Research Article

Cognitive Trajectories and Psychological Well-Being of Severe SARS-CoV-2 Patients admitted to the Intensive Care Unit: A One-Year Longitudinal Analysis Including Caregiver Perspectives

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Abstract

We investigated the cognitive profile and psychological well-being of severe SARS-CoV-2 patients admitted to the Intensive Care Unit (ICU), including caregiver perspectives. We assessed caregivers' quality of life, psychological distress and satisfaction with the information received by healthcare professionals. Consecutive patients with SARS-CoV-2 infection requiring ICU admission were recruited together with a caregiver. Patients with previous cognitive disorders were excluded. Comprehensive neuropsychological evaluation was conducted at three months (T1) and 12 months (T2) after ICU discharge and both patients and caregivers filled out validated questionnaires.

Out of 158 patients admitted to ICU in the study period, 28 met the inclusion criteria. All 28 patients (23 males) completed the assessment at 3 and 12 months. Cognitive performance analysis revealed that 40% had cognitive impairment at T1, decreasing to 33% at T2. Long-term memory was the most impaired domain at T1 and T2. [1] One-way MANOVA showed significant improvement in global cognitive efficacy and phonemic access over time. Lower performances in long-term memory were significantly associated with longer ICU stay, duration of mechanical ventilation, higher Sequential Organ Failure Assessment (SOFA) score and longer treatment with benzodiazepines, opioids, antipsychotic drugs and propofol over time.

Quality of life (QoL) analysis indicated that 71% of patients had a reduced QoL due to physical limitations at T1, which improved 12 months later. Psychological burden-related QoL remained stable. Subjectively perceived QoL worsened over time. Caregiver mental distress was moderate in 3 out of 25 caregivers on SQR-20. Caregivers reported high satisfaction (90%) with communication between caregivers and healthcare staff evaluated by COSM-R.

In conclusion, our study provides valuable insights into the cognitive and psychological well-being of severe COVID-19 patients admitted to the ICU, emphasizing the importance of long-term follow-up. The study sheds light on the potential for cognitive improvement within the initial 12 months post-ICU discharge, suggesting that early and meticulous neuropsychological assessment could guide interventions to enhance prognosis. Further, the role of caregivers as a meticulous investigator of the patient's disorder emphasizes the need of holistic support.

Introduction

he early stages of the COVID-19 pandemic revealed that nearly 1 in 10 infected individuals required hospitalization and admission to an intensive care unit (ICU) due to acute respiratory distress syndrome (ARDS) necessitating mechanical ventilation [1]. Post-COVID-19 syndrome has since emerged, marked by prevalent and debilitating cognitive impairment and psychological distress [2], especially in ICU patients who experience more severe impairment compared to those not requiring ICU care [3].

Reports of persistent cognitive impairment following ICU discharge in COVID-19 patients have been described [4,5,6] but the variability in cognitive assessment tools, ranging from surveys to telephone assessments, challenges the determination of the true prevalence of cognitive impairment in this population.

The profile of post-COVID-19 cognitive impairment, often assessed through cognitive screening tests (e.g., the MoCA or Mini–Mental State Examination), administered either in person [6,7,8,9] or by telephone [10], limits the reliability of the data. Comprehensive neuropsychological assessment, although carried out in a few studies, suggests the involvement of processing speed and long-term memory [4], potentially compromising executive functions.

Psychological distress is a further concern, affecting over 50% of the patients with critical SARS-CoV-2 infection, manifesting as anxiety, depression, trauma and stress-related disorders [4,11]. Caregivers facing isolation and inability to communicate with the patients also experience heightened psychological distress [12].

Given the extensive impact of SARS-CoV-2 infection on various mental dimensions, including both cognitive and emotional domains, there is an urgent need for a comprehensive longitudinal investigation, encompassing cognitive assessment, quality of life evaluation, and an exploration of psychological well-being among patients who have undergone critical SARS-CoV-2. The pivotal role of the caregivers, an examination of their quality of life and psychological well-being, in parallel to their interactions with ICU staff, stand as a crucial facet to be further explored. Hence, the primary objective of this study is to analyse the prevalence and nature of cognitive deficits, as well as the trajectories of quality of life and psychological well-being in a prospective, consecutive cohort of COVID-19 patients who received ICU care and mechanical ventilation due to ARDS.

To achieve these objectives, this study proposes an in-depth evaluation employing a comprehensive assessment of patients' cognition, encompassing patients and caregivers' psychological well-being and healthcare interactions, thus contributing to a more comprehensive understanding of the pandemic's consequences. This assessment was conducted at two distinct intervals, 3 and 12 months post ICU discharge, highlighting the potential persistence of cognitive impairments and exploring the impact of time on recovery trajectories. Furthermore, this study aims to identify the clinical and biometric factors associated with cognitive impairments, thereby contributing to the understanding of the mechanisms underlying such deficits.

Methods

During the first and second wave of SARS-CoV-2 infection (i.e., from March 1 to April 30, 2020, and from November 1 to 30, 2020) all consecutive patients aged 18 years or older, with SARS-CoV-2 infection confirmed by PCR on oro-nasopharyngeal swab, requiring ICU admission and mechanical intubation for acute respiratory distress syndrome (ARDS) [13], and discharged, were enrolled together with a caregiver from Sant'Orsola-Malpighi University Hospital of Bologna, Northern Italy. As caregivers we considered family members or close relatives who provide care voluntarily to patients at home. Exclusion criteria were: previous neurological and psychiatric diseases, presence of cognitive impairment or dementia, substance or alcohol abuse, assessed by in-depth caregiver interview and clinical records evaluation. Patients not living in Bologna or the province were also excluded because they could not undergo on-site clinical and neuropsychological evaluations as pandemic travel restrictions were current at that time. Patients were recruited on ICU admission (T0), when the following clinical and biometric data were collected: age, sex, PaO2/FiO2 ratio (P/F ratio), C-reactive protein (CRP), procalcitonin test (PCT), interleukin-6 (IL-6), d-dimer, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Richmond Agitation-Sedation Scale (RASS) score, sedative drugs used and days of treatment, days of mechanical ventilation and length of ICU stay. Worst P/F, worst SOFA score, worst APACHE II score, were also collected.

Cognitive function, quality of life and psychological well-being assessment

At three months (T1) and 12 months (T2) following ICU discharge, patients underwent a rigorous and standardized neuropsychological evaluation, along with self-reported questionnaires pertaining to quality of life (QoL) and psychological well-being. The neuropsychological battery, which encompassed a range of cognitive domains, was administered by two trained neuropsychologists (S.F., R.S.) in sessions lasting approximately 60 to 90 minutes each.

Likewise, caregivers completed validated questionnaires that gauged various dimensions of psychological well-being at the corresponding time point. At T1, an additional aspect of the caregiver experience, namely the degree of satisfaction with their interaction with ICU staff, was also assessed. For the purpose of classifying cognitive impairment, well-established criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) for minor and major neurocognitive disorders were employed [14].

QoL assessment was carried out through a multifaceted approach. This included the Short Form Health Survey (SF-12) [15] and the 5-level EQ-5D version (EQ-5D-5L) EuroQol Group in 2009. Additionally, a patient-centered perspective was incorporated using the Schedule for the Evaluation of Individual Quality of Life (SEIQoL) [16].

Emotional assessment was evaluated through the Hospital Anxiety and Depression Scale (HADS) [17], a widely adopted in-

strument particularly relevant for critically ill patients, as evidenced by its applicability in similar contexts [18,19]. Caregivers were engaged through the completion of the SQR-20 Self-Reporting Questionnaire (SQR-20)20 for the evaluation of physical and psycho-emotional symptoms. Furthermore, an adapted version of a questionnaire originally designed to assess satisfaction with received information and healthcare provider relationship, i.e.

the COSM-R (Communication medical doctor – patients – Revised (COSM-R) [21,22], was employed to gauge caregivers' perspective on these aspects.

Table 1 outlines the data collection timeline and the questionnaires for both patients and caregivers. Additionally, Table 2 details the specific components of the neuropsychological evaluation of patients.

Table 1: Protocol of the study.

	Data collection	Timing
Patients	Clinical and biometric data	During ICU stay
	Hospital Anxiety and Depression Scale (HADS)	T1
	Short Form Health Survey (SF-12)	T1 - T2
	Schedule for the Evaluation of Individual Quality of Life (SEIQol)	T1 - T2
	5 level EuroQol 5D version (EQ-5D-5L)	T1 - T2
	Neuropsychological evaluation (Table 2)	T1-T2
Caregivers	Questionnaire on satisfaction of doctor-patient communication (COSM-COVID-CAREGIVER)	T1
	Self Reporting Questionnaire (SQR-20)	T1 - T2
	Schedule for the Evaluation of Individual Quality of Life (SEIQol)	T1 - T2

Table 2: Neuropsychological evaluation.

Cognitive function	Test	Cut-off	References
Global cognition	Montreal Cognitive Assessment Test (MoCA)	> 15.51	Santangelo et al. 1993
Long-term Memory	Rey's 15 words: immediate recall (RAVLT IR)	> 28.52	Carlesimo et al. 1996
	Rey's 15 words: delayed recall (RAVLT DR)	> 4.68	Carlesimo et al. 1996
	Rey's figure delayed recall (Rey D)	> 9.46	Caffarra et al. 2002
Short-term Memory	Immediate visual memory (IVM)	> 13.84	Carlesimo et al. 1996
	Digit Span: forward (DA)	> 4.25	Monaco et al. 2013
	Corsi Span: forward (CA)	> 3.82	Monaco et al. 2013
Working Memory	Digit Span: backward (DI)	> 2.64	Monaco et al. 2013
	Corsi Span: backward (CI)	> 3.07	Monaco et al. 2013
Attention	Barrage test	< 2.5	Gallassi et al. 2008
	Barrage Time	< 90	Gallassi et al. 2008
	Barrage Score	> 9	Gallassi et al. 2008
	Barrage Errors	< 2	Gallassi et al. 2008
	Attentive Matrices	> 30	Spinnler and Tognoni 1987
Executive Functioning	Simple Verbal Analogies Test (SVAT)	> 13.92	Gallassi et al. 2014
	Frontal Assessment Battery (FAB)	> 13.4	Apollonio et al. 2005
	Stroop Test: time	< 36.93	Caffarra et al. 2002
	Stroop Test: errors	< 4.25	Caffarra et al. 2002
Language	Verbal Phonemic Fluency (VF)	> 17.34	Carlesimo et al. 1996
	Verbal Semantic Fluency (SF)	> 24.9	Novelli et al. 1986
Visuo-spatial and constructive functions	Rey's Copy Drawing (Rey C)	> 28.87	Caffarra et al. 2002

The current study was approved by the Ethics Committee of the Local Health Authority of Bologna, Italy (reference number 533/2020/Oss/AOUBo) and performed in accordance with the principles of good clinical practice. Participation of each patient was contingent upon obtaining written informed consent.

Statistical analysis

Initial data exploration encompassed descriptive statistics to derive concise numerical summaries of neuropsychological tests, questionnaires, and clinical data. Pearson correlations were conducted to discern potential associations between continuous variables. In order to elucidate temporal variations, separate multivariate analysis of variance (MANOVA) tests, with time as a within-subject factor (T1 vs. T2), were executed to assess cognitive and affective scores. Qualitative data stemming from open-ended responses to SEIQoL were subjected to qualitative analysis.

Results

Out of 158 patients admitted to our ICU during the study period, 28 met the inclusion criteria. All 28 patients (23 males) were included and completed the clinical assessment both at 3 and 12 months. The sample recruitment and procedure overview and demographic variables are reported in Fig.1 and Table 2a, respectively.

Cognitive Performance

Of the 28 patients, 39% (11/28) had a neurocognitive disorder at T1, overall minor except one who had a major neurocognitive impairment. At T2, 33% (9/28) presented with a neurocognitive disorder, overall mild. The only patient with T1 major neurocognitive disorder remained stable at 12 months. Long-term memory was the most impaired domain (25% of patients), followed by attention (11%), working memory (7%), language (7%) and executive functions (4%) at T1. At T2, long-term memory was still the most frequent deficit (20 %), followed by executive functions (8%), working memory (4%) and language (4%). Attention was never impaired at T2. Praxis was never impaired either at T1 or T2 (Figure 2).
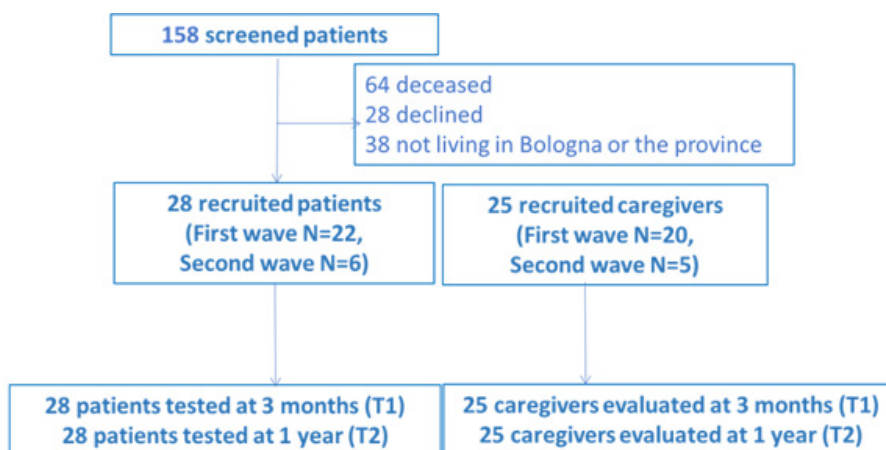

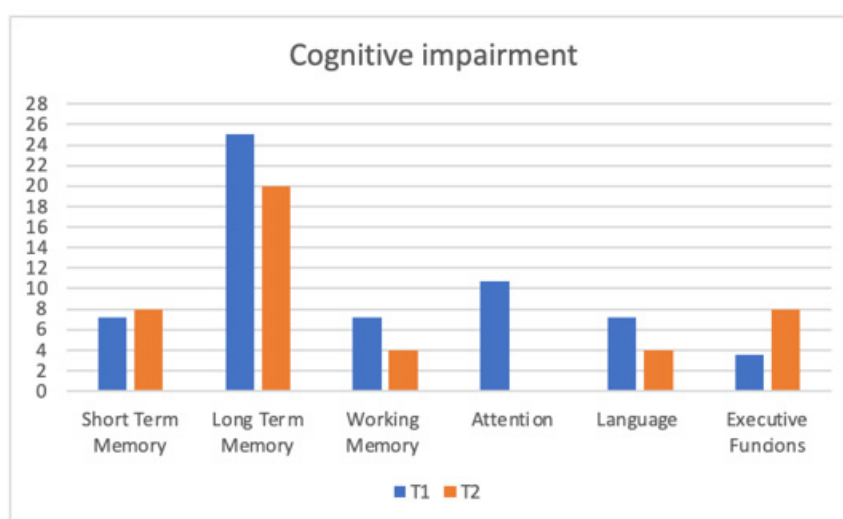**Figure 1:** Description of the sample.

Figure 2: Frequency of impaired cognitive domains.

A one-way MANOVA, with time as a within-subject factor (T1 vs. T2), showed a significant difference on cognitive performance, $F_{(6,18)} = 2.98$, $p = 0.03$, $\eta p2 = 0.49$. Specifically, global cognitive efficiency, i.e. MoCa score, $F_{(1,23)} = 6.77$, $p = 0.02$, $\eta p2 = 0.23$, and phonemic access, i.e. phonemic fluency score, $F_{(1,23)} = 9.93$, $p = 0.004$, $\eta p2 = 0.30$, improved over time (25.17 ±2.53 vs. 26.40 ±2.51; 35.41 ± 9.80 vs. 41.25 ± 15.23 respectively) (Table 3).

Table 2a: Clinical characteristics of the cohort of the patients.

	Mean	SD
Age	59.86	9.25
Education	12.14	3.23
Weight	89.36	17.402
Height	174.11	10.694
CHARLSON_COMORBIDITY_INDEX	1.96	1.454
length of stay (days)	21.30	14.829
P_F	125.04	72.655
SOFASCORE_T0	4.85	1.854
APACHE_II_T0	9.44	2.860
Worst P_F	91.93	28.563
Worst_PCT	3.00	2.000
Days of MV	14.44	11.849
Worst_SOFA_SCORE	6.33	3.174
RASS_T0	-0.48	1.528
Delirium_T0	0.04	0.192
RASS_estubation	0.48	1.189
delirium_estubation	0.15	0.362
Propofol (*days of use)	9.00	5.727
Dexa*	7.00	5.204
Benzodiazepines*	11.72	12.870
Opioids*	13.67	8.884
Antipsychotics*	9.89	11.298

Table 3: Neuropsychological evaluation at T1 and T2

Neuropsychological evaluation		T1		T2	
	p	Mean	Standard Deviation	Mean	Standard Deviation
MoCa	P= 0.02	24.61	3.06	30.00	26.41
RALVT IR	n.s.	42.57	10.67	62.10	42.36
RAVLT DR	n.s.	8.05	3.90	14.00	7.92
REY D	n.s.	18.94	4.68	35.50	22.03
IVM	n.s.	20.76	1.45	22.00	21.19
DA	n.s.	5.72	0.95	9.00	5..96
CA	n.s.	5.29	1.04	7.90	5.88
DI	n.s.	4.35	1.33	8.00	4.57
CI	n.s.	5.40	1.22	6.79	5.25
Barrage Time	n.s.	53.93	17.09	69.00	47.92
Barrage Score	n.s.	11.46	2.71	13.00	11.92
Barrage Errors	n.s.	0.43	0.92	2.00	0.08
Barrage Results	n.s.	0.67	0.91	2.30	0.32

Attentive Matrices	n.s.	46.74	9.11	60.00	49.42
Stroop Test Errors	n.s.	0.82	3.24	8.50	0.42
Stroop Test Time	n.s.	16.97	7.73	33.25	15.93
SVAT	n.s.	17.64	3.94	20.00	18.95
FAB	n.s.	17.02	1.35	18.00	17.27
VF	P= 0.04	34.58	10.82	85.90	41.25
SF	n.s.	44.72	10.68	65.93	49.23
REY C	n.s.	34.53	3.06	36.00	35.10

Lower performances in long-term memory were significantly associated with longer ICU stay, (RAVLT Delayed recall T1, r: -.491 p=.009 – RAVLT Immediate recall T2, r: -.529 p=.009), duration of mechanical ventilation (RAVLT Immediate recall T1 r=-.464, p=.015 – RAVLT Immediate recall T2 =.550, p=.007, RAVLT Delayed recall T1 r: -.529, p=.005), higher Sequential Organ Failure Assessment (SOFA) score (RAVLT Immediate recall T2 r=.450, p=.031, RAVLT Delayed recall T1 r=.503, p=.007 – T2 =.490, p=.018) and longer treatment with benzodiazepines (RAVLT Immediate recall T1 r=-.477, p=.045 – T2 =.543, p=.036, RAVLT Delayed recall T1 r=-.504, p=.033) , opioids (RAVLT Delayed recall T1 r=.490, p=.009 – RAVLT Immediate recall T2 =.564, p=.005) antipsychotic drugs (RAVLT Delayed recall T1 r=-.593 p=.007) and propofol (RAVLT Delayed recall T1 r=-.518, p=.007 – RAVLT Immediate recall T2 =-.539, p=.008).

A significant correlation between lower performances in pho-nemic fluency and longer duration of mechanical ventilation (T1 r=-.493, p=.009), longer treatment with benzodiazepines (T1 r=-.543, p=.020), antipsychotic drugs (T1 r=-.629 p=.004) and opioids (T1 r=-.528, p=.005) was observed at T1.   At T1 longer term treatment with antipsychotic drugs was related with lower scores on MoCa (r=-.662 p=.002) and digit span backward (r=-.640, p=.003).

Quality of life and psychological distress in patients

A total of 71 % of patients (24 out of 28 patients) had a reduced QoL due to physical limitations at T1 (SF-12 PCS score < 54.1, 42.42 ± 9.17), which tended to improve 12 months year later, F(1,23) = 3.59, p = 0.07, ηp2 = 0.14, (45.97 ± 8.36). A proportion of 57.14% of patients (16 out of 28) had a reduced QoL due to psychological bur-den at T1 (SF-12 MCS score < 52.9, 50.77 ± 8.78), which remained stable 12 months later, F(1,23) = 0.05, p>.05, ηp2 = 0.02, (51.22 ± 9.56) [Table 4a].

Table 4a: Quality of life (QoL) and psychological distress in patients and caregivers

	T1		T2	
	Mean	Standard Deviation	Mean	Standard Deviation
Patients				
SF12_PCS	42.51	8.81	45.97	8.36
SF12_MCS	50.66	8.97	51.22	9.56
SEIQoL	83.93	13.36	72.39	16.16
Caregivers				
SQR_20	3.76	4.77	3.44	4.13
SEIQoL	79.68	13.16	70.90	16.02

SF-12 PCS scores at T2 were significantly related to higher SOFA scores (r=.643, p=.001) and to lower digit span backward scores (r=.651, p=.001). SEIQoL showed a worsening of subjectively per-ceived quality of life between T1 and T2, F(1,23) = 17.91, p < 0.001, ηp2 = 0.44, (83.07 ± 13.52 vs. 72.39 ± 16.16). Concerning SEIQoL categories, at T1 patients reported hobbies as the most important category to consider in the quality of their life. At T2, besides hob-bies, the most important categories were also personal realization and feeding. No significant relations were detected between SF-12 MCS, SEIQoL, QoL and psychological wellbeing and patients' cog-nitive scores. No significant differences were found over time on EQ-5D score [Table 4b].

Table 4b: Health-related quality of life questionnaire in patients.

EQ-5D	T1					T2				
	No problems	*Slight problems*	*Moderate problems*	*Severe problems*	*Unable/extreme problems*	*No problems*	*Slight problems*	*Moderate problems*	*Severe problems*	*Unable/extreme problems*
Mobility	21	7	0	0	0	21	3	0	0	0
Self care	24	4	0	0	0	24	0	0	0	0
Usual activities	21	6	1	0	0	22	2	0	0	0
Pain_discomfort	12	16	0	0	0	15	9	0	0	0
Anxiety_depression	18	10	0	0	0	14	8	2	0	0

EQ-5D score at T1 was related to longer duration of treatment with benzodiazepines (T1 r=.505, p=.033) and with antipsychotics (T1 r=.507, p=.027).

Quality of life and affective outcomes in caregivers

Moderate mental distress was detected in 3 out of 25 caregivers on SQR-20 (SQR-20 >8). No significant differences were found over time on SQR-20 score and SEIQoL [Table 4].

At T1 SQR-20 score was related to T1 patients' SF12-MCS score (r=-.515, p=.008) and T2 SEIQoL total score (r=-.637, p=.001), while at T2 SQR-20 score was related to T2 patients' SF12-MCS score (r=-.576, p=.020).

At T2 the caregiver SEIQoL total score was related to patients' SEIQoL total score (r=.540, p=.031).

Concerning SEIQoL, at T1 caregivers reported mental health and autonomy as the most important category in the quality of their life, conversely at T2 the most important categories were hobbies and autonomy. Moreover, lower caregiver QoL (T2 SEIQoL) was related to higher patients' SOFA score (r=-.611; p=.012) and to LTM impairment (RAVLT Delayed T1 r=.463; p=.071, RAVLT Delayed T2 r=.459; p=.074). Concerning the communication between caregivers and healthcare staff evaluated by COSM-R, 90% of caregivers reported high satisfaction (mean score 40.36 ± SD 8.18).

Discussion

In this study, we reported a comprehensive analysis of neuropsychological performances, quality of life, and psychological well-being in severe COVID-19 patients admitted to the ICU and requiring mechanical ventilation, examined at 3 and 12 months post-discharge. Additionally, we explored the relationship between patients' conditions and the quality of life and psychological well-being of caregivers.

Several studies have focused on cognitive functions after COVID-19 infection, but the large use of cognitive screening tests as well as the frequent use of telephone assessments limit the reliability of the incidence rate of cognitive impairment. Furthermore, few studies tested long-term cognitive performances with complete neuropsychological assessment in ICU COVID-19 survivors19. Our emphasis on face-to-face comprehensive neuropsychological assessments sets this study apart. Our findings documented that 40% of patients were cognitively impaired at 3 months decreasing to 33 % at 12 months. Our data confirm that extensive neuropsychological evaluation is necessary to detect the most consistent cognitive

impairment frequency19 (up to 43%) compared to screening tests [23] (18%), both at baseline and at 12 months after ICU discharge [24]. Furthermore, beyond screening tests, also the administration of questionnaires for subjective cognitive symptoms is not recommended to define specific alterations in cognitive domains. In fact, about one-third of COVID-19 patients, regardless of the acute disease severity, reported high levels of subjective cognitive dysfunction which was not associated with results from objective cognitive evaluation but with psychological and demographic factors [25]. Thus, to define specific alterations in cognitive domains, the use of complete neuropsychological batteries is crucial to characterize the cognitive impairment to provide the best intervention in ICU discharged patients.

In our study, long-term memory was the most impaired domain both at 3 and 12 months, followed by attention, working memory, language and executive functions, instead praxis was never impaired, suggesting a predominant frontal-temporal subcortical cognitive dysfunction. This pattern is consistent with memory impairment detected in ARDS patients with or without COVID infection [26]. Long-term cognitive impairments in non-COVID ICU survivors were strictly related to hypoxemia, cardinal feature of ARDS of pulmonary etiology [27], suggesting that ARDS-mediated neurological damage could involve cytokine storm following lung injury or sepsis [28]. Mechanical ventilation was also considered an independent factor related to persistent cognitive impairment, diminished quality of life, and depression [29].

In our sample all patients had acute ARDS and all were mechanically ventilated, thus the predominant memory deficit we found could be explained by the peculiar sensitivity of medial temporal lobes to hypoxic injury.

We also observed a slight reduction in cognitive impairment frequency over time, similarly to patients with milder COVID as described by Ferrucci et al. 4 as well as in non-COVID ICU survivors [30]. Long-term memory impairment was significantly associated with higher SOFA score, longer mechanical ventilation, stay in ICU and psychotropic drugs use at 3 months. The association between long-term memory impairment, higher SOFA score and longer stays in ICU persisted at 12 months of follow-up, emphasizing the lasting impact of these clinical factors on cognitive outcomes. Our study confirmed that at 3 months post-ICU discharge patients reported a reduced QoL, primarily due to physical limitations, which tended to improve 12 months later [31-32]. However, health-related quality of life due to psychological burden remained stable 12 months later. Subjectively perceived quality of life worsened over time. Self-as-

sessed health-related quality of life was associated with duration of treatment with benzodiazepines and with antipsychotic drugs, but not cognitive scores. In our study, the majority of caregivers did not report symptoms related to mental distress either at baseline or at 1 year of follow-up. However, consistent with previous reports [33], physical and psycho-emotional symptoms reported by caregivers were related to patients' lower QoL. Moreover, lower caregiver QoL was related to higher patients' memory impairment. Generally, caregivers reported a good degree of satisfaction concerning the communication with healthcare staff.

Our study presents valuable insights into the cognitive and psychological well-being landscape of COVID-19 survivors who underwent ICU care. Despite its contributions, several key limitations warrant consideration. Notably, our sample size was modest and the absence of baseline cognitive function data limited our ability to discern pre-existing cognitive deficits. Nonetheless, we undertook meticulous measures, including comprehensive anamnesis and clinical chart review, to minimize this limitation and ensure a robust evaluation of cognitive status.

The absence of a control group is a shared limitation observed in numerous studies within the same domain. The COVID-19 pandemic has hindered the recruitment of control participants for in-person assessments due to prevailing safety concerns. This limitation highlights the challenging research landscape during the pandemic and must be taken into account when interpreting our findings.

Turning to our strengths, our study stands out for including an extensive neuropsychological battery and patient-centered perspective measures to comprehensively gauge health-related quality of life and psychological well-being. In summary, our findings reveal a significant prevalence of cognitive impairment among COVID-19 ICU survivors, as assessed through an in-depth face-to-face neuropsychological evaluation, with particular involvement of long-term memory deficits, exerting a discernible influence on quality of life as confirmed by caregiver assessment. Our data demonstrated cognitive improvement within the initial 12 months post-ICU discharge. Interestingly, the neuropsychological profile and the associated factors align with those observed in non-COVID ICU survivors, implicating the broader framework of post-intensive care syndrome rather than a distinct role for COVID-19 infection [27,28].

Furthermore, our study underscores the interconnectedness between patient well-being and caregiver experiences. We observe that caregivers' psychological well-being is strongly linked to patient quality of life and memory performance. In conclusion, our study improves the understanding of cognitive and psychological outcomes in COVID-19 ICU survivors. This insight bears significance in guiding clinical practices, suggesting that early and meticulous neuropsychological assessment could facilitate the identification of patients who might benefit from cognitive therapies, ultimately enhancing the prognosis of this debilitating complication.

Acknowledgement

Conflicts of Interest

There is no conflict of interest.

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