychosocial measures and nonurologic symptom scores in male and female patients with UCPPS. Women reported a tendency toward improved psychological symptoms and coping with longer duration that was partially accounted for by age, although these differences were small and not significant at the $P = .01$ level ($P = .02$ CSQ Catastrophizing unadjusted, $P = .08$ CSQ Catastrophizing adjusted; $P = .037$ unadjusted CSQ Coping, $P = .118$ CSQ Coping adjusted). Further, females with symptom duration ≥ 2 years reported less perceived stress and decreased negative affect than females with shorter duration ($P = .013$ PSS unadjusted, $P = .031$ adjusted PSS; $P = .038$ PANAS negative unadjusted, $P = .100$ PANAS adjusted). In males, average depression was higher in males with duration ≥2 years than men with <2 years ($P = .045$) after adjustment for age, but this difference was also small and not significant at the 0.01 level.

Exploratory analysis for alternative thresholds with duration as a continuous variable revealed increasing severity in most urinary symptoms for males until about 15 years duration. No strict thresholds were observed for symptoms in females. Nonurologic symptoms in females appeared to sharply decrease with increasing duration up to 5 years but gradually returned to higher levels as duration approached 20 years. The prevalence of other COPC did not consistently increase across duration categories, and no significant association was detected between ordinal symptom duration and the presence of COPC (data not shown).

DISCUSSION

This cross-sectional study examined the association of UCPPS symptom duration with symptom severity, prevalence of comorbid conditions, and psychosocial distress at baseline in patients enrolled in the MAPP Research Network. In clinical practice, it is often assumed that severity of symptoms in patients with UCPPS is associated with symptom duration. However, our analyses generally did not confirm this clinical impression. There was an association between symptom duration and severity in only limited subpopulations. Two years was used as the cutoff based on expert opinion in an attempt to differentiate those with "early" vs established disease. Although we conducted exploratory analyses using all patient data spline-based methods for an alternative threshold, none was identified to detect a difference.

Duration of symptoms was not associated with pain severity in males or females, and only males but not females had more severe urinary symptoms with longer duration of symptoms. Although this may represent the additional development of BPH in older men as reflected in age adjusted differences in AUA symptom score index, exploratory analysis for alternative thresholds with duration as a continuous variable revealed increasing severity in most urinary symptoms for males until about 15 years duration and not beyond. Surprisingly, in females, we did not find worsening urinary symptoms with longer duration of disease. This may imply gender differences in symptoms in UCPPS, gender differences in disease coping with longer duration of symptoms, or some biological or pathophysiological differences between both genders in the MAPP cohort. Indeed, females in the MAPP met IC/BPS criteria while males met CP/CPPS and/or IC/BPS criteria which may account for this variability. Consistent with this difference in inclusion criteria, females in the MAPP have more bladder-centric symptoms than males.[18,19] In addition, females had better coping with advancing age regardless of duration of symptoms. It will be interesting to see if these cross-sectional data are confirmed in future longitudinal studies of UCPPS patients followed over time in the next phase of the MAPP study.

It has long been assumed that there is a time dependent-progression in UCPPS from an organ specific (bladder) disease to a more systemic or centralized pain syndrome (involving the bladder and other organs outside of the pelvis).[3-5,7] It has been hypothesized that presence of one or more chronic overlapping pain conditions is a manifestation of more severe disease and that there is a temporal association between the onset of UCPPS and the development of other Chronic overlapping pain conditions.[20-23] This suggests that in some patients, central sensitization mechanisms contribute to the manifestation of IC/BPS. Consistent with this paradigm, other somatic syndromes associated with central sensitization have been shown to manifest increased symptom severity and more generalized systemic manifestations associated with longer duration of symptoms. An underlying implication is that

Table 1. Baseline demographic characteristics for UCPPS participants

		Male				Female			
		<2 Years	>=2 Years	Unadjusted *P* Value	Age Adjusted *P* Value	<2 Years	≥2 Years	Unadjusted *P* Value	Age Adjusted *P* Value
Number of Participants	Number of Participants	90	101			89	144		
Clinical Site	Northwestern U	17 (18.9%)	17 (16.8%)	0.833	0.739	9 (10.1%)	15 (10.4%)	0.065	0.100
	UCLA	14 (15.6%)	18 (17.8%)			16 (18.0%)	18 (12.5%)		
	U of Iowa	12 (13.3%)	15 (14.9%)			17 (19.1%)	17 (11.8%)		
	U of Michigan	10 (11.1%)	16 (15.8%)			16 (18.0%)	28 (19.4%)		
	University of Washington	22 (24.4%)	18 (17.8%)			15 (16.9%)	16 (11.1%)		
	Washington University, St. Louis	15 (16.7%)	17 (16.8%)			13 (14.6%)	30 (20.8%)		
	Stanford University					3 (3.4%)	20 (13.9%)		
Age (years)	Mean ± s.d.	42.2 ± 15.3	50.9 ± 14.3	<.001	.	38.0 ± 15.1	42.1 ± 13.7	0.035	.
Age Group	<35 years	34 (37.8%)	21 (20.8%)	<.001	0.542	50 (56.2%)	55 (38.2%)	0.010	0.596
	35-50 Years	33 (36.7%)	27 (26.7%)			15 (16.9%)	47 (32.6%)		
	50+ Years	23 (25.6%)	53 (52.5%)			24 (27.0%)	42 (29.2%)		
Race	White	79 (87.8%)	91 (90.1%)	0.048	0.180	78 (87.6%)	126 (87.5%)	0.848	0.873
	Black	2 (2.2%)	7 (6.9%)			2 (2.2%)	5 (3.5%)		
	Other	9 (10.0%)	3 (3.0%)			9 (10.1%)	13 (9.0%)		
Ethnicity	Hispanic	8 (8.9%)	2 (2.0%)	0.048	0.383	8 (9.0%)	10 (6.9%)	0.570	0.565
	Non-Hispanic	81 (90.0%)	99 (98.0%)			81 (91.0%)	134 (93.1%)		
	Unknown	1 (1.1%)	0 (0.0%)						
Highest level of education completed	High School or GED	9 (10.0%)	5 (5.0%)	0.130	0.347	6 (6.7%)	11 (7.6%)	0.829	0.926
	Some College	19 (21.1%)	23 (22.8%)			31 (34.8%)	45 (31.3%)		
	Graduated from College or University	41 (45.6%)	36 (35.6%)			34 (38.2%)	52 (36.1%)		
	Professional or graduate degree	21 (23.3%)	37 (36.6%)			18 (20.2%)	36 (25.0%)		
Employment	Employed	67 (74.4%)	67 (66.3%)	0.313	0.372	56 (62.9%)	88 (61.1%)	0.453	0.734
	Unemployed	10 (11.1%)	9 (8.9%)			18 (20.2%)	21 (14.6%)		
	Retired	11 (12.2%)	19 (18.8%)			5 (5.6%)	8 (5.6%)		
	Full-time homemaker					2 (2.2%)	10 (6.9%)		
	Disabled	2 (2.2%)	6 (5.9%)	0.313	0.372	8 (9.0%)	16 (11.1%)		
	Missing					0 (0.0%)	1 (0.7%)		
Income	$10,000 or less	6 (6.7%)	3 (3.0%)	0.124	0.285	15 (16.9%)	16 (11.1%)	0.221	0.378
	$10,001 to $25,000	6 (6.7%)	6 (5.9%)			8 (9.0%)	14 (9.7%)		
	$25,001 to $50,000	10 (11.1%)	16 (15.8%)			14 (15.7%)	29 (20.1%)		
	$50,001 to $100,000	23 (25.6%)	38 (37.6%)			27 (30.3%)	34 (23.6%)		
	More than $100,000	39 (43.3%)	29 (28.7%)			14 (15.7%)	38 (26.4%)		
	Prefer not to Answer	6 (6.7%)	8 (7.9%)			11 (12.4%)	12 (8.3%)		
	Missing	0 (0.0%)	1 (1.0%)			0 (0.0%)	1 (0.7%)		
Age at which symptoms began	Mean ± s.d.	40.5 ± 15.2	37.7 ± 14.4	0.201	<0.001	36.1 ± 15.0	28.4 ± 13.6	<.001	<0.001
Duration of Symptoms in Years	Mean ± s.d.	1.7 ± 1.4	13.3 ± 12.4	<.001	<0.001	1.6 ± 0.7	13.8 ± 11.1	<.001	<0.001

Table 2. Baseline medical history for UCPPS participants

	Male					Female				
	<2 Years	>=2 Years	Unadjusted *P* Value	Age adjusted *P* Value	Mean Difference (99% CI)	<2 Years	≥2 Years	Unadjusted *P* Value	Age Adjusted *P* Value	Mean Difference (99% CI)
Number of participants	90	101				89	144			
Other Somatic Syndrome										
None	60 (66.7%)	72 (71.3%)	0.101	0.091		50 (56.2%)	80 (55.6%)	0.887	0.935	
FM only	4 (4.4%)	1 (1.0%)			0.2 (0.0, 3.8)	5 (5.6%)	5 (3.5%)			0.8 (0.1, 4.3)
IBS only	24 (26.7%)	20 (19.8%)			0.8 (0.3, 2.1)	19 (21.3%)	30 (20.8%)			0.9 (0.4, 2.3)
CFS only	1 (1.1%)	1 (1.0%)			1.4 (0.0,71.2)	3 (3.4%)	8 (5.6%)			1.6 (0.3, 9.9)
>1 Dx	1 (1.1%)	7 (6.9%)			14.1 (0.7, 265)	12 (13.5%)	21 (14.6%)			1.1 (0.4, 3.2)
COPC										
None	60 (66.7%)	72 (71.3%)	0.490	0.977		50 (56.2%)	80 (55.6%)	0.926	0.965	
Any	30 (33.3%)	29 (28.7%)			1.0 (0.4, 2.3)	39 (43.8%)	64 (44.4%)			1.0 (0.5, 2.1)
Pain location										
Pelvic pain and beyond	65 (72.2%)	69 (68.3%)	0.556	0.738		72 (80.9%)	110 (76.4%)	0.419	0.410	
Pelvic pain only	25 (27.8%)	32 (31.7%)			1.1 (0.5, 2.6)	17 (19.1%)	34 (23.6%)			1.3 (0.6, 3.1)

central sensitivity resulting from one chronic painful condition may predispose to development of other conditions. Studies of patients with CFS have shown that patients with a more polysymptomatic phenotype are more likely to be female, have more severe symptoms and to have been ill for longer.[24,25] These patients are more likely to have comorbid IBS, anxiety, and depression than those with oligosymptomatic phenotype.[24] In individuals with migraine headaches, the prevalence of cutaneous allodynia (considered a systemic manifestation of the disease and a marker central sensitization) is increased in those with long duration of illness relative to those with migraine for less than 10 years.[26] The presence of allodynia in patients with migraines is associated with depression, anxiety, and comorbid conditions such as IBS, FM, and CFS.[27] FM patients with longer duration of symptoms and increased symptom duration manifest more sleep disturbances.

We did not find evidence of a time-dependent progression to a more centralized pain syndrome in most patients with UCPPS. MAPP participants with early vs ≥2 year symptom duration were as likely to experience COPC. Thus, our results do not support the expected temporal association between duration of symptoms and presence of comorbid conditions in the MAPP cohort. In addition, our results do not support an association between duration of symptoms and symptom severity in women, and there was only a modest association in men. These findings are consistent with those of the RAND Interstitial Cystitis Epidemiology study, which found no clear pattern of systemic symptom progression over time in a cohort of community women with IC/BPS symptoms.[28] In contrast, some studies do suggest such an association. In a cohort study of patients with IC/BPS, Nickel et al categorized patients by the presence or absence of 6 clinically identifiable and predefined domains including urinary, psychosocial, organ specific, infection and neurologic/systemic.[29] The authors found that duration of symptoms was strongly associated with an increase in the number of domains. Although the number of domains was associated with increased severity as measured by the ICSI and pain visual analog scales, it did not correlate, with other urinary symptom assessment. Patients with COPC had a modest increase in severity of UCPPS symptoms. Although we do not find an association with duration of symptoms, individuals with COPC including IBS, FM, and CFS, reported more severe urinary symptoms, pain, depression, and anxiety than individuals without COPC.[30] Patients with COPC are more likely to be younger at symptom onset than those without COPC.[30] These observations are consistent with systemic manifestations being associated with younger age at onset of disease in patients with migraine headaches and other COPC.[24,27] Thus, the presence of more systemic or centralized condition was associated with more severe symptoms and earlier onset, consistent with previous studies and with the literature of other somatic syndromes, but not with duration of UCPPS symptoms. In summary, our cross-sectional data

Table 3. Selected baseline urological symptoms scores for UCPPS participants

	Male					Female				
	<2 Years	>=2 Years	Unadjusted *P* Value	Age Adjusted *P* Value	Mean Difference (99% CI)	<2 Years	≥2 Years	Unadjusted *P* Value	Age Adjusted *P* Value	Mean Difference (99% CI)
Number of Participants	90	101				89	144			
Pain Severity (0-28)	13.5 ± 4.5	14.5 ± 6.0	0.181	0.104	1.3 (−0.8, 3.4)	16.0 ± 5.2	15.6 ± 5.9	0.631	0.972	0.0 (−1.9, 1.9)
Urinary Severity (0-25)	9.7 ± 5.8	12.9 ± 6.3	<.001	0.003	2.7 (0.3, 5.0)	14.1 ± 5.7	13.3 ± 6.3	0.320	0.416	−0.7 (−2.8, 1.5)
SYM-Q1: Baseline Pain (0-10)	4.6 ± 2.1	5.1 ± 2.4	0.142	0.112	0.5 (−0.3, 1.4)	5.3 ± 2.0	5.2 ± 2.2	0.546	0.920	−0.0 (−0.8, 0.7)
SYM-Q2: Baseline Urgency (0-10)	4.1 ± 2.5	5.2 ± 2.6	0.004	0.033	0.8 (−0.2, 1.8)	5.6 ± 2.4	5.2 ± 2.6	0.261	0.383	−0.3 (−1.2, 0.6)
SYM-Q3: Baseline Frequency (0-10)	4.2 ± 2.7	5.0 ± 2.5	0.042	0.198	0.5 (−0.5, 1.5)	5.3 ± 2.5	5.0 ± 2.6	0.365	0.468	−0.3 (−1.1, 0.6)
SYM-Q4: Baseline Void (1-4)	2.1 ± 0.9	2.5 ± 0.9	0.001	0.009	0.4 (0.0, 0.7)	2.6 ± 0.9	2.6 ± 0.9	0.714	0.769	0.0 (−0.3, 0.4)
SYM-Q5: Baseline Uro-Symptoms (0-10)	4.8 ± 2.2	5.1 ± 2.5	0.262	0.199	0.5 (−0.5, 1.4)	5.6 ± 2.2	5.2 ± 2.4	0.259	0.471	−0.2 (−1.0, 0.6)
SYM-Q6: Baseline NonUro-Symptoms (0-10)	2.9 ± 2.8	2.6 ± 2.3	0.450	0.495	−0.3 (−1.2, 0.7)	3.6 ± 2.9	3.7 ± 2.7	0.784	0.700	0.1 (−0.8, 1.1)
Baseline GUPI pain score (0-23)	11.8 ± 3.7	12.6 ± 4.7	0.202	0.098	1.1 (−0.6, 2.7)	13.1 ± 4.3	12.7 ± 4.8	0.533	0.910	−0.1 (−1.6, 1.5)
Baseline GUPI urinary subscale (0-10)	4.2 ± 2.8	5.2 ± 2.8	0.011	0.029	0.9 (−0.2, 2.0)	6.0 ± 2.7	5.6 ± 3.1	0.290	0.508	−0.3 (−1.3, 0.8)
Baseline GUPI QOL impact subscore (0-12)	7.4 ± 2.5	7.7 ± 3.0	0.410	0.179	0.6 (−0.5, 1.6)	8.2 ± 2.8	7.6 ± 3.0	0.095	0.233	−0.5 (−1.5, 0.5)
Baseline GUPI total score (0-45)	23.5 ± 7.0	25.5 ± 8.9	0.077	0.044	2.4 (−0.7, 5.6)	27.3 ± 8.3	25.9 ± 9.3	0.240	0.514	−0.8 (−3.8, 2.2)
Baseline ICINDEX-Symptom (0-20)	7.2 ± 4.1	9.6 ± 4.9	<.001	0.004	2.0 (0.2, 3.7)	11.0 ± 4.3	10.6 ± 4.6	0.569	0.647	−0.3 (−1.9, 1.3)
Baseline ICINDEX-Problem (0-16)	6.2 ± 4.3	8.3 ± 4.5	0.002	0.013	1.6 (−0.1, 3.3)	9.8 ± 3.9	9.3 ± 4.1	0.353	0.407	−0.5 (−1.9, 1.0)
AUA baseline symptom score index over the past month (0-35)	11.9 ± 7.7	15.8 ± 8.3	<.001	0.005	3.4 (0.3, 6.5)	17.2 ± 8.7	16.4± 8.5	0.463	0.628	−0.6 (−3.5, 2.4)
Baseline BPI pain severity sore (0-10)	3.5 ± 1.9	4.0 ± 2.1	0.062	0.018	0.7 (−0.1, 1.5)	4.2 ± 1.8	4.3 ± 2.0	0.839	0.627	0.1 (−0.5, 0.8)
Baseline FSFI (Female) (0-36)	0 (0.0%)	0 (0.0%)	.	.	. (.,.)	17.8 ± 10.0	16.8 ± 9.9	0.477	0.794	−0.3 (−3.7, 3.0)
Baseline IIEF-6 (Male) (0-30)	22.1 ± 8.8	20.3 ± 9.9	0.180	0.557	−0.8 (−4.4, 2.8)	0 (0.0%)	0 (0.0%)	.	.	. (.,.)

Table 4. Selected baseline nonurological symptoms scores for UCPPS participants

	Male					Female				
	<2 Years	>=2 Years	Unadjusted *P* Value	Age Adjusted *P* Value	Mean Difference (99% CI)	<2 Years	≥2 Years	Unadjusted *P* Value	Age adjusted *P* Value	Mean Difference (99% CI)
Number of Participants	90	101				89	144			
SYM-Q7: Baseline Mood (0-10)	4.1 ± 2.2	4.3 ± 2.5	0.555	0.127	0.5 (−0.4, 1.4)	4.5 ± 2.2	4.2 ± 2.2	0.292	0.688	−0.1 (−0.8, 0.6)
HADS-Anxiety (0-21)	7.4 ± 4.4	7.5 ± 4.3	0.920	0.231	0.8 (−0.9, 2.4)	8.6 ± 4.9	7.5 ± 4.6	0.076	0.224	−0.7 (−2.3, 0.8)
HADS-Depression (0-21)	5.1 ± 4.1	5.8 ± 4.1	0.225	0.045	1.2 (−0.3, 2.8)	5.8 ± 4.7	5.0 ± 4.0	0.176	0.257	−0.7 (−2.1, 0.8)
IPIP:Neuroticism (24-120)	62.0 ± 16.2	60.3 ± 16.4	0.478	0.644	1.1 (−5.1, 7.3)	66.1 ± 18.1	63.0 ± 16.3	0.181	0.463	−1.6 (−7.4, 4.1)
IPIP:Extraversion (24-120)	81.3 ± 14.3	80.1 ± 12.8	0.555	0.170	−2.8 (−7.9, 2.4)	79.7 ± 14.5	80.5 ± 13.9	0.691	0.790	0.5 (−4.4, 5.5)
IPIP:Openness (24-120)	83.1 ± 13.1	80.6 ± 10.9	0.156	0.278	−2.0 (−6.7, 2.7)	83.9 ± 12.4	84.4 ± 12.8	0.781	0.611	0.9 (−3.5, 5.3)
IPIP:Agreeableness (24-120)	92.5 ± 10.5	92.8 ± 10.4	0.852	0.380	−1.4 (−5.3, 2.6)	97.2 ± 9.1	99.1 ± 9.4	0.127	0.300	1.3 (−1.9, 4.4)
IPIP:Conscientiousness (24-120)	95.7 ± 13.3	95.1 ± 14.0	0.780	0.125	−3.1 (−8.3, 2.1)	95.5 ± 13.9	97.9 ± 12.4	0.166	0.283	1.9 (−2.6, 6.4)
CSQ: CAT (0-36)	10.1 ± 8.3	11.2 ± 8.7	0.377	0.078	2.2 (−1.0, 5.5)	15.8 ± 9.0	13.1 ± 8.5	0.022	0.080	−2.0 (−4.9, 0.9)
CSQ: baseline average of questions 1 to 6 (0-6)	1.7 ± 1.4	1.9 ± 1.5	0.377	0.078	0.4 (−0.2, 0.9)	2.6 ± 1.5	2.2 ± 1.4	0.022	0.080	−0.3 (−0.8, 0.2)
CSQ: ability to control pain with coping (0-6)	2.8 ± 1.4	3.0 ± 1.5	0.418	0.885	0.0 (−0.5, 0.6)	2.9 ± 1.4	3.3 ± 1.4	0.037	0.117	0.3 (−0.2, 0.8)
CSQ: ability to decrease pain with coping (0-6)	2.4 ± 1.5	2.7 ± 1.5	0.132	0.308	0.2 (−0.3, 0.8)	2.8 ± 1.2	3.0 ± 1.4	0.233	0.505	0.1 (−0.3, 0.6)
Baseline PANAS positive affect (5-50)	31.1 ± 7.4	30.0 ± 7.2	0.297	0.037	−2.2 (−5.0, 0.5)	28.4 ± 7.9	29.8 ± 7.9	0.189	0.369	0.9 (−1.7, 3.6)
Baseline PANAS negative affect (5-50)	21.0 ± 7.3	20.3 ± 7.8	0.564	0.578	0.6 (−2.2, 3.4)	23.1 ± 9.5	20.6 ± 7.6	0.038	0.100	−1.8 (−4.6, 1.0)
Baseline perceived stress scale (PSS) (0-40)	15.7 ± 7.1	15.0 ± 7.2	0.502	0.599	0.5 (−2.1, 3.2)	19.1 ± 9.3	16.2 ± 7.6	0.013	0.031	−2.3 (−5.1, 0.4)

do not support temporal progression of UCPPS from an organ-specific to a more centralized condition in most patients. It is possible that UCPPS and COPC represent manifestations of the similar pathophysiological mechanisms that are limited to some UCPPS patient subsets. It is also possible that UCPPS and COPC have no direct relationship but instead share common risk factors. Lastly, it is possible that there is indeed a temporal progression of disease from an organ centric to a more systemic syndrome manifested by other COPC but that our cross-sectional study design did not allow us to detect such a relationship. For example, central sensitization may develop early on in less than 6-12 months in a subset of (but not in all) UCPPS patients. Since the majority of patients in the MAPP cohort had UCPPS symptoms for more than 6 months (inclusion criteria) and our duration cutoff was set at $<$ vs $\geq$ 2 years, a difference may not be demonstrated between the 2 groups. Lastly, it is possible that treatments varied among the 2 groups and may account for our findings. Although, treatments were not considered in the inclusion criteria for MAPP, open-ended questionnaires, our patients reported a very wide ranging set of interventions, including pharmacologic agents and pelvic floor therapy in open-ended questionnaires. We compared baseline usage of oral opioids, tricyclics, physical therapy to the pelvic floor, Elmiron, and alpha blockers (the later in males only) between the groups with short and long duration. Only alpha blockers differed in men, with short duration patients more likely to be users (23.4% <2 years, 11.5% ≥2years, $P = .04$). There was no difference observed in any of the other medications.

Our study has some significant limitations. This is not a study of the natural history of incident cases and as such it is not designed to evaluate the natural progression of the disease. We studied potential association between symptom duration and disease manifestation, but not the progression of disease with time. The duration of symptom was reported by patients and was not verified by medical chart review. Future longitudinal MAPP studies may provide more insight into development and resolution of UCPPS and the role of COPC, mental health comorbidities, and other factors that may be associated with symptom progression and resolution. The inclusion criteria for males and females were slightly different and may account for some of the observed gender differences in the association of symptom severity and duration. Lastly, the majority of participants was recruited from referral centers and as such may not be representative of the general UCPPS population.

CONCLUSION

Symptom duration did not appear to affect severity of UCPPS pain. Males with UCPPS symptoms ≥2 years experienced more severe urinary symptoms than males with symptoms <2 years. Symptom duration was not associated with an increased rate of concomitant somatic syndromes, suggesting that UCPPS patients do not exhibit a time-dependent progression to a systemic disease phenotype.

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