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ORIGINAL RESEARCH

Anxiety in Patients with Post-COVID Syndrome: Associated Factors

Jonas Bocek[1], Dana Kamaradova Koncelikova[1], Jakub Vanek[1], Klara Latalova[1], Samuel Genzor[2], Jan Mizera[2]

[1]Department of Psychiatry, University Hospital Olomouc, Olomouc, Czech Republic; [2]Department of Respiratory Medicine and Tuberculosis, University Hospital Olomouc, Olomouc, Czech Republic

Correspondence: Jonas Bocek, Department of Psychiatry, University Hospital Olomouc, Zdravotníků 248/7, Olomouc, Czech Republic, Tel +420775992005; +420588443512, Email jonas.bocek@fnol.cz

Introduction: The term "post-COVID-19 syndrome" describes a range of symptoms persisting beyond the acute phase of the disease. These symptoms predominantly include fatigue, muscle pain, shortness of breath, and psychological issues. Research additionally suggests the possibility of long-term neurological and psychiatric impairment associated with COVID-19.

Methodology: The study included patients who visited the post-COVID outpatient clinic between April 2020 and June 2022. The examination included the detailed history taking, including the COVID-19 course, posteroanterior chest X-ray and pulmonary function tests. Anxiety level was assessed using the Beck Anxiety Inventory (BAI). The relationship between anxiety, demographic data, and course of the disease, need for hospital admission during the acute phase, oxygen therapy, post-inflammatory changes on the chest X-ray and lung function parameters was investigated.

Results: This study included 1756 patients who experienced COVID-19 and visited a post-COVID outpatient clinic. The majority of individuals experienced a mild form of the infection. The results showed that younger age and female gender were associated with significantly higher anxiety scores. Inpatients had lower BAI values than those who were not hospitalized during acute phase. Patients with post-inflammatory changes on chest X-ray had surprisingly lower BAI values. Lower values of FEV1 (forced expiratory volume in 1 second), DLCO (diffusing capacity of the lungs for carbon monoxide), and KCO (carbon monoxide transfer coefficient) were associated with significantly higher BAI values. Female gender was associated with higher levels of anxiety. In contrast, higher FEV1 values reduced the risk of a pathological level of anxiety.

Conclusion: In our study, the influence of age, gender, inpatient care during the acute phase of infection, the presence of post-inflammatory changes on the chest diagram and selected parameters of lung function (FEV1, DLCO, and KCO) were shown to be important factors in the assessment of anxiety symptoms in post-COVID patients.

Keywords: post, COVID, anxiety, anxiety symptoms, associated factors, lung function parameters

Introduction

The SARS-CoV-2 (severe acute coronavirus-2) virus was first isolated in December 2019 and spread worldwide within several months. On March 11, 2020, a pandemic was declared by the World Health Organization (WHO). COVID-19, a disease caused by the SARS-CoV-2 virus, was first identified as a respiratory illness; however, the evidence for involvement of different organ systems soon began to emerge.[1] Signs and symptoms of the acute phase of COVID-19 vary between patients, and they can fluctuate over time. According to the severity of the symptoms, 5 degrees of severity of acute COVID-19 were defined (see Table 1).[2]

In the past, the world's health system has faced the SARS epidemic. The available studies could suggest a possible similarity to the disease COVID-19, which is caused by an agent from the same group of coronaviruses. Xi et al present study of patients with SARS and COVID-19 and their psychiatric symptoms. SARS patients suffered from eight psychiatric symptoms (including anxiety) during the acute phase of the disease. Furthermore, patients were followed up at regular intervals (after 1 month, 1–6 months after discharge and 12 months after discharge). Although the severity

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Table 1 Clinical Forms of COVID-19

Severity (0–4)	Symptoms and Signs
Asymptomatic (0)	Without clinical presentation
Mild (1)	Signs of respiratory infection, but no evidence of pneumonia
Moderate (2)	Non-complicated COVID-19 pneumonia
Severe (3)	Interstitial pneumonia accompanied by at least one of the three symptoms: respiratory rate >30/min; hemoglobin saturation oxygen <93%; respiratory index* (PaO2/FiO2) ≤300mmHg
Critical (4)	Necessity of inpatient ICU care, presence of at least one from the following diagnoses: manifestations of ARDS; artificial pulmonary ventilation; circulatory shock; multiorgan failure

Notes: *The respiratory index, also known as the PaO2/FiO2 ratio, is a measure used in medicine to assess the efficiency of gas exchange in the lungs. It is calculated by dividing the partial pressure of arterial oxygen (PaO2) by the fraction of inspired oxygen (FiO2).
Abbreviations: ICU, intensive care unit; ARDS, acute respiratory distress syndrome.

of psychiatric symptoms decreased in the long term, anxiety symptoms remained even after 12 months at mild levels. The changing trajectory observed with SARS suggests that psychiatric symptoms of COVID-19 may persist for a long time after discharge, and therefore, periodic monitoring of psychiatric symptoms, psychosocial support, and psychiatric treatment (when necessary) may be necessary for COVID-19 patients from the acute to convalescent stages.[3]

With the increasing number of COVID-19 cases, the number of patients with persistent symptoms also began to rise. The most common were non-specific (eg fatigue, muscle and joint pain) and respiratory symptoms (cough and shortness of breath). Some patients also reported neurological and psychiatric symptoms,[4] such as the so-called "brain fog", a term coined for cognitive difficulties. According to a study by Zeng et al the data from 1,285,407 patients show the incidence of psychiatric symptoms was 19.7%. Specifically, the most prevalent psychiatric outcomes at 6–12 months after initial infection were anxiety (15.4%). Various psychiatric manifestations of the post-COVID syndrome were reported. Patients with a critical course of the infection suffered more frequently from PTSD (post-traumatic stress disorder), sleep disorders, cognitive impairment, concentration disorders and dysgeusia. Conversely, the patients with a mild form of infection had a higher burden of anxiety and memory impairment after resolution of the acute illness.[5] In another meta-analysis, authors reported 20.3% incidence of psychiatric symptoms, including diagnoses of PTSD, depression, sleep disorders and anxiety. All the four signs and symptoms considered in this cluster had an incidence over 10%. Specifically for anxiety symptoms was the incidence 15.2–22.2%.[6]

Anxiety symptoms are frequent psychiatric symptoms in post-COVID patients. The incidence also changes over time. It is important to consider the time interval in which we are moving since the onset of the infection. For example, we present a study of 1142 patients from Fernández-de-las-Peñas et al. It was a multicenter observational study included 1200 hospitalized patients for COVID-19. Their psychological status was assessed 7 months after discharge from the hospital. The incidence of anxiety symptoms was 16.2%.[7]

One of the large studies dealing with long-COVID is the work of Taquet et al. The conducted a retrospective cohort study based on linked electronic health records (273,618 COVID-19 survivors). The incidence and co-occurrence within 6 months and in the 3 to 6 months after COVID-19 diagnosis were calculated for 9 core features of long-COVID (breathing difficulties/breathlessness, fatigue/malaise, chest/throat pain, headache, abdominal symptoms, myalgia, other pain, cognitive symptoms, and anxiety/depression). Among COVID-19 survivors 57% had one or more long-COVID feature recorded during the whole 6-month period. For anxiety/depression was incidence 22.82%.[8]

Different terms such as post-acute COVID-19 or long COVID-19 have been used for difficulties persisting for 4–12 weeks after contracting COVID-19.[9] Subsequently, the British National Institute for Health and Clinical Quality issued a guideline that defined the post-COVID syndrome as symptoms that appear during or after experiencing a COVID-19 infection and persist for more than 3 months and cannot be explained by another cause.[10]

Another direction of research was the identification of possible risk factors leading to the development of post-COVID syndrome. For example, Tsampasian et al in his meta-analysis (n = 860,783) lists the following risk factors: female gender, older age, higher BMI (Body Mass Index), smoking, presence of comorbid disease and inpatient care during the acute phase of COVID-19, including admission to the intensive care unit.[11] Similar results (older age, female sex, living in a high-income country) and a more severe form of infection were also found in the previously mentioned work by Zeng et al.[5]

Given that the COVID-19 primarily affects the respiratory system, many authors focused on the assessment of patient's respiratory functions. Since COVID-19 primarily affects the respiratory system, many authors focused on the assessment of respiratory function, reporting a decrease in vital capacity (VC) in roughly one in four patients, decreased transfer factor for carbon monoxide (DLCO) in up to one-half of the patients following moderate and severe COVID-19.[12–14]

Aims of the Study

This is a cross-sectional study, its aim is to clarify the level of anxiety in post-COVID patients and possible associated factors with anxiety symptoms.

Hypotheses

When establishing the methodology of this study, we formulated the following hypotheses:

1. Patients with a more severe acute infection will have increased anxiety level.
2. Patients who required inpatient care for acute infection will have increased anxiety level.
3. Patients who needed oxygen therapy during an acute infection will have increased anxiety level.
4. Patients with post-inflammatory changes on the chest X-ray will have increased anxiety level.
5. The lower the VC value, the higher the BAI value.
6. The lower the FEV1 value, the higher the BAI value.
7. The lower the value of DLCO, the higher the value of BAI.
8. The lower the KCO value, the higher the BAI value.
9. To determine possible associated factors for pathologic levels of anxiety from demographic and clinical data.

Methodology

Participants

The study was performed in joint effort by the Department of Respiratory Diseases and Tuberculosis and Department of Psychiatry in University Hospital Olomouc. Patients who visited the post-COVID outpatient clinic established at the Department of Respiratory Diseases and Tuberculosis University Hospital Olomouc between April 2020 and June 2022 were offered participation. The patients who refused participation were provided the same level of care as participants, but their data were not collected for the purposes of the study. The inclusion and exclusion criteria for the study are listed in Table 2.

Table 2 Inclusion and Exclusion Criteria

Inclusion criteria
• Covid-19 positivity in history
• Post-covid outpatient visit
• Age between 15 and 95 years
• Written consent with the study
Exclusion Criteria:
• Ongoing somatic disease
• Patients unable to undergo pulmonary function testing (tracheostomy, acute psychiatric disorder)
• Patients with incomplete data (insufficient medical documentation, technical difficulties, etc.)
• Pregnancy
• Patients who were unable to complete the BAI (advanced dementia)

Sample Size Calculations

No special method was used in the selection of the sample. All patients treated in the post-COVID outpatient clinic during the specified period who met the entry criteria were included in the study. Due to the large number of patients meeting the entry criteria, estimates of the required file size were not made, and all available data were processed.

Measurements

As part of the examination, basic anamnesis, a detailed history of the COVID-19 infection itself, an posteroanterior chest X-ray and a functional lung examination (spirometry and body plethysmography) were conducted in patients.

The demographic data evaluated were age and sex. Five categories of severity of acute COVID-19 were defined, ranging from asymptomatic to critical course of the disease (0–4).[2] Other evaluated parameters included the need for hospital admission and the need for oxygen therapy during the acute phase of COVID-19. The presence of post-inflammatory changes on the chest X-ray during examination was also evaluated, the assessment was qualitative - The presence or absence of post-inflammatory changes at the beginning of the follow-up.

All patients underwent lung function examination using spirometry, body-plethysmography and lung diffusion capacity testing. Vital capacity (VC), forced expiratory volume in the first second (FEV1), transfer factor (DLCO) and transfer coefficient (KCO) for carbon monoxide (parameters of lung diffusion measured by the single-breath method) were analyzed. The values of these parameters were expressed as percentage of the predicted value.[15,16]

Lung function test measurements were performed in accordance with the current European Respiratory Society/ American Thoracic Society guidelines. Body plethysmography MasterScreen by Jaeger® was used; using software SentrySuiteTM Version 2.19 by CareFusion for data retrieval.

The following scales were administered:

Anxiety levels were assessed using the Beck Anxiety Inventory (BAI). The BAI scale includes 21 items with a four-point Likert scale, which the patient used to assess the severity of anxiety symptoms last week. Kamaradova et al validated BAI in Czech.[17] The inventory exhibited excellent internal consistency (Cronbach's alpha = 0.92). A score of 17 or more is considered a pathological value. There is no validated scale for assessing anxiety in post-COVID patients in Czech Republic. When we were choosing the BAI to evaluate the level of anxiety symptoms, we were based on some studies that also evaluated the level of anxiety symptoms using the BAI.[18–20] We are aware that BAI results may be biased by some physical symptoms of post-COVID syndrome.

Limitations in the Study Design

We are aware of possible limitations of the methodology. We mention, for example, the wide age range, as well as possible somatic comorbidities. We also do not take into account the patients' possible psychiatric anamnesis. A limitation can also be the current psychological state of the patients, which can be caused by somatic problems and can thus affect the BAI value.

Ethics Statement

The study followed the latest Helsinki Declaration and the Guideline for Good Clinical Practice. The Palacky University and University Hospital's ethical committee in Olomouc approved the study design and written consent. Written informed consent was obtained from all participants after the procedures had been fully explained, and participants were not rewarded for their participation.

Statistical Analysis

IBM SPSS Statistics Version 23 statistical software (Armonk, NY: IBM Corp) was used for statistical analysis. The relationship between BAI and the course of COVID-19 was assessed using the Kruskal–Wallis test with the Mann–Whitney U post-hoc test.

The relationship between BAI and oxygen support, hospitalization, the result of X-ray examination and the gender of the patients was analyzed using the Mann–Whitney *U*-test. Spearman correlation analysis was used to assess the relationship between BAI and VC, FEV1, DLCO and KCO parameters and age.

Associated factors of pathological anxiety were calculated using logistic regression analysis with Bonferroni correction for multiple comparisons. All tests were performed at the 0.05 level of significance.

The normal distribution of the quantitative parameter BAI was tested using the Shapiro–Wilk test. Due to the significantly non-normal, right-skewed distribution of the BAI quantitative parameter and due to the ordinal nature of the defined BAI subgroups, non-parametric methods were used for data analysis.

Results

The final sample included 1756 patients: 783 men, 971 women and 2 transgender patients. The median age in the sample was 55 years (SD = 14.4). The mean time from the positive PCR test to the control in the post-COVID clinic was 2.5 months (SD = 1.5). The average BAI value was 10.5, median 8.0 points (SD = 1.5), see Table 3.

Most of the patients had experienced mild course of COVID-19. Absolute and relative frequencies of individual degrees of severity of acute infection in the sample are presented in Table 4. The Table 5 shows the frequencies of the individual investigated indicators: the need for hospital admission during the acute phase of the infection, the need for oxygen therapy, the presence of post-inflammatory changes on the chest X-ray.

Table 3 Demographic Data

	Mean	SD	Median	Minimum	Maximum
Age	53,9	14,4	55,0	15,0	94,0
Average BAI value	10,5	8,9	8,0	0,0	46,0
The mean time from the positive PCR test to the control in the post-COVID clinic (month)	2,5	1,5	2,0	0,0	13,0

Table 4 Frequency of COVID-19 Severity in Sample

Severity	Number of Patients (total n = 1756)	Percentage of Total
Asymptomatic (0)	17	1,0
Mild (1)	925	52,7
Moderate (2)	346	19,7
Severe (3)	366	20,8
Critical (4)	102	5,8

Table 5 Frequency of Included Factors

Factor	Number of patients (total n = 1756)	Percentage of total
Inpatient care	608	34,7
Oxygenotherapy	464	26,5
Post-inflammatory changes X-ray	578	32,9

Table 6 BAI Levels According to Severity of COVID-19

BAI		Mean	SD	Median	Minimum	Maximum	p-value
Severity of COVID-19	0	5,5	7,0	3,0	0	27	**< 0,0001***
	1	11,2	8,9	10,0	0	46	
	2	9,3	8,7	7,0	0	42	
	3	10,1	8,8	7,0	0	43	
	4	11,0	9,0	9,0	0	45	

Note: * values in bold font are for statistically significant p values.

Results According to Established Hypotheses

Hypothesis 1 – Patients with a More Severe Acute Infection Will Have Increased Anxiety Level

The results turned out to be inconsistent, see Table 6, Figure 1. It was not possible to demonstrate a statistically significant association between the severity of the course of the acute COVID-19 and the BAI score. Patients with a history of mild or critical COVID-19 scored significantly higher on BAI in comparison to the asymptomatic course of COVID-19 (Mann–Whitney test, **p < 0.0001**). On the contrary, patients with a history of mild COVID-19 scored significantly higher on BAI as compared to the moderate course of the disease ((Mann–Whitney test, **p < 0.0001**).

Hypothesis 2 – Patients Who Required Inpatient Care for Acute Infection Will Have Increased Anxiety Level

This hypothesis was not confirmed. On the contrary, the level of anxiety was statistically significantly lower in the group that received inpatient care, BAI = 11.0 ± 8.9 vs 9.8 ± 8.8 (Mann–Whitney test, **p = 0.006**).

Hypothesis 3 – Patients Who Needed Oxygen Therapy During an Acute Infection Will Have Increased Anxiety Level

This hypothesis was not confirmed. The need for oxygen therapy was not found to be a statistically significant factor. The BAI value in the group requiring oxygen therapy was 10.3 ± 8.9 vs 10.6 ± 8.9 (Mann–Whitney test, p = 0.544).

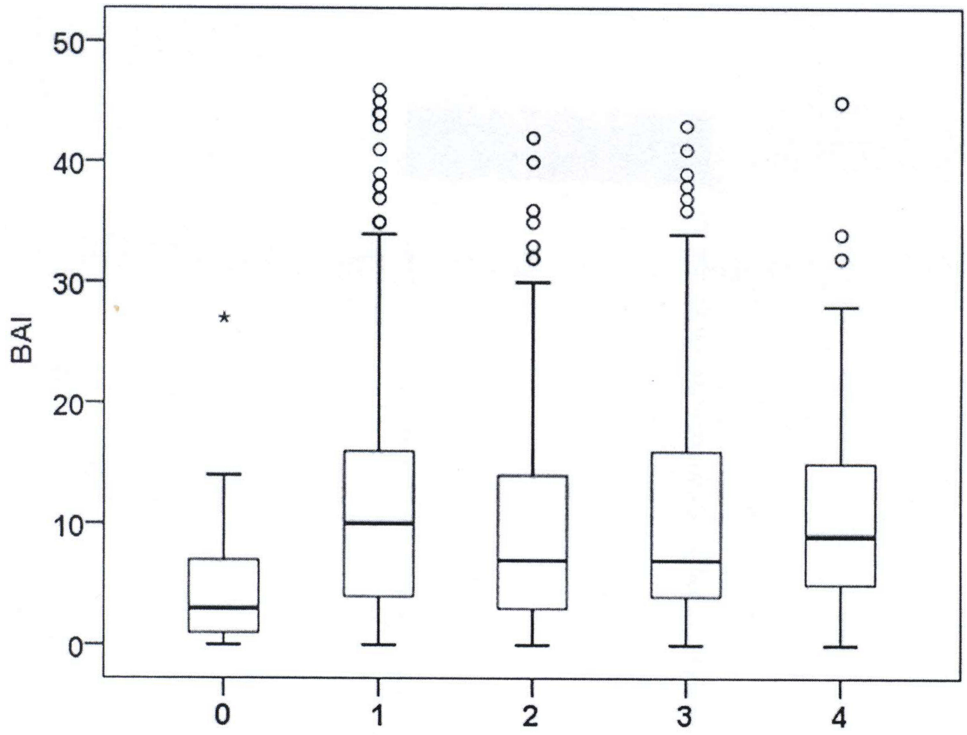

Figure 1 Quartile box plot: Distribution of BAI scores depending on the course of COVID-19.

Hypothesis 4 – Patients with Post-Inflammatory Changes on the Chest X-Ray Will Have Increased Anxiety Level

This hypothesis was not confirmed. Surprisingly, the opposite was observed when the patients with post-inflammatory changes scored significantly lower than patients without such changes: 9.9 ± 8.9 vs 10.8 ± 8.8, respectively (Mann–Whitney test, **p = 0.042**).

Hypothesis 5 – The Lower the VC Value, the Higher the BAI Value

The hypothesis was not confirmed. No significant relationship between the value VC and BAI was observed (Spearman's rank correlation coefficient = −0.022, p = 0.350).

Hypothesis 6 – The Lower the FEV1 Value, the Higher the BAI Value

This hypothesis was confirmed. A statistically significant negative correlation was observed between BAI score and FEV1 (Spearman's rank correlation coefficient = −0.096, **p = 0.0001**).

Hypothesis 7 – The Lower the Value of DLCO, the Higher the Value of BAI

This hypothesis was confirmed. A statistically significant negative correlation was observed between BAI scores and DLCO (Spearman's rank correlation coefficient = −0.064, **p = 0.007**).

Hypothesis 8 – The Lower the KCO Value, the Higher the BAI Value

This hypothesis was confirmed. Similarly, a statistically significant negative correlation was observed between BAI scores and KCO (Spearman's rank correlation coefficient = −0.052, **p = 0.028**).

Hypothesis 9 – to Determine Possible Associated Factors for Pathologic Levels of Anxiety from Demographic and Clinical Data

Results of correlations of BAI score and demographic data:

Both investigated demographic factors (gender and age) were found to be statistically significant. BAI scores were statistically significantly higher in the female group with a mean score of 12.4, SD ± 9.2 (Mann–Whitney test, **p < 0.0001**) and BAI score was statistically significantly inversely correlated with age (Spearman's rank correlation, **p = 0.002**).

Regression analysis:

The statistical results of possible associated factors for pathological anxiety levels (BAI ≥ 17) in our sample of patients are presented in Table 7. Table 7 presents the results of unadjusted estimates of the OR as a results of multiple logistic regression analysis. The most significant associated factors in our study are female gender and FEV1 value.

Furthermore, multiple logistic regression analysis was performed to determine the estimates of adjusted OR statistics seen in Table 8. Females in our sample were 2.5 times more likely to have a pathological anxiety levels than males (OR = 2.487; 95% CI: 1.943–3.183). Normal FEV1 values (FEV1 ≥ 80% of predicted) significantly but marginally predicted normal BAI scores (BAI < 17) (OR = 0.986; 95% CI: 0.979–0.993).

Discussion

The aim of this study was to investigate the factors potentially linked with increased anxiety symptoms in COVID-19 survivors. We focused on the parameters of the acute phase of the disease as well as the subjective symptoms and objective findings persisting after the resolution of the acute phase. So far, a number of studies have been published that have noted an increased incidence of psychiatric morbidity after recovering from a COVID-19.

In our study, we focused on patients who sought medical attention at the post-COVID clinic due to persistent difficulties. We present data on a total of 1756 patients. Females were slightly overrepresented in the sample (55.3%). The mean age of the patients was 53.9 years, which is in line with the findings of other authors, where post-COVID symptoms occurred in the upper middle-aged population.[21] The majority of the study participants had experienced mild course of COVID-19, which is in line with available epidemiological data suggesting mild to moderate course of the infection in the majority of subjects.[22]

The results of the comparison of BAI scores across COVID-19 severity categories are unequivocal. Although the scores were significantly higher among the mild and critical COVID-19 survivors as compared to asymptomatic infection, this was not reflected in the moderate and severe categories. One of the possible limitations may be the

Table 7 Regression Analysis of Possible Associated Factors for Pathological Anxiety Levels

	p-value	OR	95% C.I. for OR	
			Lower	Upper
Age	0,063	0,993	0,985	1,000
Gender: woman	**< 0,0001***	2,310	1,813	2,943
Severity of COVID-19	0,351	0,946	0,843	1,063
Inpatient care	0,067	0,798	0,627	1,016
Need for oxygen therapy	0,900	0,984	0,762	1,270
Post-inflammatory changes X-ray	0,062	0,792	0,620	1,011
VC %	0,492	0,998	0,991	1,005
FEV1%	**0,005***	0,990	0,984	0,997
DLCO %	0,199	0,996	0,989	1,002
KCO %	0,210	0,995	0,988	1,003

Note: *values in bold font are for statistically significant p values.

Table 8 Adjusted or for Significant Factors Predicting Pathological BAI Values

	p-value	OR	95% C.I. for OR	
			Lower	Upper
Gender: female	**< 0,0001***	2,487	1,943	3,183
FEV1%	**< 0,0001***	0,986	0,979	0,993

Notes: *Values in bold font are for statistically significant p values.

unreliable distinction between mild and moderate COVID-19, as the diagnosis of COVID-19 pneumonia might have been missed in subjects who did not undergo chest X-ray imaging during the initial work-up. Badenoch et al in their meta-analysis did not confirm the association between the severity of the acute phase of infection and the development of anxiety symptoms.[23] The opposite result was demonstrated in a study by Liu et al, where the severity of the acute phase of the infection was found to be a risk factor for the development of anxiety symptoms after experiencing a COVID-19 infection, but only in patients who needed inpatient care during the acute phase.[24]

One of the notable results is that significantly higher levels of anxiety were observed in the patients managed as outpatients compared to cases requiring hospital admission. This observation is consistent with the work of Mazza et al, which was performed on a smaller sample of patients (n = 402). In their work, they demonstrated that patients treated on an outpatient basis were more anxious than patients who were treated in hospital during the acute phase. However, the patients in the named above study were assessed 1 month post infection.[25] The opposite result was reported by Taquet et al, where comparing inpatients and outpatients demonstrated a higher probability of developing anxiety symptoms in the inpatient group.[4] There are a number of possible explanations for our observation: The inpatients may have felt safer, received a better level of care, and the possible complications could be addressed more quickly compared to outpatients. Secondly, as previously mentioned, the severity of COVID-19 may have been underestimated in the outpatients. Many patients treated on an outpatient basis were only in telephone contact with the physician or and were not sufficiently and properly treated. There is also an interpretation that from the group of patients who received the outpatient care, those

who are generally more anxious came to the examination, whereas patients without a tendency to experience anxiety symptoms did not feel the need for further assessments.

In our sample, there was no correlation between the use of oxygen therapy during the acute phase of the infection and the level of anxiety. For comparison, a study by Sperling et al showed higher levels of anxiety in patients who did not receive oxygen therapy compared to the patients treated with oxygen therapy. However, the study only included inpatients, and the anxiety symptoms was assessment was done using the Hospital Anxiety and Depression Scale,[26] pertaining direct comparison.

Based on our results, the post-inflammatory changes were not associated with increased anxiety symptoms. We based our hypothesis on the results of the study by D'Cruz et al. In this study, 119 survivors of COVID-19 were followed-up four to 6 weeks after hospital discharge. Among other findings, the authors reported higher levels of anxiety in post-COVID patients with post-inflammatory changes apparent in chest computed tomography (CT).[27] The same was not observed in our larger sample, albeit using chest X-ray, a less sensitive imaging modality, pertaining direct comparison. We hypothesize that the objective sign of impairment may not necessarily directly translate to subjective symptoms, including anxiety symptoms. A limitation in our study design is the presence of post-inflammatory changes being recorded as a binary variable, which ignores the varying extent of post-inflammatory changes.

In our study cohort, significantly lower values of FEV1, but not VC, were observed in the patients with pathological levels of anxiety. The literature search revealed several studies dealing with the possible relationship between the emotional state and the parameters of pulmonary function. For example, Livermore et al demonstrated in their study, they compared patients with chronic obstructive pulmonary disease (COPD) in combination with panic disorder with patients with COPD without panic disorder. Pulmonary parameters did not differ between these groups.[28] The same result was shown in a study by Gudmundsson et al. In their study with patients treated for COPD, they did not demonstrate an association between anxiety levels and values of lung parameters, more precisely VC and FEV1.[29] On the other hand, our findings are partially in line with the observations reported by Eren et al, who found that VC and FEV1 values were lower in patients with a higher BAI value. However, the study was conducted in patients with a primarily neurological disorder.[30] Unfortunately, as of writing this paper, the literature dealing with this topic in post-COVID patients is lacking, and the reports in patients with other respiratory disorders are brought no easily predictable results.

Both hypotheses proposing the inverse relationship between the parameters of lung diffusion capacity (DLCO and KCO) and the level of anxiety were confirmed. Lower values of both parameters were associated with a higher anxiety levels. For comparison, we present the study by Sharp et al reporting on patients suffering from sarcoidosis (n = 112). The authors noted no significant association between anxiety symptoms and DLCO value. On the contrary, the authors found an association between the presence of depressive symptoms and lower DLCO values.[31]

An important part of the present study was the determination of possible associated factors of pathological anxiety levels. The regression analyses revealed FEV1 below 80% of predicted and female sex to be significant factors of pathological levels of anxiety. The observation of female gender being significant associated factors of pathological levels of anxiety in post-COVID patients is in line with the report by Mazza et al, who surveyed COVID-19 inpatients 1 month following hospital discharge. In a questionnaire, 42% of these patients suffered from anxiety symptoms, while females were significantly more likely to self-report anxiety as compared to males.[25] Female gender is discussed in the existing literature as a risk factor for the development of post-COVID syndrome in general.[32] In our sample, FEV1 value below 80% of predicted was identified as another statistically significant associated factor of pathological levels of anxiety in post-COVID patients; however, this effect seems to be marginal.

Strengths and Limitations of the Study

The advantage of this study is the size of the patient sample. It is also the first study that deals with the possible connection between anxiety symptoms and respiratory parameters in post-COVID patients. The detected significant correlations were only at the level of very weak correlations, and their significance was only confirmed due to a large number of correlated data. As mentioned in the discussion, one of the limitations is the less than perfect reliable distinction between mild and moderate course of COVID-19 infection. In the acute phase in patients who have not been

examined and have not had an X-ray taken. The second of the mentioned limitations is the performance of an X-ray image as part of an examination in a post-covid consultation room. The X-ray image may be insufficient and inaccurate to clarify post-inflammatory changes in detail. Only the Self-Assessment Anxiety Scale (BAI) was used to assess the level of anxiety. The level of anxiety is thus not determined by an examination by a psychiatrist. In addition, the patients included in the study may have suffered from some anxiety symptoms prior to the illness of COVID-19. Finally, we are also aware that we are not taking into account psychosocial stressors (pandemic restrictions and uncertainty regarding the time of their termination, social isolation, regrets that they may have infected other people, etc.) It would be a mistake to neglect these unfavorable external factors.

In the future, further research should certainly concern the issue of anxiety in post-COVID patients. An international scale for evaluating these difficulties should also be validated.

Conclusion

Our results show that the level of subjective anxiety symptoms in patients following recovery from acute COVID-19 can be influenced by a number of factors. In our cohort, age and gender demographic data appeared as a significant factor affecting the level of anxiety. Among the investigated parameters, decreased values of FEV1, DLCO and KCO were associated with pathological levels of anxiety. The inpatient care during the acute phase of infection and resulted in lower anxiety. The effect of the severity of the acute phase proved to be inconsistent. The vital capacity and oxygen therapy did not appear to significantly influence anxiety level.

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Disclosure

The authors declare no conflicts of interest in this work.

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