



Impact of Fatigue on Cognitive Function in Post-COVID19 Survivors

Enas R. Abdelmagid¹, Ebtessam M.Fahmy², Shreen I. Taha³, Rasha M. Elrewainy^{4*}

Abstract

Background: Coronavirus 2 is the cause of COVID-19, a hazardous respiratory disease (SARS-CoV-2). More than 80% of hospitalized patients and 30% of COVID-19 survivors may have long-term effects. The most prevalent and incapacitating symptoms of the post-COVID-19 syndrome are thought to be fatigue and cognitive impairment. **Objective:** The major objective of the current study is to trace fatigue affected post-COVID survivors' cognitive function. **Subjects and Methods:** In this study, 84 cases were enlisted, and they were subdivided into two groups. The study group consisted of 42 post-COVID survivors, and the control group consisted of 42 healthy individuals who were age- and sex-matched. Addenbrooke's cognitive examination revised scale, the fatigue rating scale, and the computer-based Cognitive Assessment therapy (Rehacom system) were adopted in the current study to evaluate each case. **Results:** A clear negative correlation was found between the FSS scores and the ACE-R ($r = -0.98$, $p = 0.001$), as well as between the FSS scores and the degree of logical thinking difficulty ($r = -0.74$, $p = 0.001$) and the FSS scores and the level of figural memory difficulty ($r = -0.93$, $p = 0.001$). Clear positive correlation were detected between the FSS scores and the first quartile response time ($r = 0.94$, $p = 0.001$), the third quartile reaction time ($r = 0.96$, $p = 0.001$), the acquisition time ($r = 0.97$, $p = 0.001$), and the solution time ($r = 0.98$, $p = 0.001$). **Conclusion:** In post-COVID survivors, fatigue has a major impact on cognitive abilities.

7868

KeyWords: COVID-19, Fatigue, cognition.

DOI Number:10.14704/nq.2022.20.8.NQ44812

NeuroQuantology 2022; 20(8): 7868-7874

Introduction

The COVID-19 is a severe acute respiratory syndrome coronavirus, the seventh human coronavirus, was identified in January 2020 during the most recent pneumonia outbreak in Wuhan, Hubei Province, China. (1). The majority of people still had persistent and incapacitating symptoms after covid-19 recovery. In addition to the underlying neuropsychiatric and somatic symptoms, COVID-19 post-acute outcomes also referred to as "long COVID," can include fatigue and cognitive decline. (2, 3)

The occurrence of cognitive issues in post-COVID-19 survivors is a major source of worry, but the nature of these issues or their correlates is still ambiguous. On a broader scale, acute cognitive difficulties are typical. Even more extensive cognitive deficits in attention, memory and executive skills were found after recovery from COVID-19 disease in over 84,000 persons who had been tested online for suspected or biologically proven COVID-19. (4)

Corresponding author: Rasha M. Elrewainy

Address: ¹Demonstrator, Department of Physical Therapy for Neuromuscular Disorders and its Surgery, Faculty of Physical Therapy, Beni-Suef University, Egypt; ²Professor, Department of Neurology, Faculty of Medicine, Cairo University, Egypt; ³Assistant Professor, Department of Physical Therapy for Neuromuscular Disorders and its Surgery, Faculty of Physical Therapy, Beni-Suef University, Egypt; ⁴Assistant Professor, Department of Physical Therapy for Neurology, Faculty of Physical Therapy, Cairo University, Egypt.

E-mail: rasha.elrewainy@pt.cu.edu.eg



In observational studies on COVID-19 cases, 2-4 months after the onset of symptoms, 20%–40% of them reported having trouble in concentration, 20%–34% of them experienced memory impairment, (5) and 36% reported other cognitive issues. (6) It has also been confirmed problems in frontal lobe and, to a lesser extent, temporoparietal cortical hypometabolism are frequent findings in the acute phase of COVID-19-related encephalopathy. (7)

The most frequent long-term health problem experienced by COVID-19 survivors is post-viral tiredness. The tens of millions of disease survivors may be at risk of developing other long-term health problems. According to early findings, post-viral fatigue is the most prevalent long-term health problem affecting illness survivors. (5) The current study traces how post-COVID-19 survivors' cognitive abilities were affected by Fatigue.

Subjects and Methods

The ethical committee of faculty of physical therapy at Cairo University has accredited this cross-sectional case-control study, which was conducted on 84 participants during the course of the months from December 2021 to June 2022. The subjects were recruited from the outpatient clinic. P.T. REC/012/003782 says no. Before taking part, each participant signed an informed consent form.

Two groups were created for the cases. 42 post-COVID survivors made up the study group (GA), while 42 healthy individuals who were matched for age and sex made up the control group (GB).

The inclusion criteria cover the following aspects: Age range from 55 to 65 years, both sexes, recovery time from COVID was from three to six months and a score of at least 6 on the fatigue severity scale.

The exclusion criteria encompass the following aspects: neurological or systemic conditions that could impair cognition, weariness brought on by neurological, psychiatric, endocrine, or metabolic problems, Cognitive impairment that existed before the Covid infection, as well as current drugs such sedatives, anti-epileptics, and anti-depressants that may have an impact on cognition.

Moreover, The Addenbrooke's Cognitive Examination Revised scale, the Fatigue Severity

Scale, and the RehaCom computer-based Cognitive Assessment and Therapy were used to evaluate each case.

Methods

All subjects were assessed using Fatigue Severity Scale, Addenbrooke's Cognitive Examination Revised scale, and RehaCom computer based Cognitive Assessment and Therapy.

A- Fatigue Severity Scale (FSS):

A self-report questionnaire with nine items is called the Fatigue Severity Scale (FSS). Each statement about weariness is an item that the subject scores on a scale from 1 to 7 (totally disagree to completely agree). It is succinct, simple to administer, and exhibits internal consistency and dependability. An FSS score of at least 4 was selected as the threshold for severe fatigue (8).

B- Addenbrooke's Cognitive Examination Revised (ACE-R):

The original Addenbrooke's was developed in 1999 by the Cambridge-based medical council cognition and brain science department to recognize mild dementia and distinguish frontotemporal dementia from Alzheimer's disease. A total score of 100 was derived from the original 26 components, which were divided into 5 subscores: memory (26 points), language (26 points), fluency (14 points), attention (26 points), and visuospatial function (16 points). The deadline is between 12 and 20 minutes, with a 16-minute average (9). The 83-cut-off showed good sensitivity, specificity, likelihood ratios, and post-test probability (in memory clinic base rate) for identifying dementia and non-dementia in a clinical population (10).

C- RehaCom-Computer-based Cognitive Assessment and Therapy

The interactive computerized cognitive examination was conducted using RehaCom software. RehaCom comprises the evaluation of several cognitive processes, including executive functioning, attention, memory, and visual-spatial abilities. The application has numerous modules with varying degrees of complexity. As the subject completes easier procedures successfully, the task difficulty level automatically increases. Recording various errors, test completion times for each patient, and assessment results files allows for consistency over multiple sessions and data storage in a database. The computer provides patients with appropriate instructions and performance feedback in their language. The assessment categories were

7869



allocated among attention, concentration, reaction (length), word memory, verbal memory (i.e., the full text, not just specific words), spatial memory, and figure memory. (11)

Patients' personal information was entered first, and then the RehaCome-related parameters were changed. Figural memory and logical thinking were evaluated. Every section underwent a 30-minute evaluation. At the end of the session, a score for patients was created about the following data when the patient settled into a comfortable sitting posture at the level of the RehaCom system screen. Level of difficulty, quartile reaction time1, and quartile reaction time3 are all included in the figural memory report. Level of difficulty, quartile reaction time1, and quartile reaction time3 are included in the report on logical reasoning.

Statistical analysis

The comparison of case characteristics among groups was carried out using an unpaired t-test. For comparing FSS, ACE-R, logical reasoning, and figural memory between groups, an unpaired t-test was used. To examine the relationship between FSS, ACE-R, logical thinking, and figural memory in patients with post-covid-19, Pearson correlation coefficients were used. All statistical tests had a significance threshold of $p < 0.05$. The statistical program for social studies (SPSS) version 25 for Windows was adopted in the current study for all statistical analyses (IBM SPSS, Chicago, IL, USA).

Results

42 post-COVID-19 survivors and 42 healthy control patients in total were involved in the current study. The flow diagram of the study's cases is shown in Figure 1.

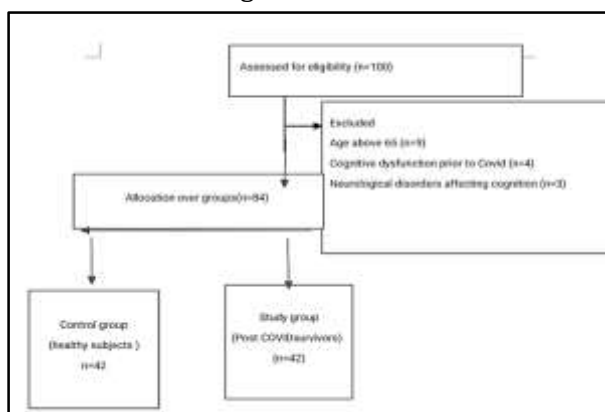


Figure (1): Consort flow diagram of subjects of the study.

Subject characteristics of the study and control groups are shown in table (1).

Table 1. Characteristics of subjects in both groups.

	Study group	Control group	MD	t-value	p-value
	Mean ± SD	Mean ± SD			
Age (years)	60.19 ± 3.14	59.37 ± 2.51	0.82	1.32	0.19
BMI (kg/m ²)	31.58 ± 5.16	31.32 ± 4.39	0.26	0.24	0.8
Duration of illness (months)	4.45 ± 1.13				
Sex, N (%)					
Females	35 (83%)	7 (17%)			
Males	35 (83%)	7 (17%)			

SD: Standard deviation; **p-value:** probability value

Comparison of FSS and ACE-R scores between study and control groups:

There was a clear increase in the mean score of FFS in the study group compared with the control group ($p < 0.001$). Also, there was a noticeable decrease in the mean total score of ACE-R in the study group compared with the control group ($p = 0.001$) (Tables 2, 3).

7870

Table 2. Comparison of mean total scores of FSS and ACE-R between study and control groups.

	Study group	Control group	MD	t-value	p-value
	Mean ± SD	Mean ± SD			
FSS score	6.45 ± 0.23	3.1 ± 0.36	3.35	50.57	0.001*
ACE-R total score	44.54 ± 11.28	93.21 ± 2.19	-48.67	-27.43	0.001*

SD: standard deviation; **MD:** mean difference; **p-value:** probability value; *Significant

Table 3. Comparison of mean scores of ACE-R domains between study and control groups.

	Study group	Control group	MD	t-value	p-value
	Mean ± SD	Mean ± SD			
ACE-R					
Attention score	14.5 ± 1.64	17.04 ± 0.58	-2.54	-9.47	0.001*
Memory score	6.69 ± 3.75	24.73 ± 0.44	-18.04	-30.96	0.001*
Fluency score	4.78 ± 1.73	12.59 ± 0.49	-7.81	-28.08	0.001*
Language score	12.78 ± 3.62	24.52 ± 0.63	-11.74	-20.7	0.001*
Visio Spatial score	5.52 ± 1.17	14.31 ± 0.47	-8.79	-45.06	0.001*
Total ACE-R score	44.42 ± 11.31	93.21 ± 2.19	-27.45	-27.45	0.001*

SD: standard deviation; **MD:** mean difference; **p-value:** probability value; *Significant



Comparison of logical reasoning and figural memory between study and control groups:

There was a significant decrease in the difficulty level of logical reasoning and figural memory in the study group compared to the control group ($p < 0.001$). There was also a significant increase in quartile reaction time 1 and quartile reaction time 3 in the study group compared with the control group ($p < 0.001$). Moreover, there was an apparent increase in the acquisition time and solution time in the study group compared with the control group ($p < 0.001$). (Table 4)

Table 4. Comparison of logical reasoning and figural memory between study and control groups.

	Study group	Control group	MD	t-value	p-value
	Mean ± SD	Mean ± SD			
Logical reasoning:					
Difficulty level	1.23 ± 0.43	4.14 ± 0.97	-2.91	-17.62	0.001*
Quartile reaction time 1 (ms)	13032.31 ± 1932.01	4947.59 ± 846.78	8084.72	24.83	0.001*
Quartile reaction time 3 (ms)	24036.76 ± 8296.44	6643.54 ± 1610.94	17393.22	13.33	0.001*
Figural memory:					
Difficulty level	1.92 ± 0.81	5.42 ± 0.99	-3.5	-17.73	0.001*
Acquisition time (s)	23.57 ± 9.01	4.14 ± 1.37	19.43	13.8	0.001*
Solution time (s)	103.23 ± 3.07	56.64 ± 12.04	46.59	24.29	0.001*

SD: standard deviation; **MD:** mean difference; **p-value:** probability value; *Significant

Correlation between FSS and ACE-R, logical reasoning, and figural memory in the study group:

There was a significant negative relation between scores of FSS and ACE-R ($r = -0.98$, $p = 0.001$). An apparent negative correlation was also found between scores of FSS and difficulty level of logical reasoning ($r = -0.74$, $p = 0.001$) and clear positive correlation was found between FSS scores and quartile reaction time 1 ($r = 0.94$, $p = 0.001$) and with quartile reaction time 3 ($r = 0.96$, $p = 0.001$).

An apparent negative correlation was highlighted between scores of FSS and difficulty level of figural memory ($r = -0.93$, $p = 0.001$), whereas, a noticeable positive correlation was found between scores of FFS with acquisition time ($r = 0.97$, $p = 0.001$) and solution time ($r = 0.98$, $p = 0.001$). (Table 5)

Table 5. Correlation between FSS, ACE-R, logical reasoning, and figural memory in the study group.

		r value	p-value
FSS score	ACE-R total score	-0.98	0.001*
	Logical reasoning		
	Difficulty level	-0.74	0.001*
	Quartile reaction time 1	0.94	0.001*
	Quartile reaction time 3	0.96	0.001*
	Figural memory		
	Difficulty level	-0.93	0.001*
	Acquisition time	0.97	0.001*
	Solution time	0.98	0.001*

r value: Pearson correlation coefficient, **p-value:** probability value; *Significant

Discussion

The outcomes of the current research showed that, in comparison to healthy controls, the study group displayed observable impairment in some cognitive domains, including figural memory, reaction behavior, attention, visuospatial ability, fluency, and language. These results supported by the findings of Hosp et al. (12), who noted that the majority of COVID-19 survivors who are hospitalized or inpatients exhibit cognitive impairment as determined by clinical screenings (e.g., the Brief Memory & Executive Test [BMET] or Montreal Cognitive Assessment [MoCA]) during the acute phase (4-6 weeks after the onset of symptoms) (12).

The present study's findings were consistent with those of a study by Jaywant et al. (13), who discovered that neuropsychological evaluations of post-COVID survivors revealed deficits primarily in executive function, with specific impairment in orientation, processing speed, set-shifting, and divided attention. (13)

Several studies have found that after COVID-19, cognitive impairments occurred in more than 25% of individuals. (14-23) Deficits were noted in verbal fluency, short-term memory, concentration, general memory loss (18, 22, 24, 26), a specific reduction in language, attention, memory, and praxis abilities, and dementia (23). (26).

Some have claimed that executive function issues following COVID-19 infection may be caused by frontal lobe illness (Ardila and Lahiri, 2020).



Within a month of the onset of symptoms, frontoparietal hypometabolism predominates together with severe executive dysfunction (13), revealing a precise neurological basis for the central executive network (CEN).

Furthermore, the outcomes of the current study showed a significant negative correlation between the FSS and ACE-R. Scores, as well as a significant negative correlation between the FSS scores and the difficulty of logical reasoning and figural memory. However, a significant negative correlation was found between the FFS scores and acquisition time and solution time. These results corroborated those of Jason et al. (27) who claimed that among sensitive people, fatigue and cognitive impairment seem to persist and may even get worse over time. Additionally, Twonsend et al. (28) observed that fatigue may negatively affect physical and cognitive abilities as well as health and safety.

On another level, the outcomes of the present study go in line with those of Townsend L et al. [29], who indicated that fatigue may negatively impact health and safety by impairing physical and cognitive functions. Although prior research in many populations has revealed a link between fatigue and physical or cognitive function

According to Jacobson et al., fatigue has been linked to long-term activity impairment (30) It should be mentioned that nine of the 14 research revealed the existence of proinflammatory markers as well as chronic tiredness and/or cognitive impairment in their sample (31,32, 33,34, 35,36, 37), and several studies identified a relationship between elevated inflammation measurements and PCS symptoms (34,35,36).

A kind of post-infectious fatigue syndrome, PCS is characterized by exhaustion and cognitive impairment. It has phenotypic characteristics with ME/CFS, which is frequently brought on by an infectious agent [38]. The chronic psychological stress experienced before and during infection appears to be the primary factor contributing to the COVID-19 effects, together with the systemic inflammation brought on by the viral infection (39). (40,41).

However, some studies were unable to establish a connection between fatigue and cognitive decline. (42,43) This might be because the Mini-Mental State Examination (MMSE) score, which has a lower sensitivity when detecting cognitive impairment, was utilized in academic work.

Conclusion

Based on the outcomes of this study, it is possible to conclude that fatigue and cognitive dysfunctions are related to post-COVID-19 survivors. Therefore, for post-COVID survivors' early detection and rehabilitation of fatigue is important for improving cognitive functioning and quality of life of post covid survivors.

Conflict of interest

Authors declare no conflict of interest.

Funding sources

The authors have no funding to report.

Acknowledgement

The authors are grateful for the patients without whom this study would not have been done.

REFERENCES

1. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020; 579(7798):270–273.
2. A. Carfi, R. Bernabei, F. Landi Persistent symptoms in patients after acute COVID-19. *J. Am. Med. Assoc.*, (2020), 324(6): 603-605.
3. A. Nalbandian, K. Sehgal, A. Gupta, M.V. Madhavan, C. McGroder, J.S. Stevens, J.R. Cook, A.S. Nordvig, D. Shalev, T.S. Sehrawat, N. Ahluwalia, B. Bikdeli, D. Dietz, C. Der-Nigoghossian, N. Liyanage-Don, G.F. Rosner, E.J. Bernstein, S. Mohan, A. A Post-acute COVID-19 syndrome. *Nat. Med.*, (2021), 27(4): 601-615.
4. Hampshire, A., Trender, W., Chamberlain, S.R., Jolly, A., Grant, J.E., Patrick, F., Miazibuko, N., Williams, C., Barnby, J.M., Hellyer, P., Mehta, M.A. Chronic COVID syndrome: the need for an appropriate medical terminology for long-COVID and COVID long-haulers. *J Med Virol*, (2020).
5. Halpin SJ, McIvor C, Whyatt G, et al. post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. *J Med Virol.*, (2021); 93:1013–1022.
6. van den Borst B, Peters JB, Brink M, et al. Comprehensive health assessment three months after recovery from acute COVID-19. *Clin Infect Dis.*, (2020). [Epub ahead of print].
7. Kas A, Soret M, Pyatigorskaya N, et al. The cerebral network of COVID-19-related encephalopathy: a longitudinal voxel-based 18F-FDG-PET study. *Eur J*



- Nucl Med Mol Imaging. (2021). [Epub ahead of print].
8. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol*, (1989); 46: 1121-3.
9. Mioshi E, Dawson K, Mitchell J, et al. The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *Int J of Geriatric Psychiatry*, (2006), 21: 1078-1085
10. Mathuranath PS, Nestor PJ, Berrios GE, et al. A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology*, (2000), 55(11): 1613-1620.
11. Schuhfried G. RehaCom Version 5. Basic Manual [Internet]. Magdeburg (DE): Hasomed; c2003. 52 p. Available from: http://www.hasomed.de/leadadmin/user_upload/Rehacom/Manuale/ENG/RehaComEN.pdf
- 12 J.A. Hosp, A. Dressing, G. Blazhenets, T. Bormann, A. Rau, M. Schwabenland, P.T. Meyer
Cognitive impairment and altered cerebral glucose metabolism in the subacute stage of COVID-19
13. A. Jaywant, W.M. Vanderlind, G.S. Alexopoulos, C.B. Fridman, R.H. Perlis, F.M. Gunning Frequency and profile of objective cognitive deficits in hospitalized patients recovering from COVID-19 *Neuropsychopharmacology* (2021)
14. M.G. Mazza, R. De Lorenzo, C. Conte, S. Poletti, B. Vai, I. Bollettini, E.M.T. Melloni, R. Furlan, F. Ciceri, P. Rovere-Querini, F. Benedetti. Anxiety and depression in COVID-19 survivors: role of inflammatory and clinical predictors. *BrainBehav. Immun.*, (2020), 89: 594-600.
15. F. Alemanno, E. Houdayer, A. Parma, A. Spina, A. Del Forno, A. Scatolini, S. Angelone, L. Brugliera, A. Tettamanti, L. Beretta, S. Iannaccone, F. Di Gennaro. COVID-19 cognitive deficits after respiratory assistance in the subacute phase: a COVID-rehabilitation unit experience.
16. de Graaf, M.A., Antoni, M.L., TerKuile, M.M., Arbous, M.S., Duiniveld, A.J.F., Feltkamp, M.C.W., Groeneveld, G.H., Hinnen, S.C.H., Janssen, V.R., Lijfering, W.M., Omara, S., Postmus, P.E., Ramai, S.R.S., Rius-Ottenheim, N., Schalijs, M.J., Schiemanck, S.K., Smid, L., Stöger, J.L., Visser, L.G., de Vries, J.J.C., Wijngaarden, M.A., Geelhoed, J.J.M., Roukens, A.H.E. Short-term outpatient follow-up of COVID-19 patients: a multidisciplinary approach. *EClinicalMedicine*, (2021), 100731. Google Scholar
17. R. De Lorenzo, C. Conte, C. Lanzani, F. Benedetti, L. Roveri, M.G. Mazza, E. Brioni, G. Giacalone, V. Canti, V. Sofia, M. D'Amico, D. Di Napoli, A. Ambrosio, P. Scarpellini, A. Castagna, G. Landoni, A. Zangrillo, E. Bosi, M. Tresoldi, F. Ciceri, P. Rovere-Querini, M. Adrish. Residual clinical damage after COVID-19: a retrospective and prospective observational cohort study. *PLoS One*, (2020), 15(10): e0239570, 10.1371/journal.pone.0239570.
18. M.M. Gennaro, P. Mariagrazia, R. De Lorenzo, M. Cristiano, P. Sara, F. Roberto, C. Fabio, R.Q. Patrizia, B. Francesco. Persistent psychopathology and neurocognitive impairment in COVID-19 survivors: effect of inflammatory biomarkers at three-month follow-up. *Brain Behav. Immun.* (2021).
19. Y. Lu, X. Li, D. Geng, N. Mei, P.-Y. Wu, C.-C. Huang, T. Jia, Y. Zhao, D. Wang, A. Xiao, B. Yin. Cerebral micro-structural changes in COVID-19 patients - An MRI-based 3-month follow-up study. *EClinicalMedicine*, (2020), 25: 100484, 10.1016/j.eclinm.2020.100484.
20. R. Méndez, V. Balanzá-Martínez, S.C. Luperdi, I. Estrada, A. Latorre, P. González-Jiménez, L. Feded, L. Bouzas, K. Yépez, A. Ferrando, D. Hervás, E. Zaldívar, S. Reyes, M. Berk, R. Menéndez. Short-term neuropsychiatric outcomes and quality of life in COVID-19 survivors. *Intern. Med.* (2021).
21. K.W. Miskowiak, S. Johnsen, S.M. Sattler, S. Nielsen, K. Kunalan, J. Rungby, T. Lapperre, C.M. Porsberg. Cognitive impairments four months after COVID-19 hospital discharge: pattern, severity, and association with illness variables. *Eur. Neuropsychopharmacol.*, (2021), 46: 39-48.
22. F. Negrini, I. Ferrario, D. Mazziotti, M. Berchicci, M. Bonazzi, A. de Sire, S. Negrini, L. Zapparoli. Neuropsychological features of severe hospitalized coronavirus disease 2019 patients at clinical stability and clues for post-acute rehabilitation. *Arch. Phys. Med. Rehabil.*, (2021), 102(1): 155-158.
23. D.L. Sykes, L. Holdsworth, N. Jawad, P. Gunasekera, A.H. Morice, M.G. Crooks. Post-COVID-19 symptom burden: what is long-COVID and how should we manage it? *Lung*, (2021), 199(2): 113-119.
24. D.M. Whiteside, V. Oleynick, E. Holker, E.J. Waldron, J. Porter, M. Kasprzak. Neurocognitive



- deficits in severe COVID-19 infection: case series and proposed model. *Clin. Neuropsychol.*, (2021), 35(4): 799-818.
25. S.E. Daugherty, Y. Guo, K. Heath, M.C. Dasmariñas, K.G. Jubilo, J. Samranvedhya, M. Lipsitch, K. Cohen. Risk of clinical sequelae after the acute phase of SARS-CoV-2 infection: retrospective cohort study. *BMJ*, (2021), 373, Article n1098.
26. Y.F. Shang, T. Liu, J.N. Yu, X.R. Xu, K.R. Zahid, Y.C. Wei, X.H. Wang, F.L. Zhou. Half-year follow-up of patients recovering from severe COVID-19: analysis of symptoms and their risk factors. *Intern. Med.*, (2021), 290(2): 444-450.
27. M. Taquet, S. Luciano, J.R. Geddes, P.J. Harrison. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. *Lancet Psychiatry*, (2021), 8(2): 130-140.
28. K. Manning, M.J. Zvolensky, L. Garey, L.J. Long, M.W. Gallagher. The explanatory role of fatigue severity in the relation between COVID-19 perceived stress and depression, anxiety, and panic severity. *Cognit. Behav. Ther.*, (2021), pp: 1-11.
29. Moore RD, Romine MW, O'Connor PJ, Tomporowski PD. The influence of exercise-induced fatigue on cognitive function. *J Sports Sci*, (2012); 30: 841-850.
31. Jacobson, K.B., Rao, M., Bonilla, H., et al. Patients with uncomplicated COVID-19 have long-term persistent symptoms and functional impairment similar to patients with severe COVID-19: a cautionary tale during a global pandemic. *Clin Infect Dis*. Published online, (2021). doi:10.1093/CID/ciab103.
32. M. Taboada, A. Cariñena, E. Moreno, N. Rodríguez, M.J. Domínguez, A. Casal, V. Riveiro, M. Diaz-Vieito, L. Valdés, J. Álvarez, T. Seoane-Pillado. Post-COVID-19 functional status six-months after hospitalization. *Infect.*, (2021), 82(4): e31-e33.
33. Fortini, A., Torrigiani, A., Sbaragli, S., et al. COVID-19: persistence of symptoms and lung alterations after 3-6 months from hospital discharge. *Infection*. Published online June 6, (2021). doi:10.1007/s15010-021-01638-1.
34. García-Abellán J, Padilla S, Fernández-González M, et al. Long-term clinical, virological and immunological outcomes in patients hospitalized for COVID-19: antibody response predicts long COVID. *bioRxiv*. Published online March 8, (2021). 03.08.21253124. doi:10.1101/2021.03.08.21253124.
35. S.W.X. Ong, S.-W. Fong, B.E. Young, Y.-H. Chan, B. Lee, S.N. Amrun, R.-L. Chee, N.-W. Yeo, P. Tambyah, S. Pada, S.Y. Tan, Y. Ding, L. Renia, Y.-S. Leo, L.F.P. Ng, D.C. Lye. Persistent symptoms and association with inflammatory cytokine signatures in recovered Coronavirus disease 2019 patients.
36. PHOSP-COVID Collaborative Group, Evans RA, McAuley H, et al. Physical, cognitive and mental health impacts of COVID-19 following hospitalization – a multi-center prospective cohort study. *bioRxiv*. Published online March 24, (2021), 03.22.21254057. doi:10.1101/2021.03.22.21254057.
37. M. Skala, M. Svoboda, M. Kopecky, E. Kosova, M. Hyrs, M. Homolac, V. Chrobok, P. Bostik, M. Fajfr, P. Prasil, S. Plisek, R. Sleha, V. Koblizek. Heterogeneity of post-COVID impairment: interim analysis of a prospective study from Czechia. *Virol J.*, (2021), 18 (1), 10.1186/s12985-021-01546-8.
38. D.L. Sykes, L. Holdsworth, N. Jawad, P. Gunasekera, A.H. Morice, M.G. Crooks. Post-COVID-19 symptom burden: What is long-COVID and how should we manage it? *Lung*, (2021), 199(2): 113-119.
39. Santis, L.V.-D., Pérez-Camacho, I., Sobrino, B., et al. Clinical and immunobiological status 12 weeks after infection with COVID-19: a prospective observational study. *bioRxiv*. Published online October 8, (2020). doi:10.1101/2020.10.06.20206060.
40. E.A. Troyer, J.N. Kohn, S. Hong. Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. *Brain Behav. Immun.* (2020), 10.1016/j.bbi.2020.04.027.
41. M. Passavanti, A. Argentieri, D.M. Barbieri, B. Lou, K. Wijayarathna, A.S.F. Mirhosseini, F. Wang, S. Naseri, I. Qamhia, M. Tãngerãs. The psychological impact of COVID-19 and restrictive measures in the world. *Affect. Disord.*, (2021), 283: 36-51.
42. Ponchel A, Bombois S, Bordet R, Hénon H. Factors associated with poststroke fatigue: a systematic review. *Stroke Res Treat.*, (2015), 347920. DOI: 10.1155/2015/347920.
43. Lees R, Selvarajah J, Fenton C, Pendlebury ST, Langhorne P, Stott DJ, et al. Test accuracy of cognitive screening tests for diagnosis of dementia and multi-domain cognitive impairment in stroke. *Stroke*. (2014), 45:3008-18.

