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Editorial

Extracorporeal Cardiopulmonary Resuscitation: Prehospital or In-Hospital Cannulation?

Extracorporeal cardiopulmonary resuscitation (E-CPR) is the establishment of venoarterial extracorporeal membrane oxygenation (ECMO) during ongoing cardiopulmonary resuscitation (CPR). Extracorporeal cardiopulmonary resuscitation is the last rescue therapy when, despite high-quality conventional CPR, it is not possible to achieve the return of spontaneous circulation in patients with out-of-hospital cardiac arrest (OHCA). The probability of achieving return of spontaneous circulation and survival declines rapidly after 10 minutes of resuscitation,[1,2] and <1% of patients survive, with a favorable neurologic outcome after 35 minutes of conventional CPR.[2] In such situations, OHCA is considered refractory, and E-CPR recently has been demonstrated to improve outcomes among patients with favorable prognostic factors (eg, young age, witnessed cardiac arrest, early bystander CPR and short no-flow time, signs of life, shockable rhythm).[3-5]

In this issue of the *Journal of Cardiothoracic and Vascular Anesthesia*, Kruit et al.[6] reported the results of a systematic review and meta-analysis investigating the effect of prehospital initiation of E-CPR on low-flow time (interval from CPR to ECMO initiation) and survival. A 2018 review identified that most evidence for prehospital E-CPR came from a small case series.[7] In their systematic review, Kruit et al.[6] included 3 new observational studies, for a total of 4 studies and 222 patients treated with prehospital E-CPR.[6] Most patients came from a study conducted in a single emergency medical service (EMS) system in Paris,[8] the first EMS system applying prehospital E-CPR since 2011.

Prehospital E-CPR is one of the 2 main strategies to provide E-CPR for patients with refractory OHCA (Fig 1). In this scenario, ECMO is established at the place of OHCA (eg, home, street, workplace, or public place), and the patient is transported to the accepting cardiac arrest center once ECMO cannulation is completed. However, prehospital E-CPR is not commonly adopted. A "load and go" strategy, in which the patient is transported rapidly with ongoing CPR to an ECPR-capable center, is far more widespread among systems offering E-CPR, and was investigated recently in 2 randomized trials.[3,4] In this scenario, ECMO cannulation is performed after hospital arrival in the emergency department, catheterization laboratory, or intensive care unit. Another strategy worth mentioning that is still not frequently applied is the *rendezvous* approach[9]: the non-ECMO ambulance rapidly transports the patient with ongoing CPR to a meeting point (eg, a spoke emergency department acting as the cannulation site) halfway with the mobile E-CPR team. The patient is then transported to the hub ECMO center for post-resuscitation care.

Initiating E-CPR at the site of OHCA potentially reduces low-flow time by avoiding delays due to patient extraction and ambulance transport, common issues in metropolitan cities. In their meta-analysis of pre-hospital E-CPR, Kruit et al. reported a pooled mean low-flow time of 61 minutes (95% CI, 45-77).[6] Because shorter low-flow times are associated with better outcomes,[10] and prehospital E-CPR pursues this goal precisely, one might expect a shorter low-flow time. A careful reader will notice that the low-flow time reported by Kruit et al. in their meta-analysis was similar to the mean low-flow times for in-hospital E-CPR in the ARREST trial (59 ± 28 minutes)[3] and in the Prague OHCA study (61 [IQR 55-70] minutes).[4] However, if moving from the setting of randomized trials to that of observational studies, the mean low-flow times for in-hospital E-CPR were highly variable and tended to have high values.[10] These observations highlight the difficulties in staying within the optimal window of 60 minutes of low flow (golden hour for E-CPR) for most patients, even when initiating E-CPR in the prehospital setting. The Paris strategy significantly reduced the mean low-flow time, with similar cannulation time, success, and complication rates compared to in-hospital E-CPR.[11]

Concerning survival after prehospital E-CPR, Kruit et al. calculated a pooled survival to hospital discharge of 23% (95% CI, 16%-34%) in patients treated with prehospital E-CPR.[6] This is a significant achievement considering the pooled low-flow time of 61 minutes. However, the absence of a comparator and the small number of studies and patients included prevented the authors from drawing any firm conclusions on the effect of prehospital E-CPR on survival. Only 1 observational study in Paris, France, compared prehospital E-CPR

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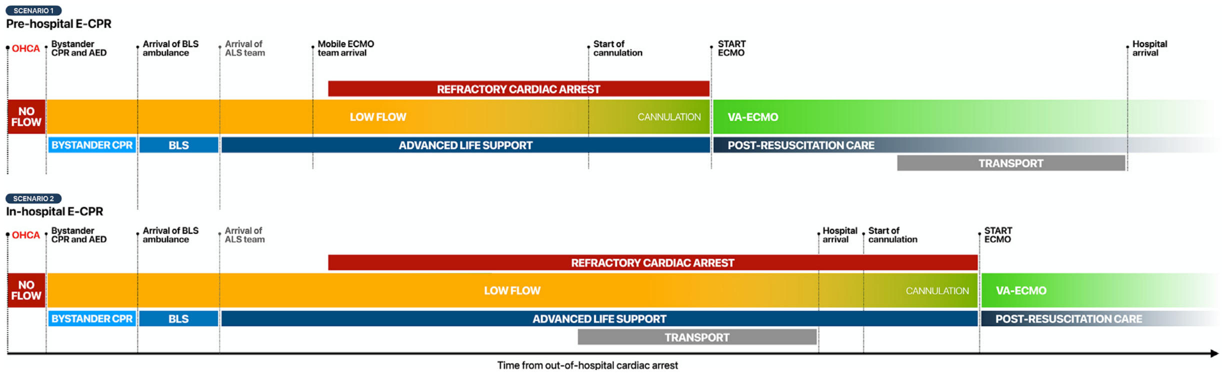

Fig 1. Comparison of the ideal prehospital versus in-hospital extracorporeal cardiopulmonary resuscitation strategies for out-of-hospital cardiac arrest.

with in-hospital E-CPR.[8] In this cohort of 525 E-CPR patients, pre-hospital cannulation was an independent predictor of higher survival and favorable neurologic outcome (odds ratio 2.9, 95% CI 1.5-5.9, p = 0.002, and odds ratio 2.9, 95% CI 1.3-6.4, p = 0.008, respectively).[8] Aiming at the goal of "no-flow zero" with early CPR and defibrillation remains the cornerstone of OHCA; bystanders have an unquestionable benefit and are the primary drivers of survival and good neurologic outcome. For example, low-cost, high-impact smartphone apps that alert citizen first responders to nearby OHCAs to provide early CPR and defibrillation should be implemented in every country.[12] Adding E-CPR to the chain of survival with the hope for favorable neurologic outcomes is only possible for patients who benefit from bystander CPR.

It is clear that treating refractory OHCA patients with E-CPR poses unique logistical challenges in addition to clinical ones. The potential reduction in low flow that prehospital E-CPR can offer and the improvement in survival are not only determined by initiating ECMO at the site of OHCA, but also by EMS system organization, rapid identification of eligible patients, and early activation of the E-CPR team and ECMO implementation. In addition, many other unpredictable factors, well-known to pre-hospital emergency medicine clinicians, may affect the desired outcome. The clinical benefits of earlier treatment and shorter low-flow time must also be balanced with the substantial costs and resources needed, including specialized equipment and personnel. Furthermore, it is essential to consider that pre-hospital E-CPR cannulation is performed in a more complex and unpredictable environment (Table 1).

On the other hand, in-hospital E-CPR is performed in a more controlled setting, with the immediate availability of advanced equipment, diagnostics, and other healthcare professionals, facilitating the procedure and the management of complications. However, it requires reaching the dedicated hospital ideally within 60 minutes, a goal that remains difficult to achieve. Although the decision to transport the patient must be made as early as possible, it should not be made at the expense of CPR quality.[13] Moreover, in-hospital E-CPR is not available everywhere (ie, in rural areas), and prehospital E-CPR can be the only solution for some patients.[14] In prehospital E-CPR, the time issue may shift to the post-cannulation phase as the patient may need to be transported to a significant distance, potentially delaying diagnosis and other treatments (eg, coronary angiography, imaging, other mechanical circulatory devices) that with in-hospital E-CPR would be immediately available after cannulation.

Randomized studies comparing prehospital versus in-hospital E-CPR are currently lacking, as observed by Kruit et al. in their systematic review.[6] Currently, the ON-SCENE trial (NCT04620070) is randomizing patients in the Netherlands to prehospital E-CPR provided through EMS helicopters versus conventional resuscitation. However, the expected study completion date is in 2026, and it will take some time to see the potential effect on survival. Long-term outcomes and quality of life after prehospital E-CPR are still unavailable and should be investigated in future studies. Until then, according to the available data, E-CPR should be anticipated and made available either way for eligible

Table 1
Pros and Cons of Prehospital Initiation of Extracorporeal Cardiopulmonary Resuscitation

Pros	Cons
• Reduction of low-flow time • Avoidance of transport with ongoing CPR • Increase the catchment of eligible patients • Equity also in rural areas or areas far from E-CPR centers	• Requirement of specialized equipment and skills not universally available in the prehospital setting • Cannulation in complex and less controlled environments • Difficulties in managing early complications • Delay of diagnosis and other treatments (eg, coronary angiography, imaging, other mechanical circulatory devices)

Abbreviations: CPR, cardiopulmonary resuscitation; E-CPR, extracorporeal cardiopulmonary resuscitation.

patients, adapting to existing local resources to limit low-flow time as much as possible.

In conclusion, there is very low certainty of evidence supporting the use of prehospital E-CPR. The work conducted by Kruit et al.[6] in this evolving field of resuscitation constitutes an important appraisal of the available evidence, helpful in informing the design of future studies and understanding current knowledge gaps. Extracorporeal cardiopulmonary resuscitation is the last rescue therapy for patients with refractory OHCA—when applied, low-flow time should be minimized, but the best strategy remains to be demonstrated and may be dependent on factors specific to each system. Nowadays, prehospital E-CPR could be the most effective way, but it requires considerable resources and skills not universally available in the prehospital setting.

Conflict of Interests

None.

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