Relationship Between Erectile Dysfunction and Moderate to Severe Prostatitis-Like Symptoms: a Propensity Score–Matched Analysis

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Abstract

Objective We assessed the relationship between chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and erectile dysfunction (ED) using propensity score matching. Methods Data from 8727 middle-aged men who had undergone health checkups were analyzed. The National Institutes of Health Chronic Prostatitis Symptoms Index (NIH-CPSI), the International Index of Erectile Function-5 (IIEF), the Premature Ejaculation Diagnostic Tool (PEDT), testosterone measurement, basic blood chemistry, and metabolic syndrome (MetS) assessment were performed in this study. As in a previous study, the symptoms were classified as "no" if respondents reported no perineal or ejaculatory pain or had an NIH-CPSI pain score of <4, and the symptoms were classified as "moderate to severe" if the pain score was >7. Of the 8727 men considered, 7181 formed the cohort for propensity score matching, including 597 men with moderate to severe prostatitis-like symptoms (case) and 6584 men with no prostatitis-like symptoms (control); ultimately, however, members of the case and control groups were matched at a 1:1 ratio by propensity score. Results After matching, the variables of age, testosterone, PEDT and MetS were evenly distributed between the groups. After matching, the mean IIEF score of the case group was significantly lower than that of the control group (17.2±5.5 vs. 14.7±5.3; P<0.001). Additionally, the severity of ED was significantly greater in the case group (no, mild, mild to moderate, moderate, and severe, respectively: 27.5%, 30.2%, 24.6%, 13.1%, and 4.7% in the control group; 10.7%, 27.0%, 33.0%, 18.9%, and 10.4% in the case group; P<0.001). Finally, the rate of moderate to severe ED was significantly higher in the case group than in the control group (17.8% vs. 29.3%; P<0.001). Conclusion Moderate to severe prostatitis-like symptoms were significantly and independently correlated with ED in middle-aged men.

Relationship between erectile dysfunction and moderate to severe prostatitis-like symptoms: a propensity score–matched analysis

ABSTRACT

Objective

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Methods

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Results

After matching, the variables of age, testosterone, PEDT and MetS were evenly distributed between the groups. After matching, the mean IIEF score of the case group was significantly lower than that of the control group (17.2±5.5 vs. 14.7±5.3; P <0.001). Additionally, the severity of ED was significantly greater in the case group (no, mild, mild to moderate, moderate, and severe, respectively: 27.5%, 30.2%, 24.6%, 13.1%, and 4.7% in the control group; 10.7%, 27.0%, 33.0%, 18.9%, and 10.4% in the case group; P <0.001). Finally, the rate of moderate to severe ED was significantly higher in the case group than in the control group (17.8% vs. 29.3%;P <0.001).

Conclusion

Moderate to severe prostatitis-like symptoms were significantly and independently correlated with ED in middle-aged men.

What is already known about this topic?

The relationship between CP/CPPS and comorbid erectile dysfunction (ED) has been investigated in several studies. However, those studies had inconsistent results and were limited by small numbers of participants, minimal adjustment for potential confounding factors, or cross-sectional study design. It is very important to investigate the association between ED and CP/CPPS because some guidelines still do not recommend screening or treatment of these two conditions, and current clinical practice focuses more on the patient's chief complaint than on screening or treating comorbidities, although both CP/CPPS and ED can seriously impact quality of life.

What does this article add?

Our propensity score matching study demonstrated that the presence of moderate to severe prostatitis-like symptoms was significantly and independently related to ED in middle-aged men. This is the first propensity score matching case-control study among studies evaluating the relationship between ED and CP/CPPS, which mimics some of the particular characteristics of randomized controlled trials. We believe our study used the most relevant methodology to reveal the relationship between ED and CP/CPPS.

1. INTRODCUTION

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a disabling condition that is primarily associated with pain in the urogenital region and disturbances in urinary function.[1] CP/CPPS is a common disease, with a prevalence of 8.2%, yet its etiologies and comorbidities are poorly understood.[2,3]

The relationship between CP/CPPS and comorbid erectile dysfunction (ED) has been investigated in several studies. However, those studies had inconsistent results and were limited by small numbers of participants,[4,5] minimal adjustment for potential confounding factors,[4-8] or cross-sectional study design.[6,7,9]

It is very important to investigate the association between ED and CP/CPPS because some guidelines[10] still do not recommend screening or treatment of these two conditions, and current clinical practice focuses more on the patient's chief complaint than on screening or treating comorbidities,[11,12] although both CP/CPPS and ED can seriously impact quality of life.

Because of the methodological limitations of previous studies and the resulting insufficiency of existing evidence, we performed the present study to establish the relationship between ED and CP/CPPS.

2. MATERIALS AND METHODS

2.1 Subjects

From August 2011 to November 2013, 8727 middle-aged men (in their 40s and 50s) underwent urological health checkups.[13] The participants applied to be part of the study. The health screening included anthropometric measurements (blood pressure measurements, waist circumference, height, and weight), testosterone levels, basic blood chemistry analyses, and a urine analysis.

Medical histories were collected using a standardized structured questionnaire. The participants were also asked to complete questionnaires concerning urological health status, including the Premature Ejaculation Diagnostic Tool (PEDT), the International Index of Erectile Function-5 (IIEF-5), and the National Institutes of Health Chronic Prostatitis Symptoms Index (NIH-CPSI). All of the participants provided written informed consent, and data concerning the participants were collected prospectively.

In order to evaluate the relationship between ED and CP/CPPS, data from the NIH-CPSI, PEDT, testosterone assays, and metabolic syndrome (MetS) assessment were used in this analysis.

2.2 CP/CPPS, and ED assessment

The NIH-CPSI and IIEF were used for the assessment of CP/CPPS and ED, respectively. Symptoms were classified as "no" if respondents reported no perineal or ejaculatory pain or had an NIH-CPSI pain score of <4 and "mild prostatitis-like symptoms" if respondents reported perineal or ejaculatory pain and had an NIH-CPSI pain score of [?]4 and <8; the symptoms were classified as "moderate to severe" if the pain score was [?]8.[14] We classified ED by severity: normal (IIEF>21), mild ED (IIEF>16 to [?]21), mild to moderate ED (IIEF>11 to [?]16), moderate ED (IIEF>7 to [?]11) or severe ED (IIEF[?]7).

2.3 MetS assessment

Two blood pressure (mmHg) measurements, obtained 5 minutes apart, were averaged using a mercury sphygmomanometer on the right arm. Waist circumference (cm), to the nearest 0.1 cm, was measured midway between the lowest rib and the ilium. Body mass (kg) and body height (cm) were also recorded. Serum was collected in the morning (between 7:00 and 9:00 AM) after an overnight fast. The biochemical analyses included measurements of fasting serum glucose levels, triglyceride levels, and high-density lipoprotein cholesterol (HDL-C) levels. A diagnosis of MetS was made if three or more of the NCEP-ATP III criteria[15] were satisfied.

2.4 Testosterone assay

Serum testosterone was measured using a radioimmunoassay kit from Cisbio Bioassays, Inc. (Parc Marcel Boiteux, Codolet). The intra-assay coefficients of variation for all of the assays were less than 9%, and the interassay coefficients of variation were less than 12%. For each assay, all samples from each subject were measured in the same assay run.

2.5 Statistical Analysis

We excluded 19 men for whom NIH-CPSI, IIEF-5, and/or PEDT data were missing. Three hundred men who had not engaged in sexual intercourse within the previous 6 months were also excluded. Additionally, 147 patients who had pyuria or had been administered certain relevant drugs, including alpha blockers, phosphodiesterase-5 inhibitors, antipsychotics, and selective serotonin reuptake inhibitors, were excluded. In addition, 1,080 men with mild prostatitis-like symptoms were excluded to focus on the relationship between ED and moderate to severe prostatitis-like symptoms. Finally, the remaining 6584 men with no prostatitis-like symptoms and 597 men with moderate to severe prostatitis-like symptoms were analyzed for pelvic pain and ED.

Demographic data were analyzed with descriptive statistics. The significance of differences in these estimates was analyzed with t-tests and χ^2 tests. The propensity score was built by means of a multivariable logistic regression model considering the following variables: age, metabolic syndrome, PEDT score, and testosterone. Propensity score matching was considered for 597 men with moderate to severe prostatitis-like symptoms

and 6584 men with no prostatitis-like symptoms, but ultimately, subjects were matched by propensity at a 1:1 ratio of controls to patients with moderate to severe prostatitis-like symptoms (n=597 controls and 597 men with moderate to severe prostatitis-like symptoms). We performed propensity score matching with the MatchIt package in the R statistical package and implemented the suggestions of Ho and colleagues for improving parametric statistical models by preprocessing data with nonparametric matching methods. After matching, the IIEF score and ED severity were compared using a t-test and $\chi 2$ test. All tests were 2-sided, with statistical significance set at P <0.05. Analyses were conducted with the R statistical package v.2.13.1 (R Foundation for Statistical Computing, Vienna, Austria).

2.6 Ethics statement The study was carried out in agreement with the applicable laws and regulations, good clinical practices, and ethical principles as described in the Declaration of Helsinki. The Institutional Review Board reviewed and approved this study protocol (approval number: 2021-05-011).

3. RESULT

The demographic data before and after propensity score matching for the patients with moderate to severe prostatitis-like symptoms and the normal controls are displayed in Tables 1 and 2, respectively. Overall, the study included 597 patients with moderate to severe prostatitis-like symptoms and 6,584 normal controls, but following propensity score matching, there were 597 moderate to severe prostatitis-like symptom cases and 597 normal controls. Before propensity score matching (Table 1), the mean age and PEDT score were significantly greater in the case group. After propensity score matching (Table 2), age, PEDT, testosterone, and MetS were evenly dispersed and did not differ significantly between the groups, thus validating the propensity score matching model.

Table 3 displays the frequency and severity of ED according to the presence of moderate to severe prostatitis-like symptoms after propensity score matching. There was a significant difference in the distribution of ED severity between the groups, and ED severity was significantly greater in the case group. The rate of moderate to severe ED was significantly higher in the case group than in the control group, and the mean IIEF score was significantly lower in the case group.

4. DISCUSSION

Our propensity score matching study demonstrated that the presence of moderate to severe prostatitis-like symptoms was significantly and independently related to ED in middle-aged men.

Several studies have investigated the relationship between ED and CP/CPPS. However, most studies are limited by a lack or minimal adjustment of potential confounding factors.[4-8,16,17]ED and CP/CPPS share many risk factors;[18] therefore, it would be important to adjust for confounding factors to examine their relationship.

To the best of our knowledge, only three studies have adjusted for confounding factors to elucidate the relationship between ED and CP/CPPS, and the results are not consistent across the studies. A cross-sectional study from Boston, MA, USA, reported that prostatitis in men was associated with ED (adjusted OR 2.36, 95% confidence interval 1.51–3.71).[9] However, this study is limited in that it adjusted only for age because of the lack of other comorbidity data. In a case-control study enrolling Egyptian patients, CP/CPPS was not a significant factor for predicting ED after adjusting for smoking, use of recreational drugs, obesity, dyslipidemia, diabetes mellitus, hypertension, and coronary heart disease.[19] However, that study enrolled only men under the age of 40 years, which might be a weak point because both ED and CP/CPPS increase with age and ED starts to significantly increase in the fifth decade of life.[20] In another case-control study from Taiwan, ED was significantly related to previous CP/CPPS (odds ratio 3.62 compared with controls, 95% confidence interval 3.07–4.26) after adjusting for patient monthly income, geographical location and urbanization level, hypertension, diabetes, coronary heart disease, renal disease, obesity and alcohol abuse/alcohol dependence syndrome status.[17] However, that study defined CP/CPPS and ED by using the ICD-9CM code rather than validated questionnaires, potentially compromising the accuracy of the diagnosis.

We adjusted for age, metabolic syndrome, premature ejaculation and testosterone because both ED and CP/CPPS increase with age,[18] chronic hyperinsulinemia (closely related to metabolic syndrome[21]) induces prostate inflammation and erectile dysfunction,[22,23] premature ejaculation is related to both ED and CP/CPPS,[13] and testosterone levels are related to CP/CPPS[24] and erectile dysfunction. To the best of our knowledge, testosterone levels and premature ejaculation have not been adjusted in previous studies. We enrolled middle-aged men, a demographic in which ED starts to increase.[20] Additionally, this is the first propensity score matching case-control study among studies evaluating the relationship between ED and CP/CPPS, which mimics some of the particular characteristics of randomized controlled trials.[25] We addressed the aforementioned limitations of previous studies.[9,17,19] Therefore, we believe our study used the most relevant methodology to reveal the relationship between ED and CP/CPPS.

Little is known about whether ED worsens as symptoms of CP/CPPS worsen. A cross-sectional study including 1,765 men (aged from 20 to 79) reported IIEF-5 scores of 20.6±0.3 for men without chronic pelvic pain symptoms, 18.3±0.7 for men with mild symptoms, and 16.5±1.1 for men with moderate/severe symptoms,[26] all of which suggest that symptoms of ED worsen as symptoms of CP/CPPS worsen. In our pilot study, mild prostatitis-like symptoms (participants who reported perineal or ejaculatory pain and had an NIH-CPSI pain score of [?]4 and <8) were not related to ED after propensity score matching. The NIH-CPSI score in the upper quartile was associated with 8.3-fold increased odds of ED in previous studies.[26] Therefore, it is unclear whether the severity of CP/CPSS correlates with the severity of ED, but it seems clear that men with moderate/severe symptoms might have a higher chance of ED than men without symptoms or moderate/severe symptoms.

Scant data are available concerning the difference in IIEF-5 scores between men with CP/CPPS and those without CP/CPPS. A population-based cross-sectional survey conducted in Singapore (including 1087 males aged 21 to 70) reported that those who had "prostatitis-like symptoms" had worse erectile function (IIEF-5: 11.92 vs. 17.16,P <0.003).[6] A case-control survey conducted in China (including 600 CP/CPPS patients aged 18–50 years) reported that those who had chronic prostatitis had worse erectile function than the controls (IIEF-5: 19.27 vs. 23.8,P =0.009).[27] In our study, the IIEF-5 scores of men with moderate to severe prostatitis-like symptoms and no prostatitis-like symptoms were 14.2 and 17.2, respectively, which was a relatively small difference compared to previous studies, potentially due to the difference in participant age and the use of propensity score–matched analysis in our study.

It is unclear why ED is significantly related to CP/CPPS, and it is hard to investigate the underlying mechanism in this clinical study setting, although vasculogenic, endocrine, neurogenic, and psychogenic mechanisms have been suggested.[16] Further clinical and experimental studies are needed to investigate the underlying mechanism to treat men with both conditions.

The limitation of this study is that the nature of our dataset makes causal inferences problematic. Nevertheless, we believe that our study provided meaningful results, as the dataset was the result of propensity score matched analysis.

In conclusion, moderate to severe prostatitis-like symptoms are significantly and independently related to ED in middle-aged men. Our data suggest the need for screening and treatment for ED in middle-aged patients with moderate to severe CP/CPPS symptoms and vice versa.

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