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Letter to the editor

# Post-intensive care syndrome in patients surviving COVID-19

**Dear Editor.** We report the clinical manifestations of post-intensive care syndrome (PICS) in COVID-19 patients, resulting in aggregate physical, cognitive and mental impairments. Such impairments were previously described as new or worsening impairments in physical, cognitive, or mental health status arising after critical illness and persisting beyond acute care hospitalization [1]. They were formulated from an observational series of 45 of 51 consecutive patients with acute respiratory distress syndrome due to COVID-19 who were discharged from an intensive care unit (ICU) in France during the first epidemic wave. Between April and September 2020, all patients underwent similar evaluations in pneumology or physical medicine and rehabilitation (PMR) departments, within the first month and 3 months after ICU discharge in follow-up consultations, by physicians of two French PMR departments. All 51 patients were alive at 3 months after ICU discharge, but 6 could not be re-evaluated (refused an appointment at 3 months). In all 45 remaining patients, COVID-19 was confirmed by a positive RT-PCR test and/or consistent CT-scan results, assessed by trained radiologists (i.e., mainly ground-glass opacities with adequate pattern and distribution for COVID-19 diagnosis).

Patient data are in the Table; 37/45 (82%) patients were men, with mean (SD) age 58.0 (11.0) years (range 27–76). The mean length of ICU stay and invasive mechanical ventilation was 31.6 (16.1) and 25.4 (12.2) days, respectively; 34/45 (76%) patients underwent prone position sessions, with mean number of sessions 3.3 (2.7). All experienced at least one complication during the hospitalization in the ICU, mainly infection (37/45 [82%]), metabolic or ionic disorder (34/45 [76%]) or thromboembolic event (22/45 [49%]).

During the first month after ICU discharge, the most frequent physical PICS manifestation was neurological impairment, with ICU-acquired weakness, defined as a Medical Research Council (MRC) score <48/60 [2], in 26/44 (59%) patients, and/or peripheral nerve injury in 14/44 (32%). Only 4/45 (9%) patients had central neurological manifestations: 2 with seizures, 1 encephalopathy and 1 cerebral haemorrhage. In all, 21/44 (48%) patients exhibited osteoarticular impairment, defined as pain and/or joint stiffness, especially in the upper limb, and 20/45 (44%) had bedsores, including 15 localizations consistent with prone positioning (i.e., face, chest and anterior tibial). Cognitive PICS manifestations were delirium, defined as time and space disorientation, hallucination, disturbed wake–sleep cycles and/or motor agitation (9/45 [20%] patients) and altered mean Montreal Cognitive Assessment questionnaire (MoCA) and/or Frontal Assessment Battery (FAB) scores: 21.9/30 (6.0) and 14.1/18 (3.8), respectively. Mental PICS manifestations were anxiety and depression, with mean scores on the Hospital Anxiety and Depression subscales of 5.7/21(3.5) and 4.4/21 (3.5).

At 3 months after ICU discharge, the most frequent physical PICS manifestation was osteoarticular impairment, in particular of the shoulder (26/45 [58%] patients), including 4 retractile capsulitis cases confirmed by MRI and 22 rotator cuff decompensations. A total of 27/45 (60%) patients had peripheral nerve injury, mainly sensitive nerve injury occulted at 1 month because of tiredness or agitation, and only 2/45 (4%) had persistent ICU-acquired weakness. Functional capacity was assessed with the modified Borg Dyspnoea scale, after the 6-min walk test, with mean score 3.5/10 (2.2); the mean SpO2 (%) at rest and after exertion was 98% (1.3) and 97% (2.2); the mean 6-min walk test score was 456.3 (158.1) m and the mean score of 5 repetitions of the sit-to-stand test was 14.2 (5.0) sec, below the expected values for healthy adults of the same age: 588 m and 7.7 s [3–5], respectively. The mean MocA and FAB scores were 23.5/30 (5.5) and 15.5/18 (2.4). The mean anxiety and depression scores on the Hospital Anxiety and Depression subscales were 6.6/21 (5.1) and 6.6/21 (5.4), and the mean Post-traumatic stress disorder CheckList-Simple (PCL-S) score was 36.4/85 (18.5). Median (interquartile range) activities of daily living score was 6 (5.5–6). Overall, 40/45 (89%) patients were hospitalized in a PMR department, 44/45 (98%) had returned home after a mean hospital stay of 74.0 (26.8) days, and 8/31 (26%) had returned to work.

In this consecutive series of COVID-19 patients surviving an ICU stay in the first COVID-19 wave in France, all experienced at least one physical impairment during the first month after ICU discharge. At 3 months, most patients still had clinically relevant physical impairment, with a high prevalence of shoulder and peripheral nerve injuries. Overall, 20% of patients exhibited delirium, a clinical expression of acute brain dysfunction, and all experienced cognitive disorder, such as memory loss or difficulty in executive functions, during the first month after ICU discharge. At 3 months, memory, attention, processing speed and executive function remained altered, and most patients did not fully recover in these areas (MocA score <26/30 and FAB score <16/18) [6,7]. For one third of patients, the anxiety and depression scores were clinically significant (>7/21) [8] at 1 and 3 months, and for more than 40% of the patients, the PCL-S score (>34) at 3 months was consistent with a possible post-traumatic stress disorder [9] possibly requiring psychological follow-up. This finding agrees with a recent study regarding the risk of psychiatric sequelae after a COVID-19 episode [10].

COVID-19 patients surviving an ICU stay can exhibit several well-identified risk factors of PICS, including prolonged mechanical ventilation (>7 days), use of a neuromuscular blocking agent and acute respiratory distress syndrome [11]. Long-term evolution is unknown, and data are lacking to determine whether neurological complications are related to direct or indirect viral action [12]. However, in this series, physical, psychological and cognitive impairments were similar to those usually observed in non-COVID patients surviving an ICU stay [13–18], and all patients but one had returned home and recovered sufficient autonomy despite remaining with osteoarticular

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**Table**
Characteristics of patients with COVID-19 and intensive care unit (ICU) stay as well as post-ICU stay features at 1 and 3 months ($n = 45$).

| Patient characteristics | | |
|---|---|---|
| Men | 37/45 (82) | |
| Age (years), mean (SD) | 58.0 (11.0) | |
| Body mass index (kg/m$^2$), mean (SD) | 28.0 (4.6) | |
| Professional categories | | |
| • High professional occupation | 6/45 (13.3) | |
| • Intermediate occupation and employees | 11/45 (24.5) | |
| • Labourer, craftsman, farmer | 14/45 (31.1) | |
| • Unemployed or retired | 14/45 (31.1) | |
| Medical history | | |
| • High blood pressure | 19/45 (42) | |
| • Diabetes | 16/45 (36) | |
| • Obesity | 13/45 (29) | |
| **ICU stay characteristics** | | |
| Length of stay (days), mean (SD) | 31.6 (16.1) | |
| Length of invasive mechanical ventilation (days), mean (SD) | 25.4 (12.2) | |
| Tracheostomy | 7/45 (16) | |
| Receiving extra-corporeal membrane oxygenation | 2/45 (5) | |
| Duration (cumulated days) under neuroblockade agent, mean (SD) | 9.1 (5.9) | |
| Weight loss in ICU (kg), mean (SD) | −6.9 (13.4)[a] | |
| Prone positioning | 34/45 (76) | |
| • number of sessions, mean (SD) | 3.3 (2.7)[b] | |
| Complications | 45/45 (100) | |
| • Infection | 37/45 (82) | |
| • Metabolic or ionic disorder | 34/45 (76) | |
| • Thromboembolic event | 22/45 (49) | |
| • Neurological event | 21/45 (47) | |
| • Other | 35/45 (78) | |
| **Post-ICU syndrome** | **At 1 month** | **At 3 months** |
| Physical impairments | | |
| • MRC score, mean (SD) /60 | 42.9 (11.2)[c] | 55.4 (6.7) |
| • Critical illness neuromyopathy (MRC score <48/60) | 26/44 (59) | 2/45 (4) |
| • Central neurological manifestation | 4/44 (9) | 3/45 (7) |
| • Peripheral nerve injury | 14/44 (32) | 27/45 (60) |
| • Osteoarticular impairment | 21/44 (48) | 37/45 (82) |
| ○ Shoulder | 17/44 (39) | 26/45 (58) |
| ○ Other upper limb | 4/44 (9) | 3/45 (7) |
| ○ Lower limb | 4/44 (9) | 9/45 (20) |
| ○ Back pain | 0/44 (0) | 5/45 (11) |
| • Bedsores | 20/45 (44) | 13/45 (29) |
| • Dysphonia | NA | 17/45 (38) |
| • Dysphagia | NA | 1/45 (2) |
| • 6MWT (m), mean (SD) | NA | 456.3 (158.1)[c] |
| • Five-repetition sit-to-stand test (sec), mean (SD) | NA | 14.2 (5.0)[d] |
| • Modified Borg Dyspnoea scale score, after 6MWT, mean (SD) /10 | NA | 3.5 (2.2)[c] |
| • SpO2 (%) at rest, mean (SD) | NA | 97.7 (1.3) |
| • Post-exertion (6MWT) SpO2 (%), mean (SD) | NA | 97.3 (2.2)[e] |
| Cognitive impairment | | |
| • Delirium | 9/45 (20) | NA |
| • MoCA, mean (SD) /30 | 21.9 (6.0)[f] | 23.5 (5.5)[e] |
| • Frontal Assessment Battery, mean (SD) /18 | 14.1 (3.8)[g] | 15.5 (2.4)[c] |
| Mental health impairments | | |
| • HAD anxiety, mean (SD) /21 | 5.7 (3.5)[b] | 6.6 (5.1)[d] |
| | 10/32 (31) | 16/42 (38) |
| ○ Including patients with score ≥8/21 | | |
| • HAD depression, mean (SD) /21 | 4.4 (3.5)[b] | 6.6 (5.4)[d] |
| | 6/32 (29) | 15/45(36) |
| ○ Including patients with score ≥8/21 | | |
| • PCL-S, mean (SD) /85 | NA | 36.4 (18.5)[h] |
| | NA | 15/35 (43) |
| ○ Including patients with score ≥ 34/85 | | |
| Other | | |
| • Hospitalization in PMR department | NA | 40/45 (89) |
| • Length of stay in PMR (days), mean (SD) | NA | 27.5 (17.8) |
| • Activities of daily living score /6, median (IQR) | 4.5 (3–6)[f] | 6 (5.5–6)[e] |
| • Return to home | *NA* | 44/45 (98) |
| • Total length of hospital stay (days), mean (SD) | *NA* | 74.0 (26.8)[c] |
| • Return to work | *NA* | 8/31 (26) |

Data are n/N (%) unless otherwise indicated.
[a] $n = 33$.
[b] $n = 32$.
[c] $n = 44$.
[d] $n = 42$.
[e] $n = 43$.
[f] $n = 38$.
[g] $n = 37$.
[h] $n = 35$.
6MWT, Six-min walk test; HAD, Hospital Anxiety and Depression scale; MoCA, Montreal Cognitive Assessment questionnaire; MRC, Medical Research Council; PCL-S, Posttraumatic stress disorder CheckList-Simple; PMR, physical medicine and rehabilitation; NA, not assessed.

and neuro-psychological impairment. These findings highlight the importance of early and multidisciplinary rehabilitation in managing PICS in survivors of an ICU stay during and after the pandemic [19,20].

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