will be used as the primary outcome measure for clinical trials in CPPS conducted by the CPCRN.

The purpose of this article is to describe the CPC study and to reproduce the baseline analysis of the cohort study recently published in the *Journal of Urology*, which is summarized here with permission.

METHODS

Patient accrual for the CPC Study began on October 16, 1998. All 488 patients who had been successfully screened and enrolled into the CPC cohort before closing recruitment on August 22, 2001, were selected for this statistical analysis. The NIH-CPSI, including subscores, was used to measure symptoms. A comprehensive history, physical examination, and demographic profile were obtained from each participant. Generalized Mantel-Haenszel procedures were used to investigate baseline associations between selected factors and symptoms.

RESULTS

CP/CPPS is a chronic syndrome, affecting men over a wide age range. Most CPC Study participants are white, well educated, and affluent. However, lower education, lower income, and unemployment were associated with more severe CPPS symptoms. Patients most frequently reported pain in the perineum and tenderness in the prostate. The most common self-reported diseases were genitourinary (55%), allergic (53%), neurologic (40%), and hematopoietic, either lymphatic or infectious (40%). CP/CPPS has a significant negative impact on both mental and physical domains of quality of life. Nearly all (95%) patients reported antimicrobial drug use. Among these 488 participants, 280 (57%) reported having used, or were currently using, ≥5 categories of prostatitis-related treatments.

Among all participants, 50% had urethral leukocytes; among 397 with EPS samples, 194 (49%) and 122 (31%) had white blood cell counts of ≥5 (5+) or ≥10 (10+) in EPS, respectively. The prevalence of category IIIA ranged from 54% to 90%, depending on the composite set of cut points. None of the CPSI measures were statistically different ($P > 0.10$) for selected leukocytosis subgroups. Based on prostate and semen cultures, 37 of 488 men (8%) had ≥1 localizing uropathogen. None of the CPSI measures were statistically different ($P > 0.10$) for selected bacterial culture subgroups.

CONCLUSION

CP/CPPS is a multifactorial problem affecting men of all ages and demographics. Patients with CPPS have a dismal quality of life, and many have benefited only minimally from empiric, goal-directed therapy. Long-term follow-up study of this CPPS cohort will answer important questions about the natural and treated history of this syndrome.

Although men with CP routinely receive anti-inflammatory and antimicrobial therapy, we found that leukocyte and bacterial counts, as we defined them, do not correlate with severity of symptoms. These findings suggest that factors other than leukocytes and bacteria also contribute to symptoms associated with CPPS.

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DISCUSSION FOLLOWING DR. SCHAEFFER'S PRESENTATION

Mark S. Litwin, MD, MPH (Los Angeles, California): If the number of white cells is not as clinically relevant as previously believed, why, then, does it make sense for us to continue to stratify patients with or without a large number of white cells?

Anthony J. Schaeffer, MD (Chicago, Illinois): We are finding that there is not a large difference, statistically, in the different populations of patients. But on an individual basis, if a patient who is complaining of pelvic pain has a large number

of white cells, it is possible that his discomfort is associated with infection or inflammation.

John N. Krieger, MD (Seattle, Washington): Let me offer a few other feasible explanations for the data you presented. There is a possibility that the National Institutes of Health (NIH) Chronic Prostatitis Symptom Index was not developed to differentiate between groups. Another possibility might be the variability in the method used to measure white cells. Then there is also the possibility of a type II error—that is, you fail to find a statistical difference because the patients in the study are either too few in number or too heterogeneous.

Dr. Schaeffer: In regard to the way the data were collected, we looked at prostatic fluid as viewed under a microscope without a counting chamber. There is no question that a counting chamber is more accurate than a white cell coverslip technique. However, I think you can tell the difference when viewing a white cell, no white cells, or 100 white cells; 100 white cells is different from 1 cell with any technique. Looking at the white cell counts in a variety of ways, we found that we could not see any relation.

Dr. Litwin: How do the chamber counts relate to 2-dimensional coverslip tests? Is there a general relation?

Dr. Krieger: The problem with a 2-dimensional coverslip test is that you are compressing cells and fluid from 3 dimensions into 2 dimensions. You can make 5 white cells look like 10 quite easily under a high-powered field. It is like looking at an x-ray versus a computed tomography scan. There is not a 1-to-1 relation between the 2 methods for establishing cell counts, and that is a problem. We have done counts both ways, and there are patients who have quite high counts using 1 method and low counts using the other method.

Dr. Litwin: So, the coverslip test will tend to overstate the number of white cells?

Dr. Krieger: It depends on how you make your coverslip, and there is much individual variation. In other words, if you have 3 people making coverslips, you get 3 different white cell counts with the same sample. That is another source of error. That is a reason why doing it by volume is superior, and why most clinical laboratories that never perform counts by coverslip use spinal fluid or seminal fluid analysis.

Michael Pontari, MD (Philadelphia, Pennsylvania): What do you mean by saying that the patients might be too heterogeneous?

Dr. Krieger: In contrast to the NIH consensus definition, the study entry criteria allowed cases with urethritis. Men at a clinic for sexually transmitted diseases (STD) might be found to have urethral white cells and would be labeled as having persistent or recurrent nongonococcal urethritis and said to have objective evidence of urethral white cells. The issue is whether you want to be inclusive or exclusive in defining the patient population. You can make an argument for either.

Dr. Schaeffer: That is a good point. Conveniently, it turned out that 50% of the men did or did not have white cells in their voided bladder urine–1 (VB-1). So we could have said that we are going to study only the 50% who have no white cells in the VB-1. In fact, there was no difference between the 2 groups in their symptoms. The other issue we should comment on is that many healthy individuals have white cells and are totally asymptomatic. Yet, if they walk into an STD clinic and are found to have white cells in the urethra, the assumption is, "Aha, that's why you are here. That's what is causing your pain."

Dr. Litwin: In fact, the study was designed to recruit a population that reflects the patients seen in usual practice, which is by nature somewhat heterogeneous, depending on how much prescreening is done. Men who go to an STD clinic tend to have a different set of symptoms and history than those who present to a urologist for chronic prostatitis.

Daniel A. Shoskes, MD (Weston, Florida): Because we are focusing on the issue of classification, a possible conclusion from the data is that inflammation or infection may be important, but is not measurable in the fluids that we have to test. In other words, there may be inflammation in a part of the prostate that is inaccessible to being expressed intraluminally. There may be bacteria that may not be expressed by these methods or measurable by the culture techniques that we use.

Dr. Schaeffer: We are really saying "inflammation, as determined by looking at the fluid using a traditional cover slide counting technique." We have to be careful to say that inflammation may be present elsewhere in the prostate, but that we either cannot find it or cannot recognize it.

Dr. Shoskes: Ultimately, we can ask whether we should have a classification as IIIA and IIIB. It may be that there is an inflammatory versus a noninflammatory condition, but not based on the number of white cells. The issue is not how many white cells are present but what the white cells are doing there. The white cells could be preventing pain and inflammation. The groups that have looked at cytokines and markers of oxidative stress in expressed prostatic secretions have seen a tighter correlation between changes in those markers and symptomatic outcome than have studies that looked at white cells and symptomatic outcome. So, it may be a feasible classification, but with different markers of inflammation.

Dr. Schaeffer: Perhaps we need to focus on new markers in these various fluids and to better define the population.

Dr. Litwin: Ultimately the endgame is clinical outcomes: does the patient feel better?

Dr. Schaeffer: Right. If we came up with some microarray technology that would define this population elegantly, it is not going to be applicable to the real world. On the other hand, another part of our goal is to identify what is causing the problem. That is why we can afford to be precise and innovative in the cohort study, and then try to apply that information so that clinicians can use it.

Robert B. Nadler, MD (Chicago, Illinois): Until you understand the etiology of the disease, it does not necessarily make sense to abandon the white cell in the fluid. Although it may not be as significant as we thought, it is still something you can measure.

J. Curtis Nickel, MD (Kingston, Ontario, Canada): What we are going to do is present a method of evaluation for general urologists in the community. So far, I have not heard anything that will justify telling general urologists that they must do that sort of evaluation, and that they must categorize patients as IIIA or IIIB. We may find that there is no evidence that it changes treatment.