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Editorial

Extracorporeal CPR: Now a standard of care?

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Despite significant improvements in the field of resuscitation, overall survival after out-of-hospital cardiac arrest (OHCA) remains low,[1,2] and many survivors have persistent neurological damage. Refractory OHCA, defined as the failure to achieve return of spontaneous circulation (ROSC) despite conventional cardiopulmonary resuscitation (CPR), is associated with an even worse prognosis. In fact, after ten minutes of conventional CPR, chances of survival start to decline rapidly.[3] After 35 minutes, less than 1% of patients achieve ROSC and survive with a favourable neurological outcome.[4,5]

One of the most recent interventions applied and investigated in the resuscitation of patients with OHCA is extracorporeal membrane oxygenation (ECMO). Extracorporeal CPR (E-CPR), the rapid deployment of veno-arterial ECMO during ongoing CPR, is a promising approach for patients with refractory OHCA.[6] Evidence supporting E-CPR is now compelling. After many observational studies,[7–13] two randomised trials demonstrated the feasibility and possible benefits of early transport to the hospital for initiation of E-CPR in patients with refractory OHCA.[14,15] In addition, a recent meta-analysis showed an improved rate of survival with good neurological outcomes.[16]

In this issue of *Resuscitation Plus*, Mørk et al.[17] described the performance of a tertiary cardiac arrest centre (CAC) in Denmark in treating patients with OHCA with a particular focus on the role of E-CPR. The authors analysed three groups of OHCA patients managed at their institution: patients admitted with ROSC, patients receiving E-CPR for refractory OHCA, and patients who arrived with refractory OHCA but were not treated with E-CPR. The rate of survival at hospital discharge was 64% in patients admitted with ROSC. While such a rate of survival may appear high compared with the literature, it probably reflects the very selected population of patients referred to a CAC characterised by favourable prognostic factors such as cardiac cause, witnessed arrest, bystander CPR, and initial shockable rhythm. In refractory OHCAs, survival at hospital discharge occurred in 27% of patients receiving E-CPR and only 1% of patients without E-CPR, confirming the very low survival of patients with prolonged refractory OHCA who do not proceed with E-CPR.[4,5] Patients with refractory OHCA were considered eligible for E-CPR after 15 minutes of conventional CPR without ROSC and if the following criteria were met: age 18–65 years, witnessed arrest, bystander CPR and preferably initial shockable rhythms, no-flow time less than ten minutes, and absence of severe comorbidity.

When interpreting studies on E-CPR, it is essential to remember that E-CPR is part of a bundle of treatments that begins in the pre-hospital setting, continues during transport, and is completed in the hospital (Fig. 1). This must be considered when trying to generalise the findings of studies conducted in successful E-CPR programs to other cities. In fact, survival rates in patients treated with E-CPR are highly variable, between 8% and 40% among studies.[13,18,19] Such high variability can be mainly explained by differences in emergency medical services (EMS) response times, quality of bystander CPR, availability of citizen first responders defibrillation,[20] patient selection, time to support on veno-arterial ECMO and post-resuscitation care.

A prolonged no-flow time, the time between collapse and initiation of bystander CPR, is one of the main factors contributing to poor survival.[21] Early bystander-initiated CPR is the most important modifiable factor in decreasing the no-flow time and increasing survival.[22] Denmark, the country of the study by Mørk et al.,[17] is one of the European countries with the highest rate of bystanders' interventions. Thanks to multiple initiatives[23] including mandatory CPR education in schools, dispatcher-assisted CPR, and a citizen first responders smartphone app,[24] bystander-initiated CPR reached 80% in 2020.[25] In fact, in the study by Mørk et al.,[17] 98% of refractory OHCAs treated with E-CPR received bystander-initiated CPR before EMS arrival and no-flow time was virtually zero. In the two recent randomised trials, rates of bystander-initiated CPR were 98% in the Prague OHCA study[15] and 87% in the ARREST trial[14] but such performances are still very far from being reached in many countries.

Low-flow time, the time between initiation of CPR and commencement of ECMO, is another crucial factor contributing to poor survival.[26] An optimal time interval for ECMO has been proposed to lie between 30 and 60 minutes after OHCA. However, the survival benefit of E-CPR can also be extended beyond 60 minutes for carefully selected patients.[13] Impressively, more than 20% of patients receiving E-CPR for refractory OHCA in the study by Mørk et al.[17] had a good neurological outcome despite low-flow times higher than

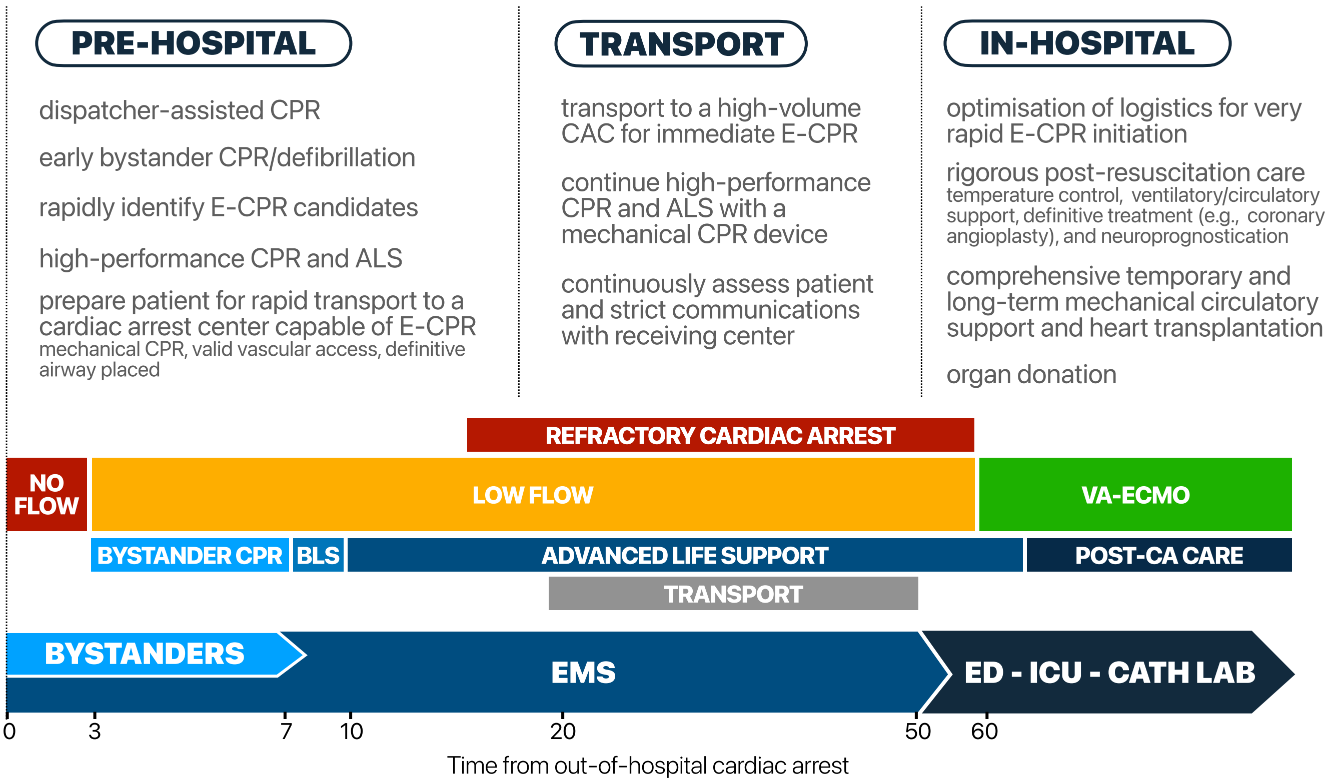

Fig. 1 – Schematic representation of the ideal structure and performance of a successful extracorporeal cardiopulmonary resuscitation (E-CPR) program for refractory out-of-hospital cardiac arrest. CPR = cardiopulmonary resuscitation, ALS = advanced life support, EMS = emergency medical services, CAC = cardiac arrest centre, VA-ECMO = veno-arterial extracorporeal membrane oxygenation, CA = cardiac arrest.

75 minutes. It is clear how bystanders play a significant role[27]: thanks to their intervention, the time window within which successful resuscitation manoeuvres can be performed and tolerated is extended. In the absence of bystander CPR, severe irreversible damage to the brain and other organs occurs, and any advanced treatments like E-CPR would likely have little or no effect on outcomes. Another important consideration, given the very long median low-flow time, is whether E-CPR increases the number of survivors with neurological impairment. In the study by Mørk et al.,[17] a good neurological outcome was found in 93% of patients discharged alive from the hospital after a refractory OHCA treated with E-CPR. Rates of patients surviving with significant neurological impairment (a score on the cerebral performance category scale of 3 or 4) were similar between patients treated with E-CPR and patients admitted with ROSC. Patient-centred outcomes such as long-term neurological outcomes and quality of life are important but were not assessed in the study by Mørk et al.[17]

Studies demonstrating the feasibility and benefits of E-CPR indirectly increase the supportive evidence for transporting and treating OHCA patients in designated CACs.[27–29] In the study by Mørk et al.,[17] 92% of patients received coronary angiography and 75% percutaneous coronary intervention. Post-arrest temperature control, easily achievable through the ECMO circuit, was also provided in 97% of patients. Percutaneous left ventricular assist devices, such as the Impella, were used in a small proportion of patients, alone or in combination with ECMO. As peripheral veno-arterial ECMO may increase left ventricular afterload with subsequent distension and pulmonary congestion, Impella can be useful for unloading and supporting the left ventricle.[30] Availability of temporary and long-term mechanical circulatory support and access to heart transplantation are also necessary. Expertise in neurological prognostication is also required in a CAC. Finally, organ donation in patients who proceed to irreversible, severe brain injury may also benefit the community.

In conclusion, Mørk et al.[17] should be congratulated for addressing this important area of research. Systems already providing E-CPR as a part of a well-organised system are now supported by further evidence. Conversely, systems considering the implementation of E-CPR must carefully reflect if the necessary services are available or can be implemented. As recent studies on E-CPR taught us, to implement a successful E-CPR program, it is imperative to have an optimised chain of survival with early bystander-initiated CPR, rapid EMS response time, high-performance CPR on-scene, mechanical CPR devices for transport of patients in refractory arrest with ongoing chest compressions, availability of high-volume CAC for immediate E-CPR, rigorous post-arrest care and careful selection of patients to undergo this expensive yet effective treatment.

Declaration of interests

TS is the Social Media Editor of Resuscitation and Resuscitation Plus and member of the ERC BLS Science and Education Committee. SB has no competing interests to declare.

REFERENCES

1. Gowens P, Smith K, Clegg G, Williams B, Nehme Z. Global variation in the incidence and outcome of emergency medical services witnessed out-of-hospital cardiac arrest: A systematic review and meta-analysis. Resuscitation 2022. https://doi.org/10.1016/j.resuscitation.2022.03.026.
2. Yan S, Gan Y, Jiang N, et al. The global survival rate among adult out-of-hospital cardiac arrest patients who received cardiopulmonary resuscitation: a systematic review and meta-analysis. Crit Care 2020;24:61.
3. Chen YS, Lin JW, Yu HY, et al. Cardiopulmonaryresuscitation with assisted extracorporeal life-support versus conventionalcardiopulmonary resuscitation in adults with in-hospital cardiac arrest: anobservational study and propensity analysis. Lancet 2008;372:554–61.
4. Goto Y, Funada A, Goto Y. Relationship between the duration of cardiopulmonary resuscitation and favorable neurological outcomes after out-of-hospital cardiac arrest: A prospective, nationwide, population-based cohort study. J Am Heart Assoc 2016;5:e002819.
5. Nehme Z, Andrew E, Bernard S, Smith K. Impact of cardiopulmonary resuscitation duration on survival from paramedic witnessed out-of-hospital cardiac arrests: An observational study. Resuscitation 2016;100:25–31.
6. Swol J, Belohlávek J, Brodie D, et al. Extracorporeal life support in the emergency department: A narrative review for the emergency physician. Resuscitation 2018;133:108–17.
7. Holmberg MJ, Geri G, Wiberg S, et al. Extracorporeal cardiopulmonary resuscitation for cardiac arrest: A systematic review. Resuscitation 2018;131:91–100.
8. Sakamoto T, Morimura N, Nagao K, et al. Extracorporeal cardiopulmonary resuscitation versus conventional cardiopulmonary resuscitation in adults with out-of-hospital cardiac arrest: a prospective observational study. Resuscitation 2014;85:762–8.
9. Nakashima T, Noguchi T, Tahara Y, et al. Patients with refractory out-of-cardiac arrest and sustained Ventricular Fibrillation as candidates for extracorporeal cardiopulmonary resuscitation – prospective multi-center observational study. Circ J 2019;83:1011–8.
10. Shin YS, Kim Y-J, Ryoo SM, et al. Promising candidates for extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest. Sci Rep 2020;10:22180.
11. Siao F-Y, Chiu C-C, Chiu C-W, et al. Managing cardiac arrest with refractory ventricular fibrillation in the emergency department: Conventional cardiopulmonary resuscitation versus extracorporeal cardiopulmonary resuscitation. Resuscitation 2015;92:70–6.
12. Bernard SA, Hopkins SJ, Ball JC, et al. Outcomes of patients with refractory out-of-hospital cardiac arrest transported to an ECMO centre compared with transport to non-ECMO centres. Crit Care Resusc 2022;24:7–13.
13. Bartos JA, Grunau B, Carlson C, et al. Improved survival with extracorporeal cardiopulmonary resuscitation despite progressive metabolic derangement associated with prolonged resuscitation. Circulation 2020;141:877–86.
14. Yannopoulos D, Bartos J, Raveendran G, et al. Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial. Lancet 2020;396:1807–16.
15. Belohlavek J, Smalcova J, Rob D, et al. Effect of Intra-arrest Transport, Extracorporeal Cardiopulmonary Resuscitation, and Immediate Invasive Assessment and Treatment on Functional Neurologic Outcome in Refractory Out-of-Hospital Cardiac Arrest: A Randomized Clinical Trial. JAMA 2022;327:737–47.
16. Scquizzato T, Bonaccorso A, Consonni M, et al. Extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest: A systematic review and meta-analysis of randomized and propensity score-matched studies. Artif Organs 2022. https://doi.org/10.1111/aor.14205.
17. Mørk SR, Bøtker MT, Christensen S, Tang M, Terkelsen CJ. Survival and neurological outcome after out-of-hospital cardiac arrest treated with and without mechanical circulatory support. Resusc Plus 2022.
18. Bartos JA, Carlson K, Carlson C, et al. Surviving refractory out-of-hospital ventricular fibrillation cardiac arrest: Critical care and extracorporeal membrane oxygenation management. Resuscitation 2018;132:47–55.
19. Bougouin W, Dumas F, Lamhaut L, et al. Extracorporeal cardiopulmonary resuscitation in out-of-hospital cardiac arrest: a registry study. Eur Heart J 2020;41:1961–71.
20. Scquizzato T, Belloni O, Semeraro F, et al. Dispatching citizens as first responders to out-of-hospital cardiac arrests: A systematic review and meta-analysis. Eur J Emerg Med 2022. https://doi.org/10.1097/MEJ.0000000000000915.
21. Guy A, Kawano T, Besserer F, et al. The relationship between no-flow interval and survival with favourable neurological outcome in out-of-hospital cardiac arrest: Implications for outcomes and ECPR eligibility. Resuscitation 2020;155:219–25.
22. Sasson C, Rogers MAM, Dahl J, Kellermann AL. Predictors of survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes 2010;3:63–81.
23. Wissenberg M, Lippert FK, Folke F. Asso-ciation of national initiatives to improve cardiacarrest management with rates of bystanderintervention and patient survival after out-of-hospital cardiac arrest. JAMA 2013;310:1377–84.
24. Andelius L, Malta Hansen C, Lippert FK, et al. Smartphone Activation of Citizen Responders to Facilitate Defibrillation in Out-of-Hospital Cardiac Arrest. J Am Coll Cardiol 2020;76:43–53.
25. The Danish Cardiac Arrest Registry 2001–2020; n.d. https://hjertestopregister.dk/ (accessed 3 April 2022).
26. Wengenmayer T, Rombach S, Ramshorn F, et al. Influence of low-flow time on survival after extracorporeal cardiopulmonary resuscitation (eCPR). Crit Care 2017;21:157.
27. Semeraro F, Greif R, Böttiger BW, et al. European Resuscitation Council Guidelines 2021: Systems saving lives. Resuscitation 2021;161:80–97.
28. Sinning C, Ahrens I, Cariou A, et al. The cardiac arrest centre for the treatment of sudden cardiac arrest due to presumed cardiac cause: aims, function, and structure: position paper of the ACVC association of the ESC, EAPCI, EHRA, ERC, EUSEM, and ESICM. Eur Heart J Acute Cardiovasc Care 2020. https://doi.org/10.1093/ehjacc/zuaa024.
29. Yeung J, Matsuyama T, Bray J, Reynolds J, Skrifvars MB. Does care at a cardiac arrest centre improve outcome after out-of-hospital cardiac arrest? – A systematic review. Resuscitation 2019;137:102–15.
30. Patel SM, Lipinski J, Al-Kindi SG, et al. Simultaneous venoarterial extracorporeal membrane oxygenation and percutaneous left ventricular decompression therapy with Impella is associated with improved outcomes in refractory cardiogenic shock. ASAIO J 2019;65:21–8.

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