

LETTER



Two-year physical, mental and cognitive outcomes among intensive care unit survivors treated for COVID-19

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Dear Editor,

Critical illness can cause new or worsened physical, mental and cognitive symptoms following intensive care unit (ICU) treatment, known as post-intensive care syndrome (PICS), which can persist for years [1]. ICU patients treated for coronavirus disease 2019 (COVID-19) frequently experience symptoms of PICS 1 year after ICU treatment; however, their long-term outcomes beyond the first year are largely unknown [2]. We therefore conducted a 2-years follow-up study to further guide ICU (after) care.

This prospective longitudinal cohort study was part of the MONITOR-IC study which was conducted in 7 Dutch hospitals [3]. All adult ICU patients admitted with COVID-19 between 1st March 2020 and 1st June 2020 who survived ICU treatment were eligible. Outcomes were measured at 1-year and 2-years follow-up using a paper or online based survey. A detailed overview of the methods is described in the electronic supplementary materials (ESM, Methods). The primary outcomes were the occurrence of physical (frail, fatigue, new physical problems), mental (anxiety, depression and post-traumatic stress disorder) and cognitive symptoms (ESM, Table 1). Secondary outcomes were Quality of Life (QoL)

and work-related problems. Differences between 1-year and 2-year outcomes were examined.

In total, 292 ICU survivors were eligible and 183 were included of whom 122 (66.7%) completed the questionnaire at both time-points (ESM, Fig. 1). Their mean age was 61.5 (standard deviation [SD], 9.5) years and 28.7% were female (ESM, Table 2). Compared to 1-year follow-up, the occurrence of physical (73.8% vs. 74.4%, $p=1.00$) and cognitive symptoms (14.2% vs 20.8%, $p=0.17$) remained significant, and the occurrence of mental symptoms even increased (19.8% vs 29.5%, $p=0.01$) after 2 years (Table 1). The most frequently experienced physical problems after 1 year, as well as after 2 years, were a weakened condition and musculoskeletal problems (ESM, Fig. 2). QoL was similar between 1-year and 2-year follow-up. At 2-year follow-up, fewer survivors experienced work-related problems compared to the 1-year follow-up (1-year: 66% vs 2-year: 32%, $p=0.04$).

Our findings show that the post-ICU sequelae after ICU treatment for COVID-19 remains significant up to 2 years after treatment. In fact, most survivors do not seem to recover from their symptoms within 2 years and even experience an increase in mental symptoms. Studies exploring PICS in non-COVID-19 patients with acute distress respiratory syndrome (ARDS) reported that survivors experience persisting or newly developed symptoms beyond the first year after ICU treatment, similar to our findings in COVID-19 survivors [1, 4]. The role of COVID-19 and the pandemic in the development of PICS remain largely unclear; however, new impairments after COVID-19, often referred to as 'long COVID', seem to be more severe in patients treated in the ICU compared to those treated in wards only or ambulatory patients at 2-year

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Table 1 Outcome scores and symptom occurrence rates in patients with COVID-19, 1 year and 2 years after ICU admission

	1-year follow-up N = 122	2-year follow-up N = 122	P value 1- vs 2-year follow-up
Physical symptoms			
At least one physical symptom—No./total (%)	90/122 (73.8)	90/121 (74.4)	1.00
Clinical Frailty Scale			
Score, median (IQR)	2 (2–3)	2 (2–3)	0.35
Frail ^a —No./total (%)	6/122 (4.9)	6/122 (4.9)	1.00
Checklist Individual Strength-8			
Score, median (IQR)	29 (17–40)	30 (20–41)	0.07
Fatigue ^b —No./total (%)	68/122 (55.7)	67/121 (55.4)	1.00
New or worsened physical problems ^c			
No. of problems—median (IQR)	2 (0–5)	2 (0–6)	0.62
≥ 1 problems—No./total (%)	85/122 (69.7)	82/122 (67.2)	0.66
Mental symptoms			
At least one mental symptom—No./total (%)	24/121 (19.8)	36/122 (29.5)	0.01
Hospital Anxiety and Depression scale—Anxiety			
Score, median (IQR)	3 (1–5)	3 (1–7)	0.06
Anxiety ^d —No./total (%)	16/122 (13.1)	26/122 (21.3)	0.03
Hospital Anxiety and Depression scale—Depression			
Score, median (IQR)	2 (1–5)	3 (1–6)	0.03
Depression ^d —No./total (%)	17/122 (13.9)	21/122 (17.2)	0.39
Impact of event scale-6			
Score, median (IQR)	0.5 (0.2–1.2)	0.5 (0–1)	0.82
PTSD ^e —No./total (%)	7/121 (5.8)	11/122 (9)	0.34
Cognitive symptoms			
Cognitive failure questionnaire-14			
Score, median (IQR)	25.4 (14.6–34.4)	28.7 (15.7–41.6)	0.03
Cognitive symptoms ^f —No./total (%)	17/120 (14.2)	25/120 (20.8)	0.17
Quality of Life			
Short form - 12 ^g - mean(SD)			
Physical component summary	46.2 (9.8)	46.1 (9.1)	0.97
Mental component summary	51 (10.2)	50.6 (10.7)	0.86
Work-related problems^h			
Not fully returned to work, No./total (%)	35/53 (66)	22/68 (32.4)	0.04

Abbreviation: IQR interquartile range

^a Frailty was measured using the CFS, a score range, 1 (very fit) to 9 (terminally ill), with a score of 5 or greater indicating frailty

^b Fatigue was measured with the Checklist Individual Strength—fatigue subscale (CIS-8) and being fatigued was defined by a CIS-8 score of ≥ 27 on the, with higher scores indicating being more fatigued

^c Physical problems were objectified by a list of 30 symptoms and were present if at least one symptom was moderate or severe

^d Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS) anxiety and depression subscales, ranging from 0 (best) to 21 (worst), with higher scores indicating worse symptoms. The presence of symptoms was defined by a HADS subscale score of ≥ 8

^e Post-traumatic stress disorder (PTSD) was measured using the Impact of Event Scale-6 and the presence of symptoms was defined by a mean of all questions ≥ 1.75. Higher scores indicate worse symptoms

^f Cognitive symptoms were defined as a score of > 43 on the abbreviated Cognitive Failure Questionnaire (CFQ-14). Higher scores indicate worse symptoms

^g Quality of Life was measured with the Short From-12 physical and mental component summary scores with a higher score indicating a better QoL

^h Work-related problems were assessed by one question with multiple answers to objectify the experienced problems

follow-up [5]. These findings highlight the importance of prolonged follow-up after ICU treatment for COVID-19, with a more attentive approach on mental rehabilitation.

We advocate for the implementation of structured, multidisciplinary, rehabilitation programs, programs for ICU patients treated for COVID-19, just as for other

ICU patients, to prevent or mitigate prolonged post-ICU related impairments.

Supplementary Information

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Author contributions

HH had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. HH, JGH, MB, MZ contributed to study concept and design. HH, MZ, MB contributed to analysis and interpretation of data. HH contributed to drafting of the article. JGH, SC, IJ, EE, KSS, DB-B, MB, MZ contributed to critical revision of the article for important intellectual content. MB, MZ both supervised the study. The corresponding author attests that all listed authors meet the ICMJE authorship criteria and that no others meeting the criteria have been omitted.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflicts of interest

All authors declare no conflict of interest.

Ethical approval

The study was approved by the medical ethical committee of Arnhem-Nijmegen, the Netherlands (CMO) (CMO-number—2020-6878).

Consent to participate

Informed consent was obtained from all participating ICU survivors and family members.

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