A Mid-to-Long Term Comprehensive Evaluation of Psychological Distress and Erectile Function in COVID-19 Recovered Patients

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ABSTRACT

Background: The psychological and sexual health of different populations are negatively affected during the coronavirus disease 2019 (COVID-19) pandemic. However, little is known about psychological distress and erectile function of male recovered patients with COVID-19 in the long term.

Aim: We aimed to evaluate psychological distress and erectile function of male recovered patients with COVID-19 in the mid-to-long terms.

Methods: We recruited 67 eligible male recovered patients with COVID-19 and followed them up twice within approximately 6 months of recovery time. The psychological distress and erectile function were assessed by validated Chinese version of paper questionnaires.

Outcomes: The primary outcomes were Symptom Checklist 90 questionnaire for psychological distress and International Index of Erectile Function-5 for erectile function.

Results: In the first visit, COVID-19 patients with a median recovery time of 80 days mainly presented the following positive symptoms: Obsessive-Compulsive, additional items (ADD), Hostility, Interpersonal Sensitivity, Depression, and Somatization; while the dimension scores in Somatization, Anxiety, ADD, and Phobia were higher than Chinese male norms. Besides, the prevalence of erectile dysfunction (ED) in the first-visit patients was significantly higher than Chinese controls. In the second visit, the primary psychological symptoms of COVID-19 patients with a median recovery time of 174 days were Obsessive-Compulsive, ADD, Interpersonal Sensitivity, and Hostility, while all dimensions scores of Symptom Checklist 90 were lower than Chinese male norms. Moreover, second-visit patients had no significant difference with Chinese controls in ED prevalence. In addition, it suggested that GSI was the independent risk factor for ED in the regression analysis for the first-visit patients.

Clinical Implications: The study showed the changes of psychological symptoms and erectile function in COVID-19 recovered patients, and provided reference on whether psychological and sexual supports are needed after a period of recovery.

Strengths and Limitations: To our knowledge, it is the first study to comprehensively evaluate the psychological distress and erectile function of COVID-19 recovered patients in the mid-to-long terms. The main limitations were the low number of analyzed participants, and the psychological distress and erectile function of healthy Chinese men over the same period were not evaluated, and the psychological and sexual related data of participants prior to COVID-19 were not available. Additionally, there was a selection bias in comparing COVID-19 patients with healthy controls.

Conclusion: With less impact of COVID-19 event, the impaired erectile function and psychological distress improved in COVID-19 recovered patients with a recovery time of nearly half a year. **Hu B, Ruan Y, Liu K, et al. A Mid-to-Long Term Comprehensive Evaluation of Psychological Distress and Erectile Function in COVID-19 Recovered Patients. J Sex Med 2021;18:1863−1871.**

INTRODUCTION

In late December 2019, a novel coronavirus disease broke out in Wuhan, China, and subsequently swept across the country and the whole world. The disease was later designated as the coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO), and the virus causing COVID-19 was identified and named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) due to high sequence similarity with SARS-CoV.[1] As of March 11, 2020, more than 118,000 cases were infected with COVID-19 in 114 countries, and over 4 thousand people had lost their lives, which was declared as a global pandemic by WHO. Due to the rapid spread of COVID-19, Chinese government firstly started the most stringent nationwide implementation of public life restrictions on January 29, 2020. Subsequently, a series of similar measures were enacted in most affected countries, including restrictions on transport, entertainment, social distancing measures, and so on.[2,3] During the pandemic, global researchers dedicated themselves to investigating the impact of COVID-19 disease and the pandemic event on public health.

Generally speaking, the outbreak of a pandemic will cause a crisis of psychological health.[4,5] During the pandemic, people's daily lives were significantly changed owing to the various disease-prevention measures.[6,7] General population experienced the loss of freedom, separation from families and friends, difficulties in securing medications, as well as the obvious economic consequences of lockdown. Health workers had an additional experience of health-threatening workload and high risk of being infected.[8] While the COVID-19 patients additionally faced the fear of dying from the disease, facing discrimination and getting stigmatized by the society.[9,10] Therefore, it was not surprising that the public was stressed and had various degrees of psychological distress, and the burden of these psychological morbidities was highest among the COVID-19 patients, followed by healthcare workers and general population amidst the COVID-19 pandemic.[10] Unfortunately, as previous studies on Severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) survivors indicated persistent mental disorder even after 1 year,[11,12] it's likely that COVID-19-related psychological distress will persist long after recovery. However, few studies reported the long-term psychological impact of COVID-19 on recovered patients.

Additionally, as both psychological and physiological components can potentially be involved in the relationship between stress and sexual function,[13] it is understandable that during the pandemic, people may have sexual dysfunction. A great number of studies demonstrated the negative influence of COVID-19 pandemic on sexual health in different populations, including sexual arousal, frequency of sexual intercourse, orgasm, sexual satisfaction, and so on.[14−17] As for men subpopulations with COVID-19, little is known about their erectile function.

As it is believed that erectile dysfunction (ED) is an excellent surrogate marker of systemic health,[18] ED patients could already have some risk factors, such as diabetes, hypertension, and dyslipidemia, increasing the possibility of COVID-19 infection. However, testicular damage and some complications of COVID-19 infection,[19−21] such as pulmonary fibrosis and myocarditis, could be potentially involved in the development of ED. Published literature also demonstrated that ED is a likely consequence of COVID-19 for survivors and reviewed the possible mechanisms contributed to the potential onset of ED.[22] Together with the number of outpatients diagnosed with ED markedly increased during the pandemic[23] and some studies reported ED in other male subgroup,[14,24−26] it is most likely that COVID-19 patients may develop ED. However, currently, the erectile function in male recovered patients with COVID-19 remains unknown. As around 55% of male COVID-19 patients were reproductive-aged in a retrospective study involving 1099 cases,[27] it is significant to evaluate their erectile function in the mid-to-long terms.

In this study, we followed up male recovered patients with COVID-19 for approximately half a year and comprehensively evaluated their psychological distress and erectile function through the paper questionnaires completed. It can provide insights into the changes of psychological symptoms and erectile function in COVID-19 recovered patients and whether they need psychological and sexual support after a period of recovery.

MATERIALS AND METHODS

Study Design

In order to evaluate the psychological distress and erectile function of male recovered patients with COVID-19 in the mid-to-long term, we designed a prospective observational study for approximately 6 months. The study was registered with ClinicalTrials.gov, number NCT04388631, and was approved by the Ethics Committee of Tongji Medical College (2020-S073). All participants gave written informed consent before starting the survey. All the information for patients, including demographic data, clinical characteristics, as well as psychometric and

sexological measures, were collected in the case report form. To ensure that there were no errors and duplicated information, 2 researchers independently converted the information of case report form into electronic records. Data were analyzed and interpreted by the authors.

Study Population

The objects of this study were male COVID-19 recovered patients with denying pre-existing ED and mental disease before COVID-19 infection. All participants were confirmed as SARS-CoV-2 positive through the real-time reverse transcriptase-polymerase chain reaction assay using pharyngeal swab specimens. Their last positive test time (considered as the beginning of recovery time) varied between January 29 and May 7, 2020. The diagnosis and classification of COVID-19 were determined according to the New Coronavirus Pneumonia Prevention and Control Program (7th ed.) published by the National Health Commission of China.

Male recovered patients with COVID-19 who met the following inclusion criteria or exclusion criteria were considered for enrolling or excluding in this study. The inclusion criteria were: (1) age between 18 and 60 years old; (2) have a fixed sexual partner and regular sexual life; (3) agree and sign the informed consent form. (4) fill in the questionnaire completely. The exclusion criteria were: (1) previously diagnosed as ED; (2) past history of psychological or mental disease; (3) traumatic or surgical history of urogenital or pelvic; (4) severe cardiovascular or cerebrovascular diseases; (5) uncontrolled hypertension or diabetes, or other severe chronic diseases.

The controls for comparison with COVID-19 recovered patients were obtained from 2 pieces of literature investigating the psychological distress and ED prevalence of large-scale Chinese men population respectively.[28,29] One of the controls ageing from 18 to 60 years (regarded as Chinese male norms) was obtained by cluster sampling in 12 Chinese provinces, and they had no history of mental disorders. The other controls between 22 and 60 years old were selected by a cross-sectional survey in different parts of China, and all of them were married and have had past intercourse experience.

Procedure

In May 2020, we contacted the male COVID-19 patients discharged from Wuhan Tongji hospital and prescreened the patients according to the inclusion and exclusion criteria. 67 patients were enrolled in this study. After signing the informed consent form, they were asked to attend the andrological laboratory and complete related examinations. The International Index of Erectile Function-5 (IIEF-5) and Symptom Checklist 90 (SCL-90) questionnaire were instructed to complete for evaluating erectile function and psychological distress, respectively. 3 months later (in August 2020), we tried to get in touch with the last eligible participants. However, only 30 eligible questionnaires of IIEF-5 and SCL-90 were completed.

Measure

Erectile function was assessed by the IIEF-5 questionnaire in its validated Chinese version, a 5-item scale scored from 1 to 5 assessing maintenance ability, erection confidence, maintenance frequency, erection firmness, and intercourse satisfaction. Total scores of 22−25, 12−21, 8−11, and 5−7 were considered to represent normal, mild, moderate, and severe ED, respectively. The cut-off value for ED was specified as 21.[30]

Psychological distress of patients was evaluated by Chinese version of SCL-90 questionnaire. The Chinese version of SCL-90 has been developed and validated as a reliable self-reporting diagnostic tool for assessing psychological distress.[31] SCL-90 contains 90 questions, measuring ten symptom dimensions in psychopathology, including Somatization (SOM), Obsessive-Compulsive (OC), Interpersonal Sensitivity (IS), Depression (DEP), Anxiety (ANX), Hostility (HOS), Phobia (PHOB), Paranoid Ideation (PAR), Psychoticism (PSY), and additional items (ADD). Additional items assess disturbances in appetite and sleep. Each question is scored on a 5-point scale (1−5) ranging from "not at all" to "extremely," which reflects the severity of symptom. The dimension score of each symptom was calculated as the mean of corresponding questions scores. The proportion of dimension scores in different ranges was obtained for reflecting the occurrence rate of symptoms of different severity. A cut-off score of ≥2 in these dimensions was used for diagnosing positive symptoms. Global Severity Index (GSI) is calculated as the mean of all 90 items in SCL-90, which provides a measure of overall psychological health.

Statistical Analysis

All the questionnaire data were electronically stored with the SPSS statistical software version 25 (IBM) for statistical analysis. The Mann-Whitney U test or independent t test was used to assess the statistical significance of continuous variables. For the categorical variables, the statistical difference among groups was determined by using Pearson's chi-square or Fisher's exact test. Univariate and multivariate logistic regression analyses were performed to explore the risk factors of ED. Statistical significance was accepted as $P < .05$.

RESULTS

In this study, we followed the enrolled subjects up in May and August 2020 respectively. After strictly prescreening according to inclusion and exclusion criteria, 67 eligible recovered patients with COVID-19 completed IIEF-5 and SCL-90 questionnaires in the first visit, whereas only 30 eligible questionnaires were completed in the second visit. The baseline demographic and clinical characteristics of the patients are shown

Table 1. Demographics, clinical characteristics of COVID-19 recovered patients

Characteristic	First visit	Second visit	P value
Individuals, n	67	30	
Age, y	31.00 (27.00−35.00)	30.50 (27.00−35.00)	.781
BMI, kg/m^2	24.49 (22.86−27.36)	24.49 (22.93−27.41)	.904
Smoker, No. (%)	19 (28.4%)	6 (20%)	.384
Drinker, No. (%)	20 (29.9%)	7 (23.3%)	.508
Married, No. (%)	45 (67.2%)	21 (70%)	.782
Classification of illness			.960
Mild, No. (%)	8 (11.9%)	3 (10.0%)	
Moderate, No. (%)	31 (46.3%)	14 (46.7%)	
Severe, No. (%)	28 (41.8%)	13 (43.3%)	
Recovery time, d	80.00 (62.00−92.00)	174.0 (150.0−184.0)	
ED, No. (%)	30 (44.8%)	9 (30.0%)	.170
IIEF-5 score	22.00 (20.00−24.00)	23.00 (21.00−24.00)	.197
GSI	1.23 (1.10−1.53)	1.15 (1.03−1.40)	.080

Data presented as median (interquartile range) or number (percentage).
BMI = Body Mass Index; ED = erectile dysfunction; GSI = Global Severity Index; IIEF-5 = International Index of Erectile Function-5.

in Table 1. COVID-19 recovered patients in the first visit (hereafter simply called first-visit patients) had a median recovery time of 80 days, and the median recovery time of recovered patients in the second visit (hereafter named second-visit patients) was 174 days. There was no statistically significant difference between first-visit and second-visit patients in demographic and clinical characteristics, including age, BMI, the rate of smoking and drinking, marriage status, and classification of illness. The prevalence of ED and GSI in second-visit patients were both lower than in first-visit patients, although not statistically significant.

Tables 2 and 3 presented the SCL-90 scale score severity distribution of recovered patients in May and August 2020, which reflected the psychological distress of patients in different periods. More than 10% of recovered patients with COVID-19 had the following positive symptom in May: OC (23.88%), ADD (19.40%), HOS (17.91%), IS (14.93%), DEP (10.45%), SOM (10.45%). In contrast, OC (20.00%), ADD (16.67%), IS (13.33%) and HOS symptoms (13.33%) occurred in more than

10% of recovered patients in August. In addition, we made comparisons of SCL-90 scores between recovered patients of different periods and the Chinese male norms (Tables 4 and 5). It

Table 3. SCL-90 scale score severity distribution of second-visit patients

Dimension	i <2	2 ≤ i < 3	3 ≤ i < 4	4 ≤ i < 5
SOM	27 (90.00%)	2 (6.67%)	1 (3.33%)	0 (0.00%)
OC	24 (80.00%)	3 (10.00%)	2 (6.67%)	1 (3.33%)
IS	26 (86.67%)	3 (10.00%)	1 (3.33%)	0 (0.00%)
DEP	27 (90.00%)	2 (6.67%)	1 (3.33%)	0 (0.00%)
ANX	27 (90.00%)	2 (6.67%)	1 (3.33%)	0 (0.00%)
HOS	26 (86.67%)	4 (13.33%)	0 (0.00%)	0 (0.00%)
PHOB	29 (96.67%)	1 (3.33%)	0 (0.00%)	0 (0.00%)
PAR	28 (93.33%)	2 (6.67%)	0 (0.00%)	0 (0.00%)
PSY	27 (90.00%)	2 (6.67%)	1 (3.33%)	0 (0.00%)
ADD	25 (83.33%)	4 (13.33%)	0 (0.00%)	1 (3.33%)

Data presented as numbers (percentages). i refers to the dimension score.

Table 2. SCL-90 scale score severity distribution of first-visit patients

Dimension	i < 2	2 ≤ i < 3	3 ≤ i < 4	4 ≤ i < 5
SOM	60 (89.55%)	7 (10.45%)	0 (0.00%)	0 (0%)
OC	51 (76.12%)	15 (22.39%)	1 (1.49%)	0 (0%)
IS	57 (85.07%)	9 (13.43%)	1 (1.49%)	0 (0%)
DEP	60 (89.55%)	7 (10.45%)	0 (0.00%)	0 (0%)
ANX	62 (92.54%)	5 (7.46%)	0 (0.00%)	0 (0%)
HOS	55 (82.09%)	12 (17.91%)	0 (0.00%)	0 (0%)
PHOB	64 (95.52%)	3 (4.48%)	0 (0.00%)	0 (0%)
PAR	63 (94.03%)	4 (5.97%)	0 (0.00%)	0 (0%)
PSY	64 (95.52%)	2 (2.99%)	1 (1.49%)	0 (0%)
ADD	54 (80.60%)	11 (16.42%)	2 (2.98%)	0 (0%)

Data presented as numbers (percentages). i refers to the dimension score.

Table 4. Comparison of SCL-90 between Chinese male norms and first-visit patients

Dimension	Chinese male norms (n = 4885)	Patients (n = 67)	P
SOM	1.34 ± 0.47	1.37 ± 0.43	.60
OC	1.62 ± 0.59	1.58 ± 0.54	.58
IS	1.49 ± 0.56	1.41 ± 0.45	.24
DEP	1.42 ± 0.52	1.38 ± 0.44	.53
ANX	1.37 ± 0.49	1.38 ± 0.42	.87
HOS	1.46 ± 0.58	1.39 ± 0.47	.33
PHOB	1.20 ± 0.39	1.22 ± 0.36	.68
PAR	1.42 ± 0.54	1.25 ± 0.34	.01
PSY	1.34 ± 0.46	1.28 ± 0.38	.29
ADD	1.50 ± 0.59	1.54 ± 0.55	.58

Data presented mean ± standard deviation.

Table 5. Comparison of SCL-90 between Chinese male norms and second-visit patients

Dimension	Chinese male norms (n = 4885)	Patients (n = 30)	P
SOM	1.34 ± 0.47	1.30 ± 0.53	.64
OC	1.62 ± 0.59	1.53 ± 0.77	.41
IS	1.49 ± 0.56	1.37 ± 0.58	.24
DEP	1.42 ± 0.52	1.33 ± 0.58	.35
ANX	1.37 ± 0.49	1.31 ± 0.58	.50
HOS	1.46 ± 0.58	1.36 ± 0.47	.35
PHOB	1.20 ± 0.39	1.20 ± 0.34	1.00
PAR	1.42 ± 0.54	1.23 ± 0.45	.06
PSY	1.34 ± 0.46	1.24 ± 0.53	.24
ADD	1.50 ± 0.59	1.45 ± 0.66	.64

Data presented mean ± standard deviation.

Table 6. Comparison of ED prevalence between recovered patients and Chinese control

	No ED	ED	P value
First-visit	37 (55.2%)	30 (44.8%)	<.0001*
Second-visit	21 (70.0%)	9 (30.0%)	.061
Chinese controls	6113 (82.9%)	1259 (17.1%)	

*P value: compared with Chinese controls.
ED = erectile dysfunction.

indicated that first-visit patients had higher scores in somatization, anxiety, phobia and additional items, and lower scores in the other symptoms than Chinese male norms, although not significant except for paranoid ideation in Table 4. Table 5 showed that second-visit patients had no significant difference with Chinese male norms and presented lower scores in all dimensions of SCL-90.

As Hao ZY, et al reported the ED prevalence of 17.1% among 7372 eligible Chinese men using the same diagnostic tool,[29] we regarded the 7372 Chinese men as a control group in this study. The recovered patients were compared with them (Table 6). It exhibited that ED prevalence of first-visit patients was significantly higher than controls, while the second-visit patients showed no significant difference with controls.

To explore the risk factors of ED in the first-visit patients, we performed univariate and multivariate logistic regression analysis (Table 7). The factors whose P value in univariate analysis was less than .3 (namely age, BMI, marital status and GSI) were included in the multivariate model. Multivariate analysis indicated that GSI was an independent risk factor for ED in the first-visit patients (OR: 8.697, P = .015).

DISCUSSION

Due to the rapid spread of COVID-19, most affected countries took stringent measures of public life restrictions with the aim to break the chain of transmission. Similar to the previous epidemic, people suffered from different degrees of psychological disorders during the COVID-19 pandemic.[31] It was reported that the most common psychological responses across different populations were depression, anxiety and traumatic stress symptoms during the COVID-19 pandemic.[32] A systematic review revealed that the prevalence of depression, anxiety, post-traumatic stress disorder (PTSD), sleep disturbances were the highest among the COVID-19 patients, followed by general population amidst the COVID-19 pandemic.[10] The overall prevalence of depression, anxiety, and sleep disturbances among COVID-19 patients was 45%, 47%, and 34%, respectively.[33]

However, the adverse consequences of COVID-19 on psychological health did not end after recovery. Some researchers continued to report some psychological symptoms in COVID-19 patients discharged 1 or 2 months later.[34−37] Nevertheless, few data are available on the long-term psychological impact of COVID-19 on recovered patients, and on reflecting psychological changes of COVID-19 recovered patients.

In this study, we assessed the psychological distress of recovered patients for approximately 6 months, and made an observation of the psychological changes. In May 2020, recovered patients with a median recovery time of 80 days mainly

Table 7. Logistic regression analysis for the risk factors of erectile dysfunction

		Univariate analysis			Multivariate analysis		
		OR	95% CI	P	OR	95% CI	P
Age		0.912	0.829−1.004	.06	0.861	0.741−1.000	.051
BMI		0.894	0.786−1.017	.089	0.918	0.791−1.066	.264
Marital status	Single	Ref.			Ref.		
	Married	0.556	0.198−1.555	.263	1.472	0.346−6.261	.601
Clinical type	Mild	Ref.					
	Moderate	0.330	0.066−1.650	.177			
	Severe	0.600	0.120−3.007	.534			
Recovery time		1.006	0.985−1.027	.566			
GSI		5.788	1.291−25.941	.022	8.697	1.533−49.354	.015

CI = confidence interval; GSI = Global Severity Index; OR = odds ratio; Ref. = Reference.

presented the following positive symptoms: obsessive-compulsive, appetite and sleep disturbances, hostility, interpersonal sensitivity, depression, and somatization. Compared with the Chinese male norms,[28] the dimension scores of somatization, anxiety, appetite and sleep disturbances, and phobia, were all higher in recovered patients, which indicated that COVID-19 patients remained the symptoms of somatization, anxiety, appetite and sleep disturbances, and phobia after a recovery time of 80 days. Similarly, Dong et al[36] evaluated the mental health of 675 recovered COVID-19 patients with an average time of 36.75 days since discharge. The results revealed that more than 10% of recovered patients had depression, anxiety and PTSD symptoms, and they had higher rates of anxiety and depression than the general adult population in China. At the median time of 61 days post-discharge, patients still reported PTSD (25%), anxiety (22%), depression (18%) and sleep disturbance (57%).[35]

COVID-19 is a highly infectious disease and could result in multiorgan dysfunction syndrome and death.[38] COVID-19 recovered patients might experience social isolation, death of family members, and perceived stigma and discrimination by others owing to the history of COVID-19. In addition, critical patients with COVID-19 might have the concern about the sequelae of corticosteroid treatment and ICU-acquired weakness which contribute to adverse long-term psychological sequelae.[39] Certainly, financial stressors due to the lockdown and quarantine are potential contributors to psychological disorders.[40] In this study, we explored whether the history of COVID-19 severity was the risk factor for psychological distress, and it suggested that the history of COVID-19 infection severity was not associated with psychological distress (supplementary table 1). In the published reports, it revealed that the main risk factors for these psychological disorders in recovered patients with COVID-19 were perceived stigma and discrimination, although they had recovered and were not infectious.[36,37] In addition to the residual psychological disorders, various proportions of recovered COVID-19 patients still experienced fatigue, breath shortness, headache, and chest pain after discharged 1 or 2 months later.[35,41,42] The above indicated that recovered patients with COVID-19 remained some psychological distress and physical discomfort after a recovery time of about 3 months, which suggested that the support and longer-term evaluation of psychological and physical disorders were warranted.

Therefore, we performed the further investigation of COVID-19 recovered patients. In August 2020, the primary psychological symptoms of patients with a median recovery time of 174 days were obsessive-compulsive, appetite and sleep disturbances, interpersonal sensitivity, and hostility. A similar investigation on 1,733 discharged patients with COVID-19 showed that fatigue or muscle weakness, sleep difficulties, and anxiety or depression were the main symptoms of discharged patients at 6 months after symptom onset.[43] Nevertheless, all dimensions scores of SCL-90 in recovered patients were lower compared with Chinese male norms. In addition, GSI, which measures the

overall psychological health, was also lower in second-visit patients compared with the first-visit patients. Taken together, the results indicated that the psychological distress in the second-visit recovered patients improved relative to the first-visit patients. However, some previous researches reported that 25% of SARS survivors had PTSD, and 15.6% had depressive disorders at 30 months post-SARS.[11] Similarly, 42.9% of MERS survivors reported PTSD, and 27% reported depression at 12 months post-MERS.[12] We speculated that the possibility for the rapid improvement in the psychological distress of the COVID-19 subjects might be as follows: Chinese government took the strict management and contained the pandemic in a short time, and meanwhile issued guidelines on psychological crisis intervention early.[6] Knowledge about COVID-19 was gradually clearer. Alternatively, it might be attributed to the participants in this study with fewer risk factors for persistent psychological disorders, such as previous psychiatric history, presence of a family member who died from COVID-19, and so on.[12]

ED refers to the inability to sustain or achieve an erection sufficient for satisfactory intercourse.[44] During the COVID-19 pandemic period, it was reported that there was a significant increase in the diagnostic rate of ED among male patients presenting to the outpatient urology clinics compared with the pre-COVID-19 pandemic period.[23] An online survey on the sexual health of 217 males through IIEF-5 questionnaire reported 31.8% of ED prevalence.[26] Moreover, ED was seen at higher rates in the healthcare professionals group compared with the control group.[24] However, few studies were specifically conducted on COVID-19 patients for erectile function.

Here, we also evaluated the erectile function of COVID-19 recovered patients for about 6 months. It revealed that recovered patients had impaired erectile function along with psychological distress in the first visit. However, it remained unclear whether the impaired erectile function was psychogenic or combined organic. Hence, we followed them up further. It showed improved erectile function along with an elevated psychological state in the second visit. As organic ED is not completely reversible, we speculated that ED for first-visit patients was mainly psychogenic.

The etiology of ED involves multiple factors which often coexist, including psychogenic, organic (neurogenic, hormonal, vasculogenic, or drug-induced) and some other factors.[45] A literature reviewed the possible mechanisms involved in the development of ED in COVID-19 survivors.[22] COVID-19 disease could cause endothelial dysfunction, subclinical hypogonadism, psychological distress and impaired pulmonary hemodynamics, which all contribute to the potential onset of ED. COVID-19 is characterized by a hyperinflammation state promoted by TNF-α, IL-6 and IL-1β,[46] which possibly promote endothelial dysfunction.[47] It has been confirmed that eNOS (endothelial Nitric Oxide Synthase) expression in the corpus cavernosum of COVID-19 (+) men and mean levels of endothelial progenitor cell from the COVID-19 (+) patients were both decreased

compared to COVID-19 (-) men, which suggested impaired endothelial function in COVID-19 (+) patients.[48] In addition, the common comorbidities of COVID-19 patients were diabetes, hypertension, chronic kidney disease and heart disease,[49] and some complications of COVID-19, such as arrhythmia, acute kidney injury, could occur in the patients.[50] Therefore, it was likely that some pharmacological treatments of COVID-19, such as the use of antihypertensive and antiarrhythmic drugs which were commonly associated with ED,[51] could contribute to the pathogenesis of ED. As a matter of fact, it was reported that the prevalence of ED in COVID-19 patients was significantly higher.[52] At 6 months after acute infection with COVID-19, a certain proportion of recovered patients remained diffusion impairment, and patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestation.[43] Therefore, it was likely that the erectile function in COVID-19 patients with a recovery time of 80 days was impaired.

To explore the risk factors of ED in the first-visit patients with COVID-19, we performed univariate and multivariate logistic regression analysis. GSI was the only independent risk factor in the multivariate analysis for ED. It suggested that erectile function was more likely affected by psychological distress rather than COVID-19 disease after about 3 months of recovery. With the prolonged time and less impact of the COVID-19 pandemic event, the psychological distress of COVID-19 recovered patients improved in the second visit, which might explain the decline in the ED prevalence of second-visit patients.

In addition to the impact on erectile function, COVID-19 could also impair sperm quality in terms of male sexual health. Angiotensin-converting enzyme 2, reported as a SARS-CoV-2 receptor, existed in almost all human testis cells, suggesting a potential effect on male fertility.[53] Actually, some of COVID-19 patients experienced scrotal discomfort,[54] and some autopsy reports of COVID-19 patients showed that there was edema, inflammatory infiltrates, and various degrees of spermatogenic cell reduction and injury in the testes,[55,56] which revealed that COVID-19 damaged the testis. Moreover, some of the reports revealed that COVID-19 recovered patients presented impaired sperm quality.[57-59]

In this study, we analyzed the changes of psychological distress and erectile function for COVID-19 patients within around 6 months of recovery time. To our knowledge, it is the first study to comprehensively evaluate the psychological distress and erectile function of COVID-19 recovered patients for such a long time. Admittedly, there are several limitations in our study. Firstly, it was an observational study, which limited the cause inference. And we did not evaluate the psychological distress and ED prevalence of healthy Chinese men over the same period, which made it hard to confirm whether the ED and psychological disorders were caused by the COVID-19 disease or the pandemic event. Secondly, we did not have any assessment of mental health and erectile function prior to COVID-19; thus we were unable to ascertain if psychological symptoms or ED were pre-existing. Additionally, there was a selection bias in comparing COVID-19 patients with healthy controls, as COVID-19 patients are overall more likely sick at baseline with more comorbidities than healthy controls. Finally, the sample size in this study was relatively small for assessing ED prevalence and psychological distress. A larger number of COVID-19 recovered patients and healthy men over the same period are needed to clarify the dynamic changes of psychological and sexual health in the longer term and determine whether the psychological and sexual disorders are affected by the disease or by the pandemic event after recovery.

CONCLUSION

With the pandemic contained and more knowledge about COVID-19, the impaired erectile function and psychological distress improved in patients who were recovered from COVID-19 for nearly half a year while without detailed clinical information on the viral infection. It is of great significance for maintaining physical and psychological health to explore SARS-CoV-2 objectively and face COVID-19 positively.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jsxm.2021.08.010.