



# Evaluation of cognitive, mental, and sleep patterns of post-acute COVID-19 patients and their correlation with thorax CT

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## Abstract

**Objective** In this study, we have evaluated the cognitive, mental, and sleep patterns of post-COVID patients 2 months after their hospitalization, and after scoring their hospitalization thorax CTs, we have compared the degree of the lung involvement with cognitive and mental states of the patients.

**Materials and methods** Forty post-COVID patients were included in our study. Patients who were hospitalized due to COVID-19 and who had thorax CT scan at the admission were included in the study. Thorax CT scans of the patients were scored using chest severity scoring (CT-SS). The Mini-Mental State Examination test (MMSE), the Montreal Cognitive Assessment Test (MoCA), the Pittsburgh Sleep Quality Index, and the Hamilton Depression and Hamilton Anxiety scales of all the participants were evaluated by the same person.

**Results** Early stage cognitive impairment was detected in 15% of post-COVID patients in the MMSE test and mean MMSE test score was  $26.9 \pm 2.1$ . The MoCA test detected cognitive impairment in 55% of the patients, and the mean MoCA score was  $19.6 \pm 5.2$ . Furthermore, all patients showed depressive symptoms in Hamilton Depression Scoring System and 57.5% of the patients showed anxiety symptoms in the Hamilton Anxiety Scoring System. The mean Pittsburg Sleep Quality Index of the patients was  $10.7 \pm 3.1$ , and it was found to be higher than normal. The mean CT-SS scores, which used to evaluate the lung involvement, of the patients were  $4.7 \pm 5.6$ . We did not find any correlation between patients' cognitive tests and CT-SS scores.

**Conclusion** When these results are taken into consideration, our study has shown that the neuropsychiatric symptoms of the patients who had COVID-19 continued even after 2 months of their illness. Therefore, long-term rehabilitation of these patients, including cognitive education and psychological services, should be continued.

**Keywords** COVID-19 · Cognition · Psychopathology · Tomography

## Introduction

A series of acute, atypical respiratory disease cases were detected in December 2019 in Wuhan, China. The source of the diseases was attributed to a new coronavirus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2); afterward, the disease caused by this virus named

Coronavirus Disease 2019 (COVID-19) [1]. Although the epidemiological and clinical features of COVID-19 patients are well defined, little attention has been paid to the psychological impact of SARS-CoV-2, such as cognitive functions. In different publications, it has been suggested that SARS-CoV-2 may affect the nervous system structures directly or indirectly [2, 3]. It has been reported that most of the SARS patients have symptoms of anxiety and depression, indicating cognitive impairment after SARS infection, along with common complaints, such as poor concentration, memory impairment, and insomnia [4]. Like other viral infections, monitoring of COVID-19 neurological sequelae has been suggested to be important in terms of potential late neuropsychological deficits [5].

In these patients, hypoxia and endothelial damage may be associated with central and peripheral nervous system

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involvement as a result of uncontrollable immune reaction and inflammation, electrolyte imbalance, hypercoagulability and disseminated intravascular coagulation, septic shock, and/or multi-organ failure [6]. According to some studies, COVID-19 has potential psychiatric and neurological complications like acute cerebrovascular events, encephalopathies, and psychosis [7, 8]. There is limited information regarding cognitive effects of COVID-19 in the literature. Cognitive deficits ranging from mild to severe are recognized as a sequela of COVID-19 infection [9, 10]. The analysis of a cohort of 87 COVID-19 patients showed that, in the subacute phase of the disease, 80% of these patients have significant impairments in cognitive functions, including memory, attention, abstraction, and spatial and time orientation [11]. In a study evaluating the impacts of COVID-19 on cognitive functions in recovered patients using neuropsychological tests, it was suggested that there might be a potential cognitive dysfunction in COVID-19 patients, especially in the domain of sustained attention [12].

Multiple studies have shown that posttraumatic stress disorder (PTSD), anxiety, and depression are increased in COVID-19 patients [13, 14]. Due to social isolation, perceived danger, uncertainty, physical discomfort, side effects of medications, and fear of infection, COVID-19 patients may experience loneliness, anger, anxiety, depression, insomnia, and PTSD [15, 16]. Clinically significant depression has been reported in approximately 30–40% of patients at 1, 3, and 6 month follow-up following COVID-19 infection [17]. Poor sleep quality also has been reported among patients recovered from COVID-19 [18].

Currently, diagnosis of COVID-19 infection depends on Real Time Reverse Transcriptase Polymerase Chain Reaction and next-generation sequencing [19]. CT findings are similar to those seen in viral pneumonias [20], with multifocal ground glass opacities and consolidation in the peripheral distribution being the most common findings [20]. Chest CT severity score (CT-SS) can be used to quickly and objectively assess the severity of pulmonary involvement in patients with COVID-19 [21].

The aim of this study is to evaluate the cognitive, mental, and sleep states of post-COVID-19 patients 2 months after hospitalization, and to assess the correlation of their cognitive and mental states with the lung involvement by scoring the hospitalization thorax CTs.

## Materials and methods

This study evaluated 40 post-COVID patients aged between 20 and 85 years who admitted to the pulmonary diseases' outpatient clinic of City Hospital, Kayseri, Turkey. The study was approved by the local ethics committee. Participants included in the study after they were briefed on evaluation

tests and written informed consents were obtained. Also, the study was conducted in accordance with the ethical principles specified in the Declaration of Helsinki.

Main inclusion criteria are hospitalization due to COVID-19 infection with PCR testing, a clinically necessary thorax CT at the time of admission to the hospital and admission to outpatient clinic 2 months after discharge from hospital, as well as not having any other known respiratory disease, no intensive-care admissions, absence of dementia, or psychiatric disease. Patients evaluated with Mini-Mental State Exam (MMSE), Montreal Cognitive Assessment (MoCA), Hamilton Rating Scale for Depression, Hamilton Anxiety Rating Scale, and Pittsburgh Sleep Quality Index (PSQI) after inclusion. Thoracic CT scans of the patients included in the study, which were taken during hospitalization, were scored with CT-SS.

Chest CT severity score uses lung opacification as a surrogate for spread of the disease in the lung. According to the anatomic structure, the 18 segments of both lungs were divided into 20 regions, in which the posterior apical segment of the left upper lobe was subdivided into apical and posterior segmental regions, whereas the anteromedial basal segment of the left lower lobe was subdivided into anterior and basal segmental regions. The lung opacities in all of the 20 lung regions were subjectively evaluated on chest CT images using a system attributing scores of 0, 1, and 2 if parenchymal opacification involved 0%, less than 50%, or equal to or more than 50% of each region, respectively [21]. The CT-SS score was defined as the sum of the individual scores in the 20 lung segment regions, ranging from 0 to 40 points. All the CT images were scored by respirologists.

The MMSE and MoCA are cognitive screening tests widely used in clinical practice. While MMSE is a 30-point questionnaire that is used to measure cognitive impairment (it contains orientation to time and place, attention, language, and visual-spatial competency domains), MoCA is a scientific screening tool developed to assess mild cognitive impairment (MCI). The test takes 10 min to administer and the total test score ranges from 0 to 30. It assesses multiple cognitive domains, including memory, language, executive functions, visuospatial skills, calculation, abstraction, attention, concentration, and orientation. A score of < 26 on the MoCA test indicates the presence of cognitive deficits [22].

PSQI is a questionnaire that evaluates sleep quality with questions asked under seven main domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disorders, use of sleep medications, and daytime functions [23]. The Hamilton Depression Scale (HDS) is a 17-item scale measuring the severity of depressive symptoms in individuals. The Hamilton Rating Scale for Depression consists of three- and five-point Likert-type items each provide an evaluation between 0–2 and 0–4. It also includes symptoms of mental and physical anxiety as

well as depression symptoms [24]. The Hamilton Anxiety Rating (HAM-A) Scale was developed by Hamilton (1959), and aims to determine the level of anxiety and symptom distribution in individuals and to measure the change in severity. It consists of 14 items that evaluates both mental and physical symptoms. The presence and severity of the items in the scale are evaluated by the interviewer [25].

## Statistical methods

All statistical analyses were carried out using the IBM SPSS for Windows, version 23.0 program. Numerical variables were summarized as mean  $\pm$  standard deviation or median [min–max], and categorical variables were summarized as numbers and percentages. The Shapiro–Wilk test was used to determine whether the numerical variables showed a normal distribution. The relationship between numerical variables was given with the Spearman correlation coefficient. Statistical significance set at  $P < 0.05$ .

**Table 1** Numbers and percentages of gender distribution, MMSE, MoCA, Hamilton depression, and Hamilton anxiety scores of the patients

	Number	Percent (%)
Gender		
Female	18	45
Male	22	55
MMSE		
Not present	34	85.0
Patients with test scores below the threshold score	6	15.0
MoCA		
Not present	18	45.0
Patients with test scores below the threshold score	22	55.0
Hamilton depression score		
Mild	2	5.0
Medium	15	37.5
Severe	23	57.5
Hamilton anxiety score		
Not present	17	42.5
Mild	4	10.0
Medium	9	22.5
Severe	10	25.0

MMSE Mini-Mental State Evaluation, MoCA Montreal cognitive assessment

## Results

Forty patients were enrolled to the study and median age was  $51.3 \pm 12.4$  years. Of the 40 patients, 55% ( $n = 22$ ) male and 45% ( $n = 18$ ) were female. In total, while MMSE was normal in 85% of patients, early stage cognitive impairment was detected in 15% of patients. The mean MMSE score of the patients was  $26.9 \pm 2.1$ . In the MoCA test, cognitive impairment was detected in 55% of the patients, and the mean MoCA score of the patients was  $19.6 \pm 5.2$ . All of the patients showed depressive symptoms in Hamilton rating scale. Anxiety symptoms were detected in 57.5% of the patients in the Hamilton anxiety scoring system (Table 1).

The average sleep quality of the patients was found to be  $10.7 \pm 3.1$  in Pittsburg sleep quality index and was higher than normal. The mean of the CT-SS, which was scored to evaluate the lung involvement of the patients, was found to be  $4.7 \pm 5.6$ . The mean CRP level of the patients at admission was  $37.1 \pm 45.5$  (Table 2).

The correlation of MoCA and MMSE tests with CT-SS showed no statistically significant relation. In addition, there was no significant correlation between Hamilton depression and anxiety tests and CT-SS. When the Hamilton depression scale was correlated with the MoCA test, the correlation coefficient was calculated as  $-0.316$  and

**Table 2** Mean values of patients' MMSE, MoCA, Pittsburg sleep scale, CT-SS, and CRP scores

	Mean $\pm$ SD	Range
MMSE	$26.9 \pm 2.1$	20–29
MoCA	$19.6 \pm 5.2$	7–27
Pittsburg sleep scale	$10.7 \pm 3.1$	6–17
CT-SS	$4.7 \pm 5.6$	0–19
CRP	$37.1 \pm 45.5$	1–156

MMSE Mini-Mental State Evaluation, MoCA Montreal cognitive assessment, CT-SS chest severity score, CRP C-reactive protein

**Table 3** The correlation of cognitive tests with CT-SS, depression, anxiety, and sleep assessment tests

	MoCA		MMSE	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
CT-SS	$-0.073$	0.665	$-0.069$	0.679
Hamilton depression scale	$-0.316$	0.047	$-0.134$	0.411
Hamilton anxiety scale	$-0.128$	0.433	0.028	0.862
Pittsburg scale	$-0.306$	0.055	$-0.064$	0.697

*r* Pearson correlation coefficient,  $p < 0.05$  statistically significant

MMSE Mini-Mental State Evaluation, MoCA Montreal cognitive assessment, CT-SS chest severity score, CRP C-reactive protein

showed a significant difference ( $p < 0.005$ ). There was also no significant correlation between the patients' MoCA and MMSE tests and Hamilton anxiety and Pittsburg sleep quality indexes (Table 3).

## Discussion

In our study, in accordance with the current literature, it has been shown that cognitive impairment continues even after the recovery phase of the disease in people who had COVID-19 infection. Furthermore, we found that the anxiety and depression scores of the patients were higher than normal. Also, it has been shown that patients had poor sleep quality according to the Pittsburgh sleep scale. However, evaluation for pulmonary involvement with CT-SS did not show any correlation with MMSE and MoCA tests, but we found a correlation between CT-SS and Hamilton depression scale and MoCA test.

The importance of detection and follow-up of COVID-19 in terms of the neuropsychological and psychological consequences has been suggested in the previous studies [5]. Therefore, in terms of appropriate cognitive rehabilitation and psychological support, it is important to learn more about these patients and to recognize them early. MMSE and MoCA can be used as early diagnosis and screening tests. Although MMSE globally accepted as a screening tool for detecting dementia, the MoCA has been shown to be more sensitive in detecting executive dysfunction. Similar to previous studies, our study showed that MoCA provided more sensitive results [26].

Neurological symptoms and cognitive dysfunctions following COVID-19 infection are likely to arise from multiple interactions, particularly direct damage by the virus to the cortex and adjacent subcortical structures, and indirect effects as part of broader systemic illness and psychological distress [15]. In a study which followed COVID-19 patients during the rehabilitation process, neuropsychological dysfunctions were shown 75% of patients in the acute phase and 70% in the post-COVID-19 period [26]. In the analysis of 87 cohort patients; in the subacute phase of the disease, 80% of the patients had been shown to have significant impairments in cognitive functions, including memory, attention, abstraction, and spatial and time orientation [11]. This study also showed that cognitive impairment continued in 70% of the patients even 1 month after discharge. Similarly, our study showed that cognitive impairment continued in 55% of the patients 2 months after their discharge. Another study evaluated the impacts of COVID-19 on cognitive functions in recovered patients, and it was shown that COVID-19 patients exhibited cognitive dysfunction, especially in sustained attention domain [12].

Thorax CT has become a prominent diagnostic method after the emergence of COVID-19 [27]. CT-SS designed to identify the severity of COVID-19 in thorax CT images and offers a simple semiquantitative scoring method [21]. In our study, we also evaluated the extent of lung involvement with CT-SS scores and investigated its correlation with cognitive tests, but we could not find a significant relationship between them. Thus, we can say that the severity of lung involvement is not correlated with cognitive and psychological deterioration of the patients.

Several studies have reported that posttraumatic stress disorder (PTSD), anxiety, and depression are increased among COVID-19 patients [13, 14]. In a study on the psychological effects of SARS-CoV-2 infection, it was shown that 40% of the patients presented with mild depression [26]. In another study, clinically significant depression was reported in approximately 30–40% of COVID-19 survivors at 1, 3, and 6 month follow-up [17]. Especially, in our study like the other studies, the high depression scores and its correlation with cognitive tests indicate the effect of psychological distress on cognitive functions [28]. The increase in depressive symptoms may be related to the emotional responses of these patients when they faced with the difficulties of daily life or when they experience feelings of uncertainty and fear. A recent meta-analysis of psychiatric and neuropsychiatric conditions associated with SARS, MERS, and COVID-19 showed that confusion, depressed mood, anxiety, and insomnia are common symptoms in hospitalized patients during acute illness [15]. Studies suggest that the social levels of symptoms associated with anxiety increase when a serious infectious disease spreads, such as the psychological burden caused by SARS-CoV-2, in which a considerable part of the sample presented anxiety disorders. Among the various impacts of COVID-19, fear and uncertainty about the disease can precipitate disorders, such as anxiety [29]. Similarly, we found high anxiety scores for COVID-19 patients in our study. Furthermore, a study among COVID-19 survivors reported poor sleep quality [18]. Another study investigating the sleep problems in 500 post-COVID-19 patients using PSQI also found poor sleep quality among COVID-19 patients [30]. Likewise, high Pittsburgh sleep scores were found in our study, and the patients were shown to have poor sleep quality. This may be associated with high anxiety scores, depressive mood, and fears.

The main limitations of our study are relatively small sample size and short follow-up period. Therefore, studies with longer follow-up periods including rehabilitation results are needed. Additionally, we used standardized tools to evaluate cognitive and emotional disturbances, but the lack of a control group without confirmed COVID-19 infection by a negative serological test may limit our interpretations.

Our study has shown that patients with COVID-19 still have neuropsychiatric symptoms, even after 2 months of



their illness. In addition to the physiological rehabilitation of COVID-19 patients, cognitive and psychological effects should also be evaluated. It has been shown that long-term rehabilitation of these patients, including cognitive education and psychological services, should be continued.

## Declarations

**Conflict of interest** The authors have no conflicts of interest to declare that are relevant to the content of this article.

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