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Improving pediatric Extracorporeal Cardiopulmonary Resuscitation means delivering best care and measuring impact beyond survival

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Children requiring extracorporeal cardiopulmonary resuscitation (ECPR) are at the edge of death. Evidence in both adult patients and children suggests that extracorporeal membrane oxygenation (ECMO) significantly improves survival when prolonged CPR is required (1,2), yet more than half of ECPR-supported children die and half of the survivors have a decline in functional status (3). Consequently, even apparently minor advancements in ECPR care offer an opportunity to save lives and improve functional status, the two most valued outcomes for parents of critically ill children (4).

In this issue of *Critical Care Medicine*, Bembea et al. link the American Heart Association (AHA) Get With The Guidelines-Resuscitation (GWTG-R) Registry and the Extracorporeal Life Support Organization (ELSO) Registry (5). The study aimed to describe the patterns of ECPR utilization among 32 hospitals and to identify risk factors for death and functional status decline as measured by a need for rehabilitation services in 568 children. The study found ECPR utilization is increasing and that longer CPR duration and complications during ECPR are associated with worse outcomes.

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This work, in combination with another recent *Critical Care Medicine* article by Meert et al (3), provides a timely opportunity to summarize the state of the art of pediatric ECPR. Similar to the article by Bembea et al (5), Meert et al (3) used an existing dataset of children who received ECPR in the Therapeutic Hypothermia After Cardiac Arrest (THAPCA) trial (6). The two studies found that 41% of children survived following ECPR and that 30% of those requiring CPR for >60 minutes survived. Both studies also demonstrated a univariate association between duration of CPR prior to ECMO and poorer outcomes, but the study by Meert et al (3) did not confirm that this association persisted in multivariate logistic regression analyses.

Perhaps surprisingly, both studies also found that the first documented cardiac rhythm was not significantly associated with survival. This contrasts with adult studies demonstrating ventricular tachycardia and ventricular fibrillation are associated with improved survival compared to other rhythms (2). However, it is worth noting that Meert et al (3) did find an association between cardiac rhythm and the composite outcome of survival with good neurological outcome (specifically, survival with Vineland Adaptive Behavior Scale, second edition, >70). Both studies also found that seizures occurred in 12-15% of children after ECPR, but there was no association between seizures and survival.

Bembea et al (5) carefully considered the impact of the burden of successive complications on survival, demonstrating that more than two complications were associated with mortality and that the association between complications and mortality increased as the number of complications increased. Neurologic and pulmonary complications carried the greatest risk of death.

Technology and electronic health records are increasingly facilitating the generation of large datasets of patient outcomes and care delivery patterns (7). The Food and Drug Administration and the Institute of Medicine (IOM) have advocated that we employ this 'real-world' data to inform patient care through learning health systems (8,9). The IOM defines the learning health care system as one "in which progress in science, informatics and care culture align to generate new knowledge as an ongoing, natural by-product of the care experience, and seamlessly refine and deliver best practices for continuous improvement in health and healthcare" (8). Rare but striking examples of pediatric learning health systems exist, such as PEDSnet (10), a national network that aims to facilitate clinical trials, observational research and quality improvement across rare pediatric diseases. PEDSnet identifies four essential attributes of a learning health system (10):

- a collaborative community of patients, families, clinicians, researchers and health system leaders to generate and apply big data;
- wide-reaching integrated multi-institutional electronic health care data sets;
- integrate point-of-care delivery of applicable research-based knowledge to ensure best care;
- facilitate clinical trials, observational research and quality improvement alongside health care delivery.

Pediatric critical illness is a heterogeneous collection of numerous, diverse, and rare conditions that require various, infrequently utilized therapies (11). This combination of patient heterogeneity and therapeutic infrequency has contributed to the small size and consequent failure of clinical trials in pediatric critical care (10, 12). The learning health system offers a path to efficiently advancing knowledge and care in pediatric critical illness. By leveraging electronic health care systems, we facilitate data collection; by reaching across centers, we gain power; by committing to use real world data to answer questions, we potentially enable the generation of generalizable, impactful clinical knowledge.

Linking two existing high-quality registries is not equivalent to developing a learning health system, but is an important and efficient example of advancing clinical knowledge through the application of existing large multi-institutional ‘real-world’ data sets. Bembea et al (5) have carefully linked two substantial registries, the AHA GTWG-R and ELSO, to draw upon the unique and distinct strengths of both. The AHA GTWG-R contributed processes of care related to CPR and hospital structural features whereas ELSO offered detail regarding the ECPR run and detail regarding patient complications.

The ELSO Registry has existed for over thirty years and across that time it has grown alongside ECMO technology and applications. It has also integrated real-time validity checks and risk-adjusted outcome reporting. In 2017, nearly 400 centers contributed data to ELSO on over 10,000 annual ECMO runs across 60 countries. Its existence across numerous institutions, geographic areas and populations of interest makes it a prime candidate for linkage with other registries (13). The ELSO Registry has been previously linked with the Organ Procurement Transplant Network database to examine ECMO in populations of patients requiring heart transplants (14), and future opportunities could include linking ELSO with administrative datasets to assess how ECMO impacts resource utilization or ventricular assist device (VAD) registries to better understand the relationship between VADs and ECMO.

This linked analysis of the GTWG-R and ELSO Registries finds ECPR utilization is expanding. Over 40% of children requiring ECPR survive and 30% survive even when CPR is required for more than one hour prior to ECMO, but mortality rates and need for rehabilitation are both significantly increased by complications. Hopefully, future work will identify ways to reduce complications and improve both survival and functional outcomes in children.

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