Phenotype, symptom severity and treatment in a "cured" cohort of chronic pelvic pain syndrome patients

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Introduction: *To identify a cohort of chronic pelvic pain syndrome (CPPS) patients who considered their symptoms completely resolved and analyze their demographics, clinical phenotype, treatments and NIH-Chronic Prostatitis Symptom Index (CPSI) scores.*

Materials and methods: *We identified 35 CPPS patients who at the follow up, reported their symptoms completely resolved ("cured"). Demographics, UPOINT phenotypes, treatments, and CPSI scores were examined. We also compared these variables to a database of 220 previously evaluated CPPS patients.*

Results: *Patients ranged in age from 19 to 72 years. Median follow up was 12 months. Mean change in CPSI sub scores before and after therapy were pain 9.7 ± 3.8 to 2.7 ± 2.9, urinary 4.0 ± 2.8 to 1.1 ± 1.2, QoL 8.1 ± 2.7 to 2.3 ± 2.5, and total 21.8 ± 6.6 to 6.2 ± 1.0 (all $p < 0.0001$). Only 9 (26%) patients reported a total score of 0. Comparing this "cured" group to a previously published cohort of phenotyped CPPS patients, the "cured" group had lower starting total and pain CPSI scores (21.8 versus 25.0 $p = 0.007$; 9.7 versus 11.5 $p = 0.006$ respectively).*

Conclusions: *Many men with CPPS can reach a subjective cure, however, the majority do not reach a CPSI score of 0. This group of "cured" patients is similar to our typical tertiary referral cohort in terms of age and phenotype but differs in having slightly lower pre-treatment CPSI scores.*

Key Words: chronic pelvic pain syndrome, chronic prostatitis, UPOINT, LUTS, cure

Introduction

Chronic pelvic pain syndrome (CPPS) is a highly prevalent urologic condition and its negative impact on quality of life of both the patients and their partners is well described.[1,2] The NIH-Chronic Prostatitis Symptom Index (CPSI) was developed to differentiate symptoms of CPPS from benign prostatic hypertrophy and quantify the extent and severity of symptoms in CPPS and its effects on quality of life. The CPSI is responsive to symptom change in clinical trials and a 6 point drop in total score correlates with perceived patient improvement.[3] While a 6 point drop from 36 to 30 may signal a "success" in a clinical trial, it is doubtful that a patient with a total CPSI of 30 would be pleased and consider themselves "cured". Given the non-specific nature of some questions in the CPSI, it is quite probable that patients, especially older men, may never achieve a score of 0. No studies have yet directly addressed the question of CPSI in patients who consider their CPPS to be completely resolved (i.e. "cured").

While it would be ideal to follow all of our CPPS patients long term, the realities of an academic tertiary care referral center make this impossible outside of

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a clinical trial. Most of our patients are from out of town, come for a second opinion and continue most of their care without direct follow up at our center and with unknown compliance to our treatment recommendations. Patients who do return often do so because their symptoms have not improved; it is rare for patients to make an out of town trip and pay for a medical visit simply to report that they are better. Nevertheless, some patients do just that and others return for other urologic issues after their CPPS has resolved. Therefore, while we are not able to report on a true incidence of symptom resolution, we are able to identify a patient cohort who presented with CPPS, followed treatment and subsequently self-reported that they were cured.

The aim of this study was to identify a cohort of CPPS patients who considered their symptoms completely resolved and analyze their demographics, treatments and CPSI scores. These patients were diagnosed and treated using the UPOINT (urinary symptoms, psychosocial dysfunction, organ specific findings, infection, neurologic, pelvic floor muscle tenderness) phenotyping system which has been previously shown to significantly improve outcomes from multi-modal treatment matched to individual phenotype compared with non-specific monotherapy.[4,5] In particular we wished to see whether "cured" patients were more likely to initially present with fewer positive domains and milder symptoms and whether cured patients had specific treatments in common.

Materials and methods

Subject selection

CPPS patients with initial clinic visits from January 2006 to January 2014 at our tertiary referral center were reviewed and data compiled on 35 patients who at a follow up visit subjectively self-reported that they felt their symptoms to be completely resolved ("cured"). Patients were entered into the database at the time of their follow up clinic visit if they volunteered a subjective assessment of their symptoms as having resolved completely. Patients were excluded if they noted improvement, but not resolution of their symptoms.

Data collection

Demographic information, clinical variables, UPOINT phenotypes, treatments, and pre-treatment and post-treatment CPSI scores were examined. This data was obtained from our IRB approved Men's Health Registry. We also compared these variables to an existing database of 220 CPPS patients previously evaluated and phenotyped at our clinic[6] that did not include these later 35 patients.

Statistical analysis

Statistical analysis was performed using GraphPad Prism v5.0 (INTER REF http://www.graphpad.com/scientific-software/prism/). Continuous variables were reported as means and standard deviations. Categorical variables were reported as frequencies and percentiles. Pairwise parametric comparisons were performed using Student's t test. Paired comparisons were used to compare pre and post-treatment groups and unpaired comparisons were used for case-control analysis. Fisher's exact test was used to assess the difference in categorical variables. Significance was established at $p < 0.05$.

Results

Patients ranged in age from 19 to 72 years; mean age was 44 ± 13. The average Charlson Comorbidity Index Score was 0.3 and average body mass index was 28 ± 6. Two thirds of patients had no history of urologic surgery. None of the cured patients had irritable bowel syndrome. Median post-void residual was 9 cc and only 6% had a residual > 100 mL. Median follow up was 12 months (range 3 to 93 months). There were a median of 3 UPOINT domains positive (range 1-5) and a median of two treatments prescribed (range 1-6), Table 1. The most

TABLE 1. **Patient characteristics cured cohort versus historical chronic pelvic pain syndrome (CPPS) cohort**

	Cured cohort	**CPPS cohort**	**p value**
Total patients (N)	35	220	-
Age [y] [range]	44 ± 13 [19-72]	45 ± 13 [11-79]	> 0.05
Positive UPOINT domains (median) [range]	3 [1-5]	3 [0-5]	> 0.05
Pre treatment total CPSI score	21.8 ± 6.6	25 ± 6.5	0.007
Pre treatment pain score	9.7 ± 3.8	11.5 ± 3.6	0.006

Data presented as mean ± standard deviation, unless otherwise noted

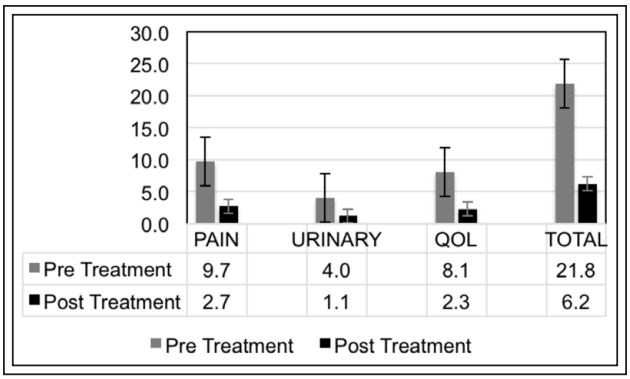

Figure 1. Chronic Prostatitis Symptom Index sub-score pre and post treatment.

prevalent treatment was pelvic floor physical therapy with 25 patients (71%) completing at least one in person session. UPOINT positive domains were 71% urinary, 29% psychosocial, 60% organ specific, 9% infectious, 26% neurologic, and 71% musculoskeletal tenderness. Mean change in CPSI sub-scores before and after therapy were pain 9.7 ± 3.8 to 2.7 ± 2.9, urinary 4.0 ± 2.8 to 1.1 ± 1.2, QoL 8.1 ± 2.7 to 2.3 ± 2.5, and total 21.8 ± 6.6 to 6.2 ± 1.0 (all $p < 0.0001$), Figure 1. Of note, only 9 (26%) patients reported a total post-treatment score of 0. The remaining patients reported post-treatment scores ranging from 1-21, Figure 2. Twenty-two percent of patients reporting a post-treatment CPSI score of 0 were still using at least one treatment modality at last follow up compared with 50% of patients reporting a post-treatment score > 0 ($p = 0.244$).

Comparing this "cured" group to a previously published cohort of phenotyped CPPS patients, the

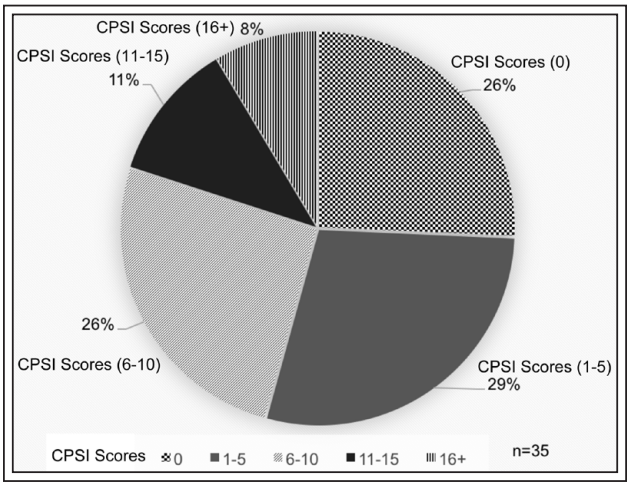

Figure 2. Total Chronic Prostatitis Symptom Index score reported at cure.

"cured" group had lower starting total and pain CPSI scores (21.8 versus 25.0 $p = 0.007$; 9.7 versus 11.5 $p = 0.006$ respectively), Table 1. There were no differences in age, proportion of positive domains, urinary sub-score or quality of life sub-score between the two groups of patients.

Discussion

Much progress has been made in the last decade in advancing the treatment of CPPS. While individual therapies have variable results in clinical trials, multimodal therapy is often effective.[7-10] In a clinical syndrome such as CPPS, it is important to focus on symptom improvement using validated metrics to quantify clinically meaningful response to therapy.[6,11] In this study, patients reported subjective cure showed significant improvement in all three CPSI sub-scores. The fact that the pain sub-category mirrors the quality of life sub-category reflects the findings of a recent review of multi-national cohorts of CPPS patients.[12] It was noted that pain contributed more to QoL differences with severity and frequency of pain being more important than pain localization/type. However, this study is unique in that in also examines patients specifically experiencing self-reported cure or resolution of symptoms.

Since the NIH-CPSI was first described in 1999 there has been attempt to improve its sensitivity by changing the "weighting" of various sub-groups so that they would be equal.[13] The revised questionnaire performed similarly to the original in discriminating between men with chronic prostatitis, BPH, and control subjects. The authors concluded that the original scoring system provided the right combination of reliable performance with ease of use. In spite of the findings that only 26% of cured patients reported a NIH-CPSI score of 0, it is unclear whether a similar attempt at revision or addition in order that patients who subjectively experience cure more reliably objectively score zero on the questionnaire would be clinically useful.

Associations between CPPS patients with irritable bowel syndrome and other pain conditions such as vulvodynia, fibromyalgia, and chronic fatigue syndrome have been described.[14-17] Interestingly, none of the patients in the cured cohort had other systemic pain syndromes or irritable bowel syndrome. While our numbers are too small to draw direct conclusions, this does support the hypothesis that CPPS patients with multiple other somatic complaints and systemic syndromes are unlikely to improve unless all their conditions are addressed as a whole.[8] Unfortunately,

data regarding the prevalence of irritable bowel syndrome in the previously phenotyped cohort of 220 CPPS patients was not available.

The main limitation of this study is the self-reported nature of patients defining themselves as cured. While we relied on patients to come forward with this assessment rather than contacting them to ask directly, reporting bias is certainly possible. We are also limited by event driven rather than time driven clinical encounters so we cannot assess long term durability of response. Furthermore, the characteristics of cured CPPS patients at a single institution tertiary referral center may not be useful to predict cure in patients treated with different protocols in different clinical settings. Nevertheless, this is the first study we are aware of that clinically describes patients with a self-reported cure and the fact that few patients do reach a score of zero may be important in future clinical trial design and potential modification of existing symptom scores to more robustly measure severity at the mild range of bother.

Conclusions

Using phenotype directed multi-modal therapy, many men with CPPS can reach a subjective cure, however having done so, the majority do not reach a CPSI score of 0. This group of "cured" patients is similar to our typical tertiary referral cohort in terms of age and phenotype but differs in having slightly lower starting CPSI score and pain sub-score. However, this study is unique in that it also examines patients specifically experiencing self-reported cure or resolution of symptoms. □

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