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Fatigue Symptoms during the First Year after ARDS

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To accompany manuscript # CHEST-Fatigue Symptoms during the First Year after ARDS

Editorial

Fatigue of ICU Survivors, No Longer to Be Neglected

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In the last decades, the world of critical care is becoming increasingly focused not only on “survival rates”, but also on the wellbeing of the critical care survivors. Acute Respiratory Distress Syndrome (ARDS) continues to represent an important public health problem despite an improvement in survival of approximately 60%.¹⁻³ The long-lasting impairment after ARDS has been suggested as a more meaningful outcome measure than mortality.⁴ Accordingly, the research has focused on the post-critical sequelae that include physical, psychological, and emotional aspects. Patients who survive ARDS are at risk for physical dysfunction, neurocognitive disorders, and worsened quality of life 6-12 months after discharge from the intensive care unit.⁴

Some years ago, a consensus workshop involving a spectrum of stakeholders identified research priorities in the field of integrative oncology through a Delphi survey.⁵ The first - ranked research topic was the “impact of integrative oncology on symptom management and quality of life (for example, dyspnea, nausea, and fatigue)”.⁵ This finding emphasizes how patients and stakeholders value these symptoms. Among these symptoms, there is fatigue, perceived by the individual as an overwhelming sense of tiredness during rest.⁶ The clinical expression of fatigue is multidimensional making evaluation challenging. ARDS patients experience a long-term stay in ICU along with prolonged mechanical ventilation, which may lead to an impairment of muscular/cardio-respiratory functions, increasing the risk of chronic fatigue. As long-term sequelae, patients might suffer from a chronic state of exhaustion, which may interfere with their functional capacity. Different types of measurement tools have been used in the reporting of functional impairment in critically ill patients to explore various domains within the

different cognitive components of cognitive, physical, emotional, and social functioning. In this field, the use of tools assessing patient reported outcomes is widespread, and, as far as fatigue is concerned, a dedicated tool to appraise the perceived fatigue in detail has been developed.⁷

In this issue, Neufeld et al⁸ investigated the occurrence of fatigue assessed by Functional Assessment of Chronic Illness Therapy (FACIT-F), after 6 and 12 months in ARDS survivors. Interestingly, 70% and 66% of former ARDS patients reported clinically significant symptoms of fatigue at 6 and 12 months respectively. In a previous study, our research group validated the FACIT- F scale in a mixed population of ICU survivors one year after hospital discharge.⁹ The mean transformed FACIT-F, that we found in our patients, was 66 (SD 12) which is quite similar to the 62 (SD 18) found by Neufeld et al.⁹ This finding may be surprising considering that our patients were less critically ill than those of Neufeld et al. (mean ICU length of stay was 10 (SD 11) and 14 (SD 11) days, respectively). Considering that the transformed FACIT-F for normal USA population is 74.7 (SD 15)⁷, both studies⁸⁻⁹ suggest that, generally, ICU survivors at one year suffer from symptoms of fatigue, especially the younger ARDS patients (mean age 49 yrs (SD15)⁸ and 68 (SD11) yrs, respectively)⁹.

Furthermore, the authors pointed out that the prevalence of fatigue at 6 months was greater than impaired physical function, impaired cognition, anxiety, or depression. Interestingly, fatigue was less severe in men and in those employed before ARDS. Specifically, patients employed prior to ARDS reported less fatigue with a mean difference of 6 points. This association between the employment prior to ARDS and the fatigue over 6 and 12 months may suggest that other factors might play a role in both. We

may hypothesize that employment is a proxy of social integration which may affect both perceived fatigue and health related quality of life (HRQoL). Orwelius et al¹⁰ showed that the level of social integration significantly affected HRQoL of the former ICU patients. Indeed, social integration affected HRQoL to a larger extent than age, sex, and the ICU related factors examined, but to a lower extent than the pre-existing diseases.¹⁰

The strengths of the study of Neufeld et al⁸ include the multicenter longitudinal prospective design, the follow up at 6- and 12-months after discharge, the high rate of responders, and the use of comprehensive measures of neurocognitive outcome in a well-defined ARDS population. Nevertheless, the high number of hospital involved in the study (38) and the long period taken to enroll patients (7 years) may reflect a selection bias, possibly testified by the quite young mean age of participants (49 years old) and the high percentage of those living independently prior to the admission in ICU (91%). This selection bias may reduce the generalizability of the study. However, the finding that a high proportion of these ARDS survivors, who suffer from fatigue, remains of a great value.

What is the next step? We firstly need to know whether fatigue occurs in survivors of other critical illnesses. For instance, the patients admitted to ICU due to severe sepsis or septic shock, could also perceive long-lasting fatigue, as well as those admitted to ICU for neurologic disease. Interestingly, Goërtz et al. found that the fatigue is more prevalent in patients with COPD with airflow limitation.¹¹ The latter is common among ICU patients and correlate with adverse outcome.¹² Future studies should focus on the influence of physical, psychological, behavioural, and systemic factors that could potentially perpetuate fatigue in patients with COPD. The malnutrition could be another

actor in the complex mechanism of the development of fatigue in ARDS survivors. We also need to understand whether the use of optimal support nutrition may represent another way in which daily practice in the ICU could affect patients' fatigue. Moreover, it would be useful to assess any relationship between fatigue and social integration. If there is a relationship, we might investigate whether interventions that promote interpersonal relationships affect fatigue and possibly introduce these interventions in the clinical practice.

REFERENCES

1. Schenck EJ, Oromendia C, Torres LK et al. Rapidly Improving ARDS in Therapeutic Randomized Controlled Trials. *Chest*. 2019;155(3):474-482.
2. Bellani G, Laffey JG, Pham T et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. *JAMA*. 2016. 23;315(8):788-800.
3. Spadaro S, Park M, Turrini C et al Biomarkers for Acute Respiratory Distress syndrome and prospects for personalised medicine. *J Inflamm (Lond)*. 2019;16:1.
4. Hopkins RO, Weaver LK, Collingridge D et al. Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2005. 15;171(4):340-7.
5. Weeks LC, Seely D, Balneaves LG et al. Canadian integrative oncology research priorities: results of a consensus-building process *Curr Oncol*. 2013;20(4):289-99.
6. Finsterer J, Mahjoub SZ. Fatigue in healthy and diseased individuals. *Am J Hosp Palliat Care*. 2014;31:562-75.
7. Cella D, Lai JS, Chang CH, Peterman A, Slavin M. Fatigue in cancer patients compared with fatigue in the general United States population. *Cancer* 2002;94:528-538.
8. Neufeld KJ, Leoutsakos JS, Yan H et al. Fatigue Symptoms during the First Year after ARDS. *Chest*. In press
9. Spadaro S, Capuzzo M, Valpiani G, et al. Fatigue in intensive care survivors one year after discharge. *Health Qual Life Outcomes* 2016;14(1):148.
10. Orwelius L, Backman C, Mats F et al. Social integration: an important factor for health-related quality of life after critical illness. *Intensive Care Med* 2011; 37:831-838
11. Goërtz YMJ, Spruit MA, Van 't Hul AJ et al. Fatigue is highly prevalent in patients with COPD and correlates poorly with the degree of airflow limitation. *Ther Adv Respir Dis* 2019

12. Volta CA, Dalla Corte F, Ragazzi R et al. Expiratory flow limitation in intensive care: prevalence and risk factors. *Crit Care*. 2019;23(1):395.

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ABBREVIATIONS LIST

ARDS = Acute Respiratory Distress Syndrome

COPD = Chronic obstructive pulmonary disease

FACIT-F = Functional Assessment of Chronic Illness Therapy

HRQoL = health related quality of life

ICU = Intensive Care Unit

SD = Standard Deviation

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