EDITORIAL

Long-term Survival after Critical Illness: Are We There Yet?

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The number of survivors after critical illness is steadily increasing due to advances in technology, a better understanding of the complex physiology of critical illness, and better care. This has led to more chronically ill patients, survivors with more disabilities, and less quality of life (QOL) in survivors. These patients may have physical, psychological, cognitive, and other mental health problems after critical illness, collectively called post-intensive care syndrome (PICS). Previous studies had shown that the survivors had severe physical impairment even many years after intensive care unit (ICU) discharge and these patients may attain age-specific health status at 5 years.[1] Management of these patients is resource intensive, usually, they need hospital care for months post ICU discharge at high dependency and rehabilitation units and they pose enormous stress on the healthcare system. The data available is largely from developed countries and very less from developing nations, so the difficulties and unique barriers for the management of such patients from developing nations are largely unknown.

In this issue of the journal, Kodati et al. studied the long-term survival and QOL among ICU survivors.[2] The study was done in a respiratory ICU for 11 months. The patients were predominantly admitted for respiratory failure and most of them required respiratory support (69% invasive mechanical ventilation and 25% non-invasive ventilation). The mean Acute Physiology and Chronic Health Evaluation II (APACHE-II) score was 14, only one-third required vasopressors, nearly 8% required renal replacement therapy, and 10% tracheostomy. The authors studied 158 patients who were discharged from ICU and measured the QOL at 3 and 6 months. Authors assessed the neuromuscular weakness by clinical examination using the Medical Research Council (MRC) score, respiratory function by forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), a 6-minute walk test (6MWT), and health-related quality of life (HRQOL) by World Health Organization Quality of Life Instrument (WHOQOL BREF – an abbreviated version of the WHOQOL-100, an abbreviated generic Quality of Life Scale developed through WHO), the Hindi version for those who visited follow-up clinic. The authors were able to follow up with every survivor except 10 patients who were lost to follow-up. In this study, nearly 19% of patients who were discharged from ICU died at 6 months and 12% required assistance in daily living, and the majority had poor QOL. The presence of neuromuscular weakness and the need for home ventilation were associated with post-ICU discharge mortality. Though many had persistent neuromuscular weakness that affected the physical and psychosocial domains of their life, the authors found severe impairment in all domains assessed, that is, physical, psychological, social, and environmental. An improving trend was observed over 6 months including mean FVC, FEV1, and 6MWT, but lower than expected normal of the individual domains. The study has brought to light the difficulties, the ICU survivors face in developing nations with limited resources, especially for follow-up and further rehabilitation. The study has its limitations in that the population studied were only medical patients admitted to the respiratory ICU, so cannot generalize the results. Moreover, no data on baseline information on the QOL before admission and at discharge. Also, there is no data on the treatment or rehabilitation provided to patients from discharge to 6 months which might have affected the outcomes. The outcome was analyzed for all patients irrespective of their ventilation status. The patients who did not receive mechanical ventilation may have better outcomes compared to patients who needed invasive ventilation. On the other hand, the QOL was assessed using WHOQOL BREF which is better compared to other scales.

Previous studies that looked at long-term survivors had a varied timeline for assessing the functional status, 1 year to 10 years with the majority assessed at either 6 months or 1 year.[3] All the domains were affected in survivors with the physical domain being affected the most. Many patients still had reduced HRQOL at 5 years compared to baseline pre-ICU status but there was improvement noted over a period and they attained good general health when adjusted for natural decline at 5 years with less effect size indicating that they regain age-specific HRQOL at 5 years. Hofhuis et al. followed up with patients till 10 years post ICU discharge, longest follow-up study to date showed that 63% of patients died at 10 years and there was a significant reduction in functioning in all domains compared to pre-ICU and age-referenced populations but with a small effect size.[4] A systemic review (19 observational cohorts and 2 case–control studies, $n = 57,712$) showed that the HRQOL was significantly affected among survivors which was not affected by the presence of acute kidney injury, delirium, or sepsis during ICU stay when compared with that of critically ill patient control groups.[3] In 5 years, there was

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a decline compared to the age-matched general population in HRQOL among ICU survivors in all domains, especially more significant in physical and social functioning, but the reduction of HRQOL may not be clinically relevant since the effect size of HRQOL reduction was weak.

These studies showed that most patients had reduced functioning in all domains but regained their age-specific HRQOL by 5–10 years. The exact burden of ICU survivors is not known and it is a real challenge to follow up with such patients due to lack of follow-up services, dedicated team, and high cost. In the recent years, the focus of intensivists has expanded from short-term outcomes and saving lives to saving lives with better QOL in ICU survivors. Moreover, it is equally important to pay attention to the caregiver's fatigue and psychosomatic problems they go through. So, this process affects both the patient and caregiver and *vice versa*. Identification of patients at ICU discharge, aggressive rehabilitation, evaluation, and management of psychological problems may alter the course of recovery toward better outcomes.

French and European Outcome Registry in Intensive Care Units (FROG-ICU) study (21 centers, France and Belgium, $n = 1,570$) identified the clinical and biological determinants of death 1-year post ICU discharge.[5] Advance age, comorbidities, chronic renal disease, severe valvular disease, recent malignancy, vascular disease, and loss of autonomy pose more risk at admission. The need for blood transfusion and length of ICU stay of more than 20 days were predictors during ICU stay. Presence of hypotension (systolic blood pressure <110 mm Hg,) and persistent inflammation identified by low temperature (<37°), low protein (protein <6 gm/dL) white blood cell count above 20,000/mm^3,platelet count below $1e^{+05}/mm^3$ at ICU discharge predicted death at 1 year. There was a 3-fold increased risk of death when all were put together in the regression model. Schandl et al. identified low education status, impaired core stability, fractures, and ICU Length of stay more than 2 days predicted occurrence of new-onset physical disability at 2 months post ICU discharge.[6] These factors at ICU discharge identify at-risk individuals at discharge and may help to focus interventions to improve their outcomes. Moreover, predicting patients who may need long rehabilitation and modifying factors during ICU stay like reducing or avoiding paralytic drugs, optimal sedation, early physiotherapy, etc. may help alter the course post ICU discharge. A recent systemic review (3 studies, one predicted mental health and the other two predicted physical health) showed that the existing prediction models are not externally validated and there is a need for methodologically rigorous models.[7] Ohbe et al. developed and validated a prediction model for new onset functional impairment after critical illness using common variables measured during the first two days of ICU admission (multicentre, retrospective cohort study, Japan, $n = 19,846$).[8] The primary outcome studied was functional impairment, measured with the Barthel index. The authors used both conventional and machine learning to develop six models to predict the functional outcomes from large databases. All six models had good discrimination and calibration with an area under the curve above 0.85. Serum albumin, blood urea nitrogen, need for mechanical ventilation, age, stroke, and acute myocardial infarction are a few factors involved in all models. The model is yet to get validated in the external population. In reality, it may take a few years before we can use it in clinical practice.

Long-term severe functional decline is common among survivors of critical illness, often underreported, and identifying at-risk patients is very important for a better outcome. We have a long way to travel and hope further studies help us identify such patients, and predict outcomes while receiving treatment in ICU.

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