Extracorporeal Cardiopulmonary Resuscitation for Refractory Out-of-Hospital Cardiac Arrest (EROCA): Results of a Randomized Feasibility Trial of Expedited Out-of-Hospital Transport

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Study objective: Outcomes of extracorporeal cardiopulmonary resuscitation (ECPR) for out-of-hospital cardiac arrest depend on time to therapy initiation. We hypothesize that it would be feasible to select refractory out-of-hospital cardiac arrest patients for expedited transport based on real-time estimates of the 911 call to the emergency department (ED) arrival interval, and for emergency physicians to rapidly initiate ECPR in eligible patients.

Methods: In a 2-tiered emergency medical service with an ECPR-capable primary destination hospital, adults with refractory shockable or witnessed out-of-hospital cardiac arrest were randomized 4:1 to expedited transport or standard care if the predicted 911 call to ED arrival interval was less than or equal to 30 minutes. The primary outcomes were the proportion of subjects with 911 call to ED arrival less than or equal to 30 minutes and ED arrival to ECPR flow less than or equal to 30 minutes.

Results: Of 151 out-of-hospital cardiac arrest 911 calls, 15 subjects (10%) were enrolled. Five of 12 subjects randomized to expedited transport had an ED arrival time of less than or equal to 30 minutes (overall mean 32.5 minutes [SD 7.1]), and 5 were eligible for and treated with ECPR. Three of 5 ECPR-treated subjects had flow initiated in less than or equal to 30 minutes of ED arrival (overall mean 32.4 minutes [SD 10.9]). No subject in either group survived with a good neurologic outcome.

Conclusion: The Extracorporeal Cardiopulmonary Resuscitation for Refractory Out-of-Hospital Cardiac Arrest trial did not meet predefined feasibility outcomes for selecting out-of-hospital cardiac arrest patients for expedited transport and initiating ECPR in the ED. Additional research is needed to improve the accuracy of predicting the 911 call to ED arrival interval, optimize patient selection, and reduce the ED arrival to ECPR flow interval. [Ann Emerg Med. 2020;■:1-10.]

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INTRODUCTION

Background

An estimated 250,000 people are treated by emergency medical services (EMS) for out-of-hospital cardiac arrest each year in the United States.[1] The modest improvement in survival rates during the past decade have been primarily attributed to better implementation of cardiopulmonary resuscitation (CPR), better advanced cardiac life support by EMS, and better post–cardiac arrest care. However, no new therapies have been proven effective in more than a decade. The result is a plateau of overall survival with good neurologic function rates at less than 10% for EMS-treated out-of-hospital cardiac arrest.[2] The limiting factor for the majority (68%) of out-of-hospital cardiac arrest patients is failure to achieve sustained return of spontaneous circulation.[3]

Extracorporeal cardiopulmonary resuscitation (ECPR) using percutaneous venoarterial extracorporeal membrane oxygenation is emerging as a feasible and potentially effective resuscitation strategy for patients with nontraumatic out-of-hospital cardiac arrest who fail standard therapy. A recent systematic review of nonrandomized studies reported that ECPR after out-of-hospital cardiac arrest was associated with long-term

Editor's Capsule Summary

What is already known on this topic

Circulatory assistance to successfully treat cardiac arrest requires rapid initiation.

What question this study addressed

Is it feasible to expedite transport for out-of-hospital cardiac arrest patients to allow earlier extracorporeal resuscitation efforts?

What this study adds to our knowledge

Using a randomized design in 1 emergency medical service, 15 subjects were enrolled out of 151 cardiac arrest patients. Only 5 out of 12 expedited transport subjects had an emergency department arrival time of 30 minutes or less and 3 out of 5 extracorporeal support subjects had a start time of 30 minutes or less.

How this is relevant to clinical practice

Different efforts are needed to address time barriers if wider use of this resuscitation path is to be implemented.

favorable neurologic outcome, with odds ratios ranging from 1.95 to 9.27.[4] Despite the promise of this emerging therapy based on observational data, it is costly, highly resource intense, and operationally difficult to implement. Randomized clinical trials will be required to definitively demonstrate its efficacy.

Yet there are many challenges to conducting a definitive multicenter clinical trial of ECPR for out-of-hospital cardiac arrest. These include an incomplete understanding of fundamental parameters such as how quickly after a patient's collapse systems of care can initiate ECPR and whether the 911 call to ECPR-flow interval can be reliably estimated in real time and used as an inclusion criterion. The Extracorporeal Cardiopulmonary Resuscitation for Refractory Out-of-Hospital Cardiac Arrest (EROCA) study is a multifaceted research effort that included a pilot randomized trial of expedited EMS transport to an ECPR-capable hospital emergency department (ED) to study these parameters.

Currently available evidence suggests that initiation of ECPR within 60 minutes of out-of-hospital cardiac arrest onset is associated with better neurologic outcome.[5] Many published case series of ECPR for out-of-hospital cardiac arrest include ECPR initiated in the ED,[5-14] whereas other programs initiate ECPR in the cardiac catheterization laboratory.[15,16] In either model, the rationale is to optimize the potential for favorable neurologic outcome by minimizing the interval from cardiac arrest onset to initiation of ECPR. For the ED model, in addition to delivering patients to the ED as soon as possible, it is essential that the clinical team reliably and rapidly initiate ECPR after ED arrival. In a study of ED-initiated ECPR, the median time from intensivist-based ECPR team arrival to initiation of ECPR was 20 minutes (interquartile range 15 to 30 minutes).[14] In our own simulation study, ECPR could be consistently initiated within 30 minutes of patient arrival by trained emergency physicians and nurses.[17] The potential advantage of cannulation performed by emergency physicians is that they are already present in ED, which could minimize delays while ECPR teams arrive. For this study, we set target intervals for our primary outcome at less than or equal to 30 minutes from 911 call to ED arrival and less than or equal to 30 minutes from ED arrival to ECPR initiation by an emergency medicine cannulation team, with the overall goal of achieving 911 call to ECPR initiation in less than or equal to 60 minutes.

The study objectives were to determine the proportion of patients with refractory out-of-hospital cardiac arrest who were randomized to expedited transport in accordance with a real-time estimated interval from 911 call to ED arrival of less than or equal to 30 minutes who actually arrived at an ECPR-capable ED within 30 minutes; and to determine the proportion of ECPR-eligible patients in whom ECPR was initiated by an emergency medicine cannulation team within 30 minutes of ED arrival.

MATERIALS AND METHODS

EROCA was a parallel-group, randomized, clinical trial. The trial focused on the feasibility and reliability of randomizing out-of-hospital cardiac arrest patients to standard care (control) versus expedited transport to an ECPR-capable hospital (experimental) when the interval from 911 call to ED arrival was estimated to be less than or equal to 30 minutes. It additionally evaluated the feasibility of emergency physicians' initiating ECPR within 30 minutes of ED arrival. Participants were assigned to the experimental group in a 4:1 ratio relative to the control group. This ratio balanced learning about the feasibility of randomization with ensuring an adequate number of ECPR-eligible patients. However, the eligible EMS transporting agencies expanded and the eligible ECMO devices changed during the trial. The study protocol is available in Appendix E1, available online at http://www.annemergmed.com.

Setting

We conducted the trial in Ann Arbor, MI. Initially, only EMS patients located within the response zone of the City of Ann Arbor Fire Department were included. Ann Arbor has a population of 123,062 and a population density of 4,409/mile^2.[18] Because of lower-than-expected enrollment, the catchment area was expanded during the trial to several adjacent first-responder agencies, including Scio Township Fire Department (population 17,949; population density 525/mile^2), Ann Arbor Township Fire Department (population 4,579; population density 271/mile^2), and Saline Area Fire Department (population 9,363; population density 2,128/mile^2). All participating fire departments were equipped with mechanical CPR devices (LUCAS-2 Physio-Control or Autopulse; Zoll, Chelmsford, MA). The ECPR-capable ED was in the Michigan Medicine/University of Michigan Hospital.

Selection of Participants

The EROCA trial screened all adult out-of-hospital cardiac arrest patients within the catchment area of the participating first-responding fire departments.

Inclusion criteria were the following:

- Present with out-of-hospital cardiac arrest, presumed nontraumatic cause and requiring CPR
- Presumed or known to be aged 18 to 70 years (before 71st birthday)
- Predicted 911 call to arrival time at ECPR-capable ED interval predicted to be within 30 minutes
- Initial shockable rhythm (ventricular tachycardia or ventricular fibrillation) or witnessed arrest with pulseless electrical activity or asystole as presenting rhythm
- Persistent cardiac arrest after initial manual paramedic cardiac rhythm analysis and shock if indicated

Exclusion criteria were the following:

- Do-not-resuscitate or do-not-intubate advance directive
- Preexisting evidence of opting out of study
- Prisoner
- Pregnant (obvious or known)
- ECPR-capable ED not at the destination hospital as determined by EMS destination protocol
- Legally authorized representative aware of study and refused study participation at the scene

The ECPR-capable hospital had a written care guideline for all ED patients with refractory cardiac arrest with predefined eligibility criteria for initiating ECPR (Figure 1).

The EMS central dispatchers identified potential cardiac arrest patients according to the reason for the call from 911. If the potential cardiac arrest occurred within the response boundaries of a participating first-responding fire department, the dispatcher completed a preassignment computer application that returned a transport strategy of either expedited transport or standard care. The computer application used real-time Web-based information from the Google Maps Application Programing Interface regarding traffic and distance from location of arrest to the ambulance bay of the ECPR-capable hospital.

Patients were enrolled under the exception from informed consent process. Enrollment occurred at randomization by the EMS providers at the scene of the out-of-hospital cardiac arrest. The study team conducted community consultation and public disclosure in each participating community. The study team approached a legally authorized representative and obtained consent to continue data collection and outcome assessment when the patient survived to hospitalization. The study team provided notification to a legally authorized representative if the patient did not survive to hospital admission or if the team was unable to contact him or her before death.

Interventions

EROCA compared 2 treatment strategies for refractory out-of-hospital cardiac arrest: continued standard care in the field (control) versus expedited transport with ongoing mechanical CPR to a hospital capable of initiating ECPR in the ED (experimental). ECPR is defined as percutaneous venoarterial extracorporeal membrane oxygenation initiated during cardiac arrest. The standard care EMS cardiac arrest protocol is provided in Appendix E2, available online at http://www.annemergmed.com. For the expedited transport group, interventions required before initiation of transport included the insertion of an advanced airway, establishment of intravenous or intraosseous access, and initiation of mechanical CPR. If the patient were to rearrest during transport, the EMS providers were instructed to deliver shocks and medications during transport rather than stopping to deliver these interventions until return of spontaneous circulation. There was no time limit to provide on-scene resuscitation before transport. The standard protocols were otherwise not modified for the expedited transport group.

A Web site available to the Huron Valley Ambulance 911 Medical Dispatch Center was used to randomize subjects. Randomization occurred in blocks of 5 with an urn method. The randomization ratio was 4:1 favoring the expedited transport group; this was intended to establish the feasibility of the randomization process while providing more opportunities to administer ECPR compared with

ECPR Inclusion Criteria

1. Age 18 to 70
2. Cardiac arrest is *EITHER:*
    a. WITNESSED OR
    b. Initial SHOCKABLE RHYTHM
3. ECPR can be initiated within 60 minutes of cardiac arrest or 911 call
4. Aggressive ICU care consistent with patient's wishes (if known by family at bedside)

ECPR Exclusion Criteria

1. Estimated BMI >40 due to morbid obesity, e.g.: >300lbs at 6' tall; >250lbs at 5'6" tall; cannot fit in a mechanical CPR device
2. Cannot anticoagulate, e.g.: Trauma, aortic dissection, intracranial hemorrhage, uncontrolled bleeding
3. Cannot perform activities of daily living at baseline (if known or reported by family), including:
    i. Brought in from nursing home, skilled nursing facility, or long term acute care
    ii. Not oriented, not conversational, not independent
4. Advanced comorbidities (if known or reported by family):
    i. Oxygen-dependent lung disease
    ii. Previously evaluated and deemed not a candidate for LVAD
    iii. End stage renal disease requiring dialysis
    iv. End stage liver disease, including jaundice, ascites, varices, and/or on transplant list
    v. Metastatic cancer and/or receiving chemotherapy or radiation
5. DNR/DNI (if known or reported by family)
6. Attending physician perception of futility, including:
    i. $ETCO_2$ <10mmHg for >20 minutes
    ii. Lactate >18mmol

Figure 1. ECPR eligibility criteria.

1:1 allocation. In situations in which the dispatcher used the Web site and gave a treatment group assignment but the patient was not enrolled or randomized in the study because he or she did not meet inclusion or exclusion criteria at the scene, that treatment group assignment was returned to the urn.

Outcome Measures

Primary endpoints were as follows:

1. Proportion of patients with a 911 call or out-of-hospital witnessed first cardiac arrest (qualifying out-of-hospital cardiac arrest event) to ED arrival interval of less than or equal to 30 minutes. We

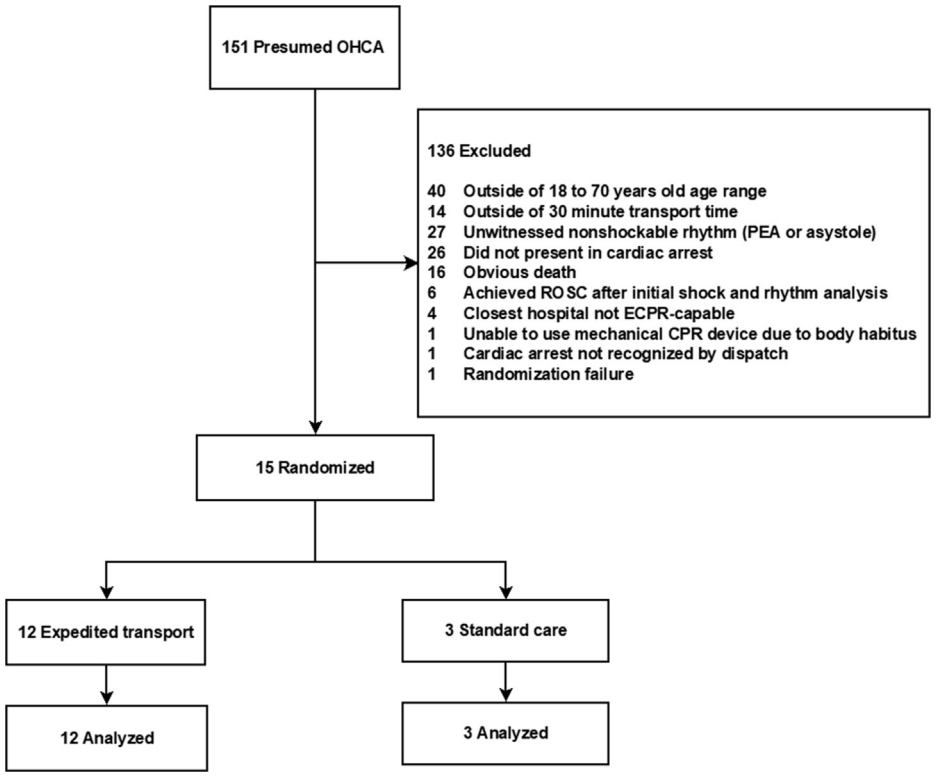

Figure 2. Consolidated Standards of Reporting Trials (CONSORT) diagram. *OHCA*, Out-of-hospital cardiac arrest; *PEA*, pulseless electrical activity; *ROSC*, return of spontaneous circulation.

selected this primary endpoint because the goal of the study was to demonstrate the feasibility and reliability of transporting patients with refractory out-of-hospital cardiac arrest to an ECPR-capable ED within a predefined interval based on real-time estimates.

2. Proportion of ECPR-eligible patients with an ED arrival to ECPR initiation interval of less than or equal to 30 minutes. We chose this interval because the estimated therapeutic window for out-of-hospital cardiac arrest ECPR is 60 minutes, and our simulation studies supported the feasibility of emergency physician–initiated ECPR within this interval.

Safety endpoints were as follows:

1. Hemorrhage requiring blood transfusion, pneumothorax requiring thoracostomy, or hemopericardium requiring pericardiocentesis.
2. Hemorrhage requiring blood transfusion (>4 units of packed RBCs per incident), vessel damage requiring vascular procedure or leading to occlusion, venous/arterial thromboembolism, stroke, renal failure, and infection. Other safety endpoints included all components of composite safety endpoints along with splenic or liver injury.

For exploratory endpoints, we measured the modified Rankin Scale score and Cerebral Performance Category score at hospital discharge and 90 days. Good neurologic outcome was predefined as 90-day modified Rankin Scale score less than or equal to 3 or Cerebral Performance Category score less than or equal to 2. We also assessed patient-reported outcomes with the Neuro-QOL battery and cognitive functioning with the NIH Toolbox.

This was a pilot trial, designed to demonstrate feasibility in preparation for a larger trial that will be powered to detect effect on patient outcomes. As such, the primary endpoints targeted process measures. The expedited transport protocol would thus have been considered acceptable if greater than or equal to 80% of patients (20/24) arrived at the ED in less than or equal to 30 minutes. Similarly, the ED ECPR initiation time would have been considered acceptable if the ED arrival to ECPR initiation interval had been less than or equal to 30 minutes for 80% or more of patients eligible for ECPR. Planned enrollment was 30 patients, with 24 enrolled in the expedited transport group (experimental) and 6 in the standard care group (control).

The EROCA trial was granted an Investigational Device Exemption from the Food and Drug Administration and was approved by the University of Michigan Institutional Review Board.

Selection of Participants

During the study period, 151 out-of-hospital cardiac arrest patients met initial prescreening criteria and 15 were randomized (Figure 2). Randomization was not used during 3% of the overall study period, primarily owing to the unavailability of qualified ECPR cannulators. During that time, there were 5 out-of-hospital cardiac arrest 911 calls. Two of these 5 out-of-hospital cardiac arrest patients had a shockable rhythm and were within the predicted time to ED arrival. Two were ineligible because the arrest was asystolic and unwitnessed, and one was outside the predicted time to ED arrival.

Recruitment occurred between May 1, 2017, and March 5, 2020. The study investigators proposed ending the trial early to the data and safety monitoring board before achieving intended accrual because of slower-than-anticipated recruitment; Food and Drug Administration–mandated pause after enrollment of initial 15 subjects, pending approval for additional enrollment on March 5, 2020; and institutionally mandated pause in clinical research operations on March 14, 2020, owing to the coronavirus disease 2019 pandemic. The data and safety monitoring board agreed to end the trial early on April 22, 2020.

RESULTS

The overall cohort (n=15) was 67% men and 80% white, with a mean age of 62 years. The initial cardiac rhythm was shockable in 53% of the cohort (n=8). Additional characteristics of the overall cohort, standard care, and expedited transport groups are available in Table 1. We reported this trial in accordance with the Consolidated Standards of Reporting Trials extension for Pilot and Feasibility Trial (Appendix E3, available online at http://www.annemergmed.com).

For primary endpoint 1, 5 of 12 participants in the expedited transport group, or 42% (95% confidence interval 19% to 68%), had a 911 call to ED arrival interval of less than or equal to 30 minutes. For primary endpoint 2 in the subset eligible for ECPR, 3 of 5 participants, or 60% (95% confidence interval 23% to 88%), had an ED arrival to ECPR initiation interval of less than or equal to 30 minutes. Table 2 compares the estimated and actual subintervals for each patient in the expedited transport group, including 911 call to scene arrival by paramedics, paramedic scene time, and transport time. These subinterval results demonstrate that our model systematically underestimated paramedic scene time and overestimated transport times.

Table 1. Characteristics of subjects by group.

Cardiac Arrest Characteristics	Overall (n=15)	Standard Care (n=3)	Expedited Transport (n=12)
Age, mean (SD), y	62 (7)	61 (3)	62 (8)
Sex, No. (%)			
Women	5 (33)	1 (33)	4 (33)
Men	10 (67)	2 (67)	8 (67)
Race, No. (%)			
White	12 (80)	3 (100)	9 (75)
Black	1 (7)	0	1 (8)
Unknown/declined	2 (13)	0	2 (17)
Asian	0	0	0
American Indian/Alaska Native	0	0	0
Native Hawaiian/Pacific Islander	0	0	0
Bystander CPR, No. (%)	10 (67)	3 (100)	7 (58)
Cardiac arrest location, No. (%)			
Home	12 (80)	2 (67)	10 (83)
Public location	3 (20)	1 (33)	2 (17)
Initial cardiac rhythm, No. (%)			
Ventricular fibrillation	8 (53)	3 (100)	5 (42)
Witnessed PEA	4 (27)	0	4 (33)
Witnessed asystole	3 (20)	0	3 (25)

Table 2. Expedited transport intervals.

Individual Subject Data by ECPR Use	911 Call to Scene Arrival Interval (Minutes)		Scene Arrival to Scene Departure Interval (Minutes)		Scene Departure to ED Arrival Interval (Minutes)		911 Call to ED Arrival Interval (Minutes)		ED Arrival to ECPR Flow Interval (Minutes)		911 Call to ECPR Flow Interval (Minutes)	
	Predicted*	Observed	Predicted*	Observed	Predicted†	Observed	Predicted	Observed	Predicted	Observed	Predicted	Observed
ECPR	5	8	8	7	12	7	25	22	30	34	60	56
	5	12	8	19	15	8	28	39	30	21	60	60
	5	6	8	29	15	8	28	43	30	30	60	73
	5	3	8	15	13	5	26	23	30	27	60	50
	5	8	8	28	5	6	18	42	30	50	60	92
No ECPR	5	11	8	19	16	7	29	37				
	5	6	8	15	12	7	25	28				
	5	4	8	26	11	2	24	32				
	5	5	8	14	17	11	30	30				
	5	7	8	22	8	4	21	33				
	5	5	8	12	12	8	25	25				
	5	6	8	23	12	7	25	36				
Mean (SD), min	5	6.8 (2.7)	8	19.1 (6.8)	12.3 (3.3)	6.7 (2.3)	25.3 (3.3)	32.5 (7.1)	30	32.4 (10.9)	60	66.2 (16.7)
Proportion ≤target		0.42		0.08		0.92		0.42		0.40		0.60
Mean Δ from predicted, min		1.8 (2.7)		11.1 (6.8)		–5.7 (2.7)		7.2 (8.1)		2.4 (10.9)		6.2 (16.7)

*The algorithm used fixed predictions for time from the 911 call until advanced life support providers arrived on scene (5 minutes) and for scene time (8 minutes).
†Transport time from scene to hospital was estimated with a call to the Google Maps Application Programing Interface to obtain estimated vehicular drive time.

Table 3. Characteristics and clinical outcomes of subjects with ECPR.

Initial Rhythm	Witnessed	Bystander CPR	911 Call to ECPR Flow Interval (Minutes)	ECPR Duration (Hours)	Cause of Death
PEA	Yes	Yes	56	92.2	Post–cardiac arrest brain injury
PEA	Yes	Yes	60	6.7	Hemorrhagic shock
Asystole	Yes	No	73	<1	Sudden cardiac death
VF	Yes	Yes	50	112.8	Multiorgan failure
VF	Yes	No	92	27	Brain death

VF, Ventricular fibrillation.

Seven of 12 patients in the expedited transport group were not ECPR candidates according to ED criteria. The reasons for their ineligibility included not consistent with goals of care, contraindication to anticoagulation, advanced cancer and receiving chemotherapy, return of spontaneous circulation achieved in the ED, body mass index greater than 40 kg/m^2, attending physician's perception of futility, and ECPR could not be initiated within 60 minutes of 911 call. The patient in the expedited transport group who achieved return of spontaneous circulation before ECPR died during hospitalization owing to post–cardiac arrest brain injury.

The 5 patients who were ECPR eligible were cannulated and had CPR flow initiated (Table 3). Three survived to hospital admission. Of the 2 who did not survive to hospital admission, one developed hemorrhagic shock from internal bleeding and the family declined operative intervention, and the other had inadequate ECPR flow despite appropriate cannula placement confirmed by autopsy. Of the 3 patients admitted to the hospital, 2 died from post–cardiac arrest brain injury (1 of whom met brain death criteria), and the third patient died from multiorgan failure despite initially recovering ability to follow commands.

The intervals for the standard care group are reported in Appendix E4, available online at http://www.annemergmed.com. All 3 standard care patients had a shockable rhythm (Table 1); none had a 911 call to ED arrival interval of less than 30 minutes, and none received ECPR. One standard care patient survived to hospital discharge and had a 90-day modified Rankin Scale score of 5 and 90-day Cerebral Performance Category score of 3. Neuro-QOL battery and cognitive functioning with the NIH Toolbox could not be performed owing to patient condition.

There were no unanticipated complications during the study. There were 3 protocol deviations. Three subjects with an unwitnessed nonshockable rhythm were transported to the ED with mechanical CPR in progress. One of these subjects was originally reported as having a witnessed arrest and subsequently determined as having an unwitnessed one. These patients were excluded from the study because they did not meet inclusion criteria.

LIMITATIONS

The main limitation of this study was the small sample size owing to lower-than-expected recruitment. This gave us less information to evaluate the precision of the estimates of 911 call to ED arrival interval, and the feasibility of consistently achieving an ED arrival to ECPR interval less than or equal to 30 minutes. With only 5 patients in the expedited transport group treated with ECPR, we also had an inadequate sample size to inform the effect of ECPR on out-of-hospital cardiac arrest patient outcomes, given that the 95% confidence interval of a 0 of 5 survival rate is 0% to 43%. Only 3 patients had ECPR initiated within 60 minutes of the 911 call and only 2 treated with ECPR had an initial shockable rhythm. Most other out-of-hospital cardiac arrest ECPR case series and ongoing clinical trials[15,19-21] included only patients with an initial shockable rhythm. Furthermore, this study was not powered to examine the safety of expedited transport versus standard resuscitation in the field. However, the rate of return of spontaneous circulation (2/3) in the standard care group suggests that there is equipoise for randomization in future trials. Expedited transport for ECPR may result in higher or lower rates of survival.

Generalizability of our findings is limited because of performance at a single site. The population density (4,408.9/mile^2), median age (27.5 years), and traffic patterns of our primary catchment area could be significantly different from those of other systems performing ECPR for out-of-hospital cardiac arrest. In addition, the ED personnel available to participate in initiating ECPR at our large academic medical center could

differ significantly from that of other academic and nonacademic EDs.

DISCUSSION

In this study, we evaluated the feasibility of using a real-time estimate of the 911 call to ED arrival interval to determine eligibility for expedited transport of refractory out-of-hospital cardiac arrest patients to an ECPR-capable ED. However, the accuracy of our methodology was less than our desired goal of 80% of patients arriving within the estimated interval. Table 2 illustrates that our fixed 5-minute estimate of 911 call to paramedic arrival time, based on historical averages, was relatively close to the overall mean of 6.9 minutes. However, there were 2 cases in which arrival time was greater than 10 minutes.

Identifying the causes of variability in 911 call to ED arrival time and incorporating them into the algorithm could improve the accuracy of the overall estimate. Our fixed scene time estimate of 8 minutes, which was based on expedited transport simulations by first responders and paramedics in our system, underestimated the average scene time by 11.7 minutes. Moreover, the variability of the scene time, ranging from 7 to 29 minutes, suggests that using a fixed interval will severely limit the accuracy of the overall estimate. The sources of this variability are likely to be multifactorial and require additional investigation. If causes of variability can be identified and known when the estimate is performed, they could be built into the algorithm to improve accuracy. Finally, the estimated transport time based on Google Maps consistently overestimated transport time by an average of 5.7 minutes. Based on these results, a modified algorithm would be improved by accounting for this systematic overestimation in predicted transport times.

A lower-than-expected number of patients were eligible for out-of-hospital enrollment and ECPR in this study. In our model, the majority of patients in the expedited transport group were not eligible for ECPR, in part because we did not expect paramedics in the field to accurately identify many of the exclusion criteria for ECPR, and some exclusion criteria developed during or after transport. Although there is the potential to more precisely select patients for expedited transport, any future study or clinical implementation of an expedited transport protocol will likely include a significant number of patients transported who are ultimately not ECPR candidates.

The accurate prediction of potential eligible subjects will be important for future studies. Reasons for out-of-hospital exclusion not accounted for in our pretrial estimates included early return of spontaneous circulation (n=6), unable to use mechanical CPR (n=1), cardiac arrest not recognized by dispatch (n=1), and randomization failure (n=1). The reasons 7 of 12 patients in the expedited transport group were not eligible for ECPR would have been difficult to predict according to historical data. Given our small sample size, the external validity of this point estimate is limited.

We also evaluated the feasibility of trained emergency physicians' ECPR initiation in the ED for refractory out-of-hospital cardiac arrest patients. However, only 3 of 5 patients achieved the goal of initiation of ECPR within 30 minutes, which fell short of our benchmark targeting 80% of cases. Despite that emergency physicians trained in ECPR cannulation participated in quarterly simulations to maintain skills, the low incidence of study cases could have limited the ability to optimize ED arrival to ECPR flow times.

In conclusion, EROCA did not meet predefined feasibility outcomes for selecting out-of-hospital cardiac arrest patients for expedited transport and initiating ECPR in the ED. The majority of subjects transported did not meet eligibility criteria for ECPR. These results provide important insight into the feasibility of ECPR clinical trials and clinical practice based on selected target intervals. Additional research is needed to improve the accuracy of predicting the 911 call to ED arrival interval, optimize patient selection, and reduce the ED arrival to ECPR flow interval.

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