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Sleep quality in individuals with post-COVID-19 condition: Relation with emotional, cognitive and functional variables

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A R T I C L E I N F O

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A B S T R A C T

The study aimed to assess sleep quality in PCC patients and its predictors by analysing its relationship with emotional, cognitive and functional variables, as well as possible differences based on COVID-19 severity. We included 368 individuals with PCC and 123 healthy controls (HCs) from the NAUTILUS Project (NCT05307549 and NCT05307575). We assessed sleep quality (Pittsburgh Sleep Quality Index, PSQI), anxiety (Generalized Anxiety Disorder, GAD-7), depression (Patient Health Questionnaire, PHQ-9), global cognition (Montreal Cognitive Assessment, MoCA), everyday memory failures (Memory Failures of Everyday Questionnaire, MFE-30), fatigue (Chadler Fatigue Questionnaire, CFQ), quality of life (European Quality of Life-5 Dimensions, EQ-5D), and physical activity levels (International Physical Activity Questionnaire, IPAQ). 203 were nonhospitalized, 83 were hospitalized and 82 were admitted to the intensive care unit (ICU). We found statistically significant differences in the PSQI total score between the PCC and HC groups ($p < 0.0001$), but there were no differences among the PCC groups. In the multiple linear regressions, the PHQ-9 score was a predictor of poor sleep quality for mild PCC patients ($p = 0.003$); GAD-7 ($p = 0.032$) and EQ-5D ($p = 0.011$) scores were predictors of poor sleep quality in the hospitalized PCC group; and GAD-7 ($p = 0.045$) and IPAQ ($p = 0.005$) scores were predictors of poor sleep quality in the group of ICU-PCC. These results indicate that worse sleep quality is related to higher levels of depression and anxiety, worse quality of life and less physical activity. Therapeutic strategies should focus on these factors to have a positive impact on the quality of sleep.

1. Introduction

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus, which has implications not only in the acute phase but also afterwards. The psychological effects of COVID-19, both in the general population and in individuals with post-COVID-19 condition (PCC), are well known and described. PCC is characterized by a wide variety of symptoms, which could be fixed or fluctuate, manifest 3 months after the onset of the disease, persist for at least 2 months, and cannot be explained by other diseases (Soriano et al., 2022).

The most common psychological effects that have been described in PCC patients are anxiety and depression disorders, as well as cognitive dysfunction and poor quality of sleep. According to different systematic reviews, COVID-19 patients display high levels of depression and post-traumatic stress symptoms and decreased psychological well-being (Bourmistrova et al., 2022; Vindegaard and Michael Eriksen Benros, 2020), as well as significantly reduced quality of life (Aiyegbusi et al., 2021). Regarding cognitive effects, it has been proven that PCC patients have poorer executive function performance (Ariza et al., 2022) and worse performance in tests measuring global cognition, such as the

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Montreal Cognitive Assessment (MoCA) (Ariza et al., 2023; García-Sánchez et al., 2022; Delgado-AlonsoValles-Salgado et al., 2022).

Additionally, many studies in the last three years have focused on demonstrating the effects of COVID-19 on sleep quality. First, there is a group of publications that have studied the effects of the pandemic and confinement on sleep quality, both in healthy subjects and COVID-19 patients (Kaur et al., 2021; Sher 2020). In fact, the exposure of people to stress during the pandemic, such as social confinement and changes in daily routines, was accompanied by various sleep disturbances, known as the 'coronasomnia' phenomenon (Semyachkina-Glushkovskaya et al., 2021). The authors report that this phenomenon is not new because the impact of major events, such as previous pandemics (Partinen and Kronholm 2017), wars, earthquakes, floods or wild fires (Lavie 2001; Belleville et al. 2019), on sleep has been previously demonstrated. Moreover, restrictions on free-living activities contribute to increased sedentary time and sleep fragmentation and have consequent effects on quality of life.

A second group of studies focused on sleep disturbances in COVID-19 patients. All of these studies concluded that COVID-19 patients had poorer sleep quality, both subjects who had been hospitalized (Akıncı and Melek Başar 2021; Samushiya et al., 2022; Al-Ameri et al. 2022; Tanriverdi et al., 2022) and those who had not (Karimi et al. 2022; Malik et al., 2022). Only a few studies differentiated the effects regarding the severity of COVID-19, such as that by Chhajer et al. (Chhajer and Shukla 2022), which showed a poorer quality of sleep in the severe COVID-19 group (intensive care unit (ICU) admission). In another study with hospitalized COVID-19 patients, the authors described that several sleep disturbances were observed after hospital discharge for COVID-19 pneumonia, but they did not find significant differences between the groups with good and poor sleep quality regarding sex, age, smoking status, hypertension, disease severity or the length of hospitalization (Kalamara et al., 2022). Poor sleep quality was associated with slow recovery from lymphopenia and an increased need for ICU care in hospitalized COVID-19 patients in a retrospective cohort study, which also showed that none of the patients in the good sleep group required ICU care (Zhang et al., 2020). According to two recent systematic reviews, the prevalence of sleep disturbances was between 57% (Alimoradi et al., 2021) and 74.8% in COVID-19 patients (Jahrami et al., 2021). In both studies, they compared the prevalence of sleep problems among the general population, health care professionals and COVID-19 patients, and it was higher in the latter group.

Additionally, the relation among cognition, emotion and sleep quality is well known. Sleep is essential for many reasons, and it has a substantial pervasive and cyclical impact on our basic psychological processes (e.g. the immune system, metabolism, brain physiology), behaviour, cognition and emotion (Pakpour et al., 2020; Medic et al. 2017). It helps to maintain daily functions, as a lack of sleep can affect psychological functioning, jeopardize the immune response, provoke mood changes, etc. Furthermore, there is a bidirectional relationship between sleep disturbances and psychiatric disorders (Sun et al., 2022).

However, few studies have focused on establishing relations between these variables and trying to identify predictors of sleep quality. In the systematic review by Alimoradi et al., only two studies reporting the association of sleep problems with depression and anxiety among the general population were found (Alimoradi et al., 2021). Furthermore, it is even less studied how these relations could be mediated by the severity of COVID-19.

Therefore, the aim of this study was i) to assess the sleep quality of PCC patients in a large, multicentric PCC cohort, ii) to analyse the relationship of sleep quality with emotional, cognitive and functional variables, iii) to identify predictors of poor sleep quality, and iv) to determine whether there are differences in these predictors according to the severity of COVID-19.

2. Materials and methods

2.1. Participants

We included 428 participants from the Nautilus Project (ClincalTrials.gov IDs: NCT05307549 NCT05307575), of which 368 had post-COVID-19 condition (PCC) and 123 were healthy controls (HCs). Of the 368 PCC patients, 203 were nonhospitalized, 83 were hospitalized and 82 were admitted to the ICU. The sample was recruited across 16 hospitals in Catalonia, Madrid and Andorra and was coordinated by the Consorci Sanitari de Terrassa (Terrassa, Barcelona, Spain). Recruitment was carried out between June 2021 and June 2022.

The inclusion criteria for the PCC group were a confirmed diagnosis of COVID-19 according to the WHO criteria with signs and symptoms of the disease during the acute phase, a period of at least 12 weeks after infection, and an age between 18 and 65 years. The exclusion criteria were an established diagnosis of a psychiatric disorder, neurological disorder, neurodevelopmental disorder, or systemic pathology known to cause cognitive deficits before COVID-19 infection and motor or sensory alterations that could interfere with the neuropsychological assessment. Additionally, patients who scored <14 points on the Montreal Cognitive Assessment (MoCA) as a general cognitive screening tool and/or <85 points on the Word Accentuation Test (TAP) as an estimate of premorbid IQ were excluded. The HCs had not had COVID-19 infection (no positive tests or compatible symptoms). The same exclusion criteria for the PCC group applied to the HC group.

PCC patients were classified into three categories depending on their COVID-19 status.

2.2. Procedure

We obtained written informed consent from all the participants before inclusion. Participation was completely voluntary, and all participants followed the same procedure to complete their participation. After the participants signed the informed consent form, we collected data on sociodemographic characteristics, previous comorbidities and COVID-19 symptoms (how they experienced COVID-19) in the first session. Afterwards, they were scheduled for a second visit during which the neuropsychological assessment was performed. To evaluate global cognition, we used the Montreal Cognitive Assessment (MoCA).

Finally, participants were given all of the questionnaires to complete online or on paper to assess different variables. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI), anxiety was assessed with the Generalized Anxiety Disorder (GAD-7), depression was assessed with the Patient Health Questionnaire (PHQ-9), everyday memory failures was assessed with the Memory Failures of Everyday Questionnaire (MFE-30), fatigue was assessed with the Chadler Fatigue Questionnaire (CFQ), quality of life was assessed with the European Quality of Life-5 Dimensions (EQ-5D), and physical activity levels were assessed with the International Physical Activity Questionnaire (IPAQ).

Participant anonymity and confidentiality were guaranteed. The Scientific Ethics Committee of the Hospital Universitari Arnau de Vilanova approved both the study and the consent procedure (CEIC 2119), as well as the Drug Research Ethics Committee (CEIm) of Consorci Sanitari de Terrassa (CEIm code: 02-20-107-070) and the Ethics Committee of the University of Barcelona (IRB00003099). Also, the investigation was carried out in accordance with the latest version of the Declaration of Helsinki.

2.3. Statistical analysis

Descriptive analyses were performed to compare healthy controls with PCC patients. For categorical variables, frequencies and percentages were obtained, and for quantitative variables, the means and standard deviations were obtained. Between-group comparisons were carried out using Pearson's nonparametric X^2 test, and only in the case of 2 × 2 tables was Fisher's exact test applied. Differences in continuous variables between groups were assessed using factorial ANOVA. For the differences between PCC patients and healthy controls, the ANOVA models were adjusted by sex, age and years of education because of the significant differences in these demographic variables. All multiple comparisons were adjusted by Bonferroni's correction.

To analyse the correlation among depression (PHQ-9), anxiety (GAD-7), quality of life (EQ-5D-total and EQ-5D-VAS), everyday memory failures (MFE-30), the level of physical activity (IPAQ), fatigue (CFQ-total and CFQ-physical), global cognition (MoCA) and the PSQI total score, multiple linear regressions were applied, adjusting for age, sex and years of education. The nonstandardized beta coefficients are shown with their 95% confidence interval, and the Akaike criterion. The CFQ-total score was not included in the multiple linear regression due to multicollinearity problems. Estimation models (factorial ANOVA, linear regression, ordinal regression) were implemented using linear models (ML) with powerful estimation (robust covariances) to handle potential violations of model assumptions. The lower the Akaike criterion value was, the better the model fit.

The statistical significance level used in the analyses was 5% ($\alpha = 0.05$). All analyses were performed with IBM SPSS statistics 26.

3. Results

3.1. Characteristics of participants

Of the 368 PCC patients, 203 had mild PCC (mean age 46.77 years, standard deviation 9.47), 83 were hospitalized (53.04 ± 8.83) and 82 were admitted to the ICU (52.27 ± 8.43). In the mild PCC group, the majority of participants were female (80.3%), while in the hospitalized and ICU groups, the majority of participants were male (50.6% and 53.7%, respectively). Patients in the ICU-PCC group consumed more alcohol (40.2%), were more obese (53.7%) and had more previous comorbidities, such as high blood pressure (29.3%) and dyslipidaemia (22%). See Table 1 for all the clinical and sociodemographic characteristics of the sample.

We found statistically significant differences between PCC patients and HCs in depression, anxiety, quality of life, daily memory failures, and global cognition (see Table 1 Supplementary material), where PCC patients obtained worse results.

3.2. Sleep quality description according to PCC severity

Healthy control subjects had better sleep quality than subjects with PCC ($p < 0.001$). However, there were no statistically significant differences between subjects with PCC based on PCC severity (Table 2). We also found significant differences between the HC and PCC groups in all of the subscales of the PSQI, except for sleep efficiency. Post hoc contrasts showed that the ICU-PCC and mild-PCC groups had poorer subjective sleep quality and a lower sleep duration than the HC group (but not with respect to the hospitalized group). Additionally, all PCC groups showed higher sleep latency than the HC group.

When analysing the percentage of participants who obtained ≥5 points on the PSQI, which indicates a poor quality of sleep, we found significant differences among the groups ($p < 0.001$). The healthy control group had a lower percentage of responses above 5 on the PSQI (57.9%) than the ICU-PCC (71.3%) and mild-PCC groups (83.3%).

3.3. Predictors of sleep quality in PCC patients

According to the multiple linear regression, female sex was a predictor of poorer quality of sleep ($p = 0.002$) but not age ($p = 0.303$). Furthermore, the PHQ-9 score was a predictor of poor quality of sleep in the mild-PCC group ($p = 0.003$). For every unit increase in the PHQ-9 score, the total PSQI score increased by 0.252 units. In the hospitalized group, two predictors were found: the GAD-7 ($p = 0.032$) and EQ-5D-total scores ($p = 0.011$). In this case, for every unit increase in the GAD-7 score, the total PSQI score increased by 0.241, and for every unit increase in the EQ-5D total score, the PSQI total score decreased by 7.567 units. Finally, in the ICU-PCC group, the GAD-7 score was also a predictor of the quality of sleep ($p = 0.045$) but also the level of physical activity (IPAQ) ($p = 0.005$). For each unit increase in the GAD-7 score, the total PSQI score increased by 0.160 points, and for each unit increase in the IPAQ score, the PSQI total score also increased by 0.00025 units. See Table 3 for the full results. Fig. 1 shows the scatterplot of predicted and observed values for each group, that is, when we included all

Table 1
Clinical and sociodemographic characteristics of the sample.

	Healthy Controls	Mild PCC	Hospitalized PCC	ICU PCC	*p value*
	n = 123	n = 203	n = 83	n = 82	
Age (years) (SD)	46.21 (9.96)	46.77 (9.47)	53.04 (8.83)	52.27 (8.43)	**<0.001***
Female (%)	75.6%	80.3%	49.4%	46.3%	**<0.001***
Years of education (SD)	15.69 (2.87)	14.33 (3.26)	13.25 (3.46)	13.09 (3.20)	**<0.001***
Days since COVID-19 (SD)	–	379.16 (206.14)	316.04 (151.15)	280.21 (114.74)	**<0.001***
MoCA (SD)	27.93 (1.82)	26.07 (2.80)	25.66 (2.94)	25.20 (2.92)	**<0.001***
BMI (SD)	25.03 (5.98)	25.48 (4.97)	27.80 (5.21)	31.27 (5.32)	**<0.001***
Tobacco smoking (%)	23.6%	8.9%	4.8%	4.9%	**<0.001***
Alcohol consumption (%)	29.3%	22.7%	27.7%	40.2%	**0.029***
Civil status					
Married (%)	71.5%	79.8%	72.3%	81.7%	0.173
Previous comorbidities					
Heart disease (%)	1.6%	2.5%	3.6%	3.7%	0.765
Respiratory disease (%)	4.9%	12.8%	14.5%	15.9%	0.050
Chronic kidney disease (%)	0.0%	1.0%	1.2%	0.0%	0.530
High blood pressure (%)	4.1%	6.9%	19.3%	29.3%	**<0.001***
Dyslipidemia (%)	9.8%	9.9%	18.1%	22.0%	**0.015***
Diabetes mellitus (%)	2.4%	0.5%	8.4%	6.1%	**0.002***
Obesity (%)	11.4%	16.3%	34.9%	53.7%	**<0.001***
Chronic liver disease (%)	0.0%	0.5%	3.6%	3.7%	**0.032***
Chronic pain (%)	4.1%	5.3%	17.5%	7.3%	**0.002***

Unless otherwise specified, results are presented as mean (standard deviation).
P-values were calculated by comparing controls, non-hospitalized COVID, hospitalized COVID and ICU COVID participants using MLG with potent estimation for continuous variables and Pearson X2 for cathegorical variables.
Level of statistical significance = *p < 0.05, **p < 0.01, ***p < 0.001.
PCC: Post-COVID-19 Condition; MoCA: Montreal Cognitive Assessment; BMI: Body Mass Index.

Table 2
Pittsburgh Sleep Quality Index (PSQI) results between healthy subjects and Post-COVID condition participants.

	Healthy Controls	Mild PCC	Hospitalized PCC	ICU PCC	*p value*
	n = 123	n = 203	n = 83	n = 82	
Subjective sleep quality (%)	2.5%	20.3%	11.0%	13.6%	**<0.001*****
Sleep latency (%)	0.8%	25.7%	21.7%	24.4%	**<0.001*****
Sleep duration (%)	10.7%	30.0%	22.2%	25.3%	**0.007****
Sleep efficiency (%)	8.9%	15.3%	9.6%	8.5%	0.428
Sleep disturbance (%)	0.0%	12.5%	21.7%	15.9%	**<0.001*****
Sleep medication (%)	5.7%	23.8%	18.1%	29.3%	**<0.001*****
Sleep daytime dysfunction (%)	16.3%	50.5%	36.1%	34.1%	**<0.001*****
Sleep total score (SD)	5.43 (3.27)	9.13 (4.13)	8.04 (4.60)	8.47 (4.45)	**<0.001*****
Prevalence of poor quality of sleep (≥5 points)	57.9%	83.3%	71.3%	78.2%	**<0.001*****

Results are presented as mean (standard deviation) for Total score, as % of 2 value for Sleep daytime dysfuntion and as % of 3 value for the rest of parameters. P-values were calculated by comparing controls. non-hospitalized COVID. hospitalized COVID and ICU COVID participants using MLG with potent estimation for continuous variables and Pearson Chi2 for cathegorical variables.
Level of statistical significance = *p < 0.05. **p < 0.01. ***p < 0.001.

possible predictors in the model, how well they predicted the overall PSQI score. In this case, the model for the ICU-PCC group better fit the observed data (had better goodness of fit) since the Akaike criteria were lower and the point cloud was narrower around the diagonal.

4. Discussion

Our results showed that PCC patients had worse sleep quality than healthy controls, determined by not only the global score but also all the PSQI subscale scores, except the sleep efficiency score. Additionally, we found that the prevalence of poor sleep quality (indicated by a PSQI global score ≥5 points) was high in all PCC groups, but there were significant differences among them. Regarding our main aim, we found that depression was a predictor of poor sleep quality in mild PCC patients, whereas anxiety was a predictor of poor sleep quality in the hospitalized PCC and ICU-PCC participants. Furthermore, quality of life was a predictor of poor sleep quality in hospitalized PCC patients and physical activity was a predictor of poor sleep quality in ICU-PCC patients.

Subjects with PCC had poorer sleep quality than HCs, as has also been previously described. In general, the PSQI global score in the majority of the studies is above 5 points, which indicates poor quality of sleep. Malik et al., (2022) found that the PSQI global score in COVID-19-positive participants was 6.96 (SD 3.770) while that in COVID-19-negative participants was 5.82 (SD 3.38), which was statistically significant. In our sample, the results for the HCs were quite similar, with a PSQI global score of 5.43 (SD 3.27), but in COVID-19 patients, the scores were slightly higher, ranging from 8.04 to 9.13, which is closer to the results of Al-Meri et al., who found a PSQI global score of 8.77 in PCC patients (Al-Ameri et al. 2022). However, not all previous studies have differentiated PCC patients regarding the severity of the disease. We only found a few studies that compared the quality of sleep among COVID-19 patients. The study most similar to ours (because it also divided PCC patients into mild, moderate and severe PCC patients) found that the latter group had worse global PSQI scores than the former group (Chhajer and Shukla 2022). In another study, the authors compared mild and moderate COVID-19 patients, with the presence of pneumonia being the main difference between the groups. They found that moderate COVID-19 patients had poorer quality of sleep (Tanriverdi et al., 2022). These results are the opposite of ours, where mild PCC patients have higher PSQI global scores. However, this could be explained by the fact that the mild groups are not the same; in their study, mild indicated not only patients without pneumonia but also inpatients, whereas in our study, mild PCC indicated patients who were not hospitalized. In addition, in our sample, the duration since COVID-19 infection was longer in the mild PCC patients than in the hospitalized PCC patients. We could assume that a longer period of persistent symptoms can worsen sleep quality. Other authors compared COVID-19 patients who had been admitted to the hospital in a respiratory care unit (RCU) versus those who had not been admitted to

Table 3
Multiple linear regression of PSQI total score, adjusted for age, sex and years of education.

	Mild PCC				Hospitalized PCC				ICU PCC			
Predictors	Coefficient	Sig.	95% Confidence Interval		Coefficient	Sig.	95% Confidence Interval		Coefficient	Sig.	95% Confidence Interval	
			Lower	Upper			Lower	Upper			Lower	Upper
PHQ9	0.252	**0,003****	0.088	0.416	0.112	0.198	−0.06	0.285	0.123	0.289	−0.107	0.352
GAD-7	0.072	0.398	−0.095	0.238	0.241	**0,032***	0.022	0.46	0.16	**0,045***	0.004	0.317
MFE-30	0.039	0.161	−0.016	0.094	0.038	0.307	−0.036	0.112	0.065	0.134	−0.021	0.152
IPAQ	−1.54E-05	0.828	−1.55E-04	1.24E-04	−6.89E-06	0.896	−1.12E-04	9.81E-05	2.48E-04	**0,005****	7.77E-05	4.18E-04
EQ-5D-TOTAL	−2.089	0.312	−6.159	1.982	−7.567	**0,011***	−13.366	−1.768	−3.641	0.141	−8.528	1.246
EQ-5D-VAS	−0.003	0.886	−0.04	0.034	0.011	0.677	−0.041	0.063	−0.04	0.053	−0.08	0.001
CFQ_Mental	−0.045	0.855	−0.531	0.441	−0.509	0.107	−1.13	0.112	0.148	0.631	−0.466	0.762
CF_Physical	0.137	0.388	−0.176	0.451	0.244	0.37	−0.295	0.782	−0.124	0.424	−0.43	0.183
MoCA	0.025	0.8	−0.167	0.216	0.008	0.952	−0.269	0.286	−0.171	0.271	−0.479	0.137
Akaike Criterion	**8,79,972**				**3,96,687**				**3,85,342**			

Outcome: PSQI global.
Level of statistical significance = *p < 0.05, **p < 0.01, ***p < 0.001.
PHQ9: Patient Health Questionnaire; GAD-7: Generalized Anxiety Disorder; MFE-30: Memory Failures of Everyday Questionnaire; IPAQ: International Physical Activity Questionnaires; EQ-5D-TOTAL: European Questionnaire of 5 Dimensions.
Total; EQ-5D-VAS: European Questionnaire of 5 Dimensions Visual Analogic Scale; CFQ-Total: Chadler Fatigue Questionnaire; MoCA: Montreal Cognitive Assessment.

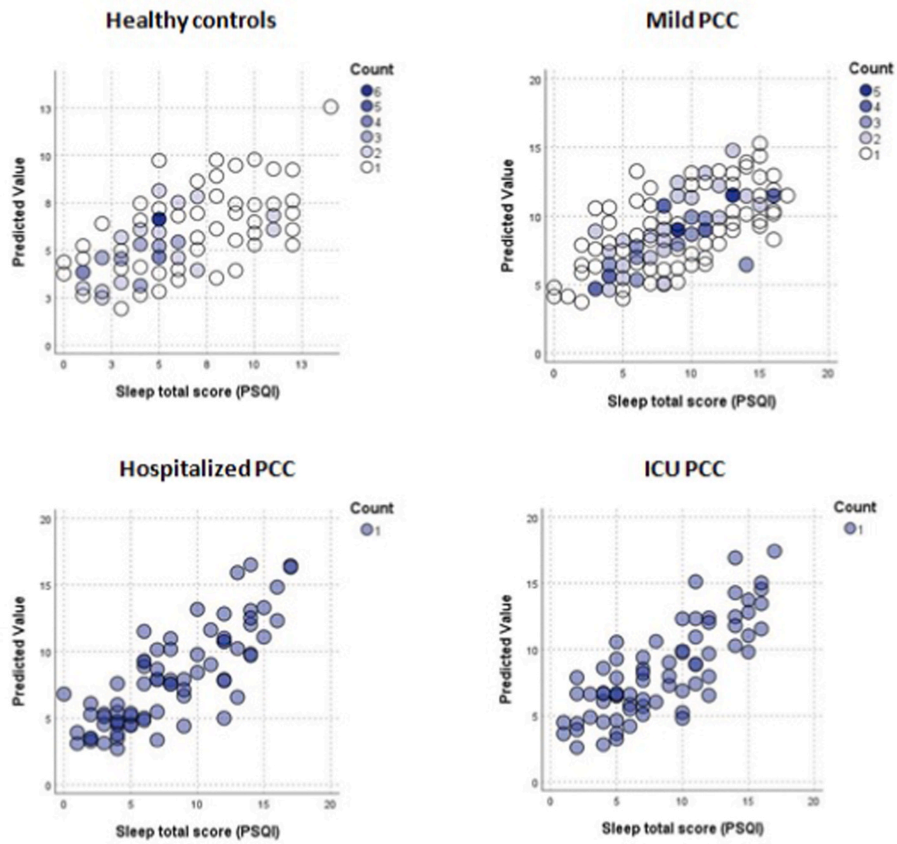

Fig. 1. Scatterplot of predicted and observed values for each group. X axis: PSQI total score observed. Y axis: PSQI values predicted by the model. Count: each color in the circle represents a number of cases (the darker the color, the more cases it represents). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

hospitals or patients who did not need admission to the RCU (Al-Ameri et al. 2022). They also reported significantly worse sleep quality in COVID-19 patients, but with no significant differences when they compared patients who had been admitted to the RCU with those who had not been.

We also analysed the PSQI components, where we found significant differences between PCC patients and HCs in all of them, except for sleep efficiency. Comparing PCC patients with HCs, we observed that the former had higher sleep latency, more disturbances and daytime dysfunction, a shorter sleep duration and the need for more sleep medications. Furthermore, they had worse subjective sleep quality. These results are similar to those published by Malik et al., (2022), but they only showed significant differences in sleep disturbances, daytime dysfunction and the use of sleep medications. Chhajer and Shukla also found significant differences in all PSQI components except for sleep duration and sleep efficiency (Chhajer and Shukla 2022). Normal healthy sleep is characterized by a sufficient duration, a good quality, an appropriate timing and regularity, and the absence of sleep disturbances or disorders (Watson et al., 2015), which can be measured subjectively with the PSQI and objectively with actigraphy and other types of wearables. Therefore, future research comparing PSQI parameters of sleep with objective measures, such as actigraphy, must be performed to clarify in which components PCC patients and HCs are more likely to experience troubles.

However, our goal was not only to describe the sleep quality of PCC patients but also to analyse its relationship with emotional, cognitive, and functional variables to identify predictors of poor sleep quality. In mild PCC patients, depressive symptoms were a predictor of poor quality of sleep, indicating that patients with major levels of depression have poorer quality of sleep. Instead, in hospitalized PCC and ICU-PCC patients, anxiety was found to be a predictor of poor quality of sleep. These results are in line with previous literature. In hospitalized COVID-19 patients, Akinci et al. found that the depression rate among those with poor sleep quality was significantly higher than that in those with good sleep quality but not in those with anxiety (Akıncı and Melek Başar 2021). Although they did not perform multiple linear regressions, Samushiya et al. demonstrated that the PSQI score had positive correlations with measurements of anxiety and depression (Samushiya et al., 2022), but they excluded patients with severe COVID-19 (defined as CT4, saturation $<93\%$, a respiratory rate >30 per min, stable elevation of the body temperature at $>39^{\circ}$, the presence of multiorgan failure). Not all the investigations found relations between sleep quality and anxiety or depression. In fact, Chhajer and Shukla did not find any association between the PSQI and global scores and anxiety (GAD-7) or depression (PHQ-4) (Chhajer and Shukla 2022). However, these results are not the usual ones, since as we have mentioned, the literature supports a relationship much more than a nonrelationship between sleep quality and emotional problems. Furthermore, this relationship between mental health problems and sleep quality has been proven in many countries, such as China (Hu et al., 2020; Zhang et al., 2020), Greece (Voitsidis et al., 2020), Italy (Cellini et al., 2020), France (Kokou-Kpolou et al., 2020), Iraq (Al-Ameri et al. 2022), and Iran (Karimi et al. 2022). Malik et al. did not analyse anxiety or depression as a predictor of poor quality of sleep, but they did show that female sex and a primary education level were significant risk factors for poorer quality of sleep (Malik et al., 2022). Hu et al. also showed that female sex was a robust risk factor for insomnia, anxiety and depression (Hu et al., 2020). We also found that females had poorer quality of sleep, although in the systematic review by Alimoradi et al., they did not confirm these findings (Alimoradi et al., 2021). They argued that this could be due to the imbalanced sex distributions of samples.

Another interesting result was the relation between physical activity and sleep quality in ICU-PCC patients. Considering that these patients had significant levels of obesity (53.7%) with a mean BMI of 31.27, it should be noted that physical activity, measured with the IPAQ, showed no significant differences among the groups ($p = 0.725$). A recent systematic review affirmed that physical activity is an effective strategy for lowering cortisol levels and improving quality of sleep (De Nys et al., 2022). However, to our knowledge, only one study to date has analysed physical activity in COVID-19 patients. The authors studied the relationship between muscle function, physical activity, and mood and sleep quality in mild and moderate COVID-19 patients. They concluded that physical performance and quality of sleep were lower in the moderate group (Tanriverdi et al., 2022). We found that many publications studied the influence of physical activity on sleep quality during the lockdown in the general population (Luciano et al., 2021; Martínez-de-Quel et al., 2021) and in special populations, such as multiple sclerosis patients (Özkeskin et al., 2021), people with asthma (Daşdemir and Suner-Keklik 2022), and patients with other medical conditions, but did not include COVID-19 patients.

The last predictor of sleep quality in PCC patients (quality of life) was found in the hospitalized group. Many authors have demonstrated the effects of COVID-19 on quality of life. Studies carried out between 1 and 3 months after COVID-19 infection showed reductions in PCC patients' health-related quality of life (HRQoL), particularly in the physical and mental components (Short Form Health Survey Questionnaire-36 (SF-36-II) (Gil et al., 2022; Rass et al., 2021) or in mobility, self-care, usual activities, pain/discomfort and anxiety/depression (EuroQoL 5D) (Halpin et al., 2021; Todt et al., 2021), even when compared to an uninfected population (Chen et al., 2020; Qu et al., 2021) or a matched healthy control group (Raman et al., 2021). In fact, most of the studies confirmed that HRQoL is affected after COVID-19 infection, both in inpatients (Garrigues et al., 2020; Jacobs et al., 2020; Sigfrid et al., 2021) and outpatients (Garratt et al., 2021). Our results indicated that the EQ-5D index score was a predictor of sleep quality in hospitalized PCC patients, which means that hospitalized PCC patients with lower quality of life also have poorer quality of sleep. This is also consistent with previous literature. Pellitteri et al. showed that poor sleepers, determined based on the PSQI score, obtained significantly worse results on the SF-36 questionnaire (Pellitteri et al., 2019). In another study, the authors found a positive correlation between the PSQI global score and various domains of the SF-36 (El Sayed et al., 2021).

The limitations and strengths of the study must be considered when interpreting the results. We did not use objective sleep measures, such as actigraphy, to compare the subjective data provided by the PSQI with objective data. Furthermore, our control group was not optimal. As explained in a previous study (Ariza et al., 2022), we wanted to enrol participants without COVID-19 but who experienced the same environmental circumstances (i.e., lockdown and stress factors). Therefore, for this reason, the HC group was not matched by age, sex or education level. However, we did collect a reasonably large sample with different COVID-19 severities, which allowed us to compare sleep quality in different PCC patients. In addition, we also had numerous data that allowed us to establish predictors of sleep quality given the robustness of the statistical calculations made.

5. Conclusions

In conclusion, our results confirm that both PCC patients and HCs have poor quality of sleep, although PCC patients have significantly worse results. Furthermore, we found that depression was a predictor of sleep quality disturbances in mild PCC patients, while anxiety, quality of life and physical activity were predictors of sleep quality disturbances in moderate and severe PCC patients. Therefore, if we implement therapeutic strategies to reduce emotional symptoms, such as depression and anxiety, or increase physical activity levels, perhaps we could increase the sleep quality of PCC patients and thus their quality of life.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors without undue reservation.

Ethics statement

The Scientific Ethics Committee of the Hospital Universitari Arnau de Vilanova approved both the study and the consent procedure (CEIC 2119), as well as the Drug Research Ethics Committee (CEIm) of Consorci Sanitari de Terrassa (CEIm code: 02-20-107-070) and the Ethics Committee of the University of Barcelona (IRB00003099). The patients/participants provided their written informed consent to participate in the study.

Author contributions

MA, MG, CJ, BS, CB and JB designed the study. ACV, NC and the NAUTILUS-Project Collaborative Group collected the data. ACV wrote the first version of the manuscript. GPR and MG critically revised the manuscript for important intellectual content. All authors revised the manuscript drafts and approved the final manuscript.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Maite-Garolera reports financial support was provided by Agency for Management of University and Research Grants (AGAUR) from the Generalitat de Catalunya (Pandemies, 202PANDE00053) and La Marató de TV3 Foundation (202111-30-31-32). Corresponding author (Gerard Piñol-Ripoll) recieved grants from the Instituto de Salud Carlos III de Madrid (PI22/01687, ISCIII) and Agency for Management of University and Research Grants (2021SGR 00761).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbih.2023.100721.

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