
Muscle Tenderness in Men With Chronic Prostatitis/Chronic Pelvic Pain Syndrome: The Chronic Prostatitis Cohort Study

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Purpose: Myofascial pain is a possible etiology for category III chronic prostatitis/chronic pelvic pain syndrome, either secondary to infection/inflammation or as the primary cause. We documented tenderness on physical examination in a large multicenter cohort of patients with chronic pelvic pain syndrome and compared to controls.

Materials and Methods: Data were reviewed from the National Institutes of Health Chronic Prostatitis Cohort study on 384 men with chronic pelvic pain syndrome and 121 asymptomatic controls who had complete unblinded physical examination data from 7 clinical centers between October 1998 and August 2001. Tenderness in 11 sites including prostate, genitals, abdomen and pelvic floor together with prostate size and consistency was evaluated. Data were correlated with cultures and symptoms.

Results: Overall 51% of patients with chronic pelvic pain syndrome and 7% of controls had any tenderness. The most common site was prostate (41% chronic pelvic pain syndrome, 5% controls), followed by external and internal pelvic floor (13% and 14% chronic pelvic pain syndrome, 0 controls) and suprapubic area (9% chronic pelvic pain syndrome, 0 controls). Of patients with chronic pelvic pain syndrome 25% had 1 tender site, 11% had 2 and 6% had 3 tender sites. Tenderness did not correlate with inflammation or infection in the prostate fluid. Prostate consistency was normal in 79% of patients with chronic pelvic pain syndrome and in 95% of controls, and did not correlate with symptom severity. Patients with chronic pelvic pain syndrome with any tenderness had significantly higher Chronic Prostatitis Symptom Index scores at baseline and at 1 year (24.1 vs 21.2 and 20.2 vs 17.5, $p < 0.0001$) compared to patients without tenderness.

Conclusions: Abdominal/pelvic tenderness is present in half of the patients with chronic pelvic pain syndrome but only 7% of controls. Extraprostatic tenderness may identify a cohort of patients with a neuromuscular source of pain.

Key Words: prostatitis, pelvic pain

Chronic pelvic pain syndrome or NIH category III prostatitis (nonbacterial prostatitis) is a common clinical syndrome with multiple potential etiologies, including infection, autoimmunity, and neuromuscular spasm.¹ Several groups have suggested that a myofascial pain syndrome with abnormal pelvic muscle spasm is the primary source of the symptoms of CPPS, although such spasm could be secondary to local infection or inflammation.² In patients with a myofascial pain syndrome palpation of the affected muscles elicits pain, typically the pain that patients attribute to their prostatitis. There have been no large scale/

multicenter studies that have assessed the incidence and distribution of such muscle tenderness.

The NIH Chronic Prostatitis Cohort Study examined 488 patients with CPPS and 121 controls, and followed their treated natural history for up to 3 years at 7 clinical centers.³ As part of the initial evaluation, the physical examination included assessment of muscle tenderness in the abdomen, genitals and pelvis, including the prostate. Tenderness was elicited by the physician performing the physical examination during palpation. This database represents a unique opportunity to study muscular pain and tenderness in men with CPPS that have been fully evaluated for symptoms, cultures and microscopy, as well as comparing these findings to asymptomatic controls.

MATERIALS AND METHODS

Data for the CPPS participants were obtained from the Chronic Prostatitis Cohort study based on a prospective,

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For another article on a related topic see page 759.

longitudinal cohort design that recruited 488 eligible, consenting participants at 7 clinical centers, described further by Schaeffer et al.³ An asymptomatic control group of 121 men were also enrolled at these clinical centers and followed under the same protocol as described in further detail by Nickel et al.⁴ Since the full physical examination was instituted after the first 79 subjects were enrolled, we have complete data on 384 men with CPPS and 121 asymptomatic controls. Tenderness was recorded as present or absent in the following locations: prostate, abdomen, flank, coccyx, pubis, suprapubic, external pelvic floor, internal pelvic floor, cord/inguinal area, epididymis and testes. The prostate examination was reported as normal or enlarged, consistency as normal, firm or soft, and nodularity as absent or present. All patients filled out an NIH CPSI, and the questions from the pain domain were analyzed according to number and location of pain sites.

Most of the analytical variables were binary or categorical, and are summarized by proportions and compared among groups using standard chi-square tests of association, and generalized Mantel-Haenszel methods, to accommodate nominal and ordinal measurement scales. Small sample methods, such as Fisher's exact test, were used in cases where large sample assumptions were not satisfied. The CPSI scores were analyzed as continuous variables. These analyses were performed to characterize tenderness using number of tender areas, overall CPSI scores and pain subscores, prostate examination variables and colony counts of localization of uropathogens. For our analyses, uropathogens were considered Gram-negative bacilli (eg *Escherichia coli*, *Klebsiella* sp.) as well as the Gram-positive *Enterococcus* species. EPS or VB3 (post-prostate massage urine) cultures were considered localized if the bacteria identified were not found in the urine culture or if the bacterial counts in EPS were at least 2 log counts higher than in urine. Statistical analyses were performed using SAS® version 8.2. For the frequencies of tenderness locations and prostate examination variables, we simply tabulated the number of subjects in each category and displayed the results. No formal tests of significance were performed because our interest was primarily in descriptive measures. In comparing baseline CPSI scores, the nonparametric Wilcoxon rank sum test was used for comparison between groups, since it is robust with respect to departures from the assumption of normality required by the usual t test. Comparisons of baseline and 12-month CPSI scores were made using a GEE model. For comparison of localization frequencies between groups, a binomial test of difference of proportions was used

TABLE 1. Incidence of tenderness by tenderness area

	No. Cases (%)	No. Controls (%)
Prostate	157 (41)	6 (5)
Trunk:		
Abdomen	21 (5)	0 (0)
Flank	4 (1)	0 (0)
Coccyx	7 (2)	0 (0)
Pubis	18 (5)	0 (0)
Suprapubic area	33 (9)	0 (0)
Cord/inguinal area	14 (4)	0 (0)
Genital:		
Epididymal	29 (8)	2 (2)
Testes	31 (8)	1 (1)
Pelvic floor:		
Internal	52 (14)	0 (0)
External	49 (13)	0 (0)

TABLE 2. Number of tender sites out of 11 possible sites

No. Tender Sites	No. Cases (%)	No. Controls (%)
0	190 (49)	113 (93)
1	95 (25)	7 (6)
2	43 (11)	1 (1)
3	24 (6)	0
4	15 (4)	0
5	9 (2)	0
6	4 (1)	0
7	1 (less than 1)	0
8	1 (less than 1)	0
9	2 (1)	0

since we have a large enough sample, and all observed proportions are sufficiently far from 0 and 1.

RESULTS

As summarized in table 1 the most common site of tenderness was the prostate (41% of cases and 5% of controls). The next most common site among cases was the internal pelvic floor (14%), followed by the external pelvic floor (13%). All other sites were tender in fewer than 10% of the cases. Two controls had epididymal tenderness and 1 had testicular tenderness. Table 2 shows the number of tender sites per subject (out of a possible 11 sites). For the cases, 49% had no sites of tenderness, 25% had 1 tender site, 11% had 2 tender sites and a total of 15% had 3 or more tender sites. In the controls 93% had no tenderness, 6% had 1 tender site and 1 patient had 2 tender sites. Evaluating the 11 individual sites of possible tenderness, no consistent combinations emerged. Indeed, of the 66 combinations seen 41 were unique and no unique combination was seen in more than 3% of patients. Given this lack of consistent pattern, we next grouped the tenderness sites into 4 geographic combinations of prostate, trunk (abdomen, flank, coccyx, pubis, suprapubic), genital (cord, epididymal, testes) and pelvic (internal/external pelvic floor). As seen in table 3 prostate tenderness was the most common (41%) followed by pelvic (19%).

We next wanted to correlate tender sites with degree of symptoms, as measured by the CPSI scores. As summarized in table 4 when patients with tenderness are compared to those without, those with tenderness had a statistically significantly higher CPSI total score and pain subscore than those who did not report tenderness. Interestingly though, the absolute difference in average CPSI score was small, ranging from 2.8 (prostate) to 5.0 (trunk). We then compared the change in baseline CPSI to the CPSI at 1 year for patients with or without tenderness in any of the geographic areas, using a GEE analysis to accommodate the longitudinal measures within patients. As seen in table 5 the negative coefficient for the patients with tenderness indicates that those with tenderness at baseline started at a higher

TABLE 3. Incidence of tenderness areas

	No. Cases (%)	No. Controls (%)
Prostate	157 (40.9)	6 (5.0)
Trunk	45 (11.7)	0 (0.0)
Genital	48 (12.5)	2 (1.7)
Pelvic	72 (18.8)	0 (0.0)

All values p < 0.0001.

TABLE 4. Comparison of mean CPSI and pain subscores for tenderness areas

Subgroups	No.	Total Score (max 43)	No.	Pain Subscore (max 21)
<i>Baseline</i>				
Any tenderness	192	23.89	192	11.14
No tenderness	192	21.23	192	9.8
Difference (p value)		2.66 (0.003)		1.35 (0.005)
Any prostate tenderness	155	24.14	157	11.34
No prostate tenderness	227	21.41	227	9.87
Difference (p value)		2.83 (0.001)		1.47 (0.002)
Any trunk tenderness	45	26.93	337	12.84
No trunk tenderness	45	21.97	339	10.15
Difference (p value)		4.96 (<0.001)		2.69 (<0.001)
Any genital tenderness	48	25.52	334	11.85
No genital tenderness	48	22.13	336	10.27
Difference (p value)		3.39 (0.015)		1.58 (0.023)
Any pelvic tenderness	72	24.96	310	12
No pelvic tenderness	72	22	312	10.12
Difference (p value)		2.96 (0.008)		1.88 (0.001)
<i>12-Mo followup</i>				
Any tenderness	133	19.65	133	9.28
No tenderness	111	17.53	111	8.29
Difference (p value)		2.12 (0.057)		0.99 (0.068)
Any prostate tenderness	151	19.88		9.24
No prostate tenderness	93	17.63		8.35
Difference (p value)		2.25 (0.051)		0.89 (0.128)

CPSI (and pain subscore). The negative coefficient for time indicates that all patients had a lower CPSI (and pain subscore) at 1 year. There was no differential improvement over time between those with and without tenderness, as reflected by the highly nonsignificant interaction term between tenderness and time.

We then compared the findings on prostate examination between patients with CPPS and controls. As seen in table 6 prostate size was enlarged in 14% of cases vs 5% of controls (p = 0.01). Mean age of patients with CPPS with a normal size prostate gland was 41.7 years vs 46.4 years for patients with CPPS with enlarged prostate (p = 0.001). Mean age of controls with normal size glands was 38.7 vs 51.9 years for controls with enlarged glands (p = 0.004). Prostate consistency was different, with a soft/boggy prostate felt in 17% of cases vs 3% of controls (p = 0.001). However, of note, 79% of patients with CPPS had normal prostate consistency.

Finally we compared tenderness with culture results for bacteria that localized to EPS or VB3. Overall, 8.0% of patients with CPPS and 8.3% of controls had localization of uropathogens. Of the 37 patients with CPPS with bacterial localization, 15 (41%) had no sites of tenderness and 11 (30%) had prostate tenderness. These numbers are similar to those without positive cultures (50% no tenderness and 43% prostate tenderness). As seen in table 7 when comparing tenderness in each of the geographic regions, there was no difference in positive cultures for uropathogens. Similarly, there was no difference in prostate fluid inflammation in patients with or without tenderness.

TABLE 6. Prostate examination results

	No. Cases (%)	No. Controls (%)	p Value
Total No.	463	121	
Size:			
Normal	397 (86)	115 (95)	0.01
Enlarged	66 (14)	6 (5)	
Consistency:			
Normal	367 (79)	115 (95)	0.0002
Firm	20 (4)	3 (3)	
Soft	76 (17)	3 (3)	
Nodularity:			
No	448 (97)	120 (99)	0.2
Yes	15 (3)	1 (1)	
Tenderness:			
No	280 (60)	115 (95)	<0.0001
Yes	183 (40)	6 (5)	

DISCUSSION

CPPS is a common and enigmatic condition of uncertain etiology. The confusion over etiology was highlighted when an NIH consensus conference developed the current diagnostic categories, which were based only on the presenting symptoms.⁵ Attempts to distinguish patients with CPPS from controls have found few significant differences apart from symptoms. Commonly measured factors such as cultures and WBC in urine, EPS and semen have failed to distinguish these groups,⁴ and we continue to search for biomarkers to make CPPS a diagnosis of inclusion rather than exclusion. Since organic pain is often associated with tenderness, it would be a reasonable assumption that patients with pelvic pain and inflammation would also have pelvic locations tender to the touch, and yet there has never been documentation of the characteristics of tenderness sites in a large scale or multicenter study. Indeed, in clinical practice, many patients receive a diagnosis of prostatitis based on prostatic tenderness during a digital rectal examination, regardless of symptoms.

Our findings confirmed the heterogeneity of patients with CPPS. While tenderness was the most discriminating factor between cases (51%) and controls (7%), it is important to note that half the patients with CPPS, while suffering from pain, had no sites of tenderness whatsoever. No distinct pattern or combination of tenderness sites emerged. Of the 194 patients who did have tenderness, there were 66 different combinations of sites. There are several possible explanations for sites of extraprostatic tenderness. One is that locations in direct contact with the prostate may have elicited prostate tenderness. Indeed, while 3% of patients had pelvic floor tenderness without prostate tenderness, 11% had pelvic floor tenderness plus prostate tenderness. Another possibility is that extraprostatic muscle spasm may mimic the symptoms of CPPS in the absence of current prostate pathology.² Another possibility is that patients

TABLE 5. GEE models of CPSI and pain subscores vs time and presence of tenderness

No Tenderness vs Any	CPSI		Pain Subscore	
	Estimate	p Value	Estimate	p Value
Intercept (value at baseline)	23.75	<0.0001	11.13	<0.0001
Tenderness—none vs any (1 vs 0)	-2.63	0.0022	-1.39	0.0022
Time—12 mos vs baseline (1:0)	-3.92	<0.0001	-1.66	<0.0001
Tenderness * time	0.2448	0.809	0.02	0.9709

TABLE 7. Comparison of incidence of localization of uropathogens by tenderness area

	Frequency Localized/No. (%)	p Value
Prostate tenderness	11/157 (7.01)	0.6245
No prostate tenderness	19/227 (8.37)	
Trunk tenderness	6/45 (13.33)	0.1419
No trunk tenderness	24/315 (7.62)	
Genital tenderness	3/48 (6.25)	0.6663
No genital tenderness	27/336 (8.04)	
Pelvic tenderness	6/72 (8.33)	0.855
No pelvic tenderness	24/312 (7.69)	

with CPPS have greater sensitivity to pain, and may report pain during an examination as opposed to a control patient, who might report it as simply unpleasant.⁶ Central neural sensitization is a common feature of many chronic pain conditions and could be the final common pathway through which the pain in CPPS becomes autonomous from its initial trigger, whether that trigger is infection, inflammation, trauma or neuromuscular stress. Finally, since neither patient nor examiner was blinded to who had CPPS and who was a control, operator and reporter bias may have influenced the results, with a belief that a patient who has pain should have or report tenderness in the area. While subgroup analysis was not statistically possible due to low numbers, all examiners reported heterogeneous findings in the patients. There were no sites with "true believers" who reported everyone with tenderness, nor were there "hyper-skeptics" who reported tenderness in nobody. Nevertheless, this examination is, by its nature, objective, and a challenge for future research is the development of stimulation techniques that could be used objectively across examiners. Furthermore, as symptoms typically wax and wane in this disorder, multiple assessments in future studies could help address reproducibility.

Using the NIH-CPSI to assess degree of symptoms, presence of tenderness in any of the geographic areas was associated with a higher symptom score, both for total score and for the pain subdomain. Nevertheless these differences were clinically small, and their average magnitude was below the threshold that patients describe as clinically relevant. Patients in this observational cohort study were treated at each local center according to best local practices, and while overall scores decreased at 1 year on average for all patients, the presence of tenderness did not make this improvement in symptoms any more or less likely. It was not recorded which therapies were used for which patients, and it is possible that treatment selection was tailored to the physical findings, but given the clinical practice at most of the centers, this is not likely.

The lack of correlation between tenderness sites and culture results is not surprising, given the selection criteria of the patients. As category III, none would have had recurrent urinary tract infections (category II) and most patients seen in the primarily tertiary care settings of the study sites had previously been treated with antibiotics, and almost all would have failed or recurred. It is likely, therefore, that the 8% of patients with cultures of uropathogens that localized to prostatic secretions had colonization with these bacteria and not acute infection, defined as associated local tissue damage with an inflammatory response. Indeed, prostatic inflammation as measured by WBC in a wet mount of EPS did not correlate with tenderness. However this method of

assessing inflammation, while most commonly used in the clinic, may not truly reflect soluble mediators of inflammation within the prostate that do cause tissue injury.⁷

The abnormal consistency of the prostate was more often seen in patients with CPPS compared to controls. However, these changes were not common in the patients with CPPS as a whole. Indeed, the notion that prostatitis is associated with a soft or boggy prostate is pervasive in urological practice, but without any basis in data. In reality, 79% of patients with CPPS in our study had a normal prostate consistency.

CONCLUSIONS

Approximately half of the patients with CPPS have areas of tenderness that are elicited during the physical examination, compared with only 7% of asymptomatic controls. It is noteworthy that half of symptomatic patients with CPPS do not. Tenderness is associated with a modest increase in symptom score, but not with prostatic cultures or WBC, and does not predict response to therapy. Documentation of tenderness should be a part of the physical examination in men with CPPS, and may aid in the diagnosis. If men with extraprostatic tenderness truly have a distinct neuromuscular or central chronic pain syndrome, then physical examination may help the classification and treatment stratification for these patients in the future.

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Abbreviations and Acronyms

CPPS	=	chronic pelvic pain syndrome
CPSI	=	Chronic Prostatitis Symptom Index
EPS	=	expressed prostatic secretions
GEE	=	Generalized Estimating Equations
NIH	=	National Institutes of Health
WBC	=	white blood cell count

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