Is there a role for ECMO-facilitated resuscitation for the management of out-of-hospital cardiac arrest (OHCA) with refractory ventricular fibrillation (VF)?

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Article Type: Therapy

Ratings: *Methods*—3.5/5, *Usefulness*—3.5/5

Objectives

To compare ED based standard ACLS resuscitation to early ECMO-facilitated resuscitation in adult (18–75 years) patients with OHCA and refractory VF.

Structured methods

Design

Phase 2, single centre, open-label, adaptive, safety and efficacy randomized controlled trial.

Setting

University of Minnesota Medical Centre.

Subjects

Adults (18–75 years) with OHCA and refractory VF or pulseless VT (pVT), < 30 min transfer time to ED and body morphology able to accommodate mechanical CPR device.

Intervention

Patients were randomly assigned to receive ED based standard ACLS treatment or early ECMO-facilitated resuscitation.

Outcomes

The primary outcome was survival to hospital discharge; secondary outcomes included safety, survival, and functional assessment at hospital discharge and at 3 months and 6 months after discharge.

Introduction

Background

Among patients with OHCA and ventricular fibrillation (VF), more than half present with refractory VF unresponsive to initial standard ACLS treatment.

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Analysis

The authors incorporated a Bayesian “play the winner” adaptive trial design to decrease the number of patients randomized to a possibly inferior treatment.

Main results

In total, 29 patients were included in the primary intention-to-treat analysis, with 15 patients in the standard ACLS group and 14 patients in the ECMO-facilitated resuscitation group. Survival to hospital discharge was significantly improved in the ECMO group (6 out of 14 patients, 43%; CrI 21.3–67.7) compared to the standard ACLS treatment group (1 out of 15 patients, 7%; 95% CrI 1.6–30.2) (ARR: 36.2%; 95% CrI 3.7–59.2; posterior probability of ECMO superiority 0.9861). Cumulative 6-month survival was significantly better in the early ECMO group compared to the standard ACLS group (43% vs 0% $p=0.006$), and no unanticipated serious adverse events were observed. The study was terminated early after the first preplanned interim analysis because the posterior probability of ECMO superiority exceeded the prespecified monitoring boundary.

Appraisal

Strengths

- Important clinical question assessing patient-important outcomes
- Patients randomized
- Allocation concealed
- While the treating teams were not blinded, critical care teams and functional assessment evaluators were blinded to group assignment
- Primary analysis based on intention to treat
- No missing outcome data

Limitations

- Small sample size
- Numerous baseline differences between the groups including fewer women in the ECMO group and more

baseline CAD, smoking and renal disease in the ACLS group

- Trial stopped early for benefit. Truncated trials often overestimate treatment effects due to small numbers of outcome events and early trial random error
- Limited generalizability to other institutions—this centre has a robust ECMO program
- Extremely high rate of bystander CPR
- Based on their own prior research, the authors hypothesized a 25% absolute difference in survival to hospital discharge (37% in the ECMO group vs 12% in the ACLS group), which is unrealistic in most settings and which far exceeds the MICD for cardiac arrest studies
- Fragility index = 1—a fragility index of 1 means that a change in the outcome for a single patient is sufficient to make the results not statistically significant

Context

Previously reported survival rates range from 5.5 to 43.5% for ECMO in OHCA and up to 55.6% in patients with VF/VT [1, 2]. However, all previous studies were observational and most were retrospective with inherent study bias. The results of this RCT are encouraging, but must be interpreted in the context of superb prehospital care, early ECMO initiation and excellent post-resuscitation care. The recent findings from the EROCA trial demonstrate how challenging these results are to replicate [3]. Centres should consider local ECMO expertise, rates of bystander CPR, pre-hospital treatment including mechanical CPR and transport times, in-hospital care when interpreting the generalizability of these results. Local expert opinion is that ECMO has great potential but the required human resources will be very expensive.

Bottom line

The ARREST trial was a small study of 30 patients terminated early after the first interim analysis. Early initiation of ECMO resulted in an impressive 43% survival to hospital discharge for refractory shockable OHCA, however results should be interpreted with caution due to the extremely small sample size and fragility of the findings. The trial was conducted in a setting with a well-developed ECMO program and exceptional infrastructure/resources, reducing the external generalizability. While this is a promising early RCT on the use of ECMO for the management of OHCA with refractory VF, larger multi-centre trials are required to

confirm the benefits seen in this study before this resource intensive strategy is adopted.

Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

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