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**Original Article** 

# Health-related quality of life and stress-related disorders in COVID-19 ICU survivors: Are they worse than with other causes of ARDS?



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Diego Gil<sup>1,\*</sup>, Carlos Tiscar<sup>1</sup>, Maria Gómez<sup>1</sup>, Javier Felices<sup>1</sup>, Luis Gajate<sup>1</sup>, Patricia Fernandez<sup>2</sup>, David Pestaña<sup>1</sup>, Tommaso Bardi<sup>1</sup>

<sup>1</sup> Department of Anaesthesiology and Critical Care, Ramón y Cajal Hospital, 28034 Madrid, Spain <sup>2</sup> Department of Psychology, Ramón y Cajal Hospital, 28034 Madrid, Spain

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#### ABSTRACT

*Background:* There are insufficient data regarding the impact of acute respiratory distress syndrome related to coronavirus disease 2019 (C-ARDS) – caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – on health-related quality of life (HRQoL) and the occurrence of stress-related disorders in coronavirus disease 2019 (COVID-19) intensive care unit (ICU) survivors. The aim of this study is to assess HRQoL and the occurrence of stress-related disorders (acute stress disorder [ASD] and post-traumatic stress disorder [PTSD]) in C-ARDS ICU survivors at 1 and 6 months following hospital discharge.

*Methods:* This prospective observational study included 90 patients treated for C-ARDS between March and May 2020 in the ICU and discharged alive from the hospital. All patients included in the study were contacted by telephone 1 month and 6 months post-hospital discharge to assess the presence of symptoms of stress-related disorders and HRQoL using the 8-item Treatment Outcome Post-traumatic Stress Disorder scale (TOP-8) and 36-item Short Form survey (SF-36). We performed univariate analyses to evaluate differences between patients who developed stress and those who did not. We also compared SF-36 scores in our sample with data from the general Spanish population and from cohorts of non–C-ARDS and severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1) survivors.

*Results*: There are 24.1% of patients showed symptoms of ASD; in 13.5% of cases the symptoms persisted 6 months later. Risk factors for the development of symptoms of ASD and PTSD are younger age, female sex, obesity, a previously diagnosed psychiatric disease and disease severity at ICU admission (P < 0.05). HRQoL was greatly affected by C-ARDS; however, there was improvement on all scales of the SF-36 at the 6-month follow-up (P < 0.05). The mean SF-36 score of our sample was higher than those previously reported in non–C-ARDS survivors (P < 0.05) for physical functioning (78.0 vs. 52.0), role functioning/physical (51.0 vs. 31.0), bodily pain (76.1 vs. 57.0), vitality (58.6 vs. 48.0), social function (72.6 vs. 63.0) and role emotional (77.4 vs. 55.0), except on the general health scale. C-ARDS survivors also scored better than SARS-CoV-1 survivors on all scales except for body pain (P < 0.05).

*Conclusions:* The impact of C-ARDS on HRQoL is substantial, with frequent occurrence of PTSD symptoms. Patients are heavily affected in all areas of health in the first month of post-hospital discharge but show a dramatic improvement within 6 months, especially in terms of physical health.

#### Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) started in 2020 and is still ongoing, and has greatly affected most countries. Severe COVID-19 induces acute respiratory distress syndrome (ARDS) often requiring mechanical ventilation and intensive care. Patients with acute respiratory distress syndrome related to coronavirus disease 2019 (C-ARDS) who require intensive care unit (ICU) admission have a high mortality rate ranging from 30% to 50%.<sup>[1]</sup> Most countries have seen ICUs overwhelmed with patients and were forced to adopt exposure restrictions. Moreover, the post-ICU environment of patients after their discharge from the hospital was altered by the imple-

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<sup>\*</sup> Corresponding author: Diego Gil, Department of Anaesthesiology and Critical Care, Ramón y Cajal Hospital, 28034 Madrid, Spain. *E-mail address:* dgilm@salud.madrid.org (D. Gil).

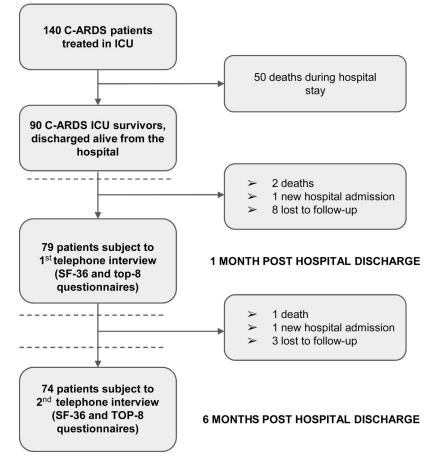


Figure 1. Flow diagram of patient selection.

ARDS: Acute respiratory distress syndrome; C-ARDS: Coronavirus disease 2019-related acute respiratory distress syndrome; HRQoL: Health-related quality of life; ICU: Intensive care unit; PTSD: Post-traumatic stress disorder.

mentation of lockdowns and social distancing. The impact of ICU stay on health-related quality of life (HRQoL) and the occurrence of stress disorders – known as post-intensive care syndrome – in ICU survivors is well established.<sup>[2,3]</sup> Acute stress disorder (ASD) occurs soon after a traumatic event, while posttraumatic stress disorder (PTSD) can be diagnosed >1 month after the event. A global effort has been made to investigate many aspects of COVID-19, mainly focusing on acute treatment and disease pathophysiology. More recently, evidence of the impact of COVID-19 on HRQoL has begun to emerge.<sup>[4,5]</sup> However, data for C-ARDS ICU survivors remain scarce. The aim of this study was to assess HRQoL and the occurrence of stress-related disorders in C-ARDS ICU survivors at 1 and 6 months after hospital discharge.

#### Methods

#### Study design

We conducted a prospective observational study on patients treated for C-ARDS between March and May 2020 in the ICU of Ramón y Cajal Hospital (Madrid, Spain), a tertiary urban academic hospital. The study combined interviews with ICU survivors at 1 month and 6 months post-ICU discharge and a retrospective review of hospital records to collect clinical data on ICU and hospital stay. The study was approved by the hospital ethics committee and informed consent was granted by all participants before inclusion through a phone call, with written, informed consent later obtained by post. The study complied with the Declaration of Helsinki. As all adult patients discharged alive from the hospital following ICU stay due to C-ARDS were included, no sample size calculation was performed. A positive COVID-19 status was determined by nasal swab polymerase chain reaction (PCR) testing.

#### Follow-up protocol

All patients who agreed to participate in the study were contacted by telephone 1 month and 6 months post-hospital discharge. Patients were subjected to a short, structured interview to assess the presence of symptoms of stress-related disorders using the 8-item Treatment Outcome Post-traumatic Stress Disorder scale (TOP-8) derived from the Davidson Trauma Scale. HRQoL was evaluated using the 36-item Short Form survey (SF-36). To minimise differences between interviewers, interviews were conducted by four researchers in a standardised manner according to a script that was developed in collaboration with the clinical psychology department. Interviewers were blinded to the clinical data of the patients. Only patients who completed both interviews and answered all questions were included in the analysis. All participating patients were able to respond to the telephone interview autonomously (i.e., no answers from caregivers or family members needed to be recorded). The flow diagram of patient selection is shown in Figure 1.

Demographic and clinical information was retrospectively collected for all patients who completed both interviews. The data included age; sex; body mass index; relevant comorbidities; duration of ICU stay; mechanical ventilation; biochemical markers of inflammation during ICU stay; pharmacologic treatments during ICU stay with a special focus on sedation, corticosteroids and other immunomodulators; complications during ICU stay; and occurrence of nosocomial infections.

The TOP-8 questionnaire evaluates the presence of symptoms of stress-related disorders through a short interview with eight questions [Supplementary Material]. Each answer is scored and ASD/PTSD is considered to be present if the total score is  $\geq 12$ .<sup>[6]</sup> Additionally, by grouping the questions into re-experiencing symptoms (questions 1 and 2), avoidance symptoms (questions 3–6) and alertness symptoms (questions 7 and 8) and calculating the mean score of each group, we identified the predominant symptoms at each time point. We also examined the presence of risk factors for the development of stress-related disorders post–C-ARDS by reviewing clinical variables in medical records including the sedation regimen used during ICU stay and the occurrence of delirium (as assessed with the Confusion Assessment Method for the ICU).

SF-36 is a validated tool for the assessment of HRQoL in ICU survivors comprising eight scales: physical functioning (PF), role functioning/physical (RP), bodily pain (BP), general health (GH), vitality (V), social functioning (SF), role functioning/emotional (RE) and mental health (MH).<sup>[7]</sup> The survey was administered during the phone interview, and responses for each item were recorded and then scored.

We compared the SF-36 score at 1 month and 6 months in our sample with data from the general Spanish population.<sup>[8]</sup> We also compared the SF-36 score at 6 months in our sample to the previously published data for cohorts of non–C-ARDS and severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1) ARDS survivors at 6 months.<sup>[9,10]</sup>

#### Statistical analysis

Quantitative variables were described with the mean and standard deviation or with the median and 25th and 75th percentiles for variables that did not follow a normal distribution. Categorical variables were described as absolute values with corresponding relative frequencies. In all statistical tests, the level of significance was  $\alpha = 0.05$ .

Continuous normal data were compared with the Student's *t*-test. Non-normally distributed data were compared with the Mann–Whitney *U test*, and categorical data were compared with the chi-squared test or Fisher's exact test when appropriate. We performed univariate analyses to evaluate differences between patients who developed stress and those who did not. A multivariate analysis could not be performed because the number of patients was insufficient. To evaluate the change in SF-36 score at 1 month and 6 months, we used the paired Student's *t*-test. Statistical analysis was performed using SPSS v20.0 (SPSS Inc., Chicago, IL, USA).

Table 1

Demographic and clinical characteristics of the study population (n = 79).

Variable	Data			
Age (years)	61 (54–66)			
Sex, male	58 (73.4)			
BMI $(kg/m^2)$	30 (6.6)			
Comorbidities				
Hypertension	33 (41.8)			
Diabetes mellitus	13 (16.5)			
Myocardial ischaemia	7 (8.9)			
Dyslipidaemia	17 (21.5)			
Chronic kidney disease	2 (2.5)			
Chronic pulmonary disease	4 (5.1)			
MH disorders	7 (8.9)			
Neurological disorders	6 (7.6)			
SAPS II	42 (32-48)			
Length of ICU stay (days)	11 (8–17)			
Length of hospital stay (days)	28 (21-42)			
Intubated	72 (91.1)			
Duration of invasive mechanical ventilation, days	7 (5-12)			
Delirium in ICU	49 (62)			
Sedation*				
Propofol	67 (84.8)			
Dexmedetomidine	50 (63.3)			
Sevoflurane	5 (6.3)			
Benzodiazepines	35 (44.3)			
Opioids	35 (44.3)			
Specific COVID-19 treatment				
High-dose corticosteroids <sup>†</sup>	39 (49.4)			
Low-dose corticosteroids	40 (50.6)			
Tocilizumab	45 (57)			
Hydroxychloroquine	74 (93.7)			
Vasopressors	50 (63.3)			
Number of prone positioning sessions				
Mean $\pm$ standard deviation	$2.29 \pm 1.70$			
Median (interquartile range)	2 (1-3)			
Minimum–maximum	0-8			
Peak IL-6 level (pg/mL)				
Median (interquartile range)	93.0 (21.2-340.0)			
Minimum–maximum	1.25-13,809			
Peak C-reactive protein level (mg/L)				
Median (interquartile range)	241.0 (171.7-316.0)			
Minimum–maximum	0–473			

Data are expressed as mean  $\pm$  standard deviation or median (interquartile range), and categorical variables are expressed as absolute *n* (%). BMI: Body mass index; COVID-19: Coronavirus disease 2019; ICU: Intensive care unit; IL-6:, Interleukin 6; MH: Mental health; SAPS: Simplified Acute Physiologic Score.

\* Most patients received at least two sedatives.

<sup>†</sup> Bolus doses  $\geq 1 \text{ mg/kg}$  of methylprednisolone or equivalent.

#### Results

Between March and May 2020, 140 C-ARDS patients were admitted to our ICU and 90 were discharged alive from the hospital [Figure 1]. The general characteristics of the study population and ICU treatment received are shown in Table 1.

#### Incidence of and risk factors for stress-related disorders

One month after hospital discharge, 24.1% of patients showed symptoms of ASD. The symptoms were still present in 13.5% of cases after 6 months [Table 2]. All patients who had a positive score for stress disorder at 6 months also had a positive score at 1 month; no patients developed these symptoms between the two follow-up time points. The most frequent symptoms of ASD and PTSD were those of avoidance (mean score of 2.42 at 1 month and 1.99 at 6 months), reliving (mean score of 2.10 at 1 month and 1.55 at 6 months) and increased arousal (mean score of 1.59 at 1 month and 1.19 at 6 months).

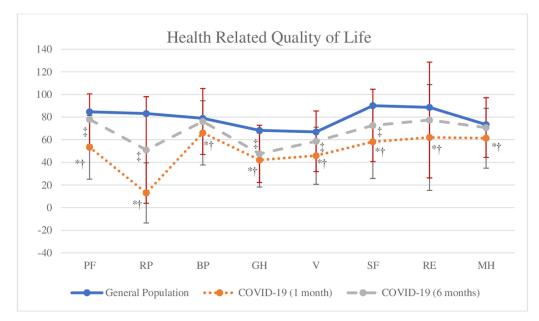


Figure 2. Results of SF-36 at the 1 month and 6 months follow-up and in the general population.

BP: Bodily pain; COVID-19: Coronavirus disease 2019; GH: General health; MH: Mental health; PF: Physical functioning; RE: Role functioning/emotional; RP: Role functioning/physical; SF: Social functioning; SF-36: 36-Item Short Form survey; V: Vitality.

\*P < 0.05 for COVID-19 (1 month) *vs.* general population;

<sup>†</sup>P < 0.05 for COVID-19 (1 month) vs. COVID-19 (6 months);

 $^{\ddagger}P < 0.05$  for COVID-19 (6 months) vs. general population.

#### Table 2

Characteristics of patients who developed symptoms of stress-related disorders at the 1- and 6-month follow-ups.

	1 month			6 months		
Variable	ASD	No ASD	P-value	PTSD	No PTSD	P-value
Number of patients	19 (24.1)	60 (75.9)	NA	10 (13.5)	64 (85.5)	NA
Age (years)	54.2 (8.3)	61.6 (8.6)	0.002	55.6 (8.7)	59.6 (9.6)	0.200
Sex						
Male	9 (15.5)	49 (84.5)	0.006	3 (30.0)	53 (82.8)	0.001
Female	10 (47.6)	11 (52.4)	0.006	7 (70.0)	11 (17.2)	0.001
BMI (kg/m <sup>2</sup> )	31.4(5.9)	29.5 (6.8)	0.200	33.7(7.2)	29.1(5.8)	0.040
Previously diagnosed MH disorders	6 (31.1)	1 (1.6)	0.001	5 (50.0)	2 (3.0)	0.001
SAPS II	36.9 (11.1)	43.6 (12.9)	0.04	41.6 (11.8)	41.8 (13.0)	0.900
Duration of mechanical ventilation (days)	7.0 (4.0-12.0)	7.0 (5.0-12.8)	0.700	9.5 (2.5–11.3)	7.0 (5.0-13.0)	0.500
Length of ICU stay (days)	9.0 (7.0-13.0)	12.5 (8.0–19.5)	0.100	9.0 (3.8-12.0)	12.0 (8.0-19.5)	0.070
Length of hospital stay (days)	27.0(15.0-30.0)	30.5 (24.0-43.8)	0.800	31.0 (32.0)	34.4 (19.0)	0.600
Peak IL-6 level (pg/mL)	93.0 (21.2-383)	104.0 (21.0-333.3)	0.600	53.0 (20.0-310.3)	94.3 (24.9-372.3)	0.400
Delirium in ICU	11 (57.9)	38 (63.3)	0.400	6 (60.0)	40 (62.5)	0.500
Benzodiazepines	10 (52.6)	25 (41.7)	0.200	4 (40.0)	32 (50.0)	0.400
Hydroxychloroquine	19 (24.1)	60 (75.9)	NA	10 (13.5)	64 (85.5)	NA

Data are expressed as mean  $\pm$  standard deviation or median (interquartile range); and categorical variables are expressed as absolute *n* (%).

ASD: Acute stress disorder; BMI: Body mass index; ICU: Intensive care unit; IL-6: Interleukin 6; MH: Mental health; NA: not available; PTSD: Post-traumatic stress disorder; SAPS: Simplified Acute Physiologic Score.

Factors associated with the development of ASD symptoms 1 month post-discharge were younger age, female sex, previously diagnosed psychiatric disorders and disease severity at ICU admission [Table 2]. Female sex, obesity and previously diagnosed psychiatric disorders were associated with PTSD symptoms at 6 months post-discharge.

#### HRQoL at 1 vs. 6 months post-discharge

The HRQoL of C-ARDS survivors was low 1 month after hospital discharge; however, there was improvement on all scales of the SF-36 at the 6-month follow-up, most notably in role limitation due to physical problems (average score of 13.0 at 1 month and 51.0 at 6 months, P < 0.05) and PF (average score of 53.3 at 1 month and 78.0 at 6 months, P < 0.05) [Figure 2].

## HRQoL at 1 and 6 months post-discharge in C-ARDS ICU survivors vs. general population

One month after hospital discharge, the HRQoL of C-ARDS ICU survivors was significantly lower than that of the general Spanish population<sup>[8]</sup> on all scales of the SF-36. The largest differences were observed in the physical domains [Figure 2]: in particular, 69 patients (87.3%) reported a significant impairment in the PF domain, 71 (89.8%) experienced role reduction due to physical problems, 57 (72.1%) had significant fatigue and 43 (54.4%) had BP. When data were adjusted for age and sex,

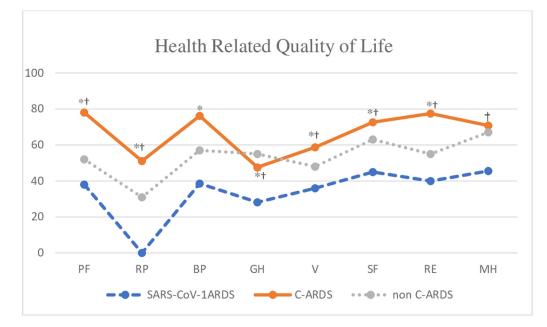


Figure 3. Results of SF-36 of SARS-CoV-1 ARDS, C-ARDS and non-C-ARDS survivors at 6 months.

ARDS: Acute respiratory distress syndrome; BP: Bodily pain; GH: General health; MH: Mental health; PF: Physical function; RE: Role functioning/emotional; RP: Role functioning/physical; SARS-CoV-1: Severe acute respiratory syndrome coronavirus-1; SF: Social function; SF-36: 36-Item Short Form survey; V: Vitality. \*P < 0.05 for C-ARDS survivors (6 months) vs. non–C-ARDS survivors (6 months);

 $^{\dagger}P < 0.05$  for C-ARDS survivors (6 months) vs. SARS-CoV-1 ARDS survivors (6 months).

#### Table 3

SF-36 scores of COVID-19 ICU survivors aged 55-64 years compared to the general Spanish population.

SF- 36 scale		1 month			6 months			
	Male Diff.	P-value	Female Diff.	<i>P</i> -value	Male Diff.	P-value	Female Diff.	<i>P</i> -value
PF	-32.1	0.001	-33.7	0.003	-3.4	0.400	-17.2	0.050
RP	-65.4	0.001	-64.2	0.001	-25.2	0.020	-58.2	0.010
BP	-3.9	0.400	-10.9	0.300	2.2	0.700	-2.9	0.800
GH	-22	0.001	-37.4	0.001	-14	0.010	-33.8	0.009
v	-18.2	0.002	-35.2	0.005	-10.6	0.050	-28.8	0.006
SF	-22.9	0.002	-37.9	0.010	-17	0.030	-36.1	0.040
RE	-23.4	0.020	-37.4	0.100	-17.8	0.050	-46.9	0.070
MH	-9.8	0.090	-26.2	0.060	-2.4	0.600	-21.8	0.040

BP: Bodily pain; COVID-19: Coronavirus disease2019; Diff.: Difference between mean values in the general Spanish population and COVID-19 survivors; GH: General health; ICU: Intensive care unit; MH: Mental health; PF: Physical functioning; RE: Role functioning/emotional; RP: Role functioning/physical; SF: Social functioning; SF-36: 36-Item Short Form survey; V: Vitality.

the reduction in HRQoL remained significant except for the BP, MH and RE scales [Table 3].

At 6 months, the reduction in HRQoL among C-ARDS ICU survivors as compared to the general Spanish population remained significant for all scales of the SF-36 except BP, RE and MH [Figure 2]. At 6 months post-discharge, 38 subjects (51.3%) still had significant impairment in PF and 42 (56.7%) reported a role reduction due to physical problems. When data were adjusted for age and sex, there were significant differences in RP, GH and SF among men between the two time points. In addition to these three scales, among women there were significant differences in V and MH [Table 3].

#### HRQoL of C-ARDS ICU survivors vs. non-C-ARDS and SARS-CoV-1 ARDS survivors

The mean SF-36 scores of non–C-ARDS survivors were higher than those previously reported.<sup>[9]</sup> This was true for all scales of

the survey except for GH, for which C-ARDS survivors scored lower than non–COVID ARDS patients. The differences were all statistically significant except for MH score. For PF (78.0 *vs.* 52.0), RP (51.0 *vs.* 31.0), BP (76.1 *vs.* 57.0), vitality (58.6 *vs.* 48.0), social function (72.6 *vs.* 63.0) and role emotional (77.4 *vs.* 55.0) [Figure 3]. C-ARDS patients had significantly higher scores than SARS-CoV-1 ARDS patients<sup>[10]</sup> on all SF-36 scales except for BP.

#### Discussion

The results of our study reveal the occurrence of symptoms of stress-related disorders and a significant impact of C-ARDS ICU admission on HRQoL after hospital discharge, although there was improvement in all scores at 6 months. The incidence of ASD symptoms was similar to that reported in a meta-analysis of COVID-19 survivors<sup>[11]</sup> and in more recent studies on COVID-19 ICU<sup>[12]</sup> and ARDS<sup>[13]</sup> survivors.

In our study, patients with the highest risk of developing symptoms of ASD and PTSD were young females with a history of psychiatric disease. These results are in line with previous findings.<sup>[14]</sup> Patients who developed ASD symptoms were more frequently obese and had a lower Simplified Acute Physiologic Score (SAPS) at ICU admission. This may be related to the influence of age on SAPS, with younger patients having a lower score but being more prone to developing ASD. The incidence of post-ICU ASD symptoms in our patients was similar to that reported by others<sup>[11,13]</sup>; however, we found that the proportion of patients developing PTSD symptoms declined significantly at 6 months whereas in the previous studies, it remained stable during the first year post-hospital discharge. It is hard to explain this discrepancy, but during the COVID-19 outbreak, a system of psychological assistance for hospital survivors and their families was implemented at our hospital and most patients received regular psychological telephone consultations in the months following discharge. Moreover, socially accepted behaviours and social support from family and friends - which can alleviate stress<sup>[15]</sup> – could have contributed to the decrease in prevalence of stress disorder although our study did not evaluate this specific aspect of recovery. The most frequent psychological symptoms in our sample at 1 month and 6 months were those related to avoidance - specifically, of information related to the pandemic to which patients were exposed after hospital discharge. This aspect is unique to the COVID-19 pandemic and difficult to compare with previous studies.

SF-36 scores in our patients were unsurprisingly lower than those in the general Spanish population. SF-36 scales most affected in COVID-19 ICU survivors were those of physical function and health, as previously observed in a mixed population of ICU survivors.<sup>[16]</sup> It should be noted that 1 month after hospital discharge, the percentage of patients with significant impairment in the physical domain was very high (93%) and higher than what would be expected from previous studies,<sup>[17,18]</sup> but in line with recently published data from a cohort of C-ARDS ICU survivors.<sup>[4,12]</sup> Moreover, a recent study on severe COVID-19 patients who did not require mechanical ventilation reported a high rate of dyspnoea (81%) at the 3-month follow-up, which was associated with chest computed tomography changes and a reduced diffusing capacity for carbon monoxide.<sup>[4]</sup>

In the 6-month follow-up of COVID-19 ICU survivors, there was significant improvement in all aspects of HRQoL explored by the SF-36, especially in the physical dimensions. Nonetheless, the scores on several scales were significantly lower than in the general Spanish population, and these differences remained significant after adjusting for age and sex. Notably, at the 6-month follow-up in the adjusted analysis, women showed a significant reduction in MH score compared to the general Spanish population. As mentioned earlier, women have a higher risk of mood disorders after hospital discharge, which should be taken into account in future post-ICU psychological care programs.

When we compared data on HRQoL of COVID-19 ICU survivors 6 months after discharge with those of non–C-ARDS survivors from a historical cohort,<sup>[9]</sup> we found that our patients were less affected in the PF, RP, RE, V and BP domains. It should be noted that patients in the ARDS study required more days of mechanical ventilation and had longer ICU and hospital stays, which may explain the observed differences. However, GH scores were more affected in C-ARDS ICU survivors; this

may be related to the novelty of SARS-CoV-2 and uncertainty about disease relapses and long-term effects as well as the general uncertainty that social restrictions and lockdowns during the pandemic have created in everyday life.

Compared to mechanically ventilated SARS-CoV-1 ARDS patients,<sup>[10]</sup> the C-ARDS patients in our study scored significantly higher on all SF-36 scales except for BP. As in the previously mentioned general non–C-ARDS cohort, the SARS-CoV-1 ARDS patients had more days of mechanical ventilation and longer ICU and hospital stays. Overall, our data showed an improved recovery of COVID-19 ICU survivors compared to allcause ARDS and SARS-CoV-1 survivors, especially in the physical dimensions of the SF-36. It is unclear whether this is due to an intrinsic characteristic of severe COVID-19 or the shorter course of mechanical ventilation and ICU stay in our cohort as a result of overall improvement in ICU practices (e.g. protective mechanical ventilation, care bundles, early physical therapy), as the studies on SARS-CoV-1 and ARDS patients were published more than a decade ago.

The results of this study highlight the considerable impact that C-ARDS has on the lives of patients who survive the ICU. These results can inform the future allocation of healthcare resources according to the needs of the growing population of COVID-19 and ICU survivors. Another strength of our study is its prospective design and ongoing nature, which may provide future insights into the post-ICU phase of COVID-19 recovery.

#### Limitations

There were several limitations to our study. First, it was a single-centre study and the results may have been influenced by centre-specific practices such as the regular psychological follow-up of COVID-19 patients after their discharge from the ICU. Second, the small sample size may have influenced the power of the study and therefore, the difference between groups should be interpreted with caution. Third, the TOP-8 instrument has been validated for the diagnosis of PTSD and is administered through a telephone interview.<sup>[6]</sup> However, we did not evaluate factors that may have played a role in the patient's response to trauma and consequent development of disorders related to stress (family situation, return to work, socioeconomic status and other social issues and psychological treatment other than the one offered via telephone by our hospital follow-up team). Fourth, the SF-36 is a widely used instrument in followup studies of ICU survivors, but the data on non-C-ARDS and SARS-CoV-1 ARDS survivors that we used for comparisons with our patients were derived from studies conducted more than a decade ago; as such, confounding factors related to general improvements in ICU practice and ARDS care may have introduced bias. Fifth, we could not normalise the comparison of clinical variables between studies although HRQoL and stress disorders include cultural aspects that could hinder comparisons between different cultures. Finally, this study included patients from the first wave of the COVID-19 pandemic, a large proportion of whom received pharmacologic treatments that were later shown to be ineffective. However, it should be noted that the two pillars of current COVID-19 treatment - namely, corticosteroids and tocilizumab - were widely used in our sample.

#### Conclusions

In conclusion, C-ARDS greatly impacted HRQoL and the occurrence of PTSD in COVID-19 patients who required ICU admission. Patients were affected in all areas of health in the first month post-hospital discharge although there was a dramatic improvement in the first 6 months, especially in terms of physical health. Additionally, the incidence of PTSD symptoms declined significantly over the 6 months post-discharge. Nonetheless, the burden of C-ARDS on patient health remained very high at the 6-month follow-up and patients' HRQoL was significantly worse than that of the general population. These results can guide future plans for post–COVID-19 healthcare, but more studies investigating the post-ICU recovery period in COVID-19 patients are needed to optimise strategies to effectively manage this healthcare crisis.

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#### **Conflicts of Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Supplementary materials

Supplementary material associated with this arbe found, the online version, ticle can in at doi:10.1016/j.jointm.2022.02.002.

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