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RESEARCH ARTICLE

The role of sleep and dreams in long-COVID

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Summary

Recent investigations show that many people affected by SARS-CoV2 (COVID-19) report persistent symptoms 2–3 months from the onset of the infection. Here, we report the Italian findings from the second International COVID-19 Sleep Study survey, aiming to investigate sleep and dream alterations in participants with post-acute symptoms, and identify the best determinants of these alterations among patients with long-COVID. Data from 383 participants who have had COVID-19 were collected through a web-survey (May–November 2021). Descriptive analyses were performed to outline the sociodemographic characteristics of long-COVID ($N = 270$, with at least two long-lasting symptoms) and short-COVID ($N = 113$, with none or one long-lasting symptom) participants. They were then compared concerning sleep and dream measures. We performed multiple linear regressions considering as dependent variables sleep and dream parameters discriminating the long-COVID group. Age, gender, work status, financial burden, COVID-19 severity and the level of care were significantly different between long-COVID and short-COVID subjects. The long-COVID group showed greater sleep alterations (sleep quality, daytime sleepiness, sleep inertia, naps, insomnia, sleep apnea, nightmares) compared with the short-COVID group. We also found that the number of long-COVID symptoms, psychological factors and age were the best explanatory variables of sleep and oneiric alterations. Our findings highlight that sleep alterations are part of the clinical presentation of the long-COVID syndrome. Moreover, psychological status and the number of post-acute symptoms should be considered as state-like variables modulating the sleep problems in long-COVID individuals. Finally, according to previous investigations, oneiric alterations are confirmed as a reliable mental health index.

KEYWORDS
COVID-19, nightmares, oneiric activity, post-acute symptoms, sleep concerns

1 | INTRODUCTION

After more than two yearsof battling the pandemic caused by the spread of the novel coronavirus infection (COVID-19), many countries are still facing a growing number of new cases every day and the consequences of the virus. Clinical manifestation of COVID-19 consists of a severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2), nevertheless it is considered a *multi-organ* disease that could range from asymptomatic or mild to lethal infection (Zaim et al., 2020).

International (Fränkl et al., 2021; Merikanto et al., 2022a; Morin et al., 2021; Scarpelli et al., 2022a) and Italian investigations (Cellini et al., 2020; Franceschini et al., 2020; Gorgoni et al., 2021) report an increase of sleep difficulties during the pandemic. These changes appear to be associated with negative consequences on mental health and wellbeing (Fränkl et al., 2021; Merikanto et al., 2022a; Morin et al., 2021). Recent meta-analyses highlight that the pandemic affected sleep–wake rhythm among different kinds of populations (Jahrami et al., 2021; Scarpelli et al., 2022b), and patients with COVID-19 show a very high rate (50%–75%) of sleep disorders (Jahrami et al., 2021). Recent studies also report that oneiric activity, especially nightmares, were more frequent during the pandemic (Scarpelli et al., 2021), and a higher rate of nightmares was related to the severity of the infection among people who have contracted the virus (Scarpelli, Nadorff, et al., 2022).

Although the duration of COVID-19 varies from 7–10 days to > 1 month (Walsh et al., 2020), many experience persistent and debilitating symptoms, including sleep problems, 2–3 months from the onset of the infection (Davis et al., 2021).

The profile, duration and incidence of this prolonged condition are largely unknown (Al-Aly et al., 2021; Arnold et al., 2021; Lopez-Leon et al., 2021; Michelen et al., 2021). The World Health Organization (WHO, 2021) defines the so-called long-COVID (LC) syndrome as "*Post COVID-19 condition occurring in individuals with a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis*." LC appears to be composed of heterogeneous symptoms that may impact multiple organ systems (Davis et al., 2021). Symptoms may oscillate over time, and the relationship between infection severity and LC condition is not clear (Petersen et al., 2021).

A recent meta-analysis showed that the most common persistent symptoms in the months following the acute phase of COVID-19 are fatigue, headache and attention dysfunction (Lopez-Leon et al., 2021). While sleep impairment is one of the most frequent prolonged symptoms (Alkodaymi et al., 2022; Davis et al., 2021; Huang et al., 2021), most studies have examined sleep difficulties without considering the different and specific aspects of sleep (e.g. subjective sleep quality, daytime sleepiness, risk of sleep apnea; Huang et al., 2021; Xiong et al., 2021) or mainly focused on insomnia symptoms (Arnold et al., 2021; Orrù et al., 2021). Only one study considered oneiric changes as potential long-lasting symptoms (Davis et al., 2021). To the best of our knowledge, no studies have systematically investigated different kinds of sleep features and dream alterations among LC subjects.

Because little is known about this aspect of LC, herein we report results from the second ICOSS survey (Merikanto et al., 2021) administered to an Italian sample. Our objective was to investigate the impact of sleep and dream measures in patients with post-acute symptoms (LC; i.e. subjects with two or more persistent symptoms lasting at least 3 months). First, we compared self-reported sleep and oneiric parameters between patients with short-COVID (SC; i.e. subjects with zero or just one persistent symptom) and LC, and second, we identified specific variables related to sleep and dream alterations among patients with LC. We hypothesized that sleep and dream disturbances may have a pivotal role in the clinical presentation of patients with LC, and that the specific sleep symptoms and oneiric alterations would help to categorize the LC group.

TABLE 1 Post-acute symptoms of the ICOSS-2 questionnaire

Fatigue
Shortness of breath or difficulty breathing and/or chest pain
Joint pain (arthralgia) and/or muscle pain
Migraine headaches
Headache, different from migraine
Abdominal pain, colics
Palpitations and/or cardiac arrhythmia
Tachycardia, fast pulse rate
Post-exertional malaise
Dizziness when standing
Low blood pressure (hypotension)
Urinary problems
Problems of sweating and/or trouble of tolerating cold/heat
Problems of attention or of concentration and/or brain fog, cognitive dysfunction
Memory problems
Loss of smell and/or taste
Delusion, psychotic symptoms
Feverishness and/or flu-like symptoms such as sore throat, runny nose, etc.
Diarrhoea and/or nausea

2 | METHODS

2.1 | Study design and participants

The current study is part of the ICOSS 2nd protocol (Merikanto et al., 2021). This survey has been designed to better understand the impact of the pandemic on sleep-related aspects, with a specific focus on post-infection symptoms. Data have been collected between May and November 2021 in Italy and in 15 other countries: Austria, Brazil, Bulgaria, Canada, China (Hong Kong), Croatia, Finland, France, Germany, Israel, Japan, Norway, Portugal, Sweden and USA. In this study, we are analysing only the Italian data. The online-survey was implemented through the Qualtrics platform. To recruit the largest number of participants, the web-survey was promoted through university communication systems, social media platforms (e.g. Facebook, Twitter, Instagram), sleep societies' websites, The Huffington Post Blog, a Facebook group of people who have contracted COVID, and through Neuroscience and Psychology social pages. The survey took about 40 min to complete.

The study was approved by the Institutional Ethics Committee of the Department of Psychology of the Sapienza University of Rome, and was conducted in accordance with the Declaration of Helsinki (protocol number: 0000861, 24 April 2021).

Subjects agreed voluntarily and anonymously to take part in the survey. To access the questions, participants at least 18 years old signed an informed consent. To ensure anonymity, the Qualtrics platform generated an automatic code for each participant. Subjects could interrupt the survey at any time and did not receive any monetary compensation. General data protection regulations were enforced to ensure privacy and confidentiality.

The present work includes participants who reported to have had COVID-19 with a positive test. We included only participants that completed ICOSS-2 questionnaires after at least 3 months from the date in which they were tested positive for COVID-19. Specifically, the long-lasting symptoms (at least 3 months) were used to distinguish between participants with SC and LC. To this aim, we defined the LC group had at least two long-lasting LC symptoms, while the SC group had zero or one persistent symptom. The sleep symptoms: (1) excessive daytime sleepiness; and (2) difficulties falling or staying asleep were excluded from the definition of LC subjects because of the specific aims of this study. The 19 items investigating post-acute symptoms are listed in Table 1.

Subjects who answered at least 50% of the questionnaire and who had < 25% missing data relative to the variables of interest were included. According to mentioned criteria, data from 383 COVID-19 participants were included in the current investigation.

2.2 | Outcomes

The survey consists of several questions addressed to both controls (i.e. subjects without infection) and COVID-19 participants, while some sections include questions only to those reporting having had the infection. We considered: (a) socio-demographic information (i.e. age, gender, residential area, cohabitation, relationship status, education, work, financial burden); (b) COVID-19-related information about the acute phase such as the level of infection severity (no marked symptoms/mild, moderate, severe/life-threatening) and level of care (at home, hospital, Intensive Care Unit [ICU admission]); and (c) the individual's chronotype, considered as a trait-like feature of sleep (Montaruli et al., 2021).

In order to assess sleep and dream measures, we considered the following variables from the Basic Nordic Sleep Questionnaire with additional items for oneiric activity (Partinen & Gislason, 1995) with reference to current symptoms: sleep quality; daytime sleepiness; sleep inertia; naps; sleep talking; dream-recall frequency (DRF); pandemic content frequency; nightmare frequency (NMF); lucid dreaming—awareness frequency; lucid dreaming—manipulation frequency. Participants rated each item on a scale from 1 to 5, based on how many nights *per* week sleep problems occurred (1 = "Never or less frequently than once per month"; 2 = "Less frequently than once per week"; 3 = "1–2 nights per week"; 4 = "3–5 nights per week"; 5 = "Nightly or almost nightly").

Additionally, two other questionnaires were used to assess sleep disturbances:

- The Insomnia Severity Index (ISI; Bastien et al., 2001), a seven-item questionnaire used to evaluate the severity of nighttime and daytime symptoms of insomnia during the past week before answering the survey, rated on a scale of 0–4. A total score of 0–7 indicates no insomnia, 8–14 subthreshold clinical insomnia, 15–21 insomnia of moderate severity, and 22 and above indicates severe insomnia.

- A Tool to Screen Patients for Obstructive Sleep Apnea, the STOP questionnaire is a screening questionnaire consisting of four yes/no questions on snoring, tiredness, observed apnea and high blood pressure. In the ICOSS survey, instead of answering yes or no, participants provided ratings on five-point Likert scales for snoring, tiredness, observed apnea (never, less than once per week, 1–2 days per week, 3–5 days per week, and daily or almost daily) and blood pressure (yes/no; Chung et al., 2008). The highest possible STOP score was 4. STOP scores of 2 or greater were classified as high risk, and a score of 0–1 as low-risk of obstructive sleep apnea (OSA; Chung et al., 2008).

Also, we considered the following psychological measures:

- Anxiety: the Generalized Anxiety Disorder-2 (GAD-2; Kroenke et al., 2009) was used to assess symptoms of anxiety. Two items assessed anxiety on scales of 0–3. Sum scores are calculated, and the cut-off score is ≥ 3.
- Stress (Elo et al., 2003): a single item assessed the current stress from "not at all" to "very much" (1–5 rating). The considered cut-off is 3.
- Because Italian participants reported several missing responses on the Patient Health Questionnaire-2 (PHQ-2; Kroenke et al., 2009), the current investigation could not consider depressive symptoms among analysed variables.

2.3 | Statistical analysis

First, descriptive analyses were performed to outline the sociodemographic characteristics of the SC and LC groups, considering the following variables: age, gender, residential area, cohabitation, relationship status, education, work status, financial burden, severity of infection, and level of care. The Chi-Square statistic was used for testing differences of categorical variables between the SC and LC groups.

Concerning sleep and dream parameters, a between one-way MANOVA was carried out to assess differences between SC and LC groups, considering the following dependent variables: (a) sleep quality; (b) daytime sleepiness; (c) sleep inertia; (d) naps; (e) sleep talking; (f) DRF; (g) pandemic content frequency; (h) NMF; (i) lucid dream frequency—awareness; (j) lucid dream frequency—manipulation; (k) ISI score; and (l) STOP score. In the case of a significant group effect, a one-way ANOVA was carried out for each measure. Eta squared values (η^2) have been also calculated as measure of effect size. Then, predictors of SC or LC groups were evaluated using discriminant function analyses.

Finally, with the aim to assess the best explanatory variables of the sleep and dream measures discriminating the LC group, we performed multiple linear regressions considering the following independent variables: age; number of post-acute/LC symptoms (long-lasting: at least 3 months); level of infection severity; level of care; anxiety score; stress score. Gender has been excluded from the independent variables because of the very unbalanced categories (females represent 81% of LC subjects). We carried out a multiple linear regression for each dependent variable resulting in significant differences between LC and SC groups in the previous analysis. We entered the variables simultaneously into a single model. Multicollinearity between the independent variables was assessed before running the regression by calculating variable inflation factors (VIF). The VIF statistics for all variables included in the regression model were under 3, indicating only moderate correlation.

All statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS) version 25.0 and MATLAB R2019. The criterion used to determine statistical significance was $p < 0.05$.

3 | RESULTS

3.1 | Characteristics of the sample

Descriptive features of the SC and LC samples are detailed in Table 2. Data from 383 subjects with COVID-19 revealed that the majority of participants can be categorized as patients with LC having two or more persistent symptoms ($N = 270$, 70.5%). Furthermore, the sample comprised of mainly women in both the SC (women: 62.8%) and LC (women: 81.1%) groups. However, the prevalence of women among LC participants was significantly higher than in the SC group ($p < 0.001$). Also, the prevalence of subjects aged < 25 years was significantly lower ($p < 0.001$) in the LC (3.3%) than in the SC (21.2%) group. The most represented age range in the LC group was 45–54 years (28.9%), followed by the 35–44 years age group (21.1%). More than 70% of the subjects in both groups resided in urban areas (SC: 71.7%; LC: 77.1%). Most of the individuals were in a relationship in both groups, with a greater percentage of engaged people in the LC group (69.3%). Almost all subjects live with other people in both groups (> 80%).

Respondents were mostly graduates with a higher or bachelor's degree both among SC (56.6%) and LC (58.5%) participants. In both groups, more than half of the subjects were employed in work (SC subjects: 57.6%; LC subjects: 76%), but the prevalence of students was significantly lower ($p < 0.001$) in the LC (4.4%) compared with the SC group (27.3%). Notably, a greater percentage of LC individuals reported the highest degree of financial burden ("a lot", 17%) than SC subjects (4.1%).

The sample mainly included subjects who reported mild or no acute COVID-19 symptoms in both the SC group (77%) and the LC group (49.3%). The distribution of participants along the three levels of COVID-19 severity (no marked symptoms or mild/moderate/severe or life-threatening) significantly differed in the LC group ($P \leq 0.001$). Indeed, they showed a higher percentage of people having severe infection or life-threatening (17.0%) compared with the SC group (8.0%). Similarly, the LC group showed a greater percentage of people that required treatment in hospital (10.4%) or ICU admission (6.7%) than the SC group (2.7%; 4.5%; $p = 0.025$). Both SC and LC groups showed a higher percentage of morning chronotype (SC: 54%; LC: 45.9%), but this difference was not significant.

TABLE 2 Characteristics of the sample

	SC participants		LC participants		
	N	%	N	%	Chi-squared (p)
Gender					
(SC = 113; LC = 270)					
Male	42	37.2	51	18.9	**14.5 (< 0.001)**
Female	71	62.8	219	81.1	
Age (years)					
(SC = 113; LC = 270)					
< 25	24	21.2	9	3.3	**35.7 (< 0.001)**
25–34	26	23.0	52	19.3	
35–44	16	14.2	57	21.1	
45–54	24	21.2	78	28.9	
55–64	15	13.3	52	19.3	
65+	8	7.1	22	8.1	
Residential area					
(SC = 99; LC = 231)					
Urban	71	71.7	178	77.1	1.1 (0.33)
Rural	28	28.3	53	22.9	
Relationship status					
(SC = 99; LC = 231)					
Yes	58	58.6	160	69.3	3.5 (0.075)
No	41	41.4	71	30.7	
Cohabitation					
(SC = 98; LC = 231)					
Alone	10	10.2	41	17.7	2.9 (0.097)
With other people	88	89.8	190	82.3	
Education					
(SC = 99; LC = 229)					
Primary	3	3.0	12	5.2	1.1 (0.576)
Secondary	40	40.4	83	36.2	
Bachelor or higher degree	56	56.6	123	58.5	
Work status					
(SC = 99; LC = 229)					
Student	27	27.3	10	4.4	**36.8 (< 0.001)**
Employed	57	57.6	174	76.0	
Unemployed	4	4.0	17	7.4	
Retired	11	11.1	28	12.2	
Financial burden					
(SC = 97; LC = 229)					
Not at all	61	62.9	126	55.0	**9.9 (0.007)**
Little	32	33.0	64	27.9	
A lot	4	4.1	39	17.0	
COVID-19 severity					
(SC = 113; LC = 270)					
No marked symptoms/mild	87	77.0	133	49.3	**25.1 (< 0.001)**
Moderate	17	15.0	91	33.7	
Severe/life-threatening	9	8.0	46	17.0	

(Continues)

TABLE 2 (Continued)

	SC participants		LC participants		
	N	%	N	%	Chi-squared (*p*)
Level of care					
(SC = 112; LC = 269)					
At home	104	92.9	223	82.9	**7.4 (0.025)**
Hospital	3	2.7	28	10.4	
ICU admission	5	4.5	18	6.7	
Chronotype					
(SC = 113; LC = 270)					
Morning	61	54	124	45.0	2.71 (0.257)
Intermediate	19	16.8	63	23.3	
Evening	33	29.2	83	30.7	

Abbreviations: ICU, Intensive Care Unit; LC, long-COVID; SC, short-COVID. Bold values denote statistical significance at the $p < 0.05$ level.

3.2 | Differences between SC and LC participants

The one-way MANOVA performed on sleep and dream variables showed statistically significant differences between the SC and LC groups (Wilks' lambda = 0.77, $F_{1,12} = 10.414$, $p < 0.001$, $\eta^2 = 0.230$). This analysis has been carried out on 331 subjects with post-infectious symptoms (98 SC versus 233 LC participants).

Specifically, subsequent ANOVAs revealed that the LC group has poorer sleep quality ($F_{1,329} = 46.05$, $p < 0.001$, $\eta^2 = 0.123$), greater daytime sleepiness ($F_{1,329} = 43.40$, $p < 0.001$, $\eta^2 = 0.117$), greater sleep inertia ($F_{1,329} = 54.23$, $p < 0.001$, $\eta^2 = 0.142$), higher nap frequency ($F_{1,329} = 4.86$, $p = 0.028$, $\eta^2 = 0.015$), greater ISI score ($F_{1,329} = 66.36$, $p < 0.001$, $\eta^2 = 0.168$) and higher OSA risk ($F_{1,329} = 17.73$, $p < 0.001$, $\eta^2 = 0.051$) than the SC group. Concerning dream activity, LC participants reported higher NMF ($F_{1,329} = 5.54$, $p = 0.019$, $\eta^2 = 0.017$) than SC participants. All results from univariate ANOVAs are reported in Table 3.

When the sleep and dream measures were used as predictors in the discriminant analysis, they could correctly classify 77.0% of patients into SC and LC groups (Wilks' lambda, 0.77; $\chi^2 = 84.26$; $p < 0.001$). *R* canonical correlation analyses showed that "insomnia" ($R^2 = 0.823$), "sleep inertia" ($R^2 = 0.744$), "sleep quality" ($R^2 = 0.685$) and "daytime sleepiness" ($R^2 = 0.665$) are the largest contributors to the model, and play a pivotal role in predicting the LC and SC membership. Canonical discriminant function coefficients along with structure coefficient matrices are shown in Table S1.

3.3 | Variables associated with sleep and dream alterations in LC participants

The second aim of our study was to identify specific variables associated with the sleep and dream alterations characterizing the LC group. Multiple linear regressions were carried out on 222 LC participants (after excluding subjects with missing values).

Except for the regression on lucid dreaming (awareness component), all models were significant with the following results.

a. Poor sleep quality ($F_{6,215} = 8.59$, $p < 0.001$; adjusted $R^2 = 0.171$) was associated with higher number of LC symptoms ($\beta = 0.25$, $t = 3.75$, $p < 0.001$) and higher stress score ($\beta = 0.20$, $t = 2.23$, $p = 0.027$).
b. Higher daytime sleepiness ($F_{6,215} = 7.47$, $p < 0.001$; adjusted $R^2 = 0.149$) was related to higher number of LC symptoms ($\beta = 0.37$, $t = 5.62$, $p < 0.001$).
c. Higher sleep inertia ($F_{6,215} = 9.07$, $p < 0.001$; adjusted $R^2 = 0.180$) was related to higher number of LC symptoms ($\beta = 0.32$, $t = 4.87$, $p < 0.001$), higher stress score ($\beta = 0.20$, $t = 2.25$, $p = 0.026$) and younger age ($\beta = -0.22$, $t = -3.26$, $p = 0.001$).
d. Higher nap frequency ($F_{6,215} = 3.69$, $p = 0.002$; adjusted $R^2 = 0.068$) was associated with higher number of LC symptoms ($\beta = 0.26$, $t = 3.76$, $p < 0.001$).
e. Higher risk of insomnia ($F_{6,215} = 15.62$, $p < 0.001$; adjusted $R^2 = 0.284$) was related to higher number of LC symptoms ($\beta = 0.37$, $t = 6.11$, $p < 0.001$) and greater stress score ($\beta = 0.20$, $t = 2.49$, $p = 0.013$).
f. Higher risk of OSA ($F_{6,215} = 6.59$, $p < 0.001$; adjusted $R^2 = 0.132$) was associated with higher number of LC symptoms ($\beta = 0.29$, $t = 4.41$, $p < 0.001$) and older age ($\beta = 0.19$, $t = 2.83$, $p = 0.005$).
g. Higher NMF ($F_{6,215} = 9.03$, $p < 0.001$; adjusted $R^2 = 0.179$) was associated with higher number of LC symptoms ($\beta = 0.28$, $t = 4.34$, $p < 0.001$), higher anxiety symptoms ($\beta = 0.21$, $t = 2.42$, $p = 0.016$) and younger age ($\beta = -0.17$, $t = -2.59$, $p = 0.010$).

The β-values (i.e. β standardized coefficients), *t*-values (i.e. *t*) and *p*-values (*p*) are all reported in Tables S2–S8.

4 | DISCUSSION

We aimed to investigate sleep and oneiric alterations associated to the LC syndrome. First, with the purpose of better characterizing the

TABLE 3 Univariate ANOVAs (SC versus LC patients), $N = 331$

	Mean (SD) SC patients $N = 98$	Mean (SD) LC patients $N = 233$	F-values (p-values)	η^2
Sleep quality	2.41 (1.120)	3.31 (1.103)	**46.05 (< 0.001)**	**0.123**
Daytime sleepiness	2.44 (1.400)	3.59 (1.469)	**43.40 (< 0.001)**	**0.117**
Sleep inertia	2.60 (1.477)	3.86 (1.398)	**54.23 (< 0.001)**	**0.142**
Nap frequency	2.45 (1.415)	2.85 (1.526)	**4.86 (0.028)**	**0.015**
Insomnia (ISI)	7.21 (5.755)	13.12 (6.135)	**66.36 (< 0.001)**	**0.168**
Apnea (STOP)	0.265 (0.547)	0.635 (0.793)	**17.73 (< 0.001)**	**0.051**
NMF	1.46 (0.827)	1.74 (1.064)	**5.54 (0.019)**	**0.017**
DRF	2.99 (1.312)	3.03 (1.440)	0.06 (0. 812)	0.000
Pandemic content frequency	1.43 (0.931)	1.43 (0.936)	0.00 (0.996)	0.000
Lucid dream frequency—awareness	2.63 (1.327)	2.97 (1.488)	3.87 (0.050)	0.012
Lucid dream frequency—manipulation	2.21 (1.341)	2.31 (1.436)	0.34 (0.560)	0.001
Sleep talking	1.27 (0.618)	1.35 (0.823)	0.88 (0.350)	0.003

Abbreviations: DRF, dream-recall frequency; ISI, Insomnia Severity Index; LC, long-COVID; NMF, nightmare frequency; SC, short-COVID; SD, standard deviation; STOP, tool to screen patients for obstructive sleep apnea. Bold values denote statistical significance at the $p < 0.05$ level.

profile of the LC subjects, we carried out a descriptive analysis showing that participants with two or more long-lasting symptoms represented > 70% of the total sample, and the majority were women. Indeed, being a woman was one of the best determinants of the LC condition in an Italian sample (Boscolo-Rizzo et al., 2021). Additionally, an investigation on 1733 patients from Wuhan, China found that 76% of the sample reported at least one post-acute symptom, with a predominance of the female gender (Huang et al., 2021). Female predisposition to insomnia is well known (Zhang & Wing, 2006) and, during the pandemic, many studies have highlighted that women have more significant sleep alterations (Scarpelli et al., 2022b). The stress associated with lockdown status and family duties could further exacerbate women's likelihood of developing sleep problems (Alfonsi et al., 2021; Salfi et al., 2021). Additionally, the "self-selection bias", typically reported in most of the investigations using surveys (Cellini et al., 2020; Franceschini et al., 2020), might have amplified the gender effect.

Consistent with Italian epidemiological data (Boscolo-Rizzo et al., 2021), the LC group was composed of a high percentage of people in the age group 40–54 years, while the youngest group, as well as students, were less affected by persistent symptoms. Interestingly, most LC participants did not report being hospitalized or having a high level of COVID-19 severity. This is partly coherent with the findings showing that LC symptoms may be unrelated to the initial disease severity. Even patients not requiring significant interventions in the acute phase can experience long-term symptoms (Krishnan et al., 2022). However, we observed that the percentage of subjects in the highest categories of care (hospitalization and ICU admission) and severity (moderate and severe infection) was greater in the LC than SC group. In this regard, some authors suggested that an increased risk gradient of new sequelae was linked with higher COVID-19 severity (Al-Aly et al., 2021; Daugherty et al., 2021). For instance, recent investigations assessed the chance of new sequelae at a 6-month follow-up showing a greater risk of long-term complications after the acute phase of the infection among non-hospitalized patients compared with control subjects, and the same pattern was observed among hospitalized COVID-19 patients compared with hospitalized none-COVID-19 individuals affected by influenza or viral lower respiratory tract diseases (Al-Aly et al., 2021; Daugherty et al., 2021).

Second, we focused on a series of sleep alterations, and found that LC reported poorer subjective sleep quality and increased sleep problems than SC participants. Specifically, the LC group showed frequent insomnia symptoms, sleep inertia, daytime sleepiness, nap frequency and apnea risk. Actually, we showed for the first time that several sleep parameters are crucial in distinguishing LC from SC subjects. Indeed, we underlined by the discriminant function analysis that insomnia and subjective sleep quality, as well as sleep inertia and daytime sleepiness, allow us to correctly classify COVID-19 patients in the SC or LC group with a classification accuracy of ~77%.

Our findings are partly in line with a recent study from the ICOSS-2 group on an international sample comparing individuals with long-lasting symptoms and healthy subjects (Merikanto et al., 2022b). The authors highlighted that long-lasting sleep symptoms are at the core of post-acute sequelae of COVID-19. In particular, LC subjects after hospitalizations reported a high rate of fatigue (61.3%), insomnia symptoms (49.6%) and excessive daytime sleepiness (35.8%; Merikanto et al., 2022b).

Our results are consistent with previous findings showing that a high proportion of patients with COVID-19 reported difficulties with sleep (Davis et al., 2021; Huang et al., 2021; Orrù et al., 2021; Xiong et al., 2021). Davis et al. (2021) revealed that insomnia symptoms are the most reported sleep alterations (60% of cases). Further, Xiong et al. (2021) found that among 538 patients with COVID-19, 17.7%

suffered from difficulty falling asleep and short or interrupted sleep after a median of 3 months from hospital discharge. Notably, a recent meta-analysis revealed that at 6–9 months, but also > 12-month follow-up, sleep disorders are commonly reported as persistent symptoms along with fatigue and dyspnea (Alkodaymi et al., 2022). It is worth noting that the higher sleep problem rate among LC individuals could represent a perpetuating factor of post-acute symptoms via the adverse effects of poor sleep on inflammation parameters. Indeed, some findings highlighted that reduced sleep duration and quality enhance viral infection risk (Gamaldo et al., 2012; Xiao et al., 2020) and, more directly, insomnia provoked an abnormal cortisol synthesis negatively impacting on immune system function (Vgontzas & Chrousos, 2002).

As far as we know, no studies have previously explored the risk of sleep apnea in follow-up studies involving patients with COVID-19. To date, some findings showed a relationship between OSA and poor COVID-19 outcomes, considering sleep apnea as a pre-existent condition that may negatively impact the course of infection. Importantly, the obstructive respiratory episodes provoking intermittent hypoxia during the night may exacerbate the hypoxia due to COVID-19 pneumonia, resulting in more negative consequences (Memtsoudis et al., 2020). We have to consider that the relationship between OSA and COVID-19 could be mediated by overweight or comorbidities such as hypertension, diabetes and cardiovascular disease, which all adversely affect COVID-19-related severity mortality outcomes (Yang et al., 2020).

Regarding oneiric activity, LC had a higher NMF than SC participants. The increased rate of nightmares could be related to the original infection as a traumatic experience and the expression of a high risk of post-traumatic stress disorder (PTSD). Indeed, one of the earliest systematic reviews on the long-term clinical effects of other respiratory syndromes such as those caused by the viruses Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-1) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) revealed that one-third of patients have prolonged anxiety, mood alterations and PTSD up to 6 months after full recovery from the acute phase of the infection (Ahmed et al., 2020). In addition, a previous investigation on SARS-CoV-1 consequences suggested the persistence of chronic fatigue syndrome and psychiatric disorders up to 4 years post-infection (Lam et al., 2009). Also, subjects reporting post-acute symptoms after COVID-19 seem to be more susceptible to suffering from PTSD (Janiri et al., 2021). More directly, Davis and colleagues (Davis et al., 2021) showed that subjects reported nightmares with a prevalence of 26% among prolonged sleep symptoms.

In order to better understand the relationship between sleep patterns and the chronic COVID-19 condition, we focused on patients with LC, showing that the number of long-lasting symptoms, age and psychological variables (i.e. anxiety and stress) are the best determinants for most sleep parameters in the LC group. Surprisingly, specific factors related to the original infection, i.e. the level of care and severity, did not predict sleep or oneiric alterations. Conversely, the number of long-lasting symptoms and specific psychological factors represent state-like variables impacting on sleep and dreams. Interestingly, the number of LC symptoms shows a significant relationship with all considered sleep measures and NMF. To some extent, our result is also consistent with the recent study by Alzueta et al. (2022), showing that the greater severity of COVID-19 symptoms was the best predictor of poor current sleep health. In this regard, we must consider that the persistent symptoms could stem from the multi-systems involvement during acute infection, and some hypothesized that patients with LC could host the virus in tissue reservoirs across the body, causing the long-lasting symptoms (Alkodaymi et al., 2022). In other words, LC syndrome can chronically affect multiple organs and, although the definition of this condition is still uncertain, we showed that the greater extension of post-acute symptoms to multiple systems would imply a general sleep impairment, both in terms of nighttime sleep quality and daily consequences. In fact, studies show that chronic medical conditions are frequently associated with sleep problems (i.e. short or long sleep, fragmented sleep, altered sleep timing, and perceptions of poor sleep/insomnia; Conley et al., 2019). The extension of persistent COVID-19 complaints to different systems and domains can also influence people's lifestyles, limiting activities and provoking changes in sleep–wake patterns (Conley et al., 2019).

Nevertheless, the underlying mechanisms of the sleep consequences of COVID-19 could be multifactorial, and may include immunological reactions, use of different medications such as corticosteroids, and psychosocial factors such as social isolation and social stigma (Fisher et al., 2021). Indeed, consistent with previous findings (Jahrami et al., 2021), we showed that the stress score was related to sleep quality, sleep inertia and insomnia. In other words, our results confirmed that stress and sleep are closely associated (Kalmbach et al., 2018). This relationship is not surprising as the persistent exposition to stressful situations such as long-lasting COVID-19 symptoms could activate stress reaction involving the autonomic nervous system and activate the hypothalamic–pituitary–adrenocortical circuit (Ulrich-Lai & Herman, 2009). In particular, as postulated by the 3P Model according to which predisposing, precipitating and perpetuating factors can contribute to insomnia (Spielman et al., 1987), we hypothesize that the physical and emotional conditions among LC subjects might provoke a hyperarousal, and promote the developing of numerous compensatory and dysfunctional behaviours (e.g. staying in bed during the day, changing or limiting their daytime routine). These latter factors could represent precipitating or perpetuating factors in the onset and maintenance of insomnia and poor sleep quality (Spielman et al., 1987).

Moreover, in line with the literature on pandemic dream activity (Kennedy et al., 2022; Scarpelli et al., 2021; Scarpelli et al., 2022a), we found that higher anxiety symptoms are one of the best explanatory variables of NMF. This result provides support to the idea that there is a continuity between mental activity during sleep and wakefulness (for review, see Scarpelli et al., 2022c), highlighting that nightmares are an expression of mental wellbeing. Overall, mental health conditions among LC subjects may have contributed to higher sleep disturbances and oneiric alterations.

Lastly, age could be considered a trait-like factor related to sleep and dream measures. Indeed, the relationship between older age and high apnea risk is not new. In this regard, a recent meta-analysis reported that advancing age increases OSA prevalence (Senaratna et al., 2017). On the other hand, younger age seemed to be associated with high sleep inertia, reported as excessive morning sleepiness. Interestingly, several studies have revealed that older subjects may show less vulnerability to sleep loss or underestimate their sleepiness, while young adults tend to report a lower level of vigilance (Bartolacci et al., 2020). Further, aging predicted a lower NMF, and this may depend on the reduced interest in dreaming during senescence, as well as a consequence due to cognitive impairment (Scarpelli et al., 2019).

5 | LIMITATIONS

Our survey has some limitations. One of the significant limitations is represented by the fact that we did not examine all 55 persistent COVID-19 symptoms identified by the existing literature (Lopez-Leon et al., 2021). This did not prevent us from analysing all aspects of the prolonged COVID-19 condition.

Like most pandemic studies, the present investigation suffers from the self-selection problem. Indeed, those with interest in LC would be more likely to participate in the survey. In addition, as mentioned, our sample included a significantly higher percentage of women. Hence, our findings should be generalized to the entire population with great caution.

Finally, we have no objective sleep measurement (e.g. actigraphic measures) and no longitudinal sleep data. These aspects would provide better understanding of sleep alterations as possible components of the LC syndrome, which future studies should consider.

6 | CONCLUSIONS

Overall, the present results highlight that sleep alterations are part of the clinical presentation of LC syndrome. In contrast to healthy subjects for whom longitudinal studies seem to indicate an alleviation of sleep disturbances over time (Gorgoni et al., 2021; Salfi et al., 2021), in subjects with chronic COVID-19 symptoms, sleep seems to show a crucial role and correlates with psychological factors and the number of persistent symptoms. Furthermore, previous pandemic investigations emphasized that oneiric activity could be considered a viable index of mental health (Fränkl et al., 2021; Scarpelli et al., 2022a). In this view, our findings confirmed that dreaming should be taken under consideration also in monitoring the post-acute phase among patients with COVID-19.

AUTHOR CONTRIBUTIONS

Conceptualization: S.S., V.A., M.G., L.D.G.; methodology: S.S., C.M.M., C.E., I.M., F.C., T.P., B.B., Y.D., B.H., Y.K.W., M.P., G.P., L.D.G.; data collection: S.S., A.D.S.; formal analysis: S.S., A.D.S., V.A., M.G.; data curation: S.S., A.D.S., G.P., L.D.G.; writing—original draft preparation: S.S., A.D.S., V.A., M.G.; writing—review and editing: C.M.M., C.E., I.M., F.C., T.P., B.B., Y.D., B.H., Y.K.W., M.P., G.P., L.D.G.

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CONFLICT OF INTEREST

All authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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