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Variability of extracorporeal cardiopulmonary resuscitation utilization for refractory adult out-of-hospital cardiac arrest: an international survey study

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Objective A growing interest in extracorporeal cardiopulmonary resuscitation (ECPR) as a rescue strategy for refractory adult out-of-hospital cardiac arrest (OHCA) currently exists. This study aims to determine current standards of care and practice variation for ECPR patients in the USA and Korea.

Methods In December 2015, we surveyed centers from the Korean Hypothermia Network (KORHN) Investigators and the US National Post-Arrest Research Consortium (NPARC) on current targeted temperature management and ECPR practices. This project analyzes the subsection of questions addressing ECPR practices. We summarized survey results using descriptive statistics.

Results Overall, 9 KORHN and 4 NPARC centers reported having ECPR programs and had complete survey data available. Two KORHN centers utilized extracorporeal membrane oxygenation only for postarrest circulatory support in patients with refractory shock and were excluded from further analysis. Centers with available ECPR generally saw a high volume of OHCA patients (10/11 centers care for >75 OHCA a year). Location of, and providers trained for cannulation varied across centers. All centers in both countries (KORHN 7/7, NPARC 4/4) treated comatose ECPR

patients with targeted temperature management. All NPARC centers and four of seven KORHN centers reported having a standardized hospital protocol for ECPR. Upper age cutoff for eligibility ranged from 60 to 75 years. No absolute contraindications were unanimous among centers.

Conclusion A wide variability in practice patterns exist between centers performing ECPR for refractory OHCA in the US and Korea. Standardized protocols and shared research databases might inform best practices, improve outcomes, and provide a foundation for prospective studies.

Keywords Extracorporeal membrane oxygenation; Heart arrest; Cardiopulmonary resuscitation

Capsule Summary

What is already known
Extracorporeal cardiopulmonary resuscitation is becoming an increasingly available modality for the treatment of refractory cardiac arrest.

What is new in the current study
We report variability in extracorporeal cardiopulmonary resuscitation patient selection and practice characteristics. Future guidelines and statements of best practices are needed. Comparison of data across centers may be limited by this practice variability.

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) is a significant global health burden with an annual incidence ranging from 29 to 55 cases per 100,000 population, of which only 2% to 11% survive to hospital discharge.[1] Approximately 75% of adult patients treated for OHCA do not achieve return of spontaneous circulation (ROSC) despite conventional cardiopulmonary resuscitation (CPR) and advanced cardiac life support.[2] Many patients who do not survive to hospital admission after OHCA have autopsy evidence of acute coronary occlusion.[3] Similarly, patients with other reversible etiologies of cardiac arrest, such as fulminant myocarditis, variant angina, and massive pulmonary embolism, are sometimes refractory to standard resuscitation measures.[4-6]

Emergent extracorporeal cardiopulmonary resuscitation (ECPR), which consists of implementing veno-arterial extracorporeal membrane oxygenation (VA ECMO), is a potential therapy for patients with a reversible cause of arrest who are refractory to conventional CPR and advanced cardiac life support interventions. Historically, ECPR was used primarily to treat pediatric in hospital cardiac arrest patients.[7-9] Over time, the scope of ECPR has expanded to adult in hospital cardiac arrest, and now to select candidates with OHCA. A 2010 Japanese review of multiple case series, originally published in Japanese language journals, demonstrated a 26.7% survival rate for more than 500 OHCA patients treated with ECPR.[10] In 2016, a meta-analysis of observational

evidence suggested improved 1-year survival (relative risk, 1.96; 95% confidence interval, 1.00 to 3.87) and 1-year neurological outcome defined as a cerebral performance category of one or two (relative risk, 2.63; 95% confidence interval, 1.11 to 6.21).[11] As the necessary equipment becomes smaller and more portable, ECPR has also been successfully deployed in both the emergency department (ED) and in prehospital settings.[12-16] The 2015 American Heart Association guidelines state, "In settings where it can be rapidly implemented, ECPR may be considered for select cardiac arrest patients for whom the suspected etiology of the cardiac arrest is potentially reversible during a limited period of mechanical cardiorespiratory support (class IIb, LOE C-LD)."[17]

Though a growing interest in ECPR exists, relatively little is known about the current practice patterns, including patient selection criteria, programmatic structure, and cannulation practices. One recent review of the published literature found a wide variation in indications such as CPR duration, age, and initial rhythm when considering ECPR as well as use of postarrest therapies such as coronary angiography and therapeutic hypothermia.[18] In addition, the Extracorporeal Resuscitation Consortium (ERECT) Research Group recently published a survey data from 99 Emergency Life Support Organization (ELSO) members who report performing ECPR and found that 50% of the respondents had performed ECPR in the ED, but more than 90% of cannulations were performed by consulting cardiothoracic (CT) surgeons.[19] Further information is needed. In addition to the published literature, we

surveyed ECPR practice in centers participating in one of two large national research consortia in the US and Korea. We hypothesized that the indications for ECPR, cannulation practices, and use of targeted temperature management (TTM) would vary among centers and countries.

METHODS

We performed an internet-based survey (Qualtrics, Provo, UT, USA) of postarrest care practices including TTM, neurological prognostication, and ECPR in English and Korean, which we have previously described in detail.[20] A dedicated 18-question sub-survey focused specifically on ECPR. The survey was distributed to 35 sites across Korea (Korean Hypothermia Network, KORHN) and 7 sites across the US (National Post-Arrest Research Consortium, NPARC).[21-23] The investigators from these sites were also asked to submit any hardcopy of institutional ECPR protocols. The University of Pittsburgh institutional review board granted institutional review board exemption for all aspects of this study.

We asked a single investigator from each KORHN and NPARC site to complete the survey. Only centers with an ECPR program completed the ECPR subsection. Investigators were instructed to answer survey questions based on local ECPR institutional protocols and practice for adult OHCA patients. The survey was sent in December 2015 and final data collection was completed in January 2016. Survey responses were included in the analysis if > 50% of questions were answered. We performed a descriptive statistics using the Stata ver. 13.1 (StataCorp., College Station, TX, USA).

RESULTS

Of the 33 KORHN and 7 NPARC surveys completed, 100% of the institutions completed the main survey. Overall, 9 KORHN and 4 NPARC institutions reported having an ECPR program and had complete survey data available. Centers using ECPR generally saw a high volume of OHCA, with 12/13 centers caring for > 75 patients per year (Table 1). Survey responders were predominantly Emergency Medicine specialists (KORHN 9/9, NPARC 3/4). In two KORHN centers, ECPR was utilized only for postarrest circulatory support in patients with refractory shock and these were excluded from further analysis. The ECPR annual caseload ranged from 0 to 30 with a median of 5 cases treated per year (interquartile range [IQR] 3 to 10) (KORHN median 5, IQR 2 to 10; NPARC median 6, IQR 5 to 19) (Fig. 1).

Location of cannulation and provider trained with cannulation for ECPR varied among centers (Table 1). Both KORHN and NPARC centers cannulate in the ED (KORHN 3/7, NPARC 3/4); however,

Table 1. ECPR cannulation characteristics

Characteristics	NPARC	KORHN
Total annual out-of-hospital cardiac arrest volume	n = 4	n = 7
< 50	0	0
50–74	0	1
75–99	1	1
100–124	2	1
> 125	1	4
Organized ECPR team		
Yes	3	3
No	1	4
24-hr ECPR capable		
Yes	2	5
No	2	2
Preferred location		
Emergency department	3	3
Operating room	0	0
Cardiac catheterization lab	0	2
Procedure suite	0	0
Depends on scenario[a]	1	2
Cannulating specialty		
Emergency medicine physician	0	4
Cardiothoracic surgeon	4	5
Surgical intensivist	1	0
Interventional cardiologist	0	4
Cannulation final decision		
Attending of record	0	1
Physician in charge of cannulation service	2	5
Other[b]	2	1
Time from vessel puncture to ECMO flow (min)	n = 1	n = 7
15	1	2
20	0	2
25	0	1
30	0	2

ECPR, extracorporeal cardiopulmonary resuscitation; NPARC, National Post-Arrest Research Consortium; KORHN, Korean Hypothermia Network; ECMO, extracorporeal membrane oxygenation.
[a]One US center preferably cannulates in the emergency department but also uses cardiac catheterization lab or operating room. Two of two Korean centers preferably cannulate in emergency department but also use cardiac catheterization lab. [b]US: 1 team decision, 1 postarrest service + cardiothoracic surgeon. Korea: either emergency department or cardiothoracic surgery attending.

other centers also primarily cannulate in the ED but in various locations depending on the situational factors (KORHN 4/7, NPARC 1/4). Patients were primarily cannulated by emergency physicians (4/7), CT surgeons (5/7), and interventional cardiologists (4/7) in KORHN centers, whereas CT surgeons (4/4) cannulated in all NPARC centers. All centers in both countries (KORHN 7/7, NPARC 4/4) used TTM for patients with persistent coma after initiating ECPR and ROSC.

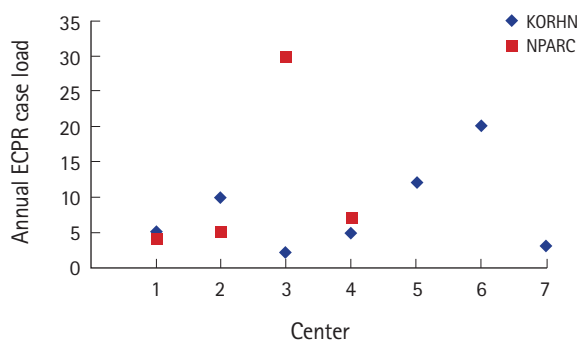All NPARC centers and four of seven KORHN centers reported

Fig. 1. Annual extracorporeal cardiopulmonary resuscitation (ECPR) case load per center. KORHN, Korean Hypothermia Network; NPARC, National Post-Arrest Research Consortium.

having a standardized hospital protocol for ECPR (Table 2). Upper age cutoff for eligibility ranged from 60 to 75 years. No absolute contraindications were unanimous among participating centers. A number of both NPARC and KORHN centers reported cannulating a high proportion of patients that meet exclusion criteria for ECPR.

DISCUSSION

We found a high level of variation in ECPR practices among the surveyed large volume cardiac arrest centers in South Korea and the US. Moreover, variability exists between centers in each country. These differences are an important potential source of bias or confounding in studies evaluating the effectiveness of ECPR in a refractory cardiac arrest.

Practice variability existed between NPARC and KORHN institutions. Organized protocols were more common at NPARC than KORHN institutions. KORHN and NPARC investigators report different locations and specialists responsible for cannulation and initiation of VA ECMO. In KORHN centers, cannulation is frequently performed in the cardiac catheterization laboratory, but not in that of NPARC centers. Institutions from both countries cannulate in the ED. In KORHN centers, multiple specialists are responsible for cannulation, while only surgical intensivists or cardiothoracic surgeons currently cannulate in NPARC centers. Other surveys have found that CT surgeons cannulate in a majority of US ECPR centers.[19] However, no interventional cardiologists were found to be primary cannulators in the surveyed NPARC centers. Absence of these specialists upon arrival of the ECPR patient in the hospital may result in delays to functional VA ECMO or no cannulation attempt at all. This may be one of the reasons for the low rate of cannulating patients who meet the exclusion criteria found in NPARC centers when compared to KORHN centers. Sim-

Table 2. ECPR selection criteria

Details on criteria	NPARC	KORHN
Standardized institutional ECPR protocol	n = 4	n = 7
Yes	4	5
No	0	2
Inclusion criteria	n = 4	n = 4
Age < 75 yr	0	2
Age < 70 yr	1	1
Age < 65 yr	1	0
Age < 60 yr	1	1
Bystander CPR	1	3
Shockable initial rhythm	1	1
Sustained VF cardiac arrest despite 30 min of resuscitation	1	3
Exclusion criteria	n = 4	n = 4
Collapse to CPR time > 30 min	0	1
Unwitnessed event	3	3
Major preexisting medical conditions[a]	3	3
Known aortic dissection	2	3
Aortic insufficiency	1	0
Recent CVA	0	2
Traumatic arrest	2	3
Body habitus	3	2
Obvious vascular disease	2	1
Preexisting neurological disease	3	3
Poor baseline neuro or functional status	2	3
Initial asystolic rhythm	2	2
Initial PEA rhythm	2	0
Other	0	0
Patients cannulated who met exclusion	n = 4	n = 3
Never	0	0
1%–10%	3	1
11%–20%	1	0
21%–30%	0	0
> 30%	0	2

ECPR, extracorporeal cardiopulmonary resuscitation; NPARC, National Post-Arrest Research Consortium; KORHN, Korean Hypothermia Network; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; CVA, cerebral vascular accident; PEA, pulseless electrical activity.
[a] Debilitating medical conditions associated with minimal odds of good outcome.

ilarly, patients who meet the inclusion criteria for cannulation may be missed in this model. Future work should determine the percentage of patients who meet the criteria for cannulation but are not treated using this therapy.

Some NPARC protocols exclude pulseless electrical activity arrest, prolonged ventricular fibrillation arrest, and age > 70 years, whereas KORHN sites do not exclude these criteria. NPARC sites appear to be more conservative in providing ECPR when compared to KORHN sites, because they may have experienced few ECPR cases, the presence of cultural differences in resuscitation care, or centers averse to cannulating in heroic situations.[20]

These findings highlight the need for future research of best

practices as well as the development of formalized hospital, regional, and national guidelines for ECPR. Variations in criteria for patient selection, eligibility, and contraindications each introduce potential for confounding in clinical research. These factors must be controlled in both observational and experimental study designs. Similar to the Utstein style standard variables collected in cardiac arrest registries,[24] a consensus set of core variables should be developed for ECPR registries to facilitate pooled analyses.

Practice variability is likely unavoidable and will require tailoring of the idiosyncrasies of each hospital/healthcare system. Both selection criteria and the nuances in cannulation logistics (location, specialty service, etc.) may require some inherent unavoidable practice variability. Ortega-Deballon et al.[18] conducted a systematic review of available literature concerning ECPR studies and found significant variability in selection criteria including patient age, initial rhythm, and duration of no flow and low flow times. The ERECT research group surveyed centers that had submitted ECPR cases to the ELSO. Most of the 70 included centers did not have formal selection criteria for ECPR.

Our study has several limitations. The large volume centers in the US and Korea that participated in this study may not reflect the full extent of ECPR practice variability. However, these large centers represent the majority of facilities that can provide emergent ECPR. Other investigators have found similar variability in ECPR practices.[18] Additional variability may exist outside the context of the provided survey questions. Finally, we did not survey the centers with regard to sedation, neuromuscular blockade, or withdrawal of care specifically for ECPR patients.

A wide variability exists at institutions performing ECPR for refractory cardiac arrest in Korea and the US, and we reported national and international variability. This variability may confound both observational and experimental research on ECPR. It also underscores the need for standardized guidelines and definitions of common ECPR variables to facilitate best practices, shared data, and research collaboration.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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