

Can anxiety and depression serve as primary factors associated with erectile dysfunction after coronavirus disease?

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Abstract. – OBJECTIVE: We investigated the association between anxiety and depression and erectile dysfunction (ED) in patients who developed ED after coronavirus disease 2019 (COVID-19).

PATIENTS AND METHODS: This study included 228 men who were hospitalized in pandemic wards between July 2021 and January 2022 with positive reverse transcription-polymerase chain reaction test results for the severe acute respiratory syndrome coronavirus 2 RNA. All patients responded to a Turkish version of the International Index of Erectile Function (IIEF) questionnaire to determine erectile status. Patients were administered the Turkish version of the Beck Depression Inventory (BDI) and Generalized Anxiety Disorder 7-item scale (GAD-7) questionnaires the day after hospitalization and also during the 1st month after diagnosis of COVID-19 to compare the COVID-19 situation with the previous situation.

RESULTS: Patients' mean age was 49.66 ± 13.3 years. The mean pre-COVID-19 erectile function score of 28.65 ± 1.33 decreased to a mean post-COVID-19 score of 26.58 ± 4.23 , which indicates a statistically significant difference ($p=0.03$). Post-COVID-19 ED occurred in 46 (20.1%) patients; 10 (4.3%) patients had mild, 23 (10.0%) had mild-to-moderate, 5 (2.1%) had moderate, and 8 (3.5%) patients had severe ED. The mean pre-COVID-19 BDI score (which indicates depression) of 1.79 ± 2.45 increased to a mean post-COVID-19 score of 2.42 ± 2.89 ($p<0.01$). Additionally, the mean pre-COVID-19 GAD-7 score of 4.79 ± 1.83 increased to a mean post-COVID-19 score of 6.79 ± 2.52 , which indicates a statistically significant difference ($p<0.01$). We observed a negative correlation between the increase in BDI and GAD-7 scores and the decrease in IIEF scores ($r=0.426$, $p<.001$, $r=0.568$, $p<.001$, respectively).

CONCLUSIONS: Our study highlights that COVID-19 can cause ED and that disease-induced anxiety and depression serve as primary contributors to ED.

Key Words:

Anxiety, Depression, Coronavirus disease, Erectile dysfunction.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has significantly affected the global population, and the long-term effects of the virus in humans have gained increasing attention in the medical community. SARS-COV2 infection is when the virus binds to the angiotensin 2 converting enzyme (ACE2) through glycoproteins membrane S. The ACE2 enzyme is strongly expressed in lung, kidney, cardiac, gastrointestinal, bladder and testicular cells^{1,2}. COVID-19-induced organ injury is primarily attributable to both the direct effects of infection and endothelial dysfunction secondary to a systemic inflammatory response³. Erectile dysfunction (ED) is one of the most common sexual dysfunctions in men; organic ED is most frequently vasculogenic in nature due to decreased blood flow, arterial insufficiency, and arterial stenosis that result from vascular diseases and endothelial dysfunction⁴. Some studies³ that investigated the association between COVID-19 and endothelial dysfunction have reported that patients with COVID-19 may develop ED as a result of subclinical hypogonadism and impaired cardiac and pulmonary hemostasis. Stress, anxiety, and depression are known pathogenetic contributors to ED, in addition to the role of endothelial dysfunction that causes organic ED⁵. The hypothesis that anxiety and depression may be equivalent to endothelial dysfunction as potent contributors

to new-onset ED in men with COVID-19 has been little investigated. We investigated whether anxiety and depression may serve as primary factors associated with development of ED in patients diagnosed with post-COVID-19 ED.

Patients and Methods

This study was approved by the Turkish Ministry of Health and the Ethics Committee of Adana City and Training and Research Hospital. We investigated 228 men hospitalized in pandemic wards between July 2021 and January 2022, with positive results on the reverse transcription-polymerase chain reaction (RT-PCR) test for SARS-CoV-2 RNA. Written informed consent was obtained from all individual participants included in the study. Patients' ages ranged between 18 and 65 years. The exclusion criteria for the study were: comorbidities such as obesity, hypertension, diabetes, or heart disease (considering that comorbidities may affect erectile function), previous diagnosis and medical/surgical treatment of ED, a history of penile and urethral surgery (for example, radical prostatectomy) that is known to be associated with ED, and administration of drugs for various unrelated conditions (for example, beta-blockers that may cause ED. All patients completed a Turkish version of the International Index of Erectile Function (IIEF) questionnaire to determine their erectile status⁶. This questionnaire includes 15 questions regarding erectile function, sexual desire, orgasmic function, sexual satisfaction, and general satisfaction. Based on IIEF scores, erectile dysfunction was defined as severe (scores 5-7), moderate (scores 8-17), mild-to-moderate (scores 17-21), mild (scores 22-25), and no ED (scores 26-30). Evaluation of depression and anxiety was performed using the Turkish version of The Beck Depression Inventory (BDI)⁷ and the Generalized Anxiety Disorder 7-item test (GAD-7)⁸, which patients completed the day after hospitalization for COVID-19. Patients were re-administered the aforementioned questionnaires during the 1st month after RT-PCR positivity, and the COVID-19 situation was compared with the previous situation.

Data Collection

This study conforms to the principles of the Declaration of Helsinki, and all methods were developed in accordance with the guidelines and regulations specified by these principles. Epide-

miological data, including demographic, clinical, and laboratory findings were extracted from the electronic hospital information system.

Statistical Analysis

All statistical analyses were performed using the SPSS software, version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables are presented as numbers and percentages and continuous variables as the mean, standard deviation, and minimum-maximum. The goodness of fit of variables for a normal distribution was determined using the Shapiro-Wilk test. The independent Student's *t*-test was used for normally distributed parameters and the Mann-Whitney U test for non-normally distributed data. The Wilcoxon test was used to determine the differences between the pre- and post-COVID-19 IIEF, BDI, and GAD-7 scores. Spearman's correlation analysis was used to compare associations between numerical variables. A statistical significance level of 0.05 was used for all tests.

Results

Patients' mean age was 49.66 ± 13.3 years; 68 (29.8%) patients were <40 years of age, 120 (52.6%) were aged 40-60 years, and 40 (17.5%) were ≥ 60 years of age. This study included 180 (78.9%) married and 48 (21.1%) unmarried men and 128 (56.1%) smokers and 100 (43.9%) non-smokers. The mean body mass index was 24.83 ± 4.26 kg/m². The mean length of hospitalization in the pandemic wards was 11.78 ± 3.59 days (Table I). The mean pre-COVID-19 IIEF score was 71.42 ± 4.43 , and the mean post-COVID-19 IIEF score was 66.18 ± 10.86 ; this difference

Table I. Patients' characteristics.

	n = 228
Age ^x	49.66±13.3
19-40 age ^y	68 (29.8%)
40-60 age ^y	120 (52.6%)
60 and over ^y	40 (17.5%)
BMI ^x	24.83±4.26
Marital status ^y	Married 180 (78.9%) Single 48 (21.1%)
Cigarette ^y	Yes 128 (56.1%) No 100 (43.9%)
Hospital stay (day) ^x	11.78±3.59

^xData was presented as Mean ± SD. ^y Data were presented as n (%).

was statistically significant ($p < 0.01$). The mean pre-COVID-19 erectile function score of 28.65 ± 1.33 decreased to a mean post-COVID-19 score of 26.58 ± 4.23 , which indicates a statistically significant difference ($p = 0.03$). Post-COVID-19 ED occurred in 46 (20.1%) patients, with mild ED in 10 (4.3%), mild-to-moderate ED in 23 (10.0%), moderate ED in 5 (2.1%), and severe ED in 8 (3.5%) patients. The mean post-COVID-19 sexual desire, orgasmic satisfaction, relationship satisfaction, and general satisfaction scores were significantly lower than pre-COVID-19 scores ($p = 0.02$, $p = 0.02$, $p = 0.04$, and $p < 0.01$, respectively) (Table II). The mean pre-COVID-19 BDI score (which is a measure of depressive symptoms) of 1.79 ± 2.45 increased to a post-COVID-19 score of 2.42 ± 2.89 ($p < 0.01$). Based on BDI scores, 146 (64.0%) patients did not show pre-COVID-19 depression; however, 80 (35.0%) patients showed minimal depression, and 2 (0.8%) patients showed mild depression. The number of patients without depression after COVID-19 increased to 110 (a reduction of 48.2%); the number of patients with minimal depression increased to 102 (44.7%) patients, and 6 (2.6%) patients developed mild depression. The mean pre-COVID-19 GAD-7 score of 4.79 ± 1.83 increased to a mean post-COVID-19 score of 6.79 ± 2.52 , which indicates a statistically significant difference ($p < 0.01$). Based on GAD-7 scores,

pre- and post-COVID-19 GAD was observed in 5 (2.1%) and 26 (11.4%) patients respectively (Table II). Correlation analysis showed a negative correlation between increased BDI and GAD-7 scores and decreased IIEF scores ($r = 0.426$, $p < .001$; $r = 0.568$, $p < .001$, respectively) (Table III).

Discussion

Endothelial dysfunction and various pathophysiological mechanisms are implicated in the pathogenesis of COVID-19-induced ED. Several studies⁹⁻¹¹ have shown that COVID-19 causes endothelial dysfunction and impairs erectile function. An increasing body of evidence has definitively established the association between primary psychogenic ED and COVID-19 and implicated endothelial dysfunction in the development of ED¹²⁻¹⁴. Elevated emotional distress levels as a result of the overall uncertainty and unpredictability created by ignorance of the COVID-19 pandemic in this psychogenic ED infrastructure may be attributed to the fact that it also affects interpersonal and close relationships during this critical period and also in the long term¹⁵. Specifically, the decline in safe close/sexual interactions and intimacy, escalation of marital conflicts, and deterioration in communication are important contributors to an indivi-

Table II. Pre- and post-COVID-19 sexual function status.

	Pre-COVID-19	Post-COVID-19	<i>p</i>
IIEF score ^x	71.42 ± 4.43	66.18 ± 10.86	<0.01
Erectile function ^x	28.65 ± 1.33	26.58 ± 4.23	0.03
Sexual desire ^x	9.71 ± 0.45	9.25 ± 1.64	0.02
Orgasmic function ^x	9.82 ± 0.26	9.20 ± 1.51	0.02
Intercourse satisfaction ^x	14.70 ± 1.34	13.39 ± 3.34	0.04
Overall satisfaction ^x	9.84 ± 0.52	8.96 ± 2.41	<0.01
BDI score ^x	1.79 ± 2.45	2.42 ± 2.89	<0.01
GAD-7 score ^x	4.79 ± 1.83	6.79 ± 2.52	<0.01

^xData were presented as Mean ± SD. BDI, beck depression inventory; GAD-7, generalized anxiety disorder-7; IIEF, international index of erectile function.

Table III. The correlation between BID, GAD-7 and IIEF score alteration.

	BID <i>r</i>	<i>p</i>	GAD-7 <i>r</i>	<i>p</i>
IIEF score before COVID-19	-0.373	.002	-0.685	<.001
IIEF score after COVID-19	-0.426	<.001	-0.568	<.001

BDI, beck depression inventory; GAD-7, generalized anxiety disorder-7; IIEF, international index of erectile function.

dual's sexual difficulties and dissatisfaction during the pandemic^{16,17}. Differences in projections of sexual desire or sexual expression and lack of privacy during incarceration also contribute to the intensification of sexual difficulties¹⁸. Many studies¹⁹⁻²¹ have reported that COVID-19 reduces frequency of sexual activity and satisfaction and negatively affects couples' sexual life. Cito et al²² observed a significant decrease in the frequency of couples' sexual intercourse during the quarantine period, primarily as a result of decreased sexual activity and lack of privacy and sexual desire. Similarly, Fang et al²¹ observed that a decline in sexual function among couples during the COVID-19 pandemic was associated with increased anxiety and depression and decreased frequency of sexual activity. In the literature has been shown that reduced sexual activity during pandemics may worsen anxiety and depression. In a case-control study performed by Mollaioli et al²³ anxiety and depression levels were lower in the sexually active than in the non-sexual groups. Therefore, sexual activity was shown to protect against psychological distress, which underscores the bidirectional association between sexual activity and psychogenic status. An important concern during the pandemic is the high levels of pornography consumption and masturbation in men, despite a significant decline in libido and overall sexual satisfaction²⁴, which is attributable to COVID-19-related social distancing and its negative consequences on physical, intellectual, and emotional well-being²⁵. The extended periods of home confinement and anxiety associated with the pandemic may promote masturbation, and an increase in the frequency of masturbation may lead to actual physical sexual intimacy, poor libido, and consequent ED²⁶⁻²⁹. In contrast, Zhang et al³⁰ reported that the COVID-19 pandemic did not affect the frequency of sexual intercourse, quality of sexual life, or emotional bond between couples. Karagöz et al¹⁷ observed that despite lower sexual activity and frequency of sexual intercourse and increased sexual avoidance and solo sexual approach behaviors (such as masturbation and pornography consumption), couples had better sex during the pandemic compared with the pre-COVID-19 period, which was attributable to spending more time together. Compared to the pre-COVID-19 period, we observed a significant post-COVID-19 decrease in the sexual desire of patients in our study, which is consistent with findings of the literature that have reported these results. An increase in BDI and GAD-7 scores

indicates that anxiety and depression may be among the main factors associated with deterioration of post-COVID-19 sexual activity. An important finding of our study is that in addition to a decrease in other sexual functions, patients experienced a decline in orgasmic function after COVID-19. In our study, we observed a significant decrease in the frequency of sexual intercourse in men with COVID-19; these findings are consistent with those reported in the literature. We also observed that COVID-19 contributed to ED and that onset of ED was negatively associated with anxiety and depression. Therefore, we conclude that anxiety and depression may precipitate ED or may worsen the pre-existing sexual difficulties as a result of ED of other organic causes triggered by anxiety and depression. ED is more severe in patients with anxiety and depression; therefore, in our view, eliminating anxiety and depression can benefit patients with COVID-19-induced ED. However, elimination of anxiety and depression alone may not successfully treat ED, and appropriate treatment decision-making is important to address other organic contributors to ED.

Limitations

Following are the limitations of this study: (a) the survey-based design of this single-center study; (b) lack of investigation of organic causes of ED, particularly the role of endothelial dysfunction and hypogonadism; and (c) inclusion of patient responses over the month immediately prior to study commencement in the IIEF questionnaire. Patients responded to the questionnaire survey while they were infected with COVID-19, which may have affected the results.

Conclusions

Our study highlights that COVID-19 can cause ED and that COVID-19-induced anxiety and depression may serve as primary risk factors for development of ED. Therefore, treatment of anxiety and depression in patients with COVID-19-induced ED may improve ED in this patient population. Further multicenter and prospective studies are warranted to more conclusively establish the effects of anxiety and depression on the development of ED in patients with COVID-19.

Ethics Approval

In accordance with the 1964 Helsinki Declaration and its later amendments, our study was approved by the Clinical

Research Ethics Committee of the Health Sciences University, Adana City Training and Research Hospital (Ethical Committee approval number: 1956/27.01.2022).

Informed Consent

Informed written consent was obtained from all individual participants included in the study.

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Authors' Contributions

S.P., K.K. and G.G. made substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data. S.P., K.K. and M.A supervised the writing of the manuscript. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

References

- 1) Delle Fave RF, Polisini G, Giglioni G, Parlavecchio A, Dell'Atti L, Galosi AB. COVID-19 and male fertility: Taking stock of one year after the outbreak began. *Arch Ital Urol Androl* 2021; 93: 115-119.
- 2) Nägele MP, Haubner B, Tanner FC, Ruschitzka F, Flammer AJ. Endothelial dysfunction in COVID-19: Current findings and therapeutic implications. *Atherosclerosis* 2020; 314: 58-62.
- 3) Kresch E, Achua J, Saltzman R, Khodamoradi K, Arora H, Ibrahim E, Ramasamy R. COVID-19 endothelial dysfunction can cause erectile dysfunction: Histopathological, immunohistochemical, and ultrastructural study of the human penis. *World J Mens Health* 2021; 39: 466-469.
- 4) Guay AT. ED2: erectile dysfunction = endothelial dysfunction. *Endocrinol Metab Clin North Am* 2007; 36: 453-463.
- 5) Pyke RE. Sexual performance anxiety. *Sex Med* 2020; 8: 183-190.
- 6) Akkus E, Kadioglu A, Esen A, Doran S, Ergen A, Anafarta K, Hattat H, Turkish Erectile Dysfunction Prevalence Study, G. Prevalence and correlates of erectile dysfunction in Turkey: A population-based study. *Eur Urol* 2002; 41: 298-304.
- 7) Hisli N. Beck depresyon envanterinin üniversite öğrencileri için geçerliliği, güvenilirliği [A reliability and validity study of Beck depression inventory in a university student sample]. *The Journal of Psychology* 1989; 7: 3-13.
- 8) Konkan R, Senormanci O, Guclu O, Aydin E, Sungur MZ. Validity and reliability study for the Turkish adaptation of the generalized anxiety disorder-7 (GAD-7) scale. *Archives of Neuropsychiatry* 2013; 50: 53-59.
- 9) Sansone A, Mollaioli D, Ciocca G, Colonnello E, Limoncin E, Balercia G, Jannini EA. "Mask up to keep it up": preliminary evidence of the association between erectile dysfunction and COVID-19. *Andrology* 2021; 9: 1053-1059.
- 10) Bakr AM, El-Sakka AI. Erectile dysfunction among patients and health care providers during COVID-19 pandemic: a systematic review. *Int J Impot Res* 2022; 34: 145-151.
- 11) Sansone A, Mollaioli D, Limoncin E, Ciocca G, Bắc NH, Cao TN, Jannini EA. The sexual long COVID (SLC): erectile dysfunction as a biomarker of systemic complications for COVID-19 long haulers. *Sex Med Rev* 2021; S2050-0521(21)00085-8.
- 12) Saad HM, GamalEl Din SF, Elbokl OM, Adel A. Predictive factors of erectile dysfunction in Egyptian individuals after contracting COVID-19: a prospective case-control study. *Andrologia* 2022; 54: e14308.
- 13) Karkin K, Alma E. Erectile dysfunction and testosterone levels prior to COVID-19 disease: what is the relationship? *Arch Ital Urol Androl* 2021; 93: 460-464.
- 14) Chu KY, Nackeeran S, Horodyski L, Masterson TA, Ramasamy R. COVID-19 infection is associated with new onset erectile dysfunction: insights from a national registry. *Sex Med* 2022; 10: 100478.
- 15) De Rose AF, Chierigo F, Ambrosini F, Mantica G, Borghesi M, Suardi N, Terrone C. Sexuality during COVID lockdown: a cross-sectional Italian study among hospital workers and their relatives. *Int J Impot Res* 2021; 33: 131-136.
- 16) Carvalho J, Pascoal PM. Challenges in the practice of sexual medicine in the time of COVID-19 in Portugal. *J Sex Med* 2020; 17: 1212-1215.
- 17) Karagöz MA, Gül A, Borg C, Erihan İB, Uslu M, Ezer M, Bağcıoğlu M. Influence of COVID-19 pandemic on sexuality: a cross-sectional study among couples in Turkey. *Int J Impot Res* 2020; 33: 815-823.
- 18) de Oliveira L, Carvalho J. Women's sexual health during the pandemic of COVID-19: declines in sexual function and sexual pleasure. *Curr Sex Health Rep* 2021; 13: 1-13.
- 19) Nessaibia I, Sagese R, Atwood L, Bouslama Z, Cocci L, Merad T, Tahraoui A. The way COVID-19 transforms our sexual lives. *Int J Impot Res* 2021; 1-3.
- 20) Lo SP, Hsieh TC, Pastuszak AW, Hotaling JM, Patel DP. Effects of SARS CoV-2, COVID-19, and its vaccines on male sexual health and reproduction: where do we stand? *Int J Impot Res* 2021; 1-7.
- 21) Fang D, Peng J, Liao S, Tang Y, Cui W, Yuan Y, Zhang Z. An online questionnaire survey on the sexual life and sexual function of Chinese adult

- men during the Coronavirus Disease 2019 epidemic. *Sex Med* 2021; 9: 100293.
- 22) Cito G, Micelli E, Cocci A, Polloni G, Russo GI, Coccia ME, Natali A. The impact of the COVID-19 quarantine on sexual life in Italy. *Urology* 2021; 147: 37-42.
- 23) Mollaioli D, Sansone A, Ciocca G. Benefits of sexual activity on psychological, relational, and sexual health during the COVID-19 breakout. *J Sex Med* 2021; 18: 35-49.
- 24) Neto RP, Nascimento BCG, Carvalho dos Anjos Silva G, Barbosa JABA, de Bessa Júnior J, Teixeira TA, Cury J. Impact of COVID-19 pandemic on the sexual function of health professionals from an epicenter in Brazil. *Sex Med* 2021; 9: 100408.
- 25) Facio Junior FN, Facio M, Spessoto A, Spessoto LCF. Sexual behavior in men during COVID-19. *Rev Assoc Med Bras.* 2020; 66: 1613-1614.
- 26) Ibarra FP, Mehrad M, Di Mauro M, Cruz EG, Nilforoushadeh MA, Russo, GI. Impact of the COVID-19 pandemic on the sexual behavior of the population. The vision of the east and the west. *Int Braz J Urol* 2020; 46: 104-112.
- 27) Pizzol D, Bertoldo A, Foresta C. Adolescents and web porn: a new era of sexuality. *Int J Adolesc Med Health* 2016; 28: 169-173.
- 28) Yu C, Zhang FJ, Zhang LL, Xian DX, Li Y, Li JJ, Wang S. An approach combining bioinformatics and machine learning to identify eight autophagy-related biomarkers and construct molecular mechanisms underlying COVID-19 and major depressive disorders. *Eur Rev Med Pharmacol Sci* 2022; 26: 8129-8143.
- 29) El Khouly RM, Elsabagh HM, Moawad AAR, Afifi S, El Hawa MA. Functional and mental health affection (depression, anxiety, stress) among Egyptian rheumatic diseases patients during COVID-19 pandemic. *Eur Rev Med Pharmacol Sci* 2022; 26: 4477-4485.
- 30) Zhang Y, Wen C, Zhang Y, Luo X, Ma ZF. The impact of mental health and stress concerns on relationship and sexuality amidst the COVID-19 lockdown. *J Sex Med* 2021; 18: 1843-1850.