An online UPOINT tool for phenotyping patients with chronic prostatitis

Christine N. Tran, MD,[1] Jianbo Li, PhD,[2] Daniel A. Shoskes, MD[1]

[1]The Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, Ohio, USA

[2]Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, Ohio, USA

TRAN CN, LI J, SHOSKES DA. An online UPOINT tool for phenotyping patients with chronic prostatitis. *Can J Urol* 2014;21(2):7195-7200.

Introduction: *To evaluate the clinical phenotypes of patients with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) using a web based online tool and to compare these clinical features with patients evaluated in a tertiary referral clinic.*

Materials and methods: *Data was collected from 720 men who gave complete online responses on a website which determines the UPOINT clinical phenotype in CP/CPPS and measures symptom severity with the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI). This was compared to phenotype and symptom severity of 220 patients evaluated in person at a tertiary referral clinic.*

Results: *The web-based cohort had CPSI scores of 11.1, 4.8, 7.6, and 23.6 for pain, urinary, quality-of-life, and total score, respectively. The percentage of patients positive for each domain was 76%, 74%, 75%, 10%, 46%, and 75% for the urinary, psychosocial, organ specific, infection, neurologic/systemic, and tenderness domains, respectively. There was a positive correlation between CPSI and number of positive UPOINT domains ($\rho = 0.25$, $p < 0.0001$). Comparison between web- and clinic-based groups showed that the clinic group had fewer UPOINT positive domains compared to the web-based group (2.9 versus 3.6, $p < 0.0001$), but had worse quality-of-life (9.0 versus 7.6, $p < 0.0001$) and CPSI total scores (25.0 versus 23.6, $p = 0.0052$).*

Conclusions: *Men using an online tool to clinically phenotype CP/CPPS show similar correlations between UPOINT domains, symptom severity, age and duration. While symptom severity was worse in patients seen in a tertiary referral clinic, the differences were small.*

Key Words: prostatitis, pelvic pain, UPOINT, web

Introduction

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), or NIH category III prostatitis, is a common clinical syndrome characterized by pain or discomfort localized to the abdomen, pelvis, and genitals, as well as irritative and obstructive lower urinary tract symptoms (LUTS) in the absence of bacteriuria.[1] These symptoms are associated with substantial morbidity and have a detrimental impact on quality-of-life and healthcare costs.[2,3]

Accepted for publication February 2014

Address correspondence to Dr. Daniel A. Shoskes, Glickman Urological and Kidney Institute, Cleveland Clinic Foundation, 9500 Euclid Avenue, Desk Q10-1, Cleveland OH 44195 USA

Physicians seeking an evidence-based approach to the management of the CP/CPPS population are frequently frustrated. Many therapies that show promise in clinical practice have failed to demonstrate efficacy when subjected to the gold standard of the randomized placebo-controlled clinical trial. There has been recent recognition that the population of men with CP/CPPS is not homogeneous with similar symptomatology and etiologic mechanisms but, rather, a diverse group of individuals with differing phenotypes requiring different therapies. The UPOINT system was developed in recognition of the need for individualized therapy.[4,5] It is a classification system that is used to categorize the phenotype of patients with CP/CPPS using six clinical domains: Urinary, Psychosocial, Organ-Specific, Infection, Neurologic/Systemic, and Tenderness of muscles. We have shown

that symptom duration and number of UPOINT domains correlated with symptom severity. Multimodal therapy using a treatment for each positive UPOINT domain simultaneously has since been shown to lead to significant improvement in symptoms and quality-of-life in CP/CPPS patients.[5] A limitation of any such system that is developed and studied in a tertiary care center is whether the findings are generalizable to the CP/CPPS patient population at large.

More recently, a web-based UPOINT tool was designed to help physicians classify patients with an established diagnosis of CP/CPPS or interstitial cystitis into the six domains of the UPOINT system (www.upointmd.com) and then recommend therapies for each positive domain. This web tool has been accessed thousands of times, both by physicians and by patients interested the process. These patients likely represent a more heterogeneous population than is typically seen in a tertiary care referral center. De-identified data that is entered into the website is stored in a MySQL database and available for download. In the present study, we report on the phenotype of a cohort of men with CP/CPPS using the web-based UPOINT tool and the correlation of phenotype with symptom severity. We also compare the results from this web-based group to data obtained from patients we have seen and examined in our own clinic.

Materials and methods

This study was reviewed and approved by the Cleveland Clinic Institutional Review Board. The web-based cohort consisted of men who had submitted information on the UPOINT website (http://www.upointmd.com) between May 7, 2009 and Feb 1, 2013. Users are brought to a homepage explaining the usefulness of the UPOINT system in the phenotypic classification of patients with a diagnosis of CP/CPPS. A disclaimer section emphasizes that this web-based tool is for physician use and was not designed to diagnose CP/CPPS but, rather, to classify patients who already have an established diagnosis. An instructions section then provides a list of suggested tests for each UPOINT domain as well as a link to the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI). Once the user has obtained the above information, they are ready to begin the survey. The survey consists of the following sections: History, NIH-CPSI scores, Physical Exam, and Other Tests. After submitting the survey, users are then provided with a list of positive UPOINT domains. For each domain, a "Yes" indicates that, based on the provided information, the patient is positive for that domain. A "No" indicates the patient is negative for that domain based on current criteria. "Unable to assess" means that insufficient evidence was provided to decide on the presence or absence of the domain. On a following webpage, a list of all potential therapies and the domains for which they may be used are provided as a basis from which the physician and patient can begin to tailor treatment strategies.

In total there were 1763 responses on the website. We excluded women and those who did not enter gender leaving 1365. We then excluded those records with significant missing data which would not allow designation of the UPOINT phenotype leaving 720.

The clinic-based cohort consisted of 220 new patients with a diagnosis of CPPS seen at the Cleveland Clinic by one physician and whose information had been recorded in an institutional review board-approved database. Each patient had had their symptom severity assessed using the NIH-CPSI; this was reported as subscores for pain, urinary symptoms, and quality-of-life, as well as a total score. Review of the history and physical examination, urine cultures, and expressed prostatic secretions or post-massage urine results led to a yes/no classification for each of the six UPOINT domains. Patients in this cohort included newly diagnosed, relatively treatment-naïve patients as well as tertiary referral patients in whom multiple therapies had failed.

For comparison between two groups, the Wilcoxon rank-sum test was used to compare continuous variables and the chi-square test was used to compare categorical variables. For correlation analysis, Spearman's rank correlation coefficient and linear regression analysis were used. All analyses were performed using the statistical software package R (version 2.15).

Results

Web-based UPOINT

The web-based cohort consisted of 720 patients. Mean age was 42 years (range 18-78) with median time since first diagnosis of 14 months (range 0-480), and median duration of current symptoms of 15 weeks (range 0-1000). The patients had CPSI scores typical of those reported in previous clinical studies: pain 11.1 ± 4.6 (range 0-21), urinary 4.8 ± 2.9 (range 0-10), quality-of-life 7.6 ± 3.1 (range 0-12), and total score 23.6 ± 7.5 (range 0-43). The number of patients with positive findings for each domain was urinary 549/720 (76%), psychosocial 531/720 (74%), organ specific 547/720 (76%), infection 75/720 (10%), neurologic/systemic 328/720 (46%), and tenderness 543/720 (75%). The

TABLE 1. **Web-based patient answers**

Question	No	Yes	Missing %	Yes
Does the pain resolve or significantly improve right after urination?	432	277	11	38.5
Hematospermia	661	54	5	7.5
Depression	435	282	3	39.2
Fibromyalgia	635	76	9	10.6
Chronic fatigue syndrome	627	88	5	12.2
Prostate cancer	703	9	8	1.25
Does the patient feel helpless or hopeless about their condition?	256	462	2	64.2
Is there pain outside the pelvis and genitals (eg. down the legs, in the chest or arms)?	455	262	3	36.4
Is the prostate specifically tender (ie. more so than other parts of the rectal exam)?	360	318	42	44.2
Is there suprapubic tenderness?	336	347	37	48.2
Is there tenderness, spasm and/or trigger points in the pelvic floor?	254	403	63	56
Improvement in symptoms following intravesical lidocaine?	87	38	595	5.3
Any bladder ulcers or glomerulations on cystoscopy?	332	22	366	3.1
Uropathogenic bacteria localized to prostate (eg. gram negative bacilli or enterococcus)?	367	52	301	7.2
Atypical bacteria in urine (eg. mycoplasma, ureaplasma)?	415	37	268	5.1

mean number of positive UPOINT domains was 3.6 ± 1.3 (median 4, range 0-6). Responses to individual questions are reported in Table 1. Using Spearman's rank correlation, we found a weak but significant positive correlation between CPSI and the number of positive UPOINT total domains ($\rho = 0.25$, $p < 0.0001$). Age and current duration of symptoms were also not related to number of positive UPOINT domains ($\rho = 0.06$, $p = 0.11$; $\rho = 0.06$, $p = 0.17$).

Clinic-based UPOINT

The clinic-based cohort consisted of 220 patients who have been previously reported on.[5] Mean age was 44 years (range 11-79) with median duration of symptoms of 24 months (range 0-440), Table 2. The patients had CPSI scores typical of those reported in previous clinical studies: pain 11.4 ± 3.6 (range 0-19), urinary 4.4 ± 3.1 (range 0-10), quality-of-life 9.0 ± 2.4 (range 0-12), and total score 25.0 ± 6.5 (range 3-39). The number of

TABLE 2. **Comparison of UPOINT domains**

Domain	Web-based group (n = 720)		Clinic-based group (n = 220)		Chi-squared p value
	Number positive	Percent positive	Number positive	Percent positive	
U	549	76.2	135	61.4	0.0000
P	531	73.8	83	37.7	0.0000
O	547	76	159	72.3	0.3070
I	75	10.4	34	15.5	0.0546
N	328	45.6	65	29.5	0.0000
T	543	75.4	158	71.8	0.3250

patients with positive findings for each domain was urinary 135/220 (61%), psychosocial 83/220 (38%), organ specific 159/220 (72%), infection 34/220 (16%), neurologic/systemic 65/220 (30%), and tenderness 158/220 (72%). The mean number of positive UPOINT domains was 2.9 ± 1.0 (median 3, range 0-5). Using Spearman's rank correlation, we found a positive correlation between CPSI and the number of positive UPOINT total domains ($\rho = 0.36$, $p < 0.0001$).

Comparison of web-based and clinic-based groups

We used the Wilcoxon rank sum test to compare the groups based on age, symptom duration, total UPOINT score, and NIH-CPSI response (pain, urinary, quality-of-life, and total score), Table 2. The clinic group was older and had longer symptom duration (57.1 versus 53.3 months, $p = 0.0088$) compared to the web-based group. The clinic group had lower UPOINT total score compared to the web-based group (2.9 versus 3.6, $p < 0.0001$), but had worse quality-of -ife (9.0 versus 7.6, $p < 0.0001$) and CPSI total scores (25.0 versus 23.6, $p = 0.0052$).

Comparison between the web- and clinic-based groups was also made for each UPOINT domain using the chi-squares test, Table 3. The web-based group had higher percentages of patients with a positive urinary (76.2% versus 61.4%, $p < 0.0001$), psychosocial (73.8% versus 37.7%, $p < 0.0001$), and neurologic/systemic domain (45.6% versus 29.5%, $p < 0.0001$).

Correlation of CPSI to UPOINT score was also assessed. There was indeed a positive correlation between CPSI and UPOINT ($p < 0.0001$) in both groups. However, the clinic-based group was found to have a higher CPSI score by 2.87 points.

Discussion

CP/CPPS is a prevalent, costly, and often clinically frustrating syndrome affecting up to 15% of all men. Recent advances in the management of this disease with the development of the UPOINT system and its use in directing multimodal therapy have the potential for wide-reaching effect. Patients now rely on the Internet moreso than ever to seek healthcare information and services. The use of web-based data collection is a well-established tool that has been used in the assessment of diseases as disparate as HIV/AIDS, ulcerative colitis and end stage renal disease.[6-8] Additionally, web-based interventions are becoming increasingly used in areas such as health behavior modification and chronic disease management.[6] In an effort to reach an even larger patient and physician base, a web-based UPOINT tool was thus recently launched to help men with CP/CPPS and their care providers systematically categorize and direct treatment for this prevalent disease. Since this web tool can collect de-identified data points in a SQL database, it allows us to analyze the self reported characteristics of patients in the general population of CPPS sufferers and compare the phenotypes and severity with patients we see in our tertiary referral clinic.

In the present study, we analyze data from a group of 720 men who completed the UPOINT online questionnaire and compare this to a population of men diagnosed with CP/CPPS at a tertiary referral center. A significant observation is that the two groups differed in terms of baseline characteristics. The clinic-based population was older, had longer symptom duration, and had worse NIH-CPSI quality-of-life and total scores. This may be explained by the fact that the clinic

TABLE 3. **Demographics, National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) and UPOINT scores**

Variable	Web-based group (n = 720)			Clinic-based group (n = 220)			Wilcoxon rank sum p value
	Responses	Mean value	Standard deviation	Responses	Mean value	Standard deviation	
Age	591	42	12.2	220	44.6	13.4	0.00708
Duration	604	53.3	125.3	220	57.1	87.5	0.00882
Pain	720	11.2	4.6	220	11.5	3.6	0.59433
Urinary	717	4.8	2.9	220	4.4	3.1	0.08732
Quality-of-life	719	7.6	3.1	220	9	2.4	0.00000
Total CPSI score	720	23.6	7.5	220	25	6.5	0.00515
UPOINT total score	720	3.6	1.3	220	2.9	1	0.00000

group was comprised of men with CP/CPPS who were evaluated at a tertiary referral center. Presumably, many of these men may have had longer-standing symptoms and may have failed more treatments prior to presentation. In contrast, a web-based questionnaire may be more reflective of characteristics of the general CP/CPPS community. Additionally, the slightly younger patient demographic in the web-based group could be indicative of higher rates of Internet use in the younger population.

Our data demonstrate that the web-based population had significantly higher percentages of patients in the urinary, psychosocial, and neurologic/systemic domains. These data lead us to several key observations. First, the user demographic for the UPOINT online tool remains unclear. While the website states that the questionnaire is intended for physician use, it is not unreasonable to assume that some subset of the data entries was made by patients themselves.

Second, there is a high missing data rate amongst the more clinically complex questions such as the presence of > 10 wbc/hpf in prostate fluid or spun VB3, the presence of prostatic stones on TRUS, uropathogenic bacteria localized to the prostate, or atypical bacteria in the urine. The low response rate could occur for the following reasons: 1) physicians who are filling out these questionnaires may not have performed these tests, or 2) if patients are filling out the questionnaire themselves, they may not have the clinical background to answer the question. Notably, some of the UPOINT domains rely more heavily than others on these missing data. For instance, the infection domain requires the exclusion of clinical category I and II prostatitis and assesses for the presence of Gram-negative bacilli or enterococci in prostate-specific specimens. If patients did not know how to respond to these questions or incorrectly responded due to lack of clinical knowledge, this has the potential to heavily skew the positive rates for this domain.

Third, nearly twice as many patients were positive for the psychosocial domain and a substantially higher proportion were positive for the neurologic/systemic domain in the web-based group. These results may be accounted for by both a patient and interviewer effect. In specific circumstances, computer-based screening has been found to be superior to standard questionnaire or interviewing methods.[6] When asked about sensitive topics by an interviewer, participants may alter their responses to present themselves in a more favorable light. For instance, participant disclosure of high risk sexual behaviors in a computer versus interviewer-based screening for HIV-related factors was found to be improved when using the online tool due to the more anonymous, web-based data collection methodology.[7] In cases where patients are filling out the UPOINT questionnaire themselves, they may be more likely to respond "yes" to questions about depression, fibromyalgia, chronic fatigue syndrome, or feelings or helplessness or hopelessness about their disease process, as compared to patients who are asked the same questions in clinic. Additionally, despite the high prevalence and impact of disorders like depression, detection and treatment rates are notoriously suboptimal.[9] In the original study describing the UPOINT system, it was noted that adequate documentation for all domains was available for the clinic-based population, with the exception that depression and catastrophizing were not always specifically questioned. Use of a standardized questionnaire ensures that these domains are always addressed during the patient interview.

The study also shows that there is only a weak correlation between UPOINT score and CPSI in the web-based population. Additionally, in contrast to the original UPOINT study, there was no correlation found between symptom duration and CPSI or number of positive UPOINT domains. This may be due to the shorter disease duration in the web cohort.

Another interesting observation is the high percentage of men (39%) in the study who responded positively to the fact that their pain resolves or significantly improves after urination, a symptom typically characteristic of interstitial cystitis (IC) patients. Recent literature has suggested that the prevalence of IC among men is much higher than previously thought.[10] Additionally, IC and CP/CPPS often have substantial overlap in clinical presentation and may even be part of a single disease process affecting the entire lower urinary tract.[10,11] As a screening tool, the UPOINT questionnaire could lead to greater recognition of the frequent coexistence of these closely related syndromes and to improved management of men who have failed prostate-targeted therapies.

Finally, the web-based questionnaire does not address sexual dysfunction. There is a growing appreciation of the high prevalence of sexual dysfunction in men with CP/CPPS.[12,13] Men with CP/CPPS are significantly more likely to experience pain at ejaculation, pain during or after sexual intercourse, partial or complete erectile dysfunction, decreased sexual desire, and premature ejaculation. While inclusion of an "S" or "sexual dysfunction" domain was not found to independently affect either CPPS symptom severity as measured by the NIH-CPSI or quality-of-life, the prevalence of sexual dysfunction in

this syndrome underlines the importance of assessing for and appropriately treating for ED in the CP/CPPS patient population.[14,15] Addition of questions regarding sexual dysfunction in a questionnaire with potential for wide-reaching use would be instructive as both a data collection tool and to guide therapy.

Conclusions

In summary, the online UPOINT tool is used frequently by patients and their physicians. Analysis of online responses shows some differences with patients presenting to a tertiary referral clinic but these self reported results continue to show a correlation between symptom severity and UPOINT domains. Reassuringly, the differences in phenotype between our more select patient population and our larger "real world" sample are small. □

References

1. Schaeffer AJ, Datta NS, Fowler JE et al. Overview summary statement. *Urology* 2002;60(6):1-4.
2. McNaughton Collins M, Pontari MA, O'Leary MP et al. Quality of life is impaired in men with chronic prostatitis the chronic prostatitis collaborative research network*. *J Gen Intern Med* 2004;16(10):656-662.
3. Litwin MS, McNaughton-Collins M, Fowler FJ et al. The national institutes of health chronic prostatitis symptom index: Development and validation of a new outcome measure. *J Urol* 1999;162(2):369-375.
4. Shoskes D, Nickel J, Rackley R, Pontari M. Clinical phenotyping in chronic prostatitis/chronic pelvic pain syndrome and interstitial cystitis: A management strategy for urologic chronic pelvic pain syndromes. *Prostate Cancer Prostatic Dis* 2008;12(2):177-183.
5. Shoskes DA, Nickel JC, Kattan MW. Phenotypically directed multimodal therapy for chronic prostatitis/chronic pelvic pain syndrome: A prospective study using UPOINT. *Urology* 2010;75(6):1249-1253.
6. Wantland DJ, Portillo CJ, Holzemer WL, Slaughter R, McGhee EM. The effectiveness of web-based vs. non-web-based interventions: a meta-analysis of behavioral change outcomes. *J Med Internet Res* 2004;6(4):e40.
7. Justice AC, Rabeneck L, Hays RD, Wu AW, Bozzette SA. Sensitivity, specificity, reliability, and clinical validity of provider-reported symptoms: a comparison with self-reported symptoms. *J Acquir Immune Defic Syndr* 1999;21(2):126-133.
8. Unruh M, Yan G, Radeva M et al. Bias in assessment of health-related quality of life in a hemodialysis population: a comparison of self-administered and interviewer-administered surveys in the HEMO study. *J Am Soc Nephrol* 2003;14(8):2132-2141.
9. Pignone MP, Gaynes BN, Rushton JL et al. Screening for depression in adults: a summary of the evidence for the US Preventive Services Task Force. *Ann Intern Med* 2002;136(10):765-776.
10. Forrest JB, Nickel JC, Moldwin RM. Chronic prostatitis/chronic pelvic pain syndrome and male interstitial cystitis: enigmas and opportunities. *Urology* 2007; 69(4):60-63.
11. Suskind AM, Berry SH, Ewing BA, Elliot MN, Suttorp MJ, Clemens JQ. The prevalence and overlap of interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome in men: Results of the RAND interstitial cystitis epidemiology male study. *J Urol* 2012;189:141-145.
12. Tran CN, Shoskes DA. Sexual dysfunction in chronic prostatitis/chronic pelvic pain syndrome. *World J Urol* 2013:31(4):741-746.
13. Hedelin HH. Evaluation of a modification of the UPOINT clinical phenotype system for the chronic pelvic pain syndrome. *Scand J Urol Nephrol* 2009;43(5):373-376.
14. Magri V, Wagenlehner F, Perletti G et al. Use of the UPOINT chronic prostatitis/chronic pelvic pain syndrome classification in european patient cohorts: Sexual function domain improves correlations. *J Urol* 2010;184(6):2339-2345.
15. Samplaski MK, Li J, Shoskes DA. Inclusion of erectile domain to UPOINT phenotype does not improve correlation with symptom severity in men with chronic prostatitis/chronic pelvic pain syndrome. *Urology* 2011;78(3):653-658.