The Importance of Rehabilitation for Functional Recovery and Long-Term Outcomes for Recovery From Critical COVID-19 Illness*

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In this issue of *Critical Care Medicine*, Stripari Schujmann et al (1) described a prospective, multicenter study analyzing the trajectory of critically ill patients with COVID-19 during their critical care illness. It described the disease course of 328 survivors admitted between July 2020 and July 2021 across four ICUs in Sao Paulo, Brazil. The primary outcome was the Barthel Index (BI) measured at ICU and at hospital discharge. Secondary outcomes included duration of mechanical ventilation, ICU and hospital length of stay (LOS), muscle and hand grip strength, development of ICU-acquired weakness, and mobility milestones including time to out of bed and ambulation. Documented ICU exposures included mechanical ventilation, sedation, renal replacement therapy, proning, and receipt of physical therapy. The authors excluded patients who died in hospital, had a short ICU stay (i.e., < 4 d), those who had a functional decline due to other complications, and those who could not participate with their assessment.

The cohort was functionally independent at baseline (i.e., BI = 100 points, described further below), relatively young (i.e., mean [sd] 55.3 (14.7) yr), and had ICU and hospital LOS of 13.9 (11.2) and 25.6 (23.0) days, respectively. Patients were quite sick with a Simplified Acute Physiology Score (SAPS)–3 score of 51.2 (16.5). Just over half of the cohort (i.e., 52.8%) received mechanical ventilation for 9.3 (8.2) days and accompanying sedation for 7.4 (6.0) days; 35.4% received neuromuscular blockade, and 33% of patients required proning during their ICU stay. The majority of the cohort (93.8%) received corticosteroids, and 11.2% required renal replacement therapy. Although no data were available on nutritional status, 56.3% of patients had reported hyperglycemia during this ICU stay. Mobility was recorded as the time to out-of-bed patient mobilization from ICU admission.

The authors identified three outcome states at hospital discharge based on BI class. The BI was a marker of functionality that included an assessment of 10 activity and mobility activities, where each item's rating reflected the amount of assistance required to complete an activity. Scores vary from 0 to 100, where higher scores reflect better function (2). It is valid and reliable for use in ICU survivors, the smallest detectable change at ICU discharge is 20 points, and scores greater than 85 reflect mild to no impairment (2). In the study by Stripari Schujmann et al (1), the authors found that 44% of included patients were functionally independent (BI score > 85 at ICU and hospital discharge), 33% recovered functionality (BI score < 85 at ICU discharge and

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> 85 at hospital discharge), and 22% were functionally dependent (BI score < 85 at both ICU and hospital discharge).

The authors developed regression models to identify factors associated with recovered functionality and functional dependence. Recovery to baseline independence during the ward stay was associated with shorter ICU LOS (odds ratio [OR] 95% CI, [0.97, 0.94–0.99]) and higher muscle strength by Medical Research Council test at ICU discharge (1.13, 1.08–1.18). The factors significantly associated with functional dependence at ICU discharge were longer time until the first day to out-of-bed patient mobilization (1.20, 1.11–1.13), older age (1.02, 1.01–1.04), hyperglycemia (2.52, 1.56–4.07), and higher SAPS-3 score (1.02, 1.01–1.04). For patients who were mechanically ventilated, longer time to out-of-bed patient mobilization and longer duration of sedation use were associated with becoming functionally dependent at ICU discharge ([1.11, 1.06–1.24] and [1.14, 1.03–1.27], respectively).

CONTEXTUALIZING THE RESULTS

How does the study by Stripari Schujmann et al (1) compare with others measuring the BI? In a cohort of 122 general ICU patients from the pre-COVID era, the median (interquartile range [IQR]) BI score at ICU discharge was 25 (10–60; rater 1) (3). In the seminal randomized clinical trial of early physical therapy and occupational therapy, the median (IQR) BI scores at hospital discharge for those who started rehabilitation within 72 hours of ICU admission was 75 (IQR 7.5–95), and those in the control group 55 (0–85) (4). Patients enrolled in the current study by Stripari Schujmann et al (1) had higher mean (SD) BI scores of 73 (24) at ICU discharge and 85 (19) at hospital discharge. Thus, in the study by Stripari Schujmann et al (1) of ICU COVID survivors, their functional status at ICU discharge was "better" than typical ICU patients and appeared "similar" at hospital discharge to those receiving early physical therapy in the pre-COVID era. However, the current study by Schujmann et al (1) restricted their analysis to survivors, which is different than Schweickert et al (4), who included decedents (and assigned a Barthel score of 0). Of the patients "excluded" from the current study by Stripari Schujmann et al (1), 56 had poor outcomes (i.e., death or cognitive/functional impairment, Fig. 1 [1]), which may contribute to a health survivor bias in the reported results. Thus, the functional status of previously healthy patients recovered from COVID-19 infection may be severely impaired.

Postintensive Care Syndrome

ICU survivors are at risk for postintensive care syndrome including physical deconditioning, cognitive impairment, mood disorders, residual physical or mental fatigue, and persistent pain (5). ICU survivors are also at risk of developing new or worsening frailty. Frailty is a multidimensional syndrome characterized by decreased reserve and diminished resistance to stressors and a state of vulnerability where minimal stress may cause catastrophic loss of function (6). Frailty is associated with an increased risk of disability, is dynamic, is preventable, and is potentially reversible (7). Impaired functional status, as indicated by a diminished BI score, may be a marker of frailty. Previous studies have demonstrated that in ICU survivors from the pre-COVID era, 46% had frailty at 3 months, and 61% progressed to a worse frailty state from baseline (7). This in turn may affect quality of lives and future disease states. Precomorbid state of frailty is associated with worse outcomes, and this may correlated with a decreased baseline BI score (8). Any intervention that may limit post-critical illness frailty is warranted and as indicated by the study by Stripari Schujmann et al (1) may encompass modifiable factors such as rehabilitation started in the ICU.

The authors provide a good foundation of baseline characteristics for future research; however, they did not report the sex or nutritional status of enrolled participants. COVID-19 is more likely to affect males than females in the ICU, and the prevalence of frailty in critically ill adults is higher for females than males (9). Females are more vulnerable for ICU-acquired weakness (10). Malnutrition leads to an increased catabolic state and deconditioning (11). Without information relating to these variables, we have an incomplete picture of factors associated with functional recovery. Future studies should focus on sex-specific factors and nutritional variables related to recovery from critical illness associated with COVID-19 infection.

Need for Rehabilitation Treatments

Clearly, rehabilitation interventions for patients with COVID-19 are important, starting from ICU and returning to the community. Mechanical ventilation, sedation, paralysis, proning, and steroids (and associated hyperglycemia) are all necessary treatments in the ICU; rehabilitation interventions are potentially modifiable exposures. In the pre-COVID era, early rehabilitation (i.e., within 1 wk of admission) is safe and can improve functional outcomes (12). The study by Stripari Schujmann et al (1) reports mobility milestones, and future studies reporting rehabilitation activities are needed. To advance the field, we need carefully designed rehabilitation interventions, ideally embedded within health systems. Rehabilitation interventions are complex, and explicit description using an approach like the Rehabilitation Treatment Specification System would help advance multidisciplinary understanding of the "active ingredients" of treatments (13).

Need for Longer Term Outcomes

We urgently need to understand posthospital outcomes in ICU COVID survivors. Although the authors of the study by Stripari Schujmann et al (1) followed patients from ICU admission to the ward and to hospital discharge, we need further studies to understand patients' disposition posthospital discharge and their reintegration into society following their critical illness. The anticipated enduring impact of COVID-19 on patients' recovery was described early in the pandemic, including functional, cognitive, and mental health dysfunction (14). Rehabilitation started in the ICU is a potentially noninvasive, modifiable intervention that could improve outcomes in patients recovering from critical illness associated with COVID-19 infection. Future work is needed to evaluate how specific rehabilitation factors (i.e., timing, intensity, type) are associated with variables related to functional recovery from critical illness (i.e., sex and nutritional status), posthospital, and long-term healthcare outcomes following COVID-19 infections. Studies embedded in healthcare systems could allow development of patient cohorts from ICU admission to hospital discharge, posthospital rehabilitation to home, and facilitate long-term longitudinal follow-up with health administrative databases (15). This in turn will allow future investigators to evaluate the most appropriate rehabilitation interventions to improve outcomes for patients recovering from critical COVID-19 illness.

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REFERENCES

1. Schujmann DS, Lunardi AC, Peso CN, et al: Functional Recovery Groups in Critically Ill COVID-19 Patients and Their Associated Factors: From ICU to Hospital Discharge. *Crit Care Med* 2022; 50:1799–1808
2. Collin C, Wade DT, Davies S, et al: The Barthel ADL index: A reliability study. *Int Disabil Stud* 1988; 10:61–63
3. Dos Reis NF, Figueiredo FCXS, Biscaro RRM, et al: Psychometric properties of the Barthel index used at intensive care unit discharge. *Am J Crit Care* 2022; 31:65–72
4. Schweickert WD, Pohlman MC, Pohlman AS, et al: Early physical and occupational therapy in mechanically ventilated, critically ill patients: A randomised controlled trial. *Lancet* 2009; 373:1874–1882
5. Rousseau A-F, Prescott HC, Brett SJ, et al: Long-term outcomes after critical illness: Recent insights. *Crit Care* 2021; 25:108
6. Rodriguez-Manas L, Feart C, Mann G, et al: Searching for an operational definition of frailty: A Delphi method based consensus statement: The frailty operative definition-consensus conference project. *J Gerontol A Biol Sci Med Sci* 2013; 68:62–67
7. Brummel NE, Girard TD, Pandharipande PP, et al: Prevalence and course of frailty in survivors of critical illness. *Crit Care Med* 2020; 48:1419–1426
8. Ferré C, Llopis F, Martín-Sánchez FJ, et al: The utility of the Barthel index as an outcome predictor in older patients with acute infection attending the emergency department. *Australas Emerg Care* 2022 Apr 6:S2588-994X(22)00023-9 [online ahead of print]
9. Hessey E, Montgomery C, Zuege DJ, et al: Sex-specific prevalence and outcomes of frailty in critically ill patients. *J Intensive Care* 2020; 8:75
10. Yang T, Li Z, Jiang L, et al: Risk factors for intensive care unit-acquired weakness: A systematic review and meta-analysis. *Acta Neurol Scand* 2018; 138:104–114
11. Singer P: Preserving the quality of life: nutrition in the ICU. *Crit Care* 2019; 23(Suppl 1):139
12. Wang YT, Lang JK, Haines KJ, et al: Physical rehabilitation in the ICU: A systematic review and meta-analysis. *Crit Care Med* 2021; 50:375–388
13. Van Stan JH, Dijkers MP, Whyte J, et al: The rehabilitation treatment specification system: Implications for improvements in research design, reporting, replication, and synthesis. *Arch Phys Med Rehabil* 2019; 100:146–155
14. Parotto M, Myatra SN, Munblit D, et al: Recovery after prolonged ICU treatment in patients with COVID-19. *Lancet Respir Med* 2021; 9:812–814
15. Lamontagne F, Rowan KM, Guyatt G: Integrating research into clinical practice: Challenges and solutions for Canada. *CMAJ* 2021; 193:E127–E131