



Long-term physical morbidity in ARDS survivors

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Survivors of ARDS have significant morbidity. Thanks to innovative investigators, we have started to accumulate robust data regarding long-term physical and neuropsychological consequences of ARDS. These prognostic data are important for clinicians, patients and family members; and will be invaluable in the development of ICU and post-ICU multi-component interventions which will reduce short- and long-term morbidity.

Herridge and her colleagues have led the way in ICU outcomes research. Their data paint a vivid and startling picture of profound—primarily extra-pulmonary—disability in survivors of critical illness [1–3]; and depressive symptoms in caregivers [4]. In ARDS survivors they showed exercise limitation, physical and psychological sequelae, decreased physical quality of life, and increased costs and use of healthcare services persisting over 5 years [1, 2]. More recently their Towards RECOVER Study described outcomes of 391 ICU survivors mechanically ventilated for at least 7 days [3]. Using recursive partitioning modeling, the authors could stratify patients into four disability risk groups based on age and ICU length of stay (LOS); these four groups determine 1-year recovery and healthcare utilization independent of admitting diagnosis and illness severity. Patients older than 66 years with ICU LOS longer than 2 weeks sustained the worse disability and had 40 % 1-year mortality. They subsequently validated the four risk groups in their ARDS cohort [5].

In an article recently published in *Intensive Care Medicine*, Pfoh and her colleagues contribute valuable data to the existing literature on ICU outcomes, with 5-year follow-up data from the Improving Care of All Patients (ICAP) study [6]. The ICAP study followed 222 acute

lung injury (ALI) survivors for physical morbidity. At discharge 36 % had muscle weakness, with most improving within 12 months [7]; weakness was associated with impairments in physical function and quality of life that persisted at 24 months. Duration of bedrest during critical illness was consistently associated with weakness throughout the 24-month follow-up.

The current study reports the trajectory of physical decline of the ICAP cohort over 5 years, and risk factors for decline. In 193 ALI survivors three measures of physical status were evaluated annually: muscle strength using Medical Resource Council (MRC) sumscore, exercise capacity as reflected in the 6 Minute Walk Test (6MWT), and the physical functioning questions of the Short Form SF36 Health Survey. Approximately 1/3 of follow-up assessments were conducted in patients' homes. For each measure, a patient was considered 'declined' if the score decreased more than the 'Reliable Change Index' at follow-up. Over 5 years, 64 patients (33 %) died and were categorized as 'declined' in all three measures. Overall 86 % of patients experienced death or decline in at least one measure; when decedents were excluded 69 % experienced decline. In the multivariable model, older age was associated with declines in muscle strength, exercise capacity and physical function; and higher Charlson index was associated with declines in muscle strength and exercise capacity. APACHE II score, sedatives/opioids, and steroids were not associated with decline.

The study by Pfoh and her colleagues contributes valuable data and supports the findings of previous studies [1, 2, 8–10]. The strengths of this study are the large cohort, excellent patient retention, a long follow-up, detailed daily evaluation of critical illness and related treatment variables, and the use of standardized clinical evaluations using validated outcome measures.

While previous studies reported disability in survivors [1–3], Pfoh reported a composite outcome of death or disability. Classifying all patients who died during

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follow-up as 'declined' provides a confusing picture of their outcomes, inflates the degree of disability in survivors, and wrongly implies that all deaths were related to sequelae of ARDS or critical illness. It is crucial to separate the outcomes of death and disability, and report any disability which occurs prior to death. Combining survivors and non-survivors does not serve to inform clinicians, patients or caregivers about expected disabilities and challenges that survivors will face. Patients and families want to know the likelihoods of dying in ICU, dying after they leave hospital, and returning to their pre-morbid functioning. Similarly, combining the stable/improved groups deprives stakeholders of important prognostic and potentially reassuring information. To address the limitations of the combined outcome, the authors conducted a sensitivity analysis which excluded decedents, in which only older age was a risk factor for physical decline, similar to the Towards RECOVER Study [3].

Another limitation of the current study, which the authors acknowledge, is the absence of a control group. This is not unique to this study, and we appreciate the challenges in identifying an appropriate control group. However, without a control group, it is unclear whether patients experienced 'normal' age-associated declines, or whether the long-term decline trajectory is indeed steeper in patients who develop critical illness or ARDS. The generalizability of these results may also be limited by patient enrolment occurring between 2004 and 2007, when ICU management was likely very different than current management, particularly relating to sedation, ventilation weaning, nutrition, steroids, and mobilization. Indeed, patients spent 35 % of ICU days in coma, a median of 11 days on bed rest, and only 52 % received physical therapy. Given advances in supportive ICU care over the last 15 years, it is possible that long-term outcomes of these patients may be better in 2016.

In contrast to the authors' conclusions, we propose a more positive perspective about their findings. Despite 'declines' in the individual measures, overall, patients showed improvements in all three measures of physical status. At 5 years, muscle strength and physical functioning appeared to be within normal range, and median 6MWT was 71 % (IQR 59, 83) of predicted. Further, while MRC sumscore, 6MWT and SF-36 provide valuable information, they do not reflect a patient's ability to independently perform daily activities. Correspondingly, it is not clear whether the declines are clinically meaningful. Granular data describing what patients can and cannot do, and their degree of independence are most valuable. This is what we need to know about survivors of critical illness: can they independently dress, feed, step into a bathtub, stand from the toilet, climb stairs, and return

to work? The ability to do these daily activities independently has a tremendous impact on the patient and caregivers, and dependence on others can be catastrophic for everyone.

The investigators identified age and Charlson index as significant risk factors for physical decline; and age alone in their sensitivity analysis of survivors. However, there are many other ICU- and post-discharge variables which could have a tremendous impact on physical health over 5 years, and are potentially modifiable. These include nutrition, delirium, rehabilitation, new illness, hospital readmission, return to work, functional status, psychological and cognitive dysfunction [11, 12], and caregiver/family support. Patient frailty [13] may be an important predictor of outcome regardless of age or comorbid illness [14]. Further, assessment of muscle contractile capacity and not just muscle mass may be prognostically valuable [15].

Patients and their family members need to know about the cognitive and physical challenges they will face in their daily lives after surviving a debilitating critical illness. They need granular and detailed data about independent function—including walking, toileting, and returning to work. They want to know if they will get better, stay the same, or improve over time. This knowledge will allow them and their families to plan their lives and organize their support networks. For clinicians and investigators, knowledge of outcomes alone is not enough—we want to know how we can improve short- and long-term outcomes. Improving outcomes will require identification of modifiable patient and care-related risk factors across the care continuum—before, during and after ICU. It is time to move forward from describing long-term morbidity, to describing the biologic mechanisms of muscle and brain dysfunction, and hopefully designing interventions which reduce morbidity.

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