

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Available online at

ScienceDirect

Letter to the editor

Early mobilization in hospitalized patients with COVID-19

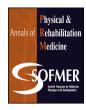
Dear Editor,

Many hospitals worldwide are overwhelmed with an unprecedented number of patients, frequently of an advanced age, who are confined to intensive care units (ICUs) due to COVID-19associated complications. In the European Union, about 32% of affected patients are hospitalized and about 9% of these are admitted to ICUs for treatment of life-threatening pneumonia; these numbers are much higher in people > 65 years old (https:// www.ecdc.europa.eu/en/publications-data/rapid-riskassessment-coronavirus-disease-2019-covid-19-pandemiceighth-update). In this context, a main, albeit often forgotten, stressor to body functional reserves, especially in older patients, is not only severe infections or other acute conditions per se but also forced inactivity. The latter can severely deteriorate the so-called intrinsic capacity (the combination of mental and physical function), which, according to the World Health Organization, is a major determinant of health in our progressively older society.

Hospitalization is likely to promote disability because of the combination of disease and low mobility levels. Most hospitalized adults (\sim 82%), especially those > 80 years old (\sim 96%), present disability, with mobility and self-care the most commonly affected domains of the International Classification of Functioning and Health [1]. Moreover, approximately one third of older adults lose their ability to independently perform 1 or more activities of daily living from hospital admission to discharge even with successful treatment of the condition that caused the hospitalization, the socalled hospital-induced disability [2]. This condition has major negative consequences in the short and long term, including an increased risk of re-admission and mortality [2]. In addition, critically ill patients experience severe muscle wasting ("ICUacquired weakness") from the first week of hospitalization [3]. No pharmacological intervention can prevent (or reverse) the functional deterioration that accompanies hospital confinement. By contrast, as confirmed in a recent meta-analysis, simple early mobilization programs have been found useful to attenuate the deleterious consequences of disuse observed upon discharge in older adults (> 60 years old) hospitalized for an acute medical condition [4].

Several studies have reported beneficial effects of in-hospital exercise programs for patients with pneumonia. For instance, an inpatient rehabilitation intervention (daily 50-min sessions for 8 days, including stretching, resistance and walking exercises) improved functional ability, muscle strength, quality of life, and dyspnoea as compared with standard respiratory physiotherapy (secretion removal, breathing exercises and walking) in adults (51–59 years old) hospitalized with community-acquired pneumonia [5]. Moreover, a recent trial reported the benefits on

Elsevier Masson France EM consulte www.em-consulte.com



physical performance and disease symptoms (fatigue, cough) of an intervention combining physical exercise and neuromuscular electrical stimulation (i.e., the generation of involuntary muscle contractions via the application of intermittent electrical stimuli to skeletal muscles) in older adults (mean age 75 years) hospitalized due to pneumonia [6].

Early rehabilitation programs have been found beneficial even for ICU patients, and indeed the international guidelines to optimize liberation from mechanical ventilation in critically ill adults such as those by the American Thoracic Society/American College of Chest Physicians recommend that these patients, particularly those with mechanical ventilation for more than 24 hr, undergo early mobilization [7]. However, despite these recommendations, early mobilization is still uncommon in most ICUs (applied in \sim 16% of patients) [8]. In this regard, a recent metaanalysis showed that this type of intervention can reduce the incidence of ICU-acquired weakness, improve functional capacity, and increase the number of ventilator-free days and the discharged-to-home rate [9]. Notably, an early exercise and mobilization program (from range-of-motion to sit-to-stand and walking exercises, depending on functional status) during periods of daily interruption of sedation increased the number of ventilator-free days and improved functional independence at discharge while decreasing the duration of delirium [10].

Of note, advanced age is not a barrier to the benefits of early mobilization. Simple interventions consisting of solely sit-to-stand and walking exercises have been found useful for preventing functional decline even in the oldest and weakest patients hospitalized for an acute medical condition (mean age 88 years), as we recently showed [11]. For individuals unable to perform volitional exercises, such as intubated patients, an alternative is neuromuscular electrical stimulation – the generation of involuntary contractions by the application of intermittent electrical stimuli to skeletal muscles. This approach, studied for decades in physiology laboratories worldwide, can attenuate muscle wasting in critically ill patients [12].

Because of the recent nature of the COVID-19 pandemic, no specific evidence is yet available on the effect of early mobilization or other physical therapies (e.g., respiratory physiotherapy) on affected patients. Moreover, the lack of personal protective equipment (at least in many European countries) and the need for rapid discharge hinders the application of early mobilization therapies. However, as recently highlighted by a group of international experts in the intensive care and acute cardiorespiratory fields, these therapies would likely play a major role in promoting a functional return to home for affected patients [13]. Once the infection curve has flattened and hospitals are no longer overwhelmed, these simple therapies could play an important role in promoting a functional return to home for patients and thus, in contributing to better management of the pandemic in general. Health professionals should be aware of the importance of preventing functional decline in hospitalized patients (particularly older ones) as well as the specific recommendations for managing COVID-19 to ensure the safety of both patients (e.g., identifying those in whom these interventions would not be indicated) and themselves (i.e., avoiding infection) [13]. Before an effective cure or vaccine is widely available, not likely in the next months, we should avoid a preventable condition, severe functional deterioration of the thousands of patients discharged after COVID-19 care.

Funding

The work of Pedro L. Valenzuela is funded by University of Alcalá (FPI2016). The work of Alejandro Lucia is supported by the Spanish Ministry of Economy and Competitiveness and Fondos FEDER (PI18/00139).

Disclosure of interest

The authors declare that they have no competing interest.

References

- Giral M, Boussat B, Lombard F, Stempfle S, François P, Pérennou D. Looking at hospitalized persons throughout the prism of the handicap. Ann Phys Rehabil Med 2018;61:12–7. <u>http://dx.doi.org/10.1016/j.rehab.2017.03.001</u>.
- [2] Covinsky KE, Pierluissi E, Story THEPS. Hospitalization-Associated Disability "She Was Probably Able to Ambulate, but I'm Not Sure.". JAMA 2011:306:1782-93.
- [3] Puthucheary Z, Rawal J, Mcphail M, Connolly B, Ratnayake G, Chan P, et al. Acute Skeletal Muscle Wasting in Critical Illness. JAMA 2013;310:1591–600. <u>http://dx.doi.org/10.1097/sa.000000000000059</u>.
- [4] Valenzuela P, Morales J, Castillo-García A, Mayordomo-Cava J, García-Hermoso A, Izquierdo M, et al. Effects of exercise interventions on the functional status of acutely hospitalised older adults: A systematic review and meta-analysis. Ageing Res Rev 2020;61:101076.
- [5] José A, Dal Corso S. Inpatient rehabilitation improves functional capacity, peripheral muscle strength and quality of life in patients with communityacquired pneumonia: A randomised trial. J Physiother 2016;62:96–102. <u>http:// dx.doi.org/10.1016/i.jphys.2016.02.014</u>.
- [6] López-López L, Torres-Sánchez I, Rodríguez-Torres J, Cabrera-Martos I, Ortiz-Rubio A, Valenza MC. Does adding an integrated physical therapy and neuromuscular electrical stimulation therapy to standard rehabilitation improve functional outcome in elderly patients with pneumonia?. A randomised controlled trial. Clin Rehabil 2019;33:1757–66. <u>http://dx.doi.org/10.1177/ 0269215519859930</u>.

- [7] Girard TD, Alhazzani W, Kress JP, Ouellette DR, Schmidt GA, Truwit JD, et al. An Official American Thoracic Society/American College of Chest Physicians Clinical Practice Guideline: Liberation from mechanical ventilation in critically ill adults rehabilitation protocols, ventilator liberation protocols, and cuff leak tests. Am J Respir Crit Care Med 2017;195:120–33. <u>http://dx.doi.org/10.1164/</u> rccm.201610-2075ST.
- [8] Hodgson C, Bellomo R, Berney S, Bailey M, Buhr H, Denehy L, et al. Early mobilization and recovery in mechanically ventilated patients in the ICU: A binational, multi-centre, prospective cohort study. Crit Care 2015;19:1–10. http://dx.doi.org/10.1186/s13054-015-0765-4.
- [9] Zhang L, Hu W, Cai Z, Liu J, Wu J, Deng Y, et al. Early mobilization of critically ill patients in the intensive care unit: A systematic review and meta-analysis. PLoS One 2019;14:1–16. <u>http://dx.doi.org/10.1371/journal.pone.0223185</u>.
- [10] Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009;373:1874–82. <u>http://dx.doi.org/10.1016/S0140-6736(09)60658-9</u>.
- [11] Ortiz-Alonso J, Bustamante-Ara N, Valenzuela PL, Vidán M, Rodríguez-Romo G, Mayordomo-Cava J, et al. Effect of a simple exercise programme on hospitalisation-associated disability in older patients: a randomised controlled trial. JAMDA 2020;21:531–7. <u>http://dx.doi.org/10.1101/19008151</u>.
- [12] Maffiuletti NA, Roig M, Karatzanos E, Nanas S. Neuromuscular electrical stimulation for preventing skeletal-muscle weakness and wasting in critically ill patients: A systematic review. BMC Med 2013;11:1. <u>http://dx.doi.org/</u> 10.1186/1741-7015-11-137.
- [13] Thomas P, Baldwin C, Bisset B, Boden I, Gosselnik R, Granger C, et al. Physiotherapy management for COVID-19 in the acute hospital setting: clinical practice recommendations. J Physiother 2020;66:73–82. <u>http://dx.doi.org/</u> 10.1016/j.jphys.2020.03.011.

Pedro L. Valenzuela^a, Michel Joyner^b, Alejandro Lucia^{c,*} ^aDepartment of Systems Biology, University of Alcalá, Madrid, Spain ^bDepartment of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN, USA

^cFaculty of Sport Sciences, Universidad Europea de Madrid, Research Institute of the Hospital 12 de Octubre ('imas12'), Madrid, Spain

*Corresponding author at: C/Tajo S/N, 28670, Villaviciosa de Odón, Madrid, Spain

E-mail address: alejandro.lucia@universidadeuropea.es (A. Lucia).

Received 23 April 2020 Accepted 26 April 2020