



Health-related quality of life in survivors of severe COVID-19 infection

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Received: 19 September 2022 / Revised: 29 October 2022 / Accepted: 31 October 2022
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Abstract

Background Long-term effects of Coronavirus Disease 2019 (COVID-19) are increasingly recognized as having a significant impact on Health-Related Quality of Life (HRQoL). Understanding HRQoL status for each patient affected by long COVID-19 and its determinants may have a key role to prevent and treat this condition.

Methods In this prospective observational study conducted in a large academic COVID-19 hospital in Rome, participants were contacted 2 years after hospital admission for severe COVID-19. To assess HRQoL, EQ-5D-5L and Visual analog scale (EQ VAS) standard questionnaires were administered by interview. Logistic regression model was used to the five health dimensions as dependent variables (0 = no problem, 1 = some/extreme problem).

Key results In 137 enrolled patients, the mean pre-COVID and post-COVID EQ-5D-5L index and EQ-VAS score were 0.97 (SD 0.06), 0.79 (SD 0.26) and 72.38 (SD 15.18), respectively. After subdivision of the participants for clinical and social variables, the EQ-5D-5L index resulted significantly lower than in the pre-COVID-19 period. Female gender, unemployed status, and chronic comorbidities were the most common predictors for having any problems in each EQ-5D-5L domain, while also older age and higher Body Mass Index (BMI) showed to be related to a lower EQ-VAS score.

Conclusion HRQoL showed to be still low in patients 2 years after acute severe COVID-19. Given the significant impact of SARS-CoV-2 on long-term chronic symptoms, predictors of poor outcomes must be considered during the acute phase of illness to plan a tailored follow-up path for each patient.

Keywords Quality of life · Health-related quality of life · HRQoL · SARS-CoV2 · COVID-19 · Post-COVID

Abbreviations

COVID-19	Coronavirus disease 2019	ANOVA	Analysis of variance
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2	ICUs	Intensive care units
HRQoL	Health-related quality of life	ECMO	Extra corporeal membrane oxygenation
EQ VAS	Visual analog scale	NHF	Nasal high-flow
SPSS	Statistical package for social sciences	CPAP	Continuous positive airway pressure

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Introduction

Decreased quality of life in patients recovered from Coronavirus Disease 2019 (COVID-19) represents a concern globally [1, 2]. Indeed, although most patients recover completely within a few weeks, some patients may develop long-term sequelae after being infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lasting several months and more [3, 4]. The “Long COVID-19”, or “Post-COVID-19 condition”, is defined as ongoing or occurrence of new symptoms after 12 weeks from the onset of COVID-19, with symptoms that last at least for

8 weeks [5]. Fatigue, post-exertional malaise, and cognitive dysfunction (“brain fog”, poor attention) are the most represented manifestations, but also cardiovascular, pulmonary, and psychiatric symptoms may occur [6–9]. For these reasons, COVID-19 may have an important long-term impact on survivors’ health-related quality of life (HRQoL) [10–12].

Establishing an estimate of the prevalence of Long COVID-19 is very difficult because of the variability of the methods, the diversity of definitions, and the different populations studied [13] but also of the missing knowledge about the follow-up of survivors after 12 months [14]. To date, the estimated proportion of individuals suffering from Long COVID-19 ranges from 13 to 80% [15, 16], a proportion that shows its heavy burden on the population worldwide. Nevertheless, the pathogenesis of Long COVID-19 is not clear, although a growing body of literature suggests that obesity, metabolic disorders, and chronic diseases may play a key role in determining the severity of the acute symptoms and the long-term sequelae [17]. Thus, to better define the impact of Long COVID-19 in patients who recovered from acute COVID-19, it is necessary to record their socio-demographic and clinical data to distinguish the enabling factors from the confounding factors related to this condition.

Beyond classical clinical outcomes such as morbidity and mortality, HRQoL is a multi-dimensional concept that represents the perspective of a patient’s health state, including mental, physical, and emotional functioning [18]. Understanding HRQoL status for each patient, in particular in the setting of Long COVID-19, is important for improving symptom relief and rehabilitation, and it is also an important predictor of treatment success [19].

To date, the 2 years follow-up of survivors from severe COVID-19 during the first wave of the pandemic is still

limited, and a lack of evidence exists about the quality of life of such patients.

To fill this gap, we performed a 2 years follow-up study aimed to investigate the HRQoL in severe COVID-19 survivors.

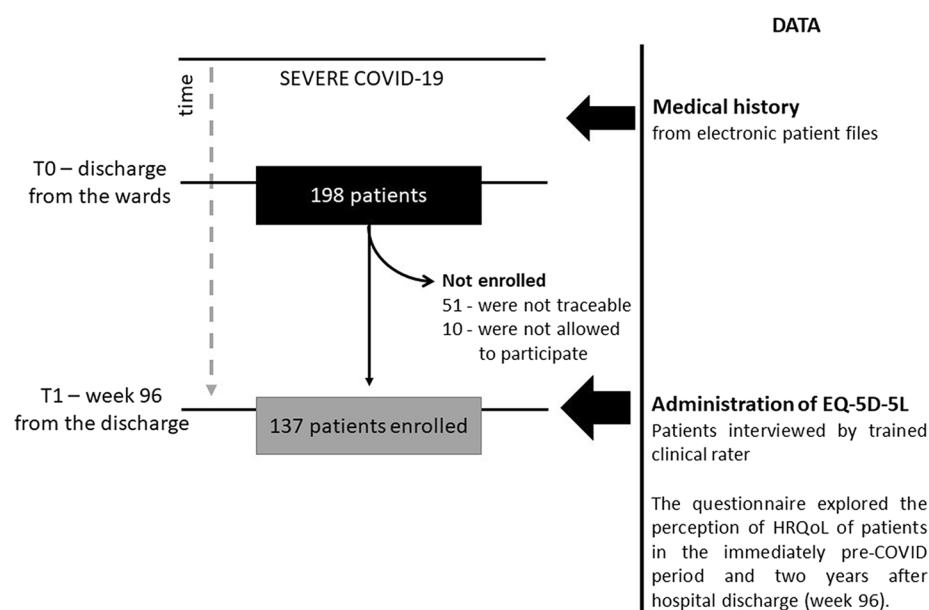
Methods

Design of study and patients

We performed a cross-sectional study of survivors of COVID-19, aged ≥ 18 , who had been hospitalized in the Infectious Diseases ward, at the Department of Public Health and Infectious Diseases of Umberto I “Sapienza” University Hospital of Rome, Italy, with confirmed COVID-19. All patients discharged to home care during the first wave of the pandemic, between March 01, 2020, and July 31, 2020, were considered for enrollment at 96 weeks from the hospital discharge. At week 96, each patient, who agreed to participate in the study, was telephone interviewed by a trained clinical rater using a standard questionnaire (Italian EQ-5D) [21–23]; we used the validated EQ-5D telephone interview mode, provided by the EuroQol group. The questionnaire explored the HRQoL in the immediately pre-COVID period and 2 years after hospital discharge (Fig. 1).

The inclusion criteria of survivors enrolled in the study were as follows: (1) confirmed COVID-19 infection by SARS-CoV-2 real-time PCR using nasal/oropharyngeal swab (2) ≥ 18 years old; (3) diagnosis of severe COVID-19, defined as indicated by NIH COVID-19 guidelines (SpO₂ < 94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired

Fig. 1 Design of the study



oxygen < 300 mm Hg, a respiratory rate > 30 breaths/min or lung infiltrates > 50%) [20].

Evaluation of quality of life

The EQ-5D is a self-completed instrument developed by the EuroQol group to assess the HRQoL defined by the EQ-5D index and comprises a short descriptive system questionnaire (EQ-5D-5L) and a visual analog scale (EQ VAS) that are cognitively undemanding, taking only a few minutes to complete [21]. The EQ-5D-5L descriptive system comprises the following five dimensions analyzing: Mobility, Self-care, Usual activities, Pain/Discomfort, and Anxiety/Depression while each dimension has three levels; no problem, some problem, extreme problem (each domain of EQ-5D 5 L is scored on a 5-point scale: 1, no problem; 2, slight problem; 3, moderate problem; 4, severe problem; and 5, unable to do). The participants were asked to indicate their health state by checking the box against the most appropriate statement concerning each dimension. The respondent's self-rated health status on a vertical VAS; the EQ VAS is a scale where patients are asked to indicate their overall health. EQ VAS is calibrated from 0 to 100 with higher scores indicating better health status; the endpoints are labeled "The best health you can imagine" and "The worst health you can imagine".

All patients were asked to rate their general health condition before and after COVID-19 disease as well as symptoms persistence at the time of the evaluation using the EQ-5D.

Data analysis

Data were analyzed with the SPSS software package (Statistical Package for Social Sciences), version 14.0. Analysis of the frequency of individual variables was conducted using descriptive statistics. The Student *t* test was performed for quantitative and the chi-square test for qualitative variables. Comparisons between groups were carried out with a *t* test, analysis of variance (ANOVA), and the Mann–Whitney *U* test for nonparametric data. The percentage of people in each dimension of EQ-5D-5L was calculated and a chi-square test was performed to examine the statistical significance of the difference between groups in the percentage of reported problems. Logistic regression model was used to the five health dimensions as dependent variables (0 = no problem, 1 = some/extreme problem). Statistical significance was set at 0.05.

Ethics

The study was approved by the Ethical Committee of Sapienza University of Rome (Ref. numb. 6484). All patients signed informed consent to participate.

Results

Out of 198 patients discharged in the analyzed period, 137 survivors of severe COVID-19 were enrolled in the present study; 61 patients were excluded from the study (51 were not traceable and 10 were not allowed to participate) (Fig. 1). No differences were found between characteristics of included and not included persons.

Demographics, comorbidities (pre-COVID-19) of the cohort, EQ VAS at week 96 from discharge, and comparison of pre-Covid EQ-5D-5L Index and post-Covid (at 2 years follow-up) Index are displayed in Table 1 and Fig. 2. Table 2 provides details of each dimension of EQ-5D-5L at a 2 years follow-up for severe COVID-19. Table 3 provides EQ-5D 5 L scores in the group pre- and post-COVID-19.

Overall, a significant worsening HRQoL at week 96 after hospital discharge compared with pre-COVID HRQoL was reported (EQ-5D-5L Index pre-COVID 0.97 (SD: 0.06) vs post-COVID 0.79 (SD: 0.26); $p < 0.01$).

After subdivision of the participants for gender, age, employment status, Body Mass Index (BMI), and suffering from chronic (respiratory, cardiac, endocrine, musculoskeletal, neurological) diseases, the mean EQ-5D-5L Index resulted significantly worsened in each of the subgroups compared to the pre-COVID-19 period ($p < 0.05$). Moreover, female gender ($p < 0.05$), older age ($p < 0.05$), BMI > 35 ($p < 0.05$), being unemployed ($p < 0.05$), suffering from chronic cardiac ($p < 0.05$), respiratory ($p < 0.05$), musculoskeletal ($p < 0.0 + 5$) diseases, were linked with lower EQ-VAS scores (Table 1).

The dimensions of EQ-5D-5L have been dichotomized, and have been used as dependent variables (0 = no problem; 1 = some/extreme problem) (Table 2). Gender, age, BMI, employment status, and suffering from chronic disease (respiratory, cardiac, endocrine, musculoskeletal, neurological) have been included as independent variables and multivariate logistic regression analysis was performed; ORs were calculated only for variables significantly linked with any dimension of EQ-5D-5L. The results showed that male gender (OR = 0.27, 95% CI 0.13–0.58), being employed (OR = 0.11, 95% CI 0.05–0.25), not suffering from chronic cardiac diseases (OR = 0.23, 95% CI 0.10–0.51) or endocrine diseases (OR = 0.39, 95% CI 0.16–0.94) were protective factors in mobility dimension; nevertheless, being unemployed may well be a result of limited mobility, thus the causal direction may be the other way around.

Self-care dimension was better preserved in employed (OR = 0.11, 95% CI 0.05–0.31) than in unemployed subjects. Not suffering from cardiovascular disease (OR = 0.39, 95% CI 0.18–0.84) and from endocrine

Table 1 Characteristics of respondents and EQ-5D-5L index and EQ-VAS scores

Patients	N (%)	EQ-5D-5L Index pre-COVID Mean (SD)	EQ-5D-5L Index post-COVID Mean (SD)	p value	EQ VAS on day of screen Mean (SD)
Total	137	0.97 (0.06)	0.79 (0.26)	<0.01	72.38 (15.18)
Sex					
Male	73 (53.3)	0.98 (0.06)	0.81 (0.24)	<0.01	75.83 (15.05)
Female	64 (46.7)	0.95 (0.08)	0.74 (0.26)	<0.01	68.20 (15.52)
Age (year)					
18–45	20 (14.6)	0.96 (0.05)	0.77 (0.31)	<0.01	80.50 (15.80)
46–70	104 (75.9)	0.98 (0.06)	0.74 (0.26)	<0.01	72.78 (17.17)
71–85	13 (9.5)	0.97 (0.06)	0.63 (0.27)	<0.01	72.70 (11.11)
Employment status					
Employed	90 (65.7)	0.95 (0.08)	0.83 (0.18)	<0.01	68.20 (15.07)
Unemployed	10 (7.3)	0.98 (0.05)	0.69 (0.29)	<0.01	62.50 (19.47)
Retired	37 (27)	0.98 (0.04)	0.69 (0.34)	<0.01	67.94 (12.13)
BMI					
< 18.5	–	–	–	–	–
18.5–24.9	44 (32.1)	0.99 (0.04)	0.83 (0.22)	<0.01	74.66 (13.18)
25–29.9	62 (45.3)	0.98 (0.05)	0.82 (0.21)	<0.01	72.82 (13.60)
30–35	26 (18.9)	0.99 (0.005)	0.79 (0.18)	<0.01	73.16 (16.00)
> 35	5 (3.7)	0.96 (0.05)	0.75 (0.18)	<0.05	56.00 (16.73)
Chronic diseases					
Chronic respiratory diseases					
Asthma	11 (8)	0.97 (0.06)	0.579 (0.30)	<0.05	65.83 (14.63)
Chronic obstructive pulmonary disease	9 (6.6)	0.903 (0.09)	0.748 (0.14)	0.07	67.5 (12.31)
Cardiovascular disease					
Heart failure					
Hypertension	35 (25.5)	0.97 (0.05)	0.73 (0.26)	<0.01	69.68 (16.27)
Ischemic heart disease	2 (1.5)	1	0.81 (0.049)	<0.05	55 (7.07)
Endocrine					
Type II diabetes	13 (9.5)	0.901 (0.13)	0.715 (0.25)	<0.05	70.77 (14.55)
Thyroid disease	12 (8.8)	0.98 (0.06)	0.63 (0.24)	<0.01	63.3 (13.20)
Musculoskeletal diseases	9 (6.6)	0.95 (0.05)	0.73 (0.30)	<0.05	67.22 (17.34)
Neurological diseases	8 (5.8)	0.93 (0.12)	0.78 (0.22)	0.13	75.62 (14.50)

diseases (OR = 0.34 95% CI 0.14–0.83) were protective in the preservation of usual activities dimension. To be aged 18–45 (OR = 0.28, 95% CI 0.09–0.89), or to be employed (OR = 0.16, 95% CI 0.06–0.31) showed a significant protective relationship in pain/discomfort dimension. Male gender (OR = 0.29, 95% CI 0.15–0.60), being employed (OR = 0.11, 95% CI 0.05–0.26), not suffering from chronic respiratory disease (OR = 0.30, 95% CI 0.11–0.83) were protective factors in Anxiety/depression dimension.

Discussion

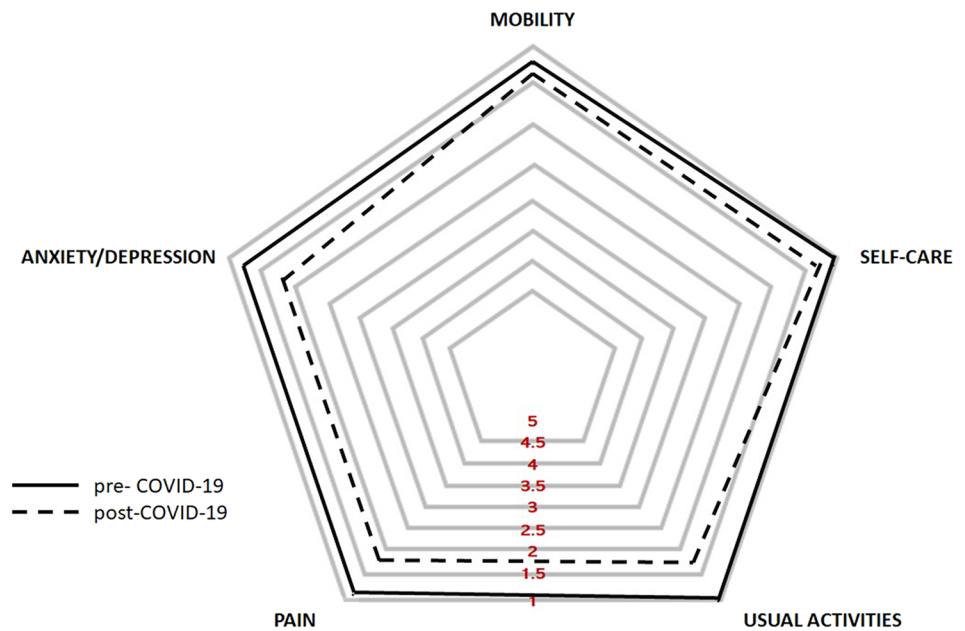
To our knowledge, this is the first study exploring health-related quality of life in patients 2 years after severe COVID-19. Our findings showed a persistent perceived worsened

health status of all the survivors of severe COVID-19 measured by EQ-5D-5L Index at 2 years follow-up (Fig. 2). The mean pre-COVID and post-COVID EQ-5D-5L index and EQ-VAS score were 0.97 (SD: 0.06), 0.79 (SD: 0.26) and 72.38 (SD: 15.18), respectively.

This study showed a week 96 EQ-5D-5L Index score of 0.79 (SD: 0.26), which is significantly lower than the general population (ranging from 0.850 to 0.949) [23, 24]. Previous studies assessing HRQoL in COVID-19 survivors using EQ-5D-5L showed instead a lower index, ranging from 0.612 to 0.714 [25–29]. However, these evaluations were performed much earlier than ours, from 4 to 12 weeks after the onset of symptoms and were not targeted on severe cases.

Regarding the mean EQ-VAS score, our findings of 72.38 (SD: 15.18) accorded to previously published results in which scores ranged from 70 to 90% [30–33], although none

Fig. 2 two-dimensional graphic representation of the pre- and post-COVID-19 EQ-5D-5L scores in the survivors of severe COVID-19 (each domain of EQ-5D-5L is scored on a 5-point scale: 1, no problem; 2, slight problem; 3, moderate problem; 4, severe problem; and 5, unable to do)



of them were performed over 6 months after acute COVID-19. In our study, the lowest EQ-VAS scores were observed in the female gender, in those aged > 71, in subjects with BMI over 35, and in those suffering from chronic diseases. Being employed was the most frequent protective variable in four domains of EQ-5D-5L (mobility, self-care, pain/discomfort, anxiety/depression), followed by the male gender (domains of mobility, anxiety/depression); moreover, being free from cardiovascular or endocrine diseases (domains of mobility, usual activities) and from chronic respiratory diseases (domain of anxiety/depression) were also protective factors.

These findings accord with the results of Peters et al., who conducted a cross-sectional study to examine the employees' consequences of COVID-19 infection, the risk factors, and the impact on quality of life over time. The author identifies older age, female gender, and medically diagnosed pre-existing illnesses, as risk factors associated with the persistence of symptoms longer than three months [35].

Problems in mobility dimension were the most frequent issue among survivors of severe COVID-19 enrolled in the present study; female gender, retired or not employed status, suffering from hypertension or endocrine diseases (type II diabetes, thyroid diseases) showed as predictors of problems in mobility dimension.

The second reported problem was anxiety/depression; female gender, unemployed or retired status, and suffering from respiratory diseases (asthma or chronic obstructive pulmonary disease) were linked to lower scores in the anxiety/depression dimension.

Pain/discomfort and issues in usual activities were the third reported problems; 46 or over years old, unemployed, or retired status were predictors for pain/discomfort;

hypertension, cardiac ischemic disease, type 2 diabetes, and thyroid diseases were linked to worsened usual activities at a 2 years follow-up.

Finally, we found a relationship between worsened self-care and unemployed status.

Our findings showed that being employed was the most common protective factor for both absolute EQ VAS/EQ-5D-5L Index scores and for each EQ-5D-5L dimension.

Unemployment status has already been found to be strongly associated with an increased risk of all-cause mortality in young people, suicide, and the development of mental illness in the general population [36, 37]. Furthermore, in our previous study, we found a relation between being unemployed or fired and the development of Post-Traumatic Stress Disorder in COVID-19 survivors [38].

Employment status has been one of the main concerns among the socio-economic consequences of the pandemic in Italy [39]. Thousands of people lost their job or experienced a large reduction in their salaries, most of them during the first wave of the pandemic. Showing the strong association between employment and HRQoL, our findings underline that new political measures in labor sectors are necessary from an economic, social but also public health point of view.

The study showed also that suffering from chronic diseases is an important variable associated with low absolute EQ VAS and EQ-5D-5L scores. In particular, being affected by chronic pulmonary diseases or cardiovascular diseases are the most represented risk factors in most of the EQ-5D-5L dimensions. Anyway, the association of chronic disease with worse quality of life could be independent from the COVID survivorship: in this sense chronic disease could

Table 2 (continued)

	Mobility		Self-care		Usual activities		Pain/discomfort		Anxiety/depression	
	No	Some or extreme	No	Some or extreme	No	Some or extreme	No	Some or extreme	No	Some or extreme
Obstructive sleep apnea	--	--	--	--	--	--	--	--	--	--
Cardiovascular diseases										
No Cardiovascular disease after Covid	57.7	15.3	64.9	8.1	51.8	21.1	43.1	29.9	37.2	35.8
	<i>p</i> < 0.01 OR = 0.23, 95% CI: 0.10–0.51		<i>p</i> = 0.60		<i>p</i> < 0.05 OR = 0.39, 95% CI: 0.18–0.84		<i>p</i> = 0.54		<i>p</i> = 0.96	
Heart failure	--	--	--	--	--	--	--	--	--	--
Hypertension	10.9	14.6	21.2	4.3	13.2	12.4	13.2	12.4	11.7	13.1
Ischemic heart disease	1.5	0	1.5	0	0	1.5	0.7	0.7	1.5	0.7
Endocrine diseases										
No Endocrine diseases	54.7	27.1	70.8	10.9	56.9	24.8	43.8	37.9	42.3	39.4
	<i>p</i> < 0.05 OR = 0.39, 95% CI: 0.16–0.94		<i>p</i> = 0.98		<i>p</i> < 0.05 OR = 0.34, 95% CI: 0.14–0.83		<i>p</i> = 0.17		<i>p</i> = 0.63	
Type II diabetes	5.1	4.4	7.3	2.2	4.4	5.1	5.1	4.4	4.4	5.1
Thyroid disease	2.9	5.8	8.1	0.7	3.6	5.1	1.5	7.3	3.7	5.1
Musculoskeletal diseases										
No Musculoskeletal diseases	58.4	35.1	81.7	11.7	59.8	33.7	48.9	44.5	45.9	47.5
	<i>p</i> = 0.47		<i>p</i> = 0.69		<i>p</i> = 0.88		<i>p</i> = 0.65		<i>p</i> = 0.95	
Musculoskeletal diseases	2.9	3.6	5.9	0.7	3.6	2.9	2.9	3.7	2.9	3.7
Neurological diseases										
No Neurological diseases	80.3	13.9	82.5	11.7	58.4	35.8	51.1	43.1	47.4	46.8
	<i>p</i> = 0.15		<i>p</i> = 0.70		<i>p</i> = 0.73		<i>p</i> = 0.58		<i>p</i> = 0.73	
Neurological diseases	4.3	1.5	4.3	1.5	3.6	2.2	2.2	3.6	2.2	3.6

Bold text indicates a statistically significant correlation with a *p*-value less than 0.05

Table 3 EQ-5D 5 L scores in the group pre- and post-COVID-19 (each domain of EQ-5D 5 L is scored on a 5-point scale: 1, no problem; 2, slight problem; 3, moderate problem; 4, severe problem; and 5, unable to do)

Dimension	Pre-COVID EQ-5D 5 L scores (mean and SD)	Post-COVID EQ-5D 5 L scores (mean and SD)	<i>p</i>
Mobility	1.13 (0.40)	1.37 (0.80)	<0.0017
Self-care	1.02 (0.15)	1.26 (0.71)	<0.0001
Usual act	1.03 (0.21)	1.72 (0.99)	<0.0001
Pain	1.12 (0.40)	1.79 (0.97)	<0.0001
Anxiety	1.18 (0.50)	1.77 (0.99)	<0.0001

be considered more an independent factor that affects the EQ-5D than a predictor of post-COVID severity.

The mobility dimension was found to be the most frequently reported problem 2 years after acute COVID-19, followed by the anxiety/depression dimension. This is a new finding compared with the previous study above mentioned [26–30], in which other dimensions are most represented, commonly pain/discomfort and anxiety/depression, and should be considered in the management of patients affected by Long COVID-19.

The study results highlight that healthcare demands related to COVID-19 will continue to grow in the near future. To address the growing health demands regarding mental and physical symptoms of long-term survivors of severe COVID-19, it is now necessary to provide scalable and sustainable health models by adopting a multidisciplinary approach to the patients. For example, Harenwall et al., offering a rehabilitation course based on integrated care of mental and somatic symptoms, showed a significant improvement in VAS score and EQ-5D-5L Index respectively 10% and 7% [40]. Despite this, to date, there is little evidence to guide the development of such rehabilitation services for patients presenting with post-COVID-19 conditions.

Given the significant impact of SARS-CoV-2 on chronic symptoms following the resolution of the acute phase, and the current lack of effective options to contrast it becomes mandatory to map all symptoms patients experienced in the acute COVID-19 and during the follow-up to and define tailored paths to initiate adequate holistic care. Given the involvement of all the five domains of EQ 5D 5L, we hypothesize that post-COVID-19 syndrome is a multisystem condition and requires a multidisciplinary approach to its management.

On the other hand, although the overall quality of life after 2 years from COVID was perceived by patients as significantly worse than pre-COVID, it should be noted that in absolute terms the impairment observed in the five dimensions oscillates between “no problem” and “slight

problem”. In no “dimension” the observed mean values reach the levels indicating “moderate problem”, “severe problem” or “unable to do”. This aspect highlights that the survivors of a severe COVID, while still remaining in a worse condition compared to the pre-COVID period, overall have an acceptable quality of life after 2 years of recovery. Given the study design, these findings could be affected by recall bias and, therefore caution should be taken before generalizing the conclusions of the present study; nevertheless, the adoption of standardized questionnaires (EQ-5D-5L and EQ VAS) could have minimized such risk of bias and, in line with other studies [41], the results should be really representative of the HRQoL in the studied population.

Limitations

The study has several limitations. First, telephone interviews had certain limitations compared with face-to-face assessments, although this method has already been used successfully in previous research during the current pandemic [1]. Second, the small sample size and the single-center design may have limited the generalizability to other settings. Third, the evaluation of pre-COVID-19 health was recorded by retrospective self-reports questionnaire. The use of this measurement has been supported by several studies, but caution should be taken in interpreting this data [2, 42].

Fourth, the results presented should be referred only to the specific population analyzed in this study: all enrolled patients were recruited between subjects hospitalized in infectious disease wards while none had been admitted to COVID intensive care units (ICUs). However, it should be noted that in our setting, only in patients undergoing orotracheal intubation or supported with Extra Corporeal Membrane Oxygenation (ECMO) were admitted to ICUs during the first pandemic wave. Conversely, subjects who needed oxygen therapy with Venturi mask or with nasal high-flow (NHF) therapy or with Continuous Positive Airway Pressure (CPAP) were hospitalized in infectious disease wards. In the analysis of the data, it was not possible to skim the results based on the type of oxygen therapy support since in most cases the patients had been subjected to more than one type of support depending on their clinical conditions.

Fifth, our findings are subject to the limitations inherent in cross-sectional data. Therefore, in future studies, causal relationships among variables should be analyzed using longitudinal study designs.

Finally, the findings of the present study are referred to the first wave of pandemic and, therefore, they are not generalizable to all severe cases of COVID occurred after the availability of Sars-Cov-2 vaccine.

Conclusions

Our findings provide important evidence on health-related quality of life in patients 2 years after acute COVID-19. In particular, principal risk factors for a poor HRQoL outcome must take into account by clinicians during the acute COVID-19 phase, to plan a tailored long-term follow-up path. Furthermore, given the significant impact of SARS-CoV-2 chronic symptoms in terms of long-term prevalence and burden for each patient, new interventions in public health and social fields are mandatory.

Author contributions Substantial contributions to the conception and design of the work and wrote the manuscript: GE, GE, GC; Acquisition of data: PV, VC, EGC, LS, LM; analysis, or interpretation of data: GE, PV, LM, SF, revising it critically for important intellectual content: CMM, GE, GC.

Funding This research received no grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that they do not have a conflict of interest.

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