Sleep and circadian health of critical COVID-19 survivors three months after hospital discharge

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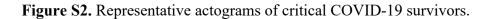**Correspondence:** Adriano D. S. Targa. Rovira Roure, 80, 25198, Lleida, Spain. Email: adrianotargads@gmail.com

Figure S1. Flowchart of the study.

Figure S2. Representative actograms of critical COVID-19 survivors.

Figure. S3. Correlations between sleep and other sequelae after hospital discharge.

Figure. S4. Correlations between fragmentation of the circadian rest-activity rhythm and other sequelae after hospital discharge.

Figure S5. Correlations between amplitude of the circadian rest-activity rhythm and other sequelae after hospital discharge.

Figure S6. Correlations between stability of the circadian rest-activity rhythm and other sequelae after hospital discharge.

Table S1. Baseline characteristics of the cohort (actigraphy).

Table S2. Other sequelae after hospital discharge.

Figure S1. Flowchart of the study.


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┌─────────────────────────┐
│ 355 patients admitted to│
│   the ICU for COVID-19  │
└─────────────────────────┘
            │
            │──────────────→  ┌─────────────────────────────┐
            │                 │          76 died            │
            │                 └─────────────────────────────┘
            │
            │──────────────→  ┌─────────────────────────────┐
            │                 │ 3 received palliative        │
            │                 │ treatment or were severely   │
            │                 │ disabled                     │
            │                 └─────────────────────────────┘
            ↓
┌─────────────────────────┐
│  276 eligible patients  │
└─────────────────────────┘
            │
            │──────────────→  ┌─────────────────────────────┐
            │                 │ 13 completed the follow-up   │
            │                 │ in another department        │
            │                 └─────────────────────────────┘
            │
            │──────────────→  ┌─────────────────────────────┐
            │                 │ 91 unreachable or declined   │
            │                 │ to attend the follow-up      │
            │                 └─────────────────────────────┘
            ↓
┌─────────────────────────┐
│   172 global analyses   │
└─────────────────────────┘
            ↓
┌─────────────────────────┐
│      65 actigraphy      │
└─────────────────────────┘
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ICU, intensive care unit.

Figure S2. Representative actograms of critical COVID-19 survivors.

The left panel represents a patient with appropriate interdaily stability, intradaily variabily, and relative amplitude; The right panel represents a patient with decreased interdaily stability, increased intradaily variabily, and decreased relative amplitude.
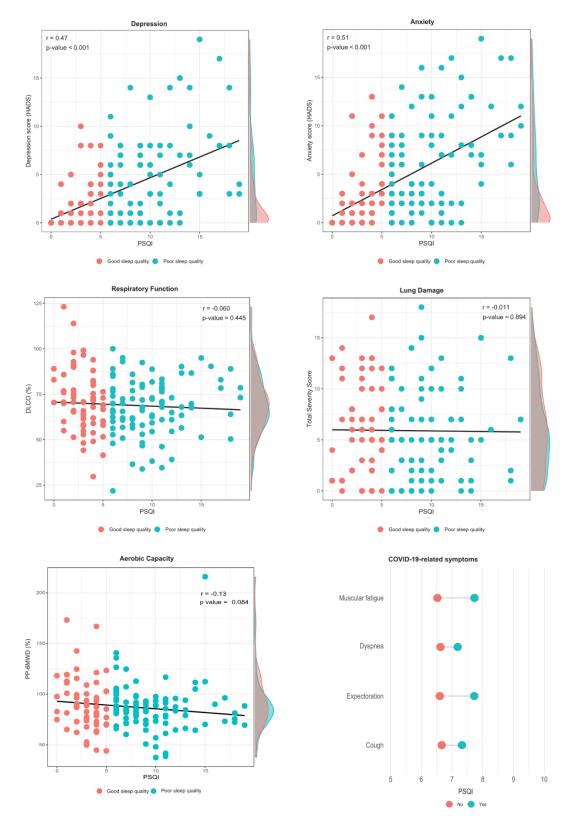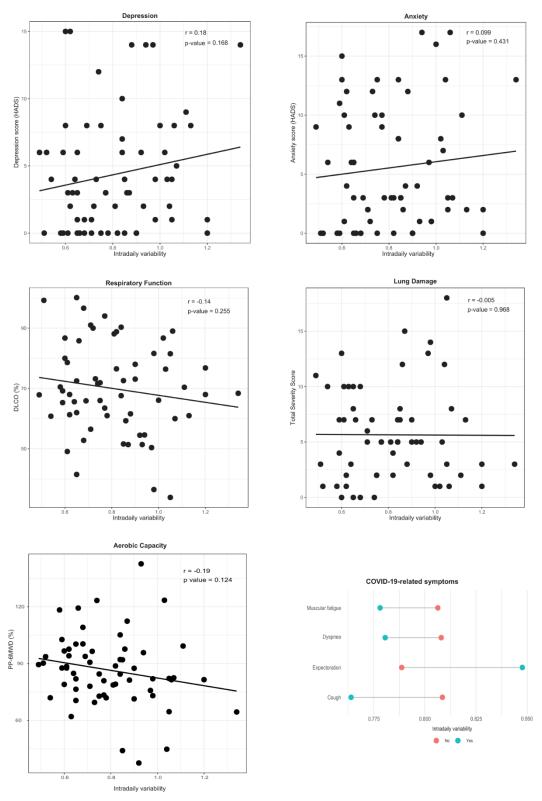
Figure. S3. Correlations between sleep and other sequelae after hospital discharge.
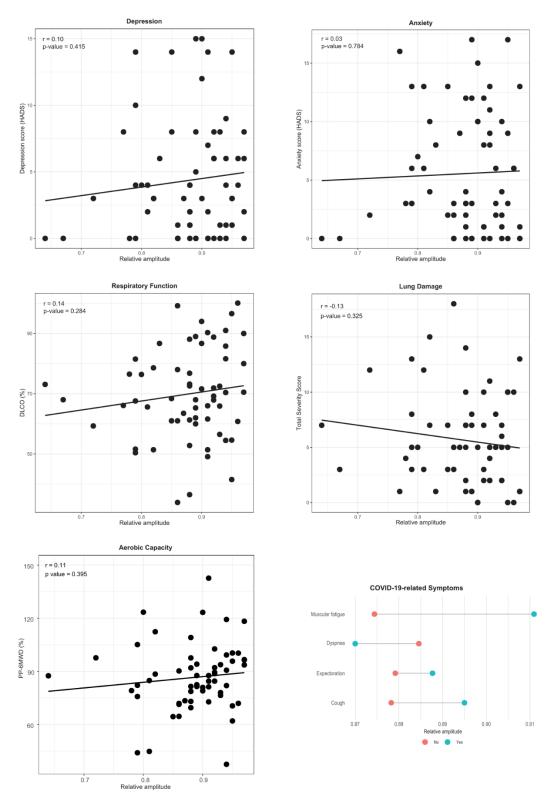

Pearson coefficient tests were performed to assess correlations between variables. The PSQI score according to the COVID-19-related symptoms are represented by the mean. The p-value threshold defining statistical significance was set at <0.05. No statistical significance was observed in relation to the COVID-19-related symptoms. DLCO, diffusing lung capacity for carbon monoxide; HADS, Hospital Anxiety and Depression Scale; PP-6MWD, percent predicted 6-minute walked distance; PSQI, Pittsburgh Sleep Quality Index.

Figure. S4. Correlations between fragmentation of the circadian rest-activity rhythm and other sequelae after hospital discharge.
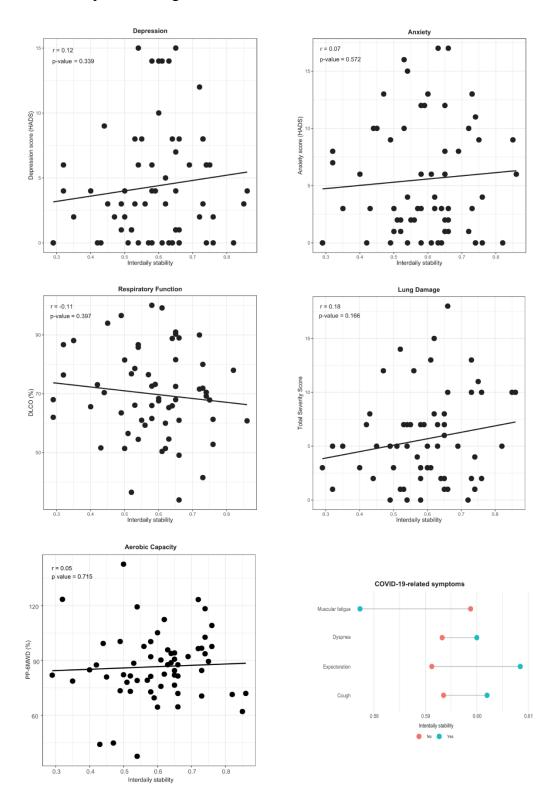

Pearson coefficient tests were performed to assess correlations between variables. The intradaily variability values according to the COVID-19-related symptoms are represented by the mean. The p-value threshold defining statistical significance was set at <0.05. No statistical significance was observed in relation to the COVID-19-related symptoms. DLCO, diffusing lung capacity for carbon monoxide; HADS, Hospital Anxiety and Depression Scale; PP-6MWD, percent predicted 6-minute walked distance.

Figure S5. Correlations between amplitude of the circadian rest-activity rhythm and other sequelae after hospital discharge.

Pearson coefficient tests were performed to assess correlations between variables. The relative amplitude values according to the COVID-19-related symptoms are represented by the mean. The p-value threshold defining statistical significance was set at <0.05. No statistical significance was observed in relation to the COVID-19-related symptoms. DLCO, diffusing lung capacity for carbon monoxide; HADS, Hospital Anxiety and Depression Scale; PP-6MWD, percent predicted 6-minute walked distance.

Figure S6. Correlations between stability of the circadian rest-activity rhythm and other sequelae after hospital discharge.

Pearson coefficient tests were performed to assess correlations between variables. The interdaily stability values according to the COVID-19-related symptoms are represented by the mean. The p-value threshold defining statistical significance was set at <0.05. No statistical significance was observed in relation to the COVID-19-related symptoms. DLCO, diffusing lung capacity for carbon monoxide; HADS, Hospital Anxiety and Depression Scale; PP-6MWD, percent predicted 6-minute walked distance.

Table S1. Baseline characteristics of the cohort (actigraphy).

Characteristics	Global n = 65
Sociodemographic data	
Sex, male	40 (61.5%)
Age, years	61.0 [53.0;66.0]
BMI, kg·m^{-2}	29.2 [27.0;33.0]
Habits	
Tobacco	
Current smoker	4 (6.15%)
Former smoker	30 (46.2%)
Non-smoker	31 (47.7%)
Chronic alcohol abuse	3 (4.61%)
Comorbidities	
Obesity	27 (42.2%)
Hypertension	34 (52.3%)
Diabetes mellitus	15 (23.1%)
Chronic lung disease	6 (9.23%)
Hospital stay	
Days	20.0 [12.0;39.0]
ICU stay	
Days	8.00 [5.00;20.0]
Minimum PaO_2 to FiO_2 ratio	138 [94.0;211]
Procedures	
Mechanical ventilation	
Invasive	28 (43.1%)
Days	18.5 [13.0;29.5]
Non-invasive	48 (73.8%)
Days	2.00 [1.00;4.00]
Prone position	30 (46.2%)
Prone position, hours	44.0 [30.5;77.5]
Pharmacotherapy	
Antibiotics	56 (86.2%)
Corticosteroids	65 (100%)
Tocilizumab	47 (72.3%)
Hydroxychloroquine	17 (26.2%)
Remdesivir	17 (26.2%)

Qualitative and quantitative data are represented as n (%) and median [p_{25};p_{75}], respectively. BMI, body mass index; FiO_2, fractional inspired oxygen; ICU, intensive care unit; n, number; p, percentile; PaO_2, arterial oxygen partial pressure. Missings: obesity, 1; minimum PaO_2/FiO_2, 5; prone position, hours, 7.

Table S2. Other sequelae after hospital discharge.

	Global	Actigraphy
	n = 172	n = 65
Respiratory evaluation		
DLCO, mL/min/mm Hg	69.1 (16.0)	69.9 (15.1)
< 60%	39 (24.7%)	13 (21.3%)
60-79%	81 (51.3%)	32 (52.5%)
≥ 80%	38 (24.1%)	16 (26.2%)
Distance (6MWT), m	408 (90.5)	395 (85.1)
Percent predicted 6MWD, %	87.8 (23.8)	86.6 (18.7)
TSS score	5.00 [2.00;8.75]	5.00 [2.00;8.00]
Mental health evaluation		
Depression score (HADS)	2.00 [0.00;6.00]	3.00 [1.00;6.00]
Normal (0-7)	143 (84.6%)	50 (76.9%)
Borderline abnormal (8-10)	16 (9.47%)	8 (12.3%)
Abnormal (11-21)	10 (5.92%)	7 (10.8%)
Anxiety score (HADS)	3.00 [1.00;8.00]	3.00 [1.00;10.0]
Normal (0-7)	126 (74.6%)	42 (64.6%)
Borderline abnormal (8-10)	19 (11.2%)	10 (15.4%)
Abnormal (11-21)	24 (14.2%)	13 (20.0%)
COVID-19-related symptoms		
Cough	28 (18.4%)	10 (16.4%)
Expectoration	25 (16.4%)	13 (21.3%)
Dyspnea		
0	74 (49.7%)	26 (42.6%)
1	42 (28.2%)	20 (32.8%)
2	28 (18.8%)	13 (21.3%)
3	4 (2.68%)	1 (1.64%)
4	1 (0.67%)	1 (1.64%)
Fever	1 (0.66%)	0 (0%)
Asthenia	1 (0.66%)	1 (1.64%)
Muscular fatigue	33 (21.7%)	11 (18.0%)

Qualitative data are represented as n (%). The means (SD) and medians [p_{25};p_{75}] were estimated for variables with normal and non-normal distributions, respectively. 6MWD, 6-minute walked distance; 6MWT, 6-minute walking test; DLCO, diffusing capacity for carbon monoxide; HADS, Hospital Anxiety and Depression Scale; n, number; p, percentile; SD, standard deviation; TSS, total severity score. Missings (global): DLCO, 14; HADS, 3; dyspnea, 23; other COVID-19-related symptoms, 20. Missings (actigraphy): DLCO, 4; dyspnea, 4; other COVID-19-related symptoms, 4.