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Post-traumatic Stress and Depressive Sequelae in ICU Hospitalized COVID-19 Patients 6 Months after Discharge: A Comparison with Non-COVID ICU Patients

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Post-Traumatic Stress and Depressive Sequelae in ICU Hospitalized COVID-19 Patients 6 Months after Discharge: A Comparison with Non-COVID ICU Patients

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Abstract: The Coronavirus Disease 2019 (COVID-19) pandemic has had a major impact on the mental and physical health of hospitalized patients. In our study we focused on the onset of symptoms correlated with Post-traumatic stress disorder (PTSD), depression and physical disabilities in patients admitted to the Intensive Care Unit (ICU) because of a severe respiratory distress related to COVID-19 (COVID Group) compared with patients admitted to the same ICU for trauma and other medical conditions than COVID-19 (No-COVID Group). The physical symptoms and the level of disability were evaluated with the Glasgow Outcome Scale-Extended (GOS-E), the Quality of Life after Brain Injury (QOLIBRI) and the 3 levels version of EQ-5D (EQ-5D-3L) questionnaire; psychiatric symptoms were investigated using the Impact of Event Scale-Revised 22-item (IES-R), the Patient Health Questionnaire, 9-Item Version (PHQ-9) and the Generalized Anxiety Disorder Assessment, 7-items version (GAD-7). These questionnaires were administered 6 months after discharge. Patients in the No-COVID Group showed statistically significant more severe scores in all the physical assessments while similar relevant PTSD and depressive symptoms were reported in both groups. The results of the present study underline the psychopathological impact of being hospitalized in ICU because of COVID-19 even after 6 months from discharge ,suggesting the importance of assessing the psychiatric effects of COVID-19 in the long term in order to create supportive measures.

Keywords: post-traumatic stress disorder; trauma; depression; physical disabilities; intensive care unit; coronavirus disease 2019

1. Introduction

Since its inception, one of the main problems caused by the Coronavirus Disease 2019 (COVID-19) pandemic worldwide has been the need for hospitalizations in a significant number of the patients affected, particularly with the need to be admitted to Intensive Care Units (ICU) for the often acute worsening of the symptoms, with rates up to 21% of the subjects affected [1-2]. Consistently, increasing literature has highlighted relevant rates of mental disorders among COVID-19 survivors. Many data showed similar prevalence rates in quality of life impairment, anxiety, depression and Post-traumatic stress disorder (PTSD) with significant impact of hospitalization in analyses of long-term outcomes in Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and COVID-19 infections, which are the 3 major Coronavirus (CoV) outbreaks that have occurred in the last 20 years [3-5]. In a Chinese cohort study on COVID-19 patients discharged from hospital, rates around 23% of anxiety or depression were reported [6]. Horn et al. found 10.4 % of somatic symptom disorder (SSD) in COVID-19 affected patients during the first and second wave in France [7]. Huang et al. reported 11.4% of PTSD in a sample of 574 COVID-19 survivors who were admitted in Chinese COVID hospitals during the first year of COVID-19 pandemic [8]. However,

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some studies suggest a particular risk for developing mental disorders among COVID-19 patients treated in the ICU with respect to patients not treated in the ICU [9-10]. In a cohort study including 45 COVID-19 ICU patients, assessed 1-month after hospital discharge, 18% of the sample reported symptoms suggestive of moderate to severe depression with scores above 10 at the Patient Health Questionnaire-9 (PHQ-9) [11]. Parallel, 17.8% of the sample reported symptoms suggestive of a diagnosis of PTSD, scoring above the threshold of 31 on the Posttraumatic Stress Syndrome Checklist for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (PCL-5) [11]. In a 4-month cohort study on 94 patients admitted in ICU for COVID-19, Morin et al. showed symptoms of anxiety in 23% of the sample besides symptoms of depression and of PTSD in a 7% and 18%, respectively [12]. Poor sleep quality has also been reported in up to 60.5% of COVID-19 ICU survivors 3 months after discharge [13]. Despite still limited, data have been reported on longer follow-up periods after discharge. In particular, Gilmartin et al. in a longer period follow-up up to 6 months after discharge from ICU, showed a high burden of psychologic and physical impairment among 22 COVID-19 survivors with persisting depressive (PHQ-9 mean score 7.8±7.4), anxiety (Generalized Anxiety Disorder Assessment, 7-items version (GAD-7) mean score 5.8±6.1) and post-traumatic stress (PCL-5 mean score 21.1±17.5) symptoms [14].

Literature data highlight that a hospitalization in ICUs represents a risk factor for the development of psychiatric symptoms, even in patients hospitalized for conditions other than the COVID-19. Indeed, there is evidence of high rates of PTSD in No-COVID-19 patients admitted to the ICU [15], with studies showing an increase in PTSD symptoms 3 to 12 months after discharge [16]. It has also been shown that high levels of anxiety during hospitalization are a risk factor for the onset of PTSD [17].

High rates of anxiety have also been documented in No-COVID-19 patients discharged from the ICU. Huang et al found that 10.3% of patients developed anxiety 6 months after hospital discharge as measured by the GAD-7 questionnaire [8]. Overall, it can be said that approximately one-third of patients admitted to the ICU develop anxiety and depression during the year after discharge [18]. In addition, patients admitted to the ICU for multiple diagnoses, most commonly polytrauma, have a less favorable course over time with worse functional outcomes at both 3 and 6 months [19]. Regarding cognitive symptoms, patients admitted to the ICU for severe illnesses such as respiratory failure or shock are known to develop cognitive deficits that may persist for up to a year or more after discharge [20].

Based on these premises, the aim of the present study was to systematically assess the physical and psychiatric long-term sequelae in all patients admitted to the ICU of a major University Hospital in Italy (Pisa), between March and November 2021, because of a severe respiratory distress related to COVID-19 (COVID Group) in comparison with a control group of all patients admitted to the same ICU during the same months but for other medical issues than COVID-19 (No-COVID Group). All patients were assessed 6 months after discharge.

2. Materials and Methods

2.1. Study sample and Procedures

Patients discharged from the ICU of the Azienda Ospedaliero Universitaria Pisana (AOUP, Pisa, Italy), between March 2021 and November 2021, were consecutively recruited for a six-month follow-up from discharge. All subjects accepted to participate to this study at the time of discharge. At a 6-month follow up visit (from September 2021 to May 2022) all subjects enrolled were assessed. Patients included were divided in two groups upon the reasons for admittance in the ICU: 1) patients admitted because of a severe respiratory distress related to COVID-19 (COVID Group); 2) other medical problems than COVID-19, including peritonitis, acute abdomen, mesenteric ischemia, BPCO exacerbation, poly-trauma, septic shock, acute pancreatitis, myocardial infarction, respiratory failure, and postoperative pancreatic cancer (No-COVID Group). The inclusion criteria were: age above 18 years; a hospitalization period in the ICU of at least 5 days. Exclusion criteria were: limitations in verbal communication that would have affected the subject's ability to follow the protocol's

assessments (e.g., lack of proficiency in Italian) and/or a lack of collaborative skills and hospitalization in the ICU for a traumatic brain injury. Assessments were conducted by anaesthesiologists working in the ICU and skilled psychiatrists and residents in psychiatry from the Psychiatric Clinic of the same AOUP, University of Pisa, Pisa, Italy.

Physical assessments of overall disability and quality of life included: the Glasgow Outcome Scale-Extended (GOS-E), a structured interview measuring the overall disability and outcome following traumatic brain injury [21-22]; the 3 levels version of EQ-5D (EQ -5D-3L), a family of instruments describing and valuing the general health [23]; the Quality of Life after Brain Injury (QOLIBRI), a questionnaire evaluating the health-related quality of life (HRQoL) of individuals after traumatic brain injury and the impact of rehabilitation or other interventions [24].

Psychiatry assessments included: the Impact of Event Scale-Revised 22-item (IES-R), a questionnaire evaluating the posttraumatic stress symptoms (PTSS) [25-26]; the PHQ-9, a questionnaire showing the presence of depressive symptoms [27-28]; the GAD-7, an instrument detecting presence of anxiety symptoms [29].

An informed consent was obtained from the patients for the study participation after receiving a full description of the study and having the possibility to ask questions. The study was conducted in accordance with the Declaration of Helsinki.

2.2. Assessment Instruments

The GOS-E is a measure of overall disability and outcome following traumatic brain injury [21-22]. The original GOS was developed in 1975 [30] and a revised scale, the GOS-E, was developed to overcome its limitations [31]. The GOS-E uses an 8-point scale to further stratify the lower and upper levels of functioning measured by the GOS [31]. This results in the following levels: dead, vegetative state, lower severe disability, upper severe disability, lower moderate disability, upper moderate disability, lower good recovery, and upper good recovery [22,32]. In the present study, the GOS-E scale was simplified into three levels of functioning: severe disability, moderate disability, and absence of disability.

The EQ-5D-3L was introduced by the EuroQol Group in 1990 [23]. It is used to assess general health and consists of two parts: the EQ-5D-3L descriptive system and the EQ visual analogue scale (EQ VAS). In the present study, we used the EQ-5D-3L descriptive system, which is composed of five dimensions: Mobility, Self-Care, Habitual Activities, Pain/Discomfort, and Anxiety/Depression [33]. Each dimension is divided into three levels of functioning: no problems, some problems, extreme problems. To simplify the results, we divided the sample into two groups: no problems and presence of problems (some problems plus extreme problems).

The QOLIBRI was developed to assess the HRQoL of individuals after traumatic brain injury and the impact of rehabilitation or other interventions [24]. The QOLIBRI is a comprehensive questionnaire with 37 items covering six dimensions of HRQoL after brain injury [24]. The questionnaire provides a quality of life profile and a total score and is divided into Section A (level of satisfaction) and Section B (domain of complaints). The two sections together consist of six scales: 'Cognition' (7 items), 'Self' (7 items), 'Daily life and autonomy' (7 items), 'Social relationships' (6 items), 'Emotions' (5 items), and 'Physical problems' (5 items) [24]. Each item is rated on a five-point scale: 1 (not at all), 2 (slightly), 3 (moderately), 4 (quite), and 5 (very) [24]. The QOLIBRI scale yields an overall score, which is the sum of the scores obtained in the individual scales [24]. In the present study, we used the QOLIBRI total scale, which was recently validated in comparison with the QOLIBRI subscales and consists of six items: "Cognition," "Self," "Daily Living and Autonomy," "Social Relationships," "Emotions," and "Physical Problems" [34]. Each of the six items is rated on a five-point scale: 1 (Not at all), 2 (Slightly), 3 (Moderately), 4 (Quite), and 5 (Very) [34]. The score for each item is added together and then the total score is then converted to a percentage scale: 0 represents the lowest quality of life and 100 represents the best possible quality of life [34]. The QOLIBRI scales meet standard psychometric criteria, and test-retest reliability and internal consistency were good [35-36]. Although GOS-E and QOLIBRI questionnaires were developed for patients with brain injury, in clinical practice they are also used in other cases.

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The IES-R [25-26] is a questionnaire that demonstrated high internal consistency [37] and was used to assess PTSS. This questionnaire is one of the most commonly scales used to screen rescue workers for trauma and stress related symptoms [38-40]. The items of the IES-R are scored on a 5-point rating scale. Individuals with a total score of 33 or more have severe PTSD; individuals with a total score of 24 or more have moderate symptoms and this score is usually considered suggestive of PTSD [37,41].

The PHQ-9 is a questionnaire that assesses the presence of depressive symptoms and it consists of nine items that are self-rated on a scale from 0 (not at all) to 3 (almost every day), such that the available range is 0-27 and scores of 0-4, 5-9, 10-14, 15-19, and 20-27 indicate minimal, mild, moderate, moderately severe, and severe depressive symptoms, respectively [27-28] [42]. The questionnaire has shown high agreement with the diagnosis of major depression based on structured interviews [43-45].

The GAD -7 is a questionnaire that showed to be a reliable and valid instrument with good test-retest reliability and high internal consistency to assess the presence of anxiety symptoms [29]. The GAD-7 consists of seven items and is commonly used to screen for generalized anxiety disorders [29,42,46]. The patient is asked to self-report how often he/she has been bothered by seven common anxiety disorder symptoms in the past two weeks [29,42,46]. For each item, the values 0, 1, 2, and 3 must be given [29,42,46]. Scores of 0-4, 5-9, 10-14, and 15-21 represent minimal, mild, moderate, and severe anxiety symptoms, respectively [29,42,46].

2.3. Statistical Analysis

All statistical analyses were performed using the Statistical Package for Social Science (SPSS), version 26.0. Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were reported as percentages. All tests were two-sided, and a p value < 0.05 was considered statistically significant. Chi-square was calculated to assess differences between the two groups on categorical variables. To compare continuous normally distributed variables among groups, t-test was used, while Man-Whitney test was used for the non-parametric ones.

3. Results

3.1. Clinical characteristics

A total sample of 143 patients discharged from the ICU in the period of observation of the present study satisfied inclusion criteria. Among these: 27 (8 of these admitted for COVID-19) could not be contacted because of change in contact data or reallocation, 5 (1 of these admitted for COVID-19) had died and 20 (7 of these admitted for COVID-19) refused to participate to the study. The final sample consisted of 91 participants (N=67, 73.6% males and N=24, 26.4% females): 30 patients (33.0%) in the COVID Group and 61 patients (67.0%) in the No-COVID Group. The whole sample presented a mean age of 52.16±17.98 years, with a statistically significant difference between the COVID and No-COVID Groups (58.56±10.71 and 49.50±19.72 years respectively, p=0.008).

The disability classification, as measured through the GOS-E simplified test, was significantly different between groups, showing a significantly higher prevalence of severe disability the No-COVID Group (25.0%) compared to the COVID Group (3.4%). Statistically significant differences between groups also emerged in the mobility and pain domains of the EQ scale, showing the No-COVID Group higher prevalence of disturbed mobility (48.3%) and pain (63.9%) compared to the COVID Group (20.0% and 36.0%, respectively). In terms of quality of life, statistically significant differences emerged in the physical problems, emotions, daily life and autonomy, and social relationships domains of the QOLIBRI scale. In all these domains, the No-COVID Group showed significantly lower scores compared to the COVID Group, suggestive of more physical problems (mean=11.3±4.72 vs. mean=13.75±3.52, p=0.018), more emotion disturbances (mean=13.89±3.35 vs. mean=11.84±4.15, p=0.026), more difficulties in daily life and autonomy (mean=11.20±4.50 vs. mean=13.43±4.45, p=0.024) and more difficulties in social relationships (mean=11.19±4.48 vs. mean=13.79±3.55, p=0.009).

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A quarter of the patients of the total sample presented a moderate level of symptoms trauma and stress related, reporting an IES-R score>24. In particular, these symptoms were reported in about a third of the patients of No-COVID Group compared in only about one sixth of the patients of COVID Group.

More than 10% of the total sample reported a PHQ-9 score>10, showing moderate to severe depressive symptoms: the percentage was more than double in the No-COVID Group (15.0%) compared to the COVID group (6.7%). Approximately 15% of the total sample presented a GAD-7 score>10 correlated with moderate to severe anxiety symptoms, with substantially the same incidence in the No-COVID and COVID Groups. See Table 1.

Table 1. Socio-demographic and clinical characteristics of the study sample and devided in No-COVID and COVID groups.

		Total Sample	**No-COVID Group**	**COVID Group**	
		N=91	*N=61*	*N=30*	
		Mean ± SD	Mean ± SD	Mean ± SD	**p-value**
	Age (years)	52.16±17.98	49.50±19.72	58.56±10.71	**0.008***
	Length of hospitalization (days)	17.30 ±15.47	16.75±12.32	18.52±21.09	0.688
		N (%)	N (%)	N (%)	**p-value**
	Gender (Female)	24 (26.4)	18 (29.5)	6 (20.0)	0.475
GOSE-simplified	Severe disability	15 (17.6)	14 (25.0)	1 (3.4)	**0.001***
	Moderate disability	20 (23.5)	17 (30.4)	3 (10.3)	
	Absence of disability	50 (58.8)	25 (44.6)	25 (86.2)	
EQ-5D-3L	EQ Mobility (disturbed)	35 (38.9)	29 (48.3)	6 (20.0)	**0.018***
	EQ Selfcare (disturbed)	14 (15.7)	12 (20.3)	2 (6.7)	0.172
	EQ Usual activities (disturbed)	37 (42.0)	28 (47.5)	9 (31.0)	0.216
	EQ Pain (disturbed)	50 (54.9)	39 (63.9)	11 (36.7)	**0.026***
	EQ Depression (disturbed)	31 (34.8)	24 (40.0)	7 (21.1)	0.217
		Mean ± SD	Mean ± SD	Mean ± SD	**p-value**
QOLIBRI	QOLIBRI-physical problems	12.13±4.48	11.3±4.72	13.75±3.52	**0.018***
	QOLIBRI-cognition	12.81±3.97	12.65±4.20	13.11±3.53	0.627
	QOLIBRI-emotions	12.53±4.00	11.84±4.15	13.89±3.35	**0.026***
	QOLIBRI-daily life and autonomy	11.95±4.29	11.20±4.50	13.43±3.45	**0.024***
	QOLIBRI-social relationships	12.07±4.34	11.19±4.48	13.79±3.55	**0.009***
	QOLIBRI-infuturation	12.70±3.59	12.24±4.01	13.61±2.37	0.100
	QOLIBRI-total score	70.83±25.86	67.74±26.02	76.80±24.89	0.120
GAD-7	GAD-7 total score	3.87±5.07	3.80±5.08	4.03±5.13	0.638

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		N (%)	N (%)	N (%)	**p-value**
	GAD-7 Score>10	13 (14.4)	9 (15.0)	4 (13.3)	1.000
		Mean ± SD	Mean ± SD	Mean ± SD	**p-value**
PHQ-9	PHQ-9 total score	4.48±4.62	4.70±4.85	4.06±4.17	0.779
		N (%)	N (%)	N (%)	**p-value**
	PHQ-9 Score>10	11 (12.2)	9 (15.0)	2 (6.7)	0.426
		Mean ± SD	Mean ± SD	Mean ± SD	**p-value**
IES-R	IES-R total score	14.96±17.41	15.65±18.01	13.63±16.40	0.940
	IES-R intrusion	0.77±0.99	0.82±1.04	0.66±0.90	0.880
	IES-R avoidance	0.58±0.77	0.60±0.77	0.53±0.79	0.745
	IES-R arousal	0.67±0.77	0.66±0.76	0.67±0.81	0.951
		N (%)	N (%)	N (%)	**p-value**
	IES-R Score>24	22 (25.0)	17 (29.3)	5 (16.7)	0.299

[1]GOS-E: Glasgow Outcome Scale-Extended; EQ-5D-3L: 3 levels version of EQ-5D; QOLIBRI: Quality of Life after Brain Injury; GAD-7: Generalized Anxiety Disorder Assessment, 7-items version; PHQ-9: Patient Health Questionnaire-9; IES-R: Impact of Event Scale-Revised 22-item; No-COVID Group: patients admitted to the Intensive Care Unit (ICU) for trauma and other medical conditions than Coronavirus Disease 2019 (COVID-19); COVID Group: patients admitted to the same ICU because of a severe respiratory distress related to COVID-19.

4. Discussion

The results of the present study show mild to moderate rates of PTSS and depressive symptoms in the COVID Group after 6 months from ICU discharge in the period between March 2021 and November 2021. Interestingly, psychopathological assessments reported comparable results with a group of subjects discharged in the same period for the same ICU where they had been hospitalized for other medical conditions than COVID-19 and trauma, despite this latter No-COVID group showed statistically significantly more severe scores in all the physical assessments including the GOS-E, EQ-5D-3L and QOLIBRI scales. In our study, the prevalence of symptomatologic PTSD in the COVID Group at 6-month follow-up was 16.7%. This percentage seems to be higher than in a cross-sectional study conducted in a Covid hospital in Wuhan, in which 11% of patients had PTSD 6 months after admission to COVID-19 [47]. This difference may be because our patients were all admitted to the ICU. Indeed, Wang et al. indicate that ICU admission is one of the factors closely associated with the occurrence of PTSD besides other factors including witnessing the suffering of other patients, the persistence of physical symptoms and the perception of having been infected by COVID-19 [47] . It's also important to recall that literature show that the presence of a previous diagnosis of mental disorders represents a risk factor for PTSD in ICU survivors, particularly a history of anxiety and depression [48-49], thus our results may underestimate the prevalence PTSD rates among all ICU CIVD-19 hospitalized patients since prior mental disorders were one of the exclusion factors in our study.

We must also consider that the prevalence of psychiatric symptoms is often high in COVID-19 patients during hospitalization. Data on the impact of these symptoms on the occurrence and severity of PTSD are contradictory. According to some studies, they decrease after discharge, instead according to others, high anxiety levels during hospitalization constitute a risk factor for the occurrence and severity of PTSD after discharge [17,50]. However, this aspect was not evaluated in our study. It is important to note that evidence suggests that the onset of PTSD symptoms may extend beyond 6 months. Studies of ICU survivors show an increase in PTSD symptoms 3 to 12 months after

discharge [16]. PTSD can still be diagnosed in up to 25% of cases even after 6 months, and this represents an exacerbation of earlier symptoms [15]. Furthermore, because the COVID-19 pandemic was still present during the 6 months after discharge, the COVID-19 ICU patients may have been fearful of re-infecting themselves or transmitting the virus to others in the months after discharge. This may have exacerbated the symptoms of hyperarousal and avoidance behaviors associated with COVID-19 [17]. Regarding symptoms of anxiety and depression, our study showed that 13.3% and 6.7% of the COVID Group developed symptoms of anxiety and depression, respectively, at 6-month follow-up. The cross-sectional study by Huang et al found that 10.3% of patients developed anxiety symptoms 6 months after hospital discharge, as assessed by the GAD -7 questionnaire [8]. We reported similar results considering that our sample consisted only of patients admitted to the ICU. Similarly, Morin et al. found that 23% of patients admitted in ICU developed anxiety while 7% and 18% developed symptoms of depression and PTSD respectively at 4-month follow-up [12. Gilmartin et al. performed a 6-month follow-up after ICU discharge in COVID-19 survivors, were they found persisting mild level of depression assessed with PHQ-9 questionnaire (mean score of 7.8±7.4), mild level of anxiety assessed with GAD-7 questionnaire (mean score 5.8±6.1) and subthreshold PTSD assessed with PCL-5 questionnaire (mean score 21.1±17.5) [14]]. In a 1-year follow-up, COVID-19 ICU patients who were treated with extracorporeal membrane oxygenation (ECMO) still showed anxiety (44%), depression (42%) and risk for PTSD (42%) [51]. From the analysis of our data, COVID and No-COVID-19 groups admitted to the ICU had the same level of anxiety, depression, and PTSD symptoms assessed with the standardized questionnaires (GAD-7, PHQ-9, IES-R), and the same level of satisfaction with their cognitive function assessed with QOLIBRI. Our results are confirmed by a study comparing COVID-19 and No-COVID-19 ICU patients with respiratory failure receiving mechanical ventilation [52].In another observational study, symptoms of anxiety, depression, and PTSD were assessed one and three months after discharge in patients hospitalized during the pandemic COVID-19. It was found that a significant proportion of patients reported psychological symptoms, but that there was no difference in severity and prevalence between COVID-19 and No-COVID-19 patients [53]. This study confirms our findings, even though the patients were examined in a shorter period after discharge than in our study. Plenty of literature highlights the relevance of psychopathological consequences of COVID-19 on affected patients and the fact that these may persist over time. However, the underlying mechanisms are not fully known, as the psychopathological consequences could be related to other factors besides the direct and indirect effects of the virus, such as living through a pandemic or surviving a severe illness.

For what concern the physical symptoms, Nguyen NN et al. found that COVID-19 ICU patients had symptoms persisting at 12 weeks after discharge: fatigue (from 31% to 64%), dyspnoea (from 31% to 54%), arthralgia (from 22% to 55%) and cough (from 5% to 46%)[54]. In our study, although the two groups had a similar psychopathological outcome, it was found that No-COVID Group had significantly more disability, greater mobility limitations, and more severe pain after 6 months than the COVID Group. These patients also showed lower satisfaction with their emotions and self-image, autonomy, and ability to manage all aspects of daily life, social relationships, and physical problems. These results can be explained by the fact that most of the No-COVID-19 patients admitted to the ICU were affected by pathologies with high physical stress. Indeed, patients admitted to the ICU for other diagnoses, mostly polytrauma, would have a less favourable course over time, with worse GCS and GOSE at both 3 and 6 months [19. The data in the literature comparing quality of life and disability between COVID-19 and No-COVID-19 patients show that there are either similar in both groups or worsen in the No-COVID-19 group. Therefore, despite greater physical impairment in the No-COVID Group, this study shows an overlap of psychopathological symptoms in the two groups at 6 months, in agreement with the literature. Some authors suggest that this overlap of psychological symptoms in the two patient groups may be due to the pandemic context shared by COVID-19 and No-COVID-19 Groups; both populations experienced pandemic containment, social alienation, and isolation [53]. However, there may be different disease management in the two groups within an ICU (eg, different levels of sedation, the need for different types of ventilation, the use of different personal protective equipment by nurses in no covid units compared with covid units, etc.). Future studies

should therefore focus to such aspects that might influence psychiatric outcome. Our research demonstrates that PTSS can be chronic and disabling in the long term, even if not extremely severe. Unfortunately, we didn't have the prevalence of PTSS at the time of ICU discharge, so we don't know if psychiatric symptoms are decreasing, remaining stable or worsening. This fact suggests the importance of a proper follow-up in these patients.

While interpreting our results, some limitations should be kept in mind. First, the limited sample size, which may have contributed to the lack of significance in some of the results of this study and could affect the generalizability of the results. Second, the lack of assessment of psychopathological symptoms before admission to the intensive care unit, although all patients with a previous diagnosis of psychiatric illness were excluded from this study. Third, although the present study was performed during the months of the COVID-19 pandemic when anticoagulation at higher doses, corticosteroids and treatment with other immunomodulators were systematically used in patients with COVID-19 infection, we had no data on whether or not the patients of this study had undergone these therapies before or during ICU hospitalization. Therefore, it was not possible to evaluate if there were differences regarding the psychiatric and physical sequelae between patients admitted in ICU because of a severe respiratory distress related to COVID-19 who had taken such therapies compared to who did not had assumed them.

5. Conclusions

The results of the present study corroborate the relevance of evaluating psychiatric symptoms in COVID-19 patients to plan effective supportive measures or long-term follow-up strategies for this population.

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