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Measuring and improving outcomes that matter to patients after cardiac arrest

Efforts to improve outcomes after out-of-hospital cardiac arrest (OHCA) have focused on early recognition, increasing the frequency and quality of layperson cardiopulmonary resuscitation (CPR) delivery, and public access defibrillation [1]. Clinical and population-based studies support that these interventions have increased the number of survivors of OHCA [2–4]. Bundled post-arrest care, with attention to cardio-cerebral resuscitation and temperature management, also contribute to improved survival [5]. As OHCA survival increases, health care providers are recognizing the importance of quantifying and maximizing quality of life after survival. Dichotomous, short-term outcomes like survival to discharge, discharge with a Cerebral Performance Category of 1 or 2 (often called "good outcome"), or other crude measures of recovery quality are increasingly being replaced with more granular and long-term measures of impairment, function, and participation, as recommended by World Health Organization and American Heart Association consensus statements [6,7]. With such measures, the durable impact of interventions in the acute phase of OHCA resuscitation on outcomes that matter to patients and their families can be studied in detail.

In this issue of *Resuscitation*, Riddersholm et al. [8] report the association between post-cardiac arrest syndrome [9] (PCAS) severity and rates of return to work among OHCA patients included in the nationwide Danish registry who were employed prior to arrest. The authors estimated PCAS severity by measuring the need for organ support therapy (mechanical ventilation, vasopressor dependence, and/or renal replacement therapy), although neither timing nor duration of organ support data were available. OHCA patients surviving to hospital care were grouped based on need for organ support therapy at any time within the first 30 days from arrest: A) non-Intensive Care Unit (ICU) patients; B) ICU with support of 0–1 organs; C) ICU with support of 2 organs; and D) ICU with support of 3 organs. Comparisons used Group B as reference, although the authors could not adjust for the dose, duration, or timing of each form of organ therapy support. The outcome of interest, return to work, was defined as not receiving social benefits, other than maternity leave, leave-of-absence, or educational grants, and identified from the Danish Labor Market Authority. Patients were followed from day 30 through the end of study (6/30/2016) for return to work, death, or emigration.

Return to work has been used previously as a "proxy for preserved function without major neurologic deficits" in OHCA survivors [10]. Kragholm, et al. [10] reported a return to work rate of up to 76% for 30-day survivors between 2001 and 2011 in Denmark. Although easy to quantify in governmental datasets or registry-based studies, as an outcome measure "return to work" risks being a difficult-to-define amalgamation of participation, impairment, and function. Deficits in any of these domains may preclude return to work, and this dichotomous variable cannot be used to determine if an inability to work was related to impairment (i.e. memory, vision, mood), function (i.e. write, type, walk stairs), job shortage, inadequate accommodation, or early retirement. Similarly, subjects may return to their prior employment, but may also assume a different job (i.e. once an engineer, now a store clerk) due to necessity or post-critical illness adaptation [11]. For these reasons, a recent study reported on return to work and participation in patients after surviving OHCA by direct patient or proxy interview at 6 months [12]. Lilja et al. [12] found that 66/142 (46.5%) of OHCA patients had returned to previous work without any change, while 32/142 (22.5%) and 36/142 (25%) were working with reduced hours or on sick leave, respectively. This methodology allowed for inquiry into changes in employment status but still likely underestimated or misclassified return to work, given the lack of serial measurements.

That increased burden of organ failure in the acute phase of post-arrest care portends worse long-term cognitive outcomes is not surprising. The most apparent explanation is that the effect of initial anoxic injury on the brain and other organ systems is roughly proportional. Insofar as this is true, extracranial organ failure may simply be an easily measurable surrogate marker of brain injury severity amenable to registry-based studies. In this paradigm, the findings of Riddersholm, et al. [8] may help inform clinicians and families as they weight the likelihood of an acceptable neurological recovery when deciding whether to continue life-sustaining therapy.

An alternative explanation for the observed association is that modifiable processes of care used in support of organ failure may directly contribute to avoidable secondary brain injury. The idea that critical care has a lasting effect on neurocognitive outcomes is not a new one. Even absent acute brain injury, a majority of patients randomized in a large trial of acute lung injury management had persistent cognitive deficits at one year, and fluid management strategy was significantly associated with this risk [13]. Duration of delirium in the ICU has a similar negative association with one-year outcomes [14,15]. Benzodiazepine administration during critical illness is independently associated with long-term impairments in executive function [15].

It is not difficult to postulate mechanisms through which post-arrest organ support might have a modifiable effect on long-term cognition in the OHCA population. Changes in post-arrest cerebrovascular autoregulation, for example, mean that higher mean arterial pressures may be necessary to maintain cerebral perfusion [16,17]. A patient with cardiovascular reserve may be able to compensate by augmenting blood pressure, maintaining



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cerebral blood flow. By contrast, clinicians managing a patient with vasopressor-dependent cardiovascular failure may target a mean arterial pressure of 65 mmHg, lower than may be needed for cerebral perfusion [18]. Among mechanically ventilated patients, both hypoxemia and hyperoxia may contribute to brain injury and cognitive impairment [13,19]. Because granular data on the therapeutic targets for organ support, dose, and duration of therapy are not available in this registry, these types of hypotheses cannot be easily tested using this dataset.

A robust understanding of the impact of critical care interventions on long-term patient outcomes is lacking. As a resuscitation community, we have achieved sustained improvements in rates of return of spontaneous circulation and survival to hospital discharge. It is now incumbent on us to move beyond these crude measures, but also to learn what outcomes matter to patients and their families. After surviving OHCA, return to work may or may not be a financial necessity, a priority, or simply an unnecessary burden for patients. Some may recover fully while others reintegrate with a revaluation of life [20]. Some may instead desire to return to playing sports, singing in church, or challenging friends to a game of cards. Moreover, return to work cannot be used to assess the large proportion of OHCA patients who are retirees. Patient-centered outcomes are not easily captured by retrospective chart review or registries, but nevertheless are the goal towards which patient care is directed.

We commend Riddersholm, et al. [8], for assessing return to work and societal participation in this study. Unraveling the complex relationship between ICU interventions and granular, patient-centered long-term outcomes is challenging and beyond the scope of any existing dataset, but is urgently needed.

Disclosures

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