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EDITORIAL

Shortening the path to perfusion: why every link in the chain of survival shapes ECPR outcomes

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1. Extracorporeal support in refractory cardiac arrest

The modern landscape of resuscitation medicine is being transformed by extracorporeal cardiopulmonary resuscitation (ECPR), an intervention that can restore perfusion when conventional cardiopulmonary resuscitation (CPR) fails. The first fundamental pillar of ECPR lies in the accurate selection of candidates, taking into account both patient-specific factors—primarily age and comorbidities—and event-related characteristics such as witnessed arrest, timing, presenting rhythm, and logistical feasibility. Yet, as the study by Liao *et al.* [1] compellingly demonstrates, even the most advanced technologies cannot compensate for one fundamental truth: time remains the central determinant of survival. Their analysis of 279 adult in-hospital and out-of-hospital cardiac arrest (OHCA) patients reveals a clear and linear relationship between delays in extracorporeal membrane oxygenation (ECMO) cannulation and in-hospital mortality, with a 3% rise in mortality for every minute of CPR-to-ECMO delay and a fourfold increase in death when cannulation occurs ≥30 minutes after arrest [1].

This finding is neither isolated nor surprising—it resonates deeply with the principles of the Chain of Survival, the conceptual backbone of cardiac arrest management [2, 3]. What Liao *et al.* [1] provide is quantitative evidence that ECPR success is not defined at the bedside where the cannulas go in, but at the moment the patient collapses. Every link—bystander action, early defibrillation, emergency medical system (EMS) coordination, and hospital readiness—shapes whether an ECMO-capable center receives a viable patient in time for extracorporeal circulation to make a difference (Fig. 1).

2. Bystander CPR: the first determinant of ECPR eligibility

High-quality bystander CPR (adequate depth and rate with minimal interruptions) is the earliest and most decisive modifiable factor in preserving organ viability. Without it, no-flow time is prolonged long before ECMO teams are activated. National cohort studies, such as Goto *et al.*'s [4] conducted in Japan, confirm that each minute without CPR decreases neurologically intact survival by as much as 10%, whereas immediate bystander compressions dramatically increase the chance of neurologically intact survival.

Liao *et al.*'s [1] data highlight that ECMO cannot reverse the cumulative metabolic debt of prolonged low-flow states. This is due to the progressive imbalance between cellular energy demand and energy supply that accrues during sustained states of inadequate tissue perfusion. If perfusion is not maintained early, even the fastest ECPR sequence cannot restore organs that have already suffered irreversible ischemia. The community's role—through CPR training, public awareness, and dispatcher-assisted CPR—thus becomes the very first safeguard for ECPR success.

3. Early defibrillation: restoring rhythm before mechanical circulation is needed

Defibrillation is the third pillar in the Chain of Survival and potentially the most time-sensitive intervention. Shockable rhythms, particularly ventricular fibrillation, deteriorate rapidly into non-shockable rhythms if defibrillation is delayed, diminishing the likelihood that ECPR will restore a perfusing rhythm.

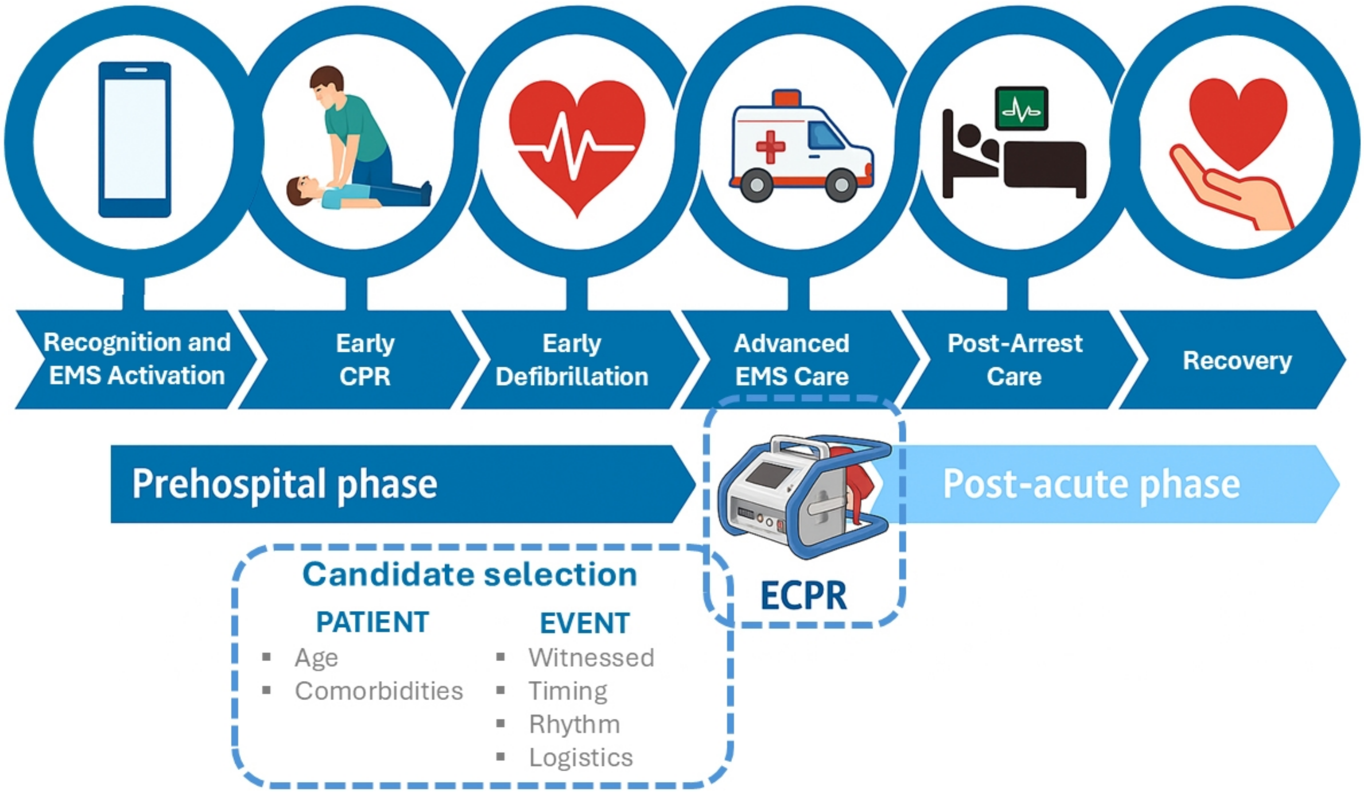

FIGURE 1. The chain of survival represents all the interconnected links required to maximize outcomes in patients experiencing cardiac arrest. ECPR represents a valuable tool to restore perfusion in selected patients, only when embedded in a structured cardiac arrest management system. ECPR: extracorporeal cardiopulmonary resuscitation; EMS: emergency medical system; CPR: cardiopulmonary resuscitation.

In their analysis, Liao *et al*. [1] show that patients with underlying coronary artery disease (CAD)—a population in whom shockable rhythms are common—suffer disproportionately from delayed ECMO deployment, with mortality rising steeply with every passing minute. This reinforces findings from Yannopoulos *et al*.'s [5] Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST) trial, where ultra-early defibrillation paired with rapid ECMO transport yielded unprecedented survival in refractory ventricular fibrillation (VF).

The convergence of evidence suggests that public automated external defibrillator (AED) access, rapid use, and continuous expansion of first-responder programs directly increase the pool of patients who can actually benefit from ECPR.

4. EMS–ECMO center coordination: the critical middle link

Even the most efficient ECMO team cannot compensate for poorly coordinated prehospital logistics. What occurs between the bystander and the hospital doors—including recognition, prioritization, and routing—largely determines the CPR-to-ECMO interval.

Liao *et al*. [1] show that patients cannulated within 14 minutes from the beginning of CPR had dramatically lower mortality (52%) compared to those cannulated after 30 minutes (nearly 80%).

Reaching such targets requires high-performance EMS systems that activate ECMO centers early, sometimes even during ongoing resuscitation in the field.

High-performing international models demonstrate common features:

Early ECMO alert protocols: Spanning from Prague to Paris, EMS systems deploy ECMO teams as soon as refractory arrest is identified—often before arrival of EMS crews on scene.

Direct transfer to ECMO-capable hospitals: Randomized trials show superior outcomes when refractory OHCA patients are transported immediately for invasive interventions, including ECPR [6].

Mechanical CPR during transport: Minimizes interruptions and preserves cerebral perfusion even in complex extrications, as suggested by international guidelines in settings where conventional CPR would be ineffective or potentially dangerous for the rescuers (evacuations, transport) [2, 3].

Prehospital identification of ECPR candidates: Initial rhythm, witnessed arrest, immediate CPR, and presumed reversible causes must be recognized by EMS within seconds.

Without these elements, the delay curves continue their relentless climb, pushing mortality higher with every minute.

5. Hospital coordination and ECMO readiness: the final determinant of survival

Once the patient reaches the ECMO center, the system must operate with the speed and precision of a trauma activation in terms of protocolized, multidisciplinary activation and intervention. Liao *et al*. [1] describe the numerous causes of cannulation delay: equipment mobilization, operator inexperience, need for interdisciplinary coordination, and variable environments (emergency department *vs.* intensive care unit *vs.* operating room).

Centers with superior outcomes share several structural features:

A 24/7 ECMO team: Evidence shows that dedicated ECPR teams reduce activation time and improve outcomes by enabling rapid cannulation and protocolized management.

Simulation-based training: Cannulation errors, vascular complications, and workflow inefficiencies all shrink when rehearsed regularly.

Pre-assembled ECMO carts: Standardized equipment placement shortens time to pump-on and reduces cognitive load during emergencies.

Ultrasound-guided vascular access: As shown in Nakatsutsumi *et al.* [7], real-time ultrasound reduces cannulation complications and substantially decreases procedural duration.

Integrated cardiac catheterization capability for CAD patients—who showed the strongest time-dependence in Liao *et al*. [1]—rapid coronary angiography and revascularization are essential.

Ultimately, the hospital's ability to convert an arriving patient into an ECMO-supported circulation within minutes is not an aspirational standard—it is a survival prerequisite, as demonstrated repeatedly in the mortality curves of Liao *et al*.'s [1] study.

6. ECPR as a system, not a procedure

The most important lesson we have learnt along the past two decades is that ECPR is not simply an intervention but a system of care spanning public, prehospital, and in-hospital environments. The survival benefit of ECMO is unlocked only when every preceding link preserve organ viability long enough for mechanical perfusion to make a difference [8].

Thus, ECPR programs must be designed around the Chain of Survival:

- Immediate bystander CPR: maximizes neurological and myocardial salvage.
- Early defibrillation: prevents rhythm deterioration and reduces the need for prolonged CPR.
- EMS coordination and rapid transport: ensures the patient reaches the appropriate hospital for the individual patient without avoidable delay.
- Hospital-level readiness and technical proficiency: eliminate cannulation delays that sharply increase mortality.

Liao *et al*.'s [1] study adds powerful, quantitative evidence to what clinicians already know intuitively: ECMO does not rescue patients from prolonged low-flow states—it is, in fact, effective only within systems that are able to minimise delays and reduce cardiac arrest duration.

7. Conclusion

ECPR is an extraordinarily powerful intervention for restoring circulation in refractory cardiac arrest, but it is not intended for every arrest victim. To maximise meaningful outcomes (*i.e.*, neurologically intact survival) and minimise ineffective interventions, programmes must adopt rigorously defined selection protocols.

The CPR-to-ECMO interval is the single modifiable variable most strongly associated with ECPR outcomes. But shortening this interval requires more than faster cannulation—it demands a seamless continuum of care, beginning in the community and ending in the ECMO-capable intensive care unit.

Besides this, a major organizational and ethical issue related to ECPR is the ability to make this resource available to all potential candidates. Unfortunately, at least for now, this is not feasible both in areas distant from ECMO centers within regions where ECPR protocols exist, and even more so in parts of the world where access to high-quality basic life support itself remains a challenge.

ECPR can never replace the preceding links in the chain of survival; rather, it relies entirely on them in order to achieve its effectiveness. If healthcare systems intend to adopt ECPR as a meaningful survival tool, they must invest not only in equipment and specialists but also in CPR education, public AED deployment, EMS integration, and efficient institutional protocols. Only when every link in the Chain of Survival is strengthened will the lifesaving potential of ECPR be fully realized.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

FS—drafted the first version. AR—revised the manuscript critically and integrated the text. Both authors were involved in the conception of the manuscript. Both authors read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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