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Measuring physical function after ICU - one step at a time

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Long term recovery after critical illness is important to patients, families and clinicians.[1] Powerful messages from patients highlight the persistent functional legacy of an intensive care unit (ICU) stay and describe the difficulties in recovering physical strength, functional capacity, and resuming domestic roles.[2, 3] In the last 10 years clinicians and researchers have focused on both measuring these long term patient outcomes and intervening in an attempt to attenuate them. This research has provided us with mixed messages relating to the best methods of measuring long term outcomes, of identifying effective interventions and the patients who may most benefit. It is in this context we review physical function outcomes through the lens of four papers published in *Intensive Care Medicine* that focused on outcomes from six months to five years after an ICU admission and outline the possible next steps of our inquiry.

Physical function can be mapped to the World Health Organisation's International Classification of Functioning[4], with outcome measures that include organ impairment (e.g. strength), activity limitation (e.g. walking distance or activities of daily living), participation restriction (e.g. return to work or leisure activities) and measures of health status or health-related quality of life that separate physical status. Each of these domains has several specific outcome assessment tools that can be used to track patient recovery.

Across physical function domains, the relationship between organ impairment (strength), activity limitation and participation restriction following critical illness is described in several studies.[5, 6] Physical function and activity may be reduced for months to years following critical illness compared with the healthy normal population and poor physical function is associated with reduced health status.[6, 7] In a multicentre longitudinal study of ARDS survivors over five years, 86% (n=166) experienced decline in physical status from their hospital discharge functional state.[6] Patients who were stable or showed improvement over the first year after discharge commonly experienced physical decline in the subsequent years and this was related to age and pre morbid co-morbidities. More than one half of the cohort experienced declines in both strength and either exercise capacity or physical functioning, as measured with the Medical Research Council Manual Muscle Test (MRC), the six-minute walking distance (6MWD) and the self-reported generic health status instrument SF-36 Physical Function domain respectively. Similarly, in a study of ICU survivors following severe sepsis and septic shock, at three months there was a decline in physical function with a

reduction in both muscle strength and physical activity levels (measured with accelerometers).[8]

Measuring activity limitation is particularly complex in ICU survivors. Techniques include performance based in-person tests of activity such as the six-minute walk test (6MWT) or the timed up and go (TUG), wearable technology such as accelerometers or wireless activity trackers that measure data such as the number of steps walked, metabolic equivalents or steps climbed[8] and patient reported outcome measures such as the activities of daily living and physical function domain or Physical Component Scores (PCS) of health related quality of life tools such as the SF-36. Performance based tests are particularly difficult since they require the patient to return to hospital or the assessor to visit the patient. This uses resources and patient loss to follow-up can be an issue.[9] Conversely using patient reported measures is less difficult as these are generally questionnaires and can be administered by phone or mail. Patient reported outcomes are important in assessing value-based health care and are recommended by the International Consortium of Health Outcomes.[10]

To date, the most common measure of physical function using patient reported outcomes is using a health-related quality of life questionnaire. Across four international studies, and at different time points, the correlations between the 6MWD, 4 m walk and the SF-36 PCS were reported to be moderately strong.[11, 12] In contrast, performance based 6MWD and TUG explained only 54% and 33% of the variance respectively in the SF-36 physical function domain at three months after ICU in 177 patients, although correlations were also moderate between these variables.[13] Researchers should be cognisant that patient report and performance tests may measure different constructs, however the benefits of questionnaire based data are the minimization of both loss to follow up and use of resources. Interestingly, in a recent Delphi process to identify a core outcome set for long term outcomes of survivors of acute respiratory failure, there was no consensus for a measure of performance-based physical function that should be used in all survivors of acute respiratory failure.[1] The six minute walk test came closest to consensus at 54% agreement, although the SF-36 was suggested as a core outcome measure.[1]

In a recent publication of impact of disability after ICU, patients who reported moderate to severe disability at six months after ICU were most likely to report problems with physical function, and this was associated with a significant reduction in health related quality of life.[2] A follow up study of health-related quality of life in survivors five years after ICU discharge also demonstrated that the domains most reduced were physical functioning, role-physical, general health and social functioning[14]. However, in contrast to Pfoh et al, these authors reported a small change in SF-36 physical function measures in survivors compared with premorbid measures that may not be clinically significant at five years after adjustment for natural decline. Reasons for these differences may be the variability around the PCS measure, the age of the populations in the two study groups and their premorbid disease state. Additionally resilience, adaptation and environmental factors (such as family support) may also have a large impact on a patient's health status.[2, 14]

Early mobilization and rehabilitation is one candidate intervention to improve physical function in ICU survivors.[5, 15] In a single centre study of n=50, patient reported physical function (SF-36) improved in the ICU exercise group at six months compared with control, although no performance based tests showed between group differences. In a recent meta-analysis of active mobilization and rehabilitation during ICU, patients who were randomized to early mobilization and rehabilitation had improved muscle strength and were more likely

to be able to walk independently at hospital discharge compared to patients who received standard care.[16] The meta-analysis showed no difference in health status measured with the SF-36 domain of Physical Function. Other randomized trials across the last 10 years provide inconsistent evidence related to the role of rehabilitation in improving physical function outcomes, perhaps due to differences in timing of the intervention, inadequate dose or heterogeneous patient populations.[17]

What are the next steps in solving the dilemma of addressing the functional deficits of ICU survivors (Figure 1)? We have evidence that physical function is an important problem for ICU patients and their families, but conflicting evidence about how and when to intervene to improve outcomes.[9] First, we need consensus on a measure of physical function that can be used across the continuum of survivorship, that is sensitive to change and agreement on the time-point of measurement. While health status questionnaires are commonly used and SF-36 is named as a core outcome[1] results across studies for this outcome are most inconsistent. Second, we need to define the most effective intervention, the timing of commencement, a dose that may need to be individually titrated and the interaction of multiple interventions (eg: sedation, nutrition, exercise). Third, we must identify the potential confounding variables such as the patient's pre-admission health trajectory, co-morbidities and frailty. Finally, understanding genetic, biological, environmental and lifestyle factors that may assist us in developing a model of precision medicine to impact functional outcomes after critical illness, such as altered inflammatory response or mitochondrial dysfunction.

While these next steps in unravelling the answer to reduced functional outcomes in ICU survivors appear numerous and daunting, we know that in addressing these issues we will find a way to the final step; that is identifying what we should do to most effectively improve our patients' functional recovery after an admission to the ICU.

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Figure 1. The next steps in measuring and improving physical function after ICU

