

CSL Behring
Supplement from
Euroanaesthesia
2017 Symposium

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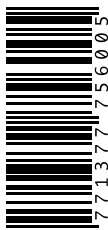
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Outcomes after 1 week of mechanical ventilation for patients and families

We review recent findings on outcomes in adults after mechanical ventilation for one week or more in the intensive care unit, exploring both patients and their family perspectives.

surgical ICUs. The understanding of such determinants is important to critical care physicians, as it may aid patient-centred care, prognostication, education, rehabilitation and study design. In parallel, knowledge around the impact of patient trajectories after ICU on their caregivers is limited, yet fundamental. A large proportion of patients who receive prolonged MV during a stay in the ICU and survive to discharge require assistance from a caregiver 1 year after ICU discharge (Chelluri et al. 2004). Although caregiver assistance is often essential for patients, such care may have several potential negative consequences affecting physical and mental health of the caregivers (Cameron et al. 2006; Van Pelt et al. 2007; Azoulay et al. 2005).

In the past few years, the literature has provided a growing body of information in these important areas of ICU practice that can help better inform the management of patients and their caregivers.

In light of the findings from recent studies, in the present article we provide a brief review on outcomes after 1 week of mechanical ventilation for patients and families, and of the predictors for these outcomes.

Patient outcomes

Some evidence is accumulating to indicate that for patients needing ICU stays longer than 7 days, admission diagnosis and physiological illness severity may not be reliable predictors of outcome and trajectories of recovery. Researchers have suggested that this might be the reflection of a transition to a different disease state, such as persistent critical illness

(Iwashyna et al. 2016), or may reflect the fundamental importance of pre-ICU illness trajectory in determining post-ICU outcome.

Recently, prospective data became available from the RECOVER Program. This initiative began in 2007 in collaboration with the Canadian Critical Care Trials Group, and was focused on risk strata post ICU (Herridge et al. 2016). The Towards RECOVER study, the first step of this multi-phase project, evaluated a multi-centre Canadian cohort of 391 medical/surgical ICU patients, who received one week or more of MV, at 7 days, 3, 6, and 12 months after ICU discharge. Patients in this cohort had a mean age of 58 years; 42% were female. The majority of them lived at home and independently prior to their critical illness. The median Acute Physiology and Chronic Health Evaluation (APACHE) II was 22 and median Multiple Organ Dysfunction score (MODS) on day 7 of MV was 6. Seven days after ICU discharge, all patients reported weakness and functional limitations, and the majority were unable to walk. Depressive symptoms were common and several patients (23%) reported features of post-traumatic stress disorder at 3 months post ICU discharge, which persisted at 1 year in the majority of cases.

A recursive partitioning model showed that disability is determined by age and ICU length of stay (LOS) based on the Functional Independence Measure (FIM) at 7 days post ICU discharge, independent of admitting diagnosis and severity of illness. Four distinct disability risk groups were identified [Young Short LOS (age <42 years, ICU stay <2 weeks); Mixed-age Variable LOS (\geq 42 years, <2 weeks

Critical illness survivorship carries a burden of physical and neuropsychological disabilities (Griffiths and Jones 1999; Herridge and Cameron 2013). These determine decreased quality of life when compared to the sex- and age-matched general populations as well as increased healthcare resource utilisation (Herridge et al. 2011; Hopkins et al. 1999; Schelling et al. 2000; Weinert et al. 1997). Previous studies suggest that age (Barnato et al. 2011; Ehlenbach et al. 2010; Herridge et al. 2003), premorbid functional status and frailty (Hopkins et al. 1999; Barnato et al. 2011; Ehlenbach et al. 2010; Herridge et al. 2003; Iwashyna et al. 2010; Pandharipande et al. 2013), reason for intensive care unit (ICU) admission (Unroe et al. 2010), burden of co-morbid illness (Herridge et al. 2011; Herridge et al. 2003; Hopkins et al. 1999), and ICU length of stay (LOS) and weakness (Unroe et al. 2010; Needham et al. 2014; Carson et al. 2012) may affect recovery trajectories after ICU discharge.

However, until recently, there was a paucity of data on determinants of outcomes in adult patients who survive one week or more of mechanical ventilation (MV) in medical and

and ≤ 45 years, ≥ 2 weeks); Older Long LOS (46–66 years, ≥ 2 weeks), and Oldest Long LOS (> 66 years, ≥ 14 days)]. These groups were characterised by different outcomes and post-ICU healthcare utilisation, with increasing disability from the Young Short LOS to the Oldest Long LOS. In the latter group, only 19% were discharged home directly from hospital, and over one-third required hospital readmission in the year after ICU discharge. Forty percent of this group died within the first 12 months after ICU discharge, and the surviving patients had severe and persistent functional dependency. Cognitive dysfunction, including problem solving and memory, was affected uniformly across risk groups.

Iwashyna and colleagues conducted a large retrospective, population-based observational study on over 1 million patients from 182 ICUs across Australia and New Zealand (Iwashyna et al. 2016). They found that among patients still in ICU, admission diagnosis and physiological derangements, which accurately predicted outcome on admission, progressively lost their predictive ability after 10 days, and no longer predicted outcome more accurately than did simple antecedent patient characteristics such as age, sex and chronic health status. Patients who were still in the ICU after one week from the onset of acute critical illness experienced higher mortality and resource utilisation, and had a much lower chance of returning directly to home at hospital discharge. In their retrospective cohort study of a random sample of 35,000 Medicare beneficiaries older than 65 years old, who received ICU care and survived to hospital discharge, Moitra et al. showed that for each day beyond 7 days in the ICU there was an increased risk of death by 1 year, irrespective of the need for MV (Moitra et al. 2016). Altogether, data from these recent studies may suggest that a complex interaction of specific physiological changes determined by acute illness with prolonged ICU stay coupled with the patient's prior functional and health status determine reserve and resiliencies that dictate outcomes and the trajectory of recovery.

The MEND-ICU Program, a pilot study led by Drs. Batt and Dos Santos, in collaboration with the RECOVER Program, (Dos Santos et al. 2016) focused on the determinants of muscle dysfunction and differential resilience and disability after critical illness. The authors

recruited patients with the goal to delineate cellular mechanisms underlying long-term persistence of weakness in ICU survivors. Assessments were conducted at 7 days and 6 months after ICU discharge, including motor functional capacity, quadriceps size, strength, voluntary contractile capacity, electromyography, nerve conduction studies, and vastus lateralis biopsies for histologic, cellular and molecular analyses. The authors concluded that long-term weakness in ICU survivors results from heterogeneous muscle pathophysiology with variable combinations of muscle atrophy and impaired contractile capacity. These findings are associated with decreased satellite cell content and compromised muscle regrowth, suggestive of impaired regenerative capacity.

critically ill patients with similar degrees of physiologic derangement may have very disparate trajectories of resolution of organ dysfunction and recovery

Caregiver outcomes

The experience of caregivers for critically ill patients is equally a life transformative one. They often present mood disorders, such as depression and post-traumatic stress disorder (Azoulay et al. 2005), and these may also affect their capability to care for the family member, whose outcomes could hence be compromised (Herridge and Cameron 2013).

Choi and colleagues prospectively studied caregivers of critically ill patients who received MV for at least 7 days (Choi et al. 2011). The family caregivers completed follow-up at 1 and 6 months after discharge from the intensive care unit. Although limited by the relatively small sample size, the findings of this study highlighted the physical and psychological burden experienced by caregivers, and reported that 20% of caregivers perceived moderate or greater restrictions in nearly all areas of daily life, particularly the areas related to social life or personal recreation. These suggest the importance that interventions designed to

enhance coping, decrease social isolation, and improve patients' functional status may have in assisting this vulnerable and often neglected population.

In parallel to the patient data, the RECOVER Program also described detailed health outcomes in caregivers of critically ill patients, identifying subgroups of caregivers with distinct health trajectories and assessing variables associated with poor caregiver outcomes (Cameron et al. 2016). The parallel caregiver cohort of the RECOVER Program enrolled family members or friends who were primarily responsible for providing or coordinating care after hospital discharge, without financial compensation, to patients who had received at least 7 days of MV and were discharged alive from ICU. The caregivers' mean age was 53 years, with the majority being women, and almost two-thirds caring for a spouse.

This study showed that mental health was severely affected in the cohort, with depressive symptoms present in a large percentage of caregivers (67% initially and 43% at one year), and although in the majority of cases depressive symptoms decreased over time, in a subgroup (16%) no signs of improvement were recorded. Conversely, physical health appeared unaffected and similar to population norms.

Interestingly, and consistently with findings from previous pilot data (Choi et al. 2012), no patient variables were associated with caregiver outcomes. Indeed, no patient demographic and clinical characteristics nor changes in patient functional and psychological outcomes over time appear to correlate with caregiver outcomes.

Instead, Cameron and colleagues identified how the characteristics of the caregiver and the caregiving situation were important determinants of caregiver outcomes during the follow-up period. The variables that were significantly associated with worse mental health outcomes include younger age, greater effect of patient care on other activities, less social support, less sense of control over life and less personal growth.

Summary and conclusions

Novel data have recently become available that describe patient outcomes after 1 week or more in the ICU. Survivors have important physical

and mental health consequences, independent of admitting diagnosis and severity of illness (Herridge et al. 2016; Moitra et al. 2016; Iwashyna et al. 2016). Long-term weakness following resolution of critical illness is associated with variable combinations of muscle atrophy and impaired voluntary contractile capacity, which result from impaired regenerative capacity. Muscle biology can be durably and even definitely altered by critical illness (Dos Santos et al. 2016).

A new perspective emerges, suggesting that critically ill patients with similar degrees of physiologic derangement may have very disparate trajectories of resolution of organ dysfunction and recovery, that appear unrelated to the admitting diagnosis or severity of disease, and fundamentally determined by their age and ICU LOS and pre-ICU health status. Hence, physiologic definitions such as those currently in use for Acute Respiratory Distress Syndrome (ARDS) (ARDS Definition Task Force 2012) or sepsis (Shankar-Hari et al. 2016) may not assist in defining the longer-term prognosis of these patients. Furthermore, as the duration of ICU stay increases, patients may transition to a different disease state in which they continue to accrue disability over time, which may be referred to as persistent or chronic critical illness, characterised by increased 1 year mortality, resource utilisation and inability to return home (Iwashyna et al. 2016; Moitra et al. 2016).

This novel information can help inform goals of care discussions, discharge planning, rehabilitation and long-term expectations for recovery and functional autonomy. Future studies are needed to better characterise individual responses to critical illness, their resilience and potential for repair, and whether different

interventions should be designed for different disability risk groups to help improve patient outcomes. The delineation of the role played by functional status pre-ICU in the trajectory of recovery, and how it relates to the response to prolonged ICU stay is of central importance, and perhaps in particular for elderly patients (Ferrante et al. 2015).

In parallel to a better understanding of the trajectory of recovery after 1 week of mechanical ventilation, we are learning how critical illness affects the entire family. Caregivers' mental health is severely affected, and the identification of those more vulnerable to such consequences may inform the provision of additional support/resources, as well as assist in the design of future studies aimed at assessing the effects of different interventions to improve caregiver outcomes.

In critical illness, as in all aspects of medicine, considering the family as a whole is fundamental and central to effective and compassionate care delivery (Wittenberg and Prosser 2016).

Conflict of interest

Matteo Parotto declares that he has no conflict of interest. Margaret Herridge declares that she has no conflict of interest.

Supported by: Canadian Institutes of Health Research, Ontario Ministry of Health Innovation Fund; University of Toronto-Department of Medicine Challenge Integration Fund; the John MacNaughton Family Fund, the Jason Tham and Andrea Chan Family fund and the Don and Jane Luck Family Fund.

Acknowledgements

We are indebted to the patients and their families for their willingness to participate

in the RECOVER Program and for graciously donating their time to this research program.

The authors are extremely grateful to the Canadian Institutes of Health Research, Ontario Ministry of Health Innovation Fund; University of Toronto-Department of Medicine Challenge Integration Fund; the John MacNaughton Family Fund, the Jason Tham and Andrea Chan Family fund and the Don and Jane Luck Family Fund for their very generous support of this programme of research.

The authors also thank the RECOVER Research Coordinators at each of our sites across Canada. Paulina Farias from University Health Network (Toronto); Cheryl Ethier, Maedean Brown, Brittany Giacomino and Sumesh Shah from Mount Sinai Hospital (Toronto); Orla Smith, Yoon Lee, Kerri Porretta, Julia Lee and Melissa Wang from St. Michael's Hospital (Toronto); Nicole Marinoff, Jane Wang, Derek Parsotam and Ashwati Raghunath from Sunnybrook Health Sciences Centre (Toronto); Andrea Tkaczyk and France Clarke from St. Joseph's Healthcare (Hamilton); Mary-Jo Lewis, Tracey McArdle and Brigitte Gomes from Ottawa Hospital Civic Campus (Ottawa); Johanne Harvey from Hôpital Maisonneuve-Rosemont (Montreal); Chantal Langevin, Karine Grondi, Joanie Lacasse-Bedard and Eugénie Pinsonnault from the University Hospital Centre of Sherbrooke (Quebec); Lynda Lazosky and Ellen Woo from St. Paul's Hospital (British Columbia)

Abbreviations

ICU intensive care unit
LOS length of stay
MV mechanical ventilation

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