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ORIGINAL ARTICLE

Erectile Function

Is mild erectile dysfunction associated with severe psychological symptoms in Chinese patients with moderate-to-severe chronic prostatitis/chronic pelvic pain syndrome?

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This study aimed to assess the association between psychological disorders and erectile dysfunction (ED) in patients with different degrees of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS). This was a retrospective study conducted from June 2017 to October 2019 and included 182 outpatients. Patients were interviewed using the Structured Interview on Erectile Dysfunction (SIEDY) for pathogenic quantification. The National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) and the International Index of Erectile Function-5 (IIEF-5) were used for the evaluation of CP/CPPS and ED. The Generalized Anxiety Disorder-7 (GAD-7) and Patient Health Questionnaire-9 (PHQ-9) were used to assess anxiety symptoms and depressive symptoms. The number of patients with mild CP/CPPS and mild ED, mild CP/CPPS and moderate-to-severe ED, moderate-to-severe CP/CPPS and mild ED, and moderate-to-severe CP/CPPS and moderate-to-severe ED was 69 (37.9%), 36 (19.8%), 35 (19.2%), and 42 (23.1%), respectively. The corresponding PHQ-9 scores of the four groups were 6.22, 7.19, 10.69, and 7.71, respectively. The corresponding GAD-7 scores of the four groups were 5.26, 6.31, 8.77, and 6.36, respectively. Among patients with moderate-to-severe CP/CPPS, the PHQ-9 and GAD-7 scores of the moderate-to-severe ED group were significantly lower than those of the mild ED group ($P = 0.007$ and $P = 0.010$, respectively). The prevalence of ED and premature ejaculation (PE) in patients with moderate-to-severe CP/CPPS was significantly higher than that in patients with mild CP/CPPS ($P = 0.001$ and $P = 0.024$, respectively). Our findings proved that the severity of ED was negatively associated with psychological symptoms in outpatients with moderate-to-severe CP/CPPS.

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Keywords: anxiety; association; chronic prostatitis/chronic pelvic pain syndrome; depression; erectile dysfunction

INTRODUCTION

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is described as pain or discomfort localized to the pelvis and genitals or lower urinary tract symptoms (LUTS) in the absence of voiding tract infection.¹ Nearly 4.5%–9% of males have a history of CP/CPPS, and older males have a 50% recurrence rate.^{2,3} Erectile dysfunction (ED), a sexual disorder, was found to be significantly correlated with CP/CPPS.⁴ ED is present in 27%–35% of patients with CP/CPPS, and its prevalence continues to increase.⁵

Anxiety disorder (AD) and depression are the most common psychological diseases in the general population.^{6,7} Both CP/CPPS and ED have a negative impact on many aspects of psychological functioning.^{8–10} Although mounting evidence has indicated that LUTS caused by CP/CPPS and ED has a significant positive association with psychological symptoms, very few studies have investigated the

association between psychological disorders and different severities of ED in patients with CP/CPPS, especially in China. It is necessary to determine the impact of ED on psychological factors in CP/CPPS patients to better manage the mental health of patients with both CP/CPPS and ED.

Thus, the present study examined the association between the degree of ED and psychological symptoms in a sample of Chinese men with CP/CPPS who attended an andrology outpatient clinic. We used a combination of various questionnaires, such as the Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), and Quality of Life (QoL), to analyze each patient's psychological symptoms and thoroughly assess patients' mental state. In addition, the Structured Interview on Erectile Dysfunction (SIEDY), a brief, multidimensional instrument designed explicitly for simultaneous assessment and quantification, was used to assess

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the contributions of the organic, relationship, and psychological components of ED.¹¹

PATIENTS AND METHODS

The study was intended to be a retrospective analysis of a consecutive series of 461 patients who were examined at the urology/andrology clinic, Xiangya International Medical Center of Central South University, Changsha, China, from June 2017 to October 2019. These patients had been affected by CP/CPPS associated with ED for at least 6 months. After excluding participants who were missing or refused to answer inquiries about their condition ($n = 62$) and those who did not complete the questionnaire or had a mental illness ($n = 217$), the remaining 182 patients were included in our investigation. This study was authorized by the Institutional Review Board of Xiangya Hospital, Changsha, China (2019-S252). The study flowchart is shown in **Supplementary Figure 1**.

All patients were interviewed prior to any diagnostic or treatment procedure using the SIEDY, the International Prostate Symptom Score (IPSS), and the National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI). We defined patients with an NIH-CPSI score >14 as having moderate-to-severe CP/CPPS and those with a score ≤ 14 as having mild CP/CPPS. The International Index of Erectile Function-5 (IIEF-5), a scale reflecting the severity of ED, was also completed by the study participants. Scores of 12–21, 8–11, and 5–7 indicate mild ED, moderate ED, and severe ED, respectively. The Premature Ejaculation Diagnostic Tool (PEDT) was used to standardize the diagnosis of premature ejaculation (PE). Scores of 0–8, 9–10, and 11–20 are defined as no PE, suspected PE, and PE, respectively. The patients were also asked to complete the GAD-7, which was used to assess anxiety symptoms, as well as the PHQ-9, which was used to evaluate depressive symptoms. In addition, we defined patients with a storage symptom score >3 on the IPSS as the storage group and those with a voiding symptom score >4 on the IPSS as the voiding group.

The SIEDY is a 13-item questionnaire consisting of three scales that identify and quantify components concurrent with sexual disorder. Specifically, scale 1 addresses organic factors and yields scores between 0 and 12; scores ≥ 4 indicate an organic problem. Scale 2 addresses marital factors and yields scores between 0 and 12; scores ≥ 2 indicate relationship impairment. Scale 3 addresses psychopathological factors and yields scores between 0 and 18; scores ≥ 3 indicate psychopathology.

All patients underwent a complete physical and andrological examination, including an evaluation of weight, height, blood pressure, pulse, respiration, and body mass index (BMI). A blood sample was drawn in the morning after an overnight fast to determine blood glucose, total cholesterol, triglyceride, high-density lipoprotein (HDL), glycated hemoglobin (GH), total testosterone (T), prolactin (PRL), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) levels. Testosterone levels were measured early in the morning after an overnight fast. Prostatic fluid was drawn to measure white blood cells, red blood cells, phospholipid bodies, and the presence of specific infections. Moreover, we detailed the general condition of the patient, including his income, masturbation history, disease history, and medication effectiveness.

The Kolmogorov–Smirnov test and Q-Q plots were used to test normality. Data were expressed as mean \pm standard deviation (s.d.) when normally distributed and as median (quartiles) for parameters with nonnormal distribution. Differences in normally distributed variables were assessed by Student's *t*-test, whereas nonnormally distributed variables were compared by the Wilcoxon rank-sum (Mann–Whitney U) test. The Chi-square test was used to compare

differences in categorical variables between participant groups. Spearman's or Pearson's method was used for linear analysis. All statistical analyses were performed using SPSS Statistics (IBM, version 22.0; SPSS, Armonk, NY, USA) for Windows. $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Comparison of the characteristics of patients with different degrees of CP/CPPS

The associations between the main sociodemographic, clinical, and biochemical characteristics and CP/CPPS are shown in **Table 1**. A total of 77 (42.3%) patients reported moderate-to-severe CP/CPPS. On univariate analysis, scores on the IIEF-5, a scale reflecting the severity of ED, showed a strong negative correlation with NIH-CPSI scores ($P < 0.001$). Psychological symptoms, reflected in the PHQ-9, GAD-7, and SIEDY-3 scores, showed significant positive relationships with the NIH-CPSI score ($P = 0.001$, $P = 0.002$, and $P = 0.027$, respectively). In addition, the QoL score showed a strong association with the NIH-CPSI score ($P < 0.001$).

Comparison of the characteristics of patients with different severities of ED

The association between the severity of ED and the scale scores is shown in **Figure 1**. The PHQ-9 scores of the mild ED, moderate ED, and severe ED groups were 7.72, 7.47, and 7.48, respectively. Similarly, the GAD-7 scores of the three groups were 6.44, 6.34, and 6.32, respectively. The SIEDY-3 scores of the three groups were 6.49, 5.40, and 6.36, respectively. Interestingly, no correlation was found between the severity of ED and any psychological variable. The SIEDY-1 score and the NIH-CPSI score showed a significant association with the severity of ED ($P < 0.001$ and $P = 0.007$, respectively). In addition, total testosterone, which suggests the presence of organic ED, had significantly decreased in patients with moderate and severe ED (data not shown).

Comparison of the symptoms of different severities of ED between patients with moderate-to-severe and mild CP/CPPS

We investigated the association of the characteristics of mild ED and moderate-to-severe ED between patients with different severities of CP/CPPS (**Table 2** and **Figure 2**). Interestingly, in patients with moderate-to-severe CP/CPPS, there were significant negative correlations between the severity of ED and the PHQ-9, GAD-7, and SIEDY-3 scores ($P = 0.007$, $P = 0.010$, and $P = 0.002$, respectively), whereas in patients with mild CP/CPPS, there were no such significant correlations ($P = 0.357$, $P = 0.191$, and $P = 0.202$, respectively; **Figure 2**). In addition, SIEDY-1 scores and age showed a positive association with the severity of ED in patients with both mild and moderate-to-severe CP/CPPS (**Table 2**). In patients with mild CP/CPPS, the prevalence of hypoactive sexual desire was significantly higher among those with moderate-to-severe ED than among those with mild ED (66.7% vs 61.1%), whereas in patients with moderate-to-severe CP/CPPS, the prevalence of hypoactive sexual desire in different groups was not significantly different (65.8% vs 66.7%).

Classification of sexual dysfunction

Table 3 shows the association between NIH-CPSI scores and sexual dysfunction. IIEF-5 scores were categorized into three groups: 12–21, 8–11, and 5–7 for mild, moderate, and severe ED, respectively. PEDT scores of 0–8, 9–10, and 11–20 represented no PE, suspected PE, and PE, respectively. Both ED severity and the presence of PE had significantly increased in moderate-to-severe CP/CPPS patients ($P = 0.001$ and $P = 0.024$, respectively; **Table 3**).

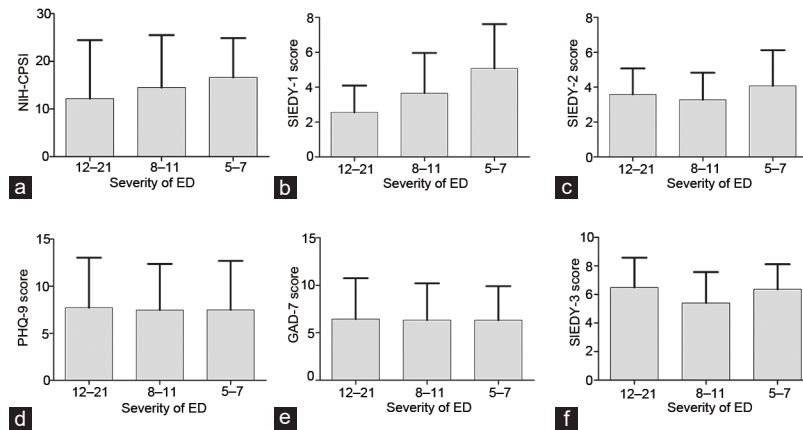


Figure 1: (a) NIH-CPSI, (b) SIEDY-1, (c) SIEDY-2, (d) PHQ-9, (e) GAD-7, and (f) SIEDY-3 scores in different degrees of ED (IIEF-5). ED: erectile dysfunction; NIH-CPSI: National Institutes of Health-Chronic Prostatitis Symptom Index; SIEDY: Structured Interview on Erectile Dysfunction; PHQ: Patient Health Questionnaire; GAD: Generalized Anxiety Disorder; IIEF: International Index of Erectile Function.

Table 1: Association between the basic data and CP/CPSP, as evaluated by the NIH-CPSI

Variables	Total case (n=182)	NIH-CPSI ≤14 (n=105)	NIH-CPSI >14 (n=77)	P
Age (year)	33.86±8.36	34.81±8.72	32.56±7.72	0.073
BMI (kg m ⁻²)	22.85±2.63	23.50±2.87	21.75±1.71	<0.001**
Systolic pressure (mmHg)	124.98±11.52	124.31±10.77	126.13±12.77	0.399
Blood sugar (mmol l ⁻¹)	5.10 (4.93, 5.48)	5.18 (4.94, 5.37)	4.99 (4.76, 5.55)	0.377
Cholesterol (mmol l ⁻¹)	4.89 (4.30, 5.49)	4.99 (4.12, 5.71)	4.81 (4.53, 5.20)	0.881
Triglyceride (mmol l ⁻¹)	1.68±0.63	1.83±0.65	1.42±0.50	<0.001**
FSH (μU l ⁻¹)	4.00 (3.24, 5.44)	4.01 (3.43, 5.17)	4.00 (2.99, 5.88)	0.655
LH (μU l ⁻¹)	5.08±1.73	5.52±1.79	4.40±1.39	<0.001**
PRL (μg l ⁻¹)	10.71±3.92	11.12±4.63	10.07±2.33	0.039*
Testosterone (nmol l ⁻¹)	19.40±6.11	19.67±6.22	18.98±5.97	0.533
IIEF-5	13.53±4.74	14.63±4.46	12.04±4.72	<0.001**
PHQ-9	7.62±5.15	6.55±5.13	9.06±4.85	0.001*
GAD-7	6.40±4.08	5.62±3.88	7.45±4.13	0.002*
QoL	2.00 (1.00, 4.00)	2.00 (1.00, 4.00)	3.00 (2.00, 4.00)	<0.001**
SIEDY scale 1	3.23±2.13	2.97±2.13	3.57±2.07	0.060
SIEDY scale 2	3.57±1.60	3.43±1.58	3.75±1.62	0.177
SIEDY scale 3	6.15±2.12	5.86±2.06	6.56±2.13	0.027*

Data are expressed as the mean±s.d. of a normal distribution and the median (quartiles) of non-normally distributed. * $P<0.05$, ** $P<0.001$. CP/CPSP: chronic prostatitis/chronic pelvic pain syndrome; NIH-CPSI: National Institutes of Health-Chronic Prostatitis Symptom Index; s.d.: standard deviation; BMI: body mass index; FSH: folliclestimulating hormone; LH: luteinizing hormone; PRL: prolactin; IIEF: International Index of Erectile Function; PHQ: Patient Health Questionnaire; GAD: Generalized Anxiety Disorder; QoL: Quality of Life; SIEDY: Structured Interview on Erectile Dysfunction

Comparison of symptoms between different LUTS groups

Table 4 shows the correlation between the storage symptom group (storage score >3) and the voiding symptom group (voiding score >4). The IIEF-5 scores of the voiding and storage + voiding groups were significantly lower than those of the mild LUTS and storage groups ($P = 0.035$). Interestingly, regarding the PHQ-9, GAD-7, and QoL scores, the average scores of the storage + voiding group were significantly higher than those of the group with only storage symptoms and the group with only voiding symptoms ($P = 0.009$, $P = 0.001$, and $P < 0.001$, respectively).

DISCUSSION

ED is more common in the elderly population than in other age groups, and several investigations have shown that severe ED can cause severe psychological symptoms.^{12,13} However, the unique age distribution of Chinese ED outpatients caused the opposite result. In

our study, the average age of the patients was only 33.86 years. This is because in China, the vast majority of people, including nearly half of the urologists, believe that ED is a natural part of aging rather than a disease.¹⁴ Accordingly, the vast majority of elderly ED patients in China, especially those with organic ED, are reluctant to see a doctor for loss of erectile function. A 5-year survey conducted in China revealed that 74.5% of ED patients who sought treatment were under the age of 50 years,¹⁵ while the literature on ED from most other countries reports an average age >50 years.^{16,17} Tan *et al.*¹⁸ proved that only 58% of ED patients in China seek help from a Western doctor, which was significantly lower than the findings for patients in other Asian countries.

ED is divided into many categories by pathophysiological factors, but it is typically classified as organic ED, psychogenic ED, and mixed ED.¹⁹ Among these classifications, mixed ED has undoubtedly accounted for the most substantial proportion of cases in several

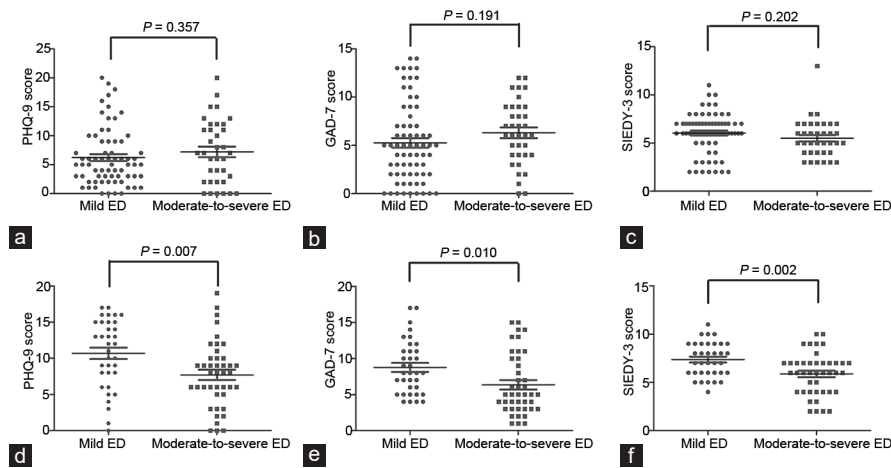


Figure 2: (a) PHQ-9, (b) GAD-7, and (c) SIEDY-3 scores of different degrees of ED in mild CP/CPPS patients. (d) PHQ-9, (e) GAD-7, and (f) SIEDY-3 scores of different degrees of ED in moderate-to-severe CP/CPPS patients. ED: erectile dysfunction; PHQ: Patient Health Questionnaire; GAD: Generalized Anxiety Disorder; SIEDY: Structured Interview on Erectile Dysfunction; CP/CPPS: chronic prostatitis/chronic pelvic pain syndrome.

Table 2: The association of characteristics between ED group in different severity levels of CP/CPPS

Variables	Mild CP/CPPS			Moderate-to-severe CP/CPPS		
	Mild ED (n=69)	Moderate-to-severe ED (n=36)	P	Mild ED (n=35)	Moderate-to-severe ED (n=42)	P
Age (year)	33.13	38.03	0.006*	29.66	34.98	0.002*
BMI (kg m ⁻²)	23.48	23.55	0.921	21.91	21.56	0.494
LH (μU l ⁻¹)	5.41	5.81	0.391	4.29	4.56	0.501
PRL (μg l ⁻¹)	11.44	10.26	0.324	10.05	10.09	0.948
QoL	1.53	1.38	0.663	3.19	3.44	0.490
SIEDY 1	2.30	4.25	0.001*	3.06	4.00	0.048*
SIEDY 2	3.57	3.17	0.222	3.63	3.86	0.540

Data are expressed as the mean values. * $P < 0.05$. ED: erectile dysfunction; CP/CPPS: chronic prostatitis/chronic pelvic pain syndrome; BMI: body mass index; LH: luteinizing hormone; PRL: prolactin; QoL: Quality of Life; SIEDY: Structured Interview on Erectile Dysfunction

Table 3: The association between National Institutes of Health-Chronic Prostatitis Symptom Index scores and sexual dysfunction

Variables	Scores	Mild CP/CPPS (n=105), n (%)	Moderate-to-severe CP/CPPS (n=77), n (%)	P
IIEF-5 score	12–21	69 (65.7)	35 (45.5)	0.001*
	8–11	28 (26.7)	25 (32.5)	
	5–7	8 (7.6)	17 (22.1)	
PEDT score	0–8	30 (28.6)	17 (22.1)	0.024*
	9–10	22 (21.0)	6 (7.8)	
	11–20	53 (50.5)	54 (70.1)	

* $P < 0.05$. CP/CPPS: chronic prostatitis/chronic pelvic pain syndrome; IIEF: International Index of Erectile Function; PEDT: Premature Ejaculation Diagnostic Tool

studies.¹⁷ One study proved that the IIEF-5 scores of patients with psychogenic ED were significantly higher than those of patients with organic ED and found that most mild ED patients had psychogenic ED.²⁰ A total of 80.2% of our participants were aged under 40 years. In China, a country with a traditional culture and a history of thousands of years, most parents and teachers are very conservative; as a result, most young Chinese people receive no sexual education. As a result, they may fail when they have sex for the first time, which may exacerbate the occurrence of psychogenic ED.²¹ One study investigating ED outpatients in five Chinese hospitals over 5 years showed that the age of patients with psychogenic ED was significantly lower than that of patients with other types of ED, and the proportion of mild ED was markedly higher among outpatients with psychogenic ED than

among those with other ED types.²² In young Chinese patients, ED is typically psychogenic and mild.²³ These young patients with mild ED feel ashamed before their partners and peers due to a lack of sexual education and may face pressure from traditional Chinese parents to produce offspring, which further exacerbate their anxiety and depressive symptoms.

The patients in our survey had different degrees of CP/CPPS in addition to sexual impairment. Our results showed that in moderate-to-severe CP/CPPS patients, sexual impairments such as ED and PE and the severity of psychological symptoms had significantly increased. Many scholars have proven an important correlation between CP/CPPS and sexual impairment.^{24,25} Hence, regular evaluation of ED in CP/CPPS patients is necessary. The significant increase in anxiety, depression, and QoL scores in patients with moderate-to-severe CP/CPPS, especially those with both storage and voiding symptoms, might be related to the excessive release of adrenocorticotrophic hormone (ACTH) and sympathetic nervous excitement.²⁶

In our study, patients with moderate-to-severe CP/CPPS and moderate-to-severe ED (IIEF-5 <12) had significantly lower PHQ-9, GAD-7, and SIEDY-3 scores than those with mild ED (11 <IIEF-5 <22). In addition to the lack of sex education for young Chinese patients, the impact of CP/CPPS cannot be ignored. Young and middle-aged people are prone to CP/CPPS, an association that is consistent with the age structure of Chinese outpatients. Many studies have shown that the psychological symptoms associated with severe CP/CPPS, such as anxiety and depression, might be important causes of ED.^{27,28}

Table 4: The correlation between the storage symptom score group (storage score >3) and the voiding symptom score group (voiding score >4) evaluated by the International Prostate Symptom Score

Variables	Mild LUTS group (n=87)	Storage group (n=18)	Voiding group (n=18)	Storage + voiding group (n=59)	P
Age (year)	34.79	33.56	33.83	32.58	0.479
BMI (kg m ⁻²)	23.50	22.28	23.35	21.72	0.011*
Systolic pressure (mmHg)	125.71	116.40	126.50	126.91	0.019*
PRL (µg l ⁻¹)	11.21	10.96	9.99	10.01	0.444
Testosterone (nmol l ⁻¹)	20.54	19.59	15.81	18.60	0.070
IIEF-5	14.24	14.50	12.33	12.56	0.035*
PHQ-9	6.55	6.61	7.94	9.39	0.009*
GAD-7	5.20	7.06	6.50	7.93	0.001*
QoL	1.42	2.00	2.25	3.57	<0.001**
SIEDY scale 1	2.79	3.67	3.67	3.59	0.073
SIEDY scale 2	3.69	2.50	3.50	3.73	0.026*
SIEDY scale 3	6.00	4.67	6.89	6.61	0.002*

*P<0.05, **P<0.001. BMI: body mass index; PRL: prolactin; IIEF: International Index of Erectile Function; PHQ: Patient Health Questionnaire; GAD: Generalized Anxiety Disorder; QoL: Quality of Life; SIEDY: Structured Interview on Erectile Dysfunction; LUTS: lower urinary tract symptoms

Zhang *et al.*²⁹ showed that most patients with CP/CPPS had ED, but few among them had moderate-to-severe ED. Therefore, the anxiety and depression caused by severe CP/CPPS in these young patients further led to the occurrence of mild ED, which in turn exacerbated their psychological symptoms. In our study, the SIEDY-1 score, reflecting organic factors, was significantly higher in patients with moderate-to-severe ED than in those with mild ED, which also proved that most patients with moderate-to-severe ED have organic ED.

The psychological symptoms of patients with moderate-to-severe CP/CPPS are typically severe,³⁰ but those with more severe ED in moderate-to-severe CP/CPPS patients had less severe psychological symptoms in our study. It has been documented that the long-term existence of chronic diseases may help ED patients better adjust to the emergence of a new disease-related problem, namely, sexual failure, which in turn causes them to have reduced concern and therefore reduced performance anxiety and depression.³¹ In fact, in our survey, among patients with mild CP/CPPS, the prevalence of hypoactive sexual desire was significantly higher in patients with moderate-to-severe ED than in patients with mild ED. However, in patients with moderate-to-severe CP/CPPS, the prevalence of hypoactive sexual desire did not differ significantly according to ED degree and was even lower in patients with moderate-to-severe ED. There was no significant difference in the prevalence of hypoactive sexual function in patients with moderate-to-severe CP/CPPS, which indicates that patients with both moderate-to-severe CP/CPPS and moderate-to-severe ED have a positive attitude toward addressing these diseases.³² As a result of the age structure of and the presence of moderate-to-severe CP/CPPS in Chinese outpatients, our study results differed from those in most Western countries.

CONCLUSIONS

Our study found that in Chinese outpatients with moderate-to-severe CP/CPPS, those with more severe ED showed milder psychological symptoms, a finding related to the unique age composition of Chinese ED outpatients. Among Chinese men with moderate-to-severe CP/CPPS, those with mild ED require further increases in the level of psychological intervention than those with moderate-to-severe ED to improve the therapeutic effect.

AUTHOR CONTRIBUTIONS

XCL, ZYT, and DJL contributed to conception and design. XCL, XBZ, ZCL, and DJL contributed to acquisition of data. XCL and ZCL contributed to analysis of data. XCL contributed in drafting the

article. XCL, XBZ, ZCL, ZYT, and DJL contributed in revising the article critically for important intellectual content. All authors read and approved the final manuscript.

COMPETING INTERESTS

All authors declared no competing interests.

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Supplementary Information is linked to the online version of the paper on the *Asian Journal of Andrology* website.

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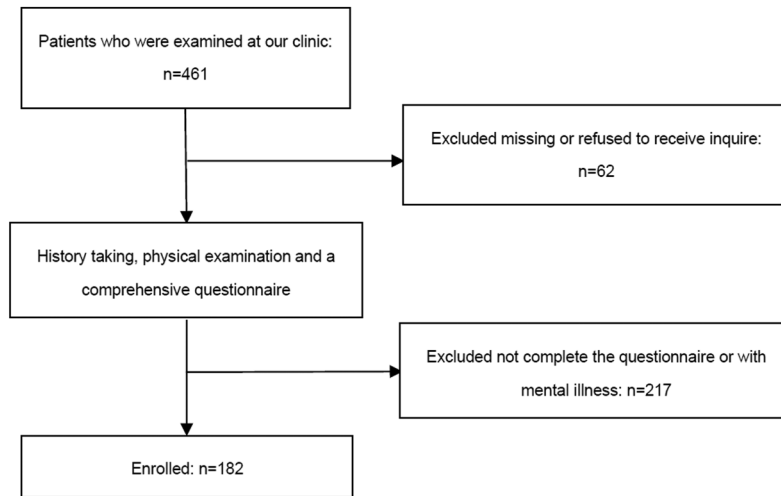
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Supplementary Figure 1: Study flowchart for enrollment of patients.