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Selected Topics: Critical Care

EMERGENCY PHYSICIAN-INITIATED RESUSCITATIVE EXTRACORPOREAL MEMBRANE OXYGENATION

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☐ **Abstract—Background: Extracorporeal membrane oxygenation (ECMO) has several applications as a resuscitative intervention, including extracorporeal cardiopulmonary resuscitation (ECPR). ECPR is rarely initiated in the emergency department (ED) by emergency physicians outside regional academic institutions. Objectives: To evaluate whether ECPR improves clinical outcomes after cardiac arrest when initiated by emergency physicians (EPs) in a nonacademic hospital. Methods and Materials: We performed a retrospective analysis of prospectively identified consecutive EP-initiated ECMO subjects from a single community hospital over a 7-year period. Logistic regression and propensity models tested the association between ECPR and survival to hospital discharge compared with concurrent ECPR-eligible control subjects. Results: Over 7 years (2010–2017), EPs initiated ECMO on 58 subjects; 44 (76%) were venoarterial cases (43 ECPR) initiated in the ED. Of those, 11 (25%) survived to discharge (n = 9 with cerebral performance category score 1) and most were still alive after 5 years (66%). Adjusting for known covariates, ECPR subjects were more likely than concurrent controls to survive to discharge (odds ratio 8.4; 95% confidence interval 1.2–60.4). Propensity analysis revealed a favorable trend toward survival to discharge after ECPR (odds ratio 2.0; 95% confidence interval 0.51–7.8). Conclusions: Emergency physicians initiated ECMO with promising clinical outcomes. Prospective trials are needed to define the efficacy, safety, and cost-effectiveness of EP-initiated ECMO.** **© 2019 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).**

☐ **Keywords—ECMO; cardiac arrest; ECPR; resuscitation**

INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) has therapeutic potential in a variety of emergency conditions and clinical settings (1–8). Extracorporeal cardiopulmonary resuscitation (ECPR), in particular, has generated much interest as a means to boost survival and favorable neurologic outcome after cardiac arrest (9). Given the inherent resource requirement, most institutional ECMO programs exist within a traditional academic center (10). Yet in many hospitals, emergency physicians (EPs) may be the only clinicians immediately available for emergent ECMO cases. Our hospital has utilized EPs for more than 7 years to initiate and manage ECMO in cases of refractory cardiac arrest and respiratory distress. To demonstrate the feasibility and clinical success of an ECMO program outside the academic center, we describe long-term clinical outcomes of ECPR cases performed by EPs at a nonacademic hospital compared with a concurrent ECPR-eligible control group.

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MATERIALS AND METHODS

Study Design and Setting

We performed a retrospective analysis of prospectively identified consecutive EP-initiated ECMO cases at a single community hospital. Over the study period, annual ED patient census increased from 56,000 to 94,000 patients, and EP staffing increased from 25 to 40 providers. We employ no resident physicians or midlevel providers, and physician coverage expanded over the study period in a commensurate fashion from 72 to 112 daily physician-hours. Cardiothoracic Surgery and Cardiology specialties do practice within the hospital but are not routinely immediately available at bedside during off-hours. The Sharp Institutional Review Board approved this analysis.

Data Source

Two investigators (ZS and LP) abstracted ECMO patient data while adhering to bias-reducing practices described by Kaji et al. (11). Data were obtained primarily through existing quality-improvement records, which include a database of all ECMO patients treated in the hospital. This is maintained by our mechanical circulatory support division. We reviewed the electronic medical record as needed to collect additional or missing Utstein variables. Conflicting data abstraction was resolved by consensus (Kappa = 0.99). The hospital code sheet and our data collection sheet are included in the Supplementary Materials (available online).

Institutional ECMO Program

The EP-ECMO program began in 2010 with a small group of interested providers (ZS, JB, CH) initiating ECMO in an ad hoc fashion. As of December 2017, most of the EPs at our hospital have been trained in ECMO and 73% have performed at least one case (median 2 [interquartile range (IQR) 1–4] cases; range 1–17 cases) in a procedural or supervisory role. EP-ECMO coverage has since expanded throughout the hospital to include the intensive care unit (ICU), inpatient wards, radiology suite, cardiac catheterization suite, and trauma bay. Provider training evolved over the study period from self-directed learning and individual instruction from cardiologists and cardiothoracic surgeons to extensive biannual simulation and regular didactic training. We also maintain active quality assurance and process improvement.

Our multidisciplinary panel of institutional stakeholders typically adheres to the following selection criteria: age < 75 years, witnessed collapse, the presence of bystander cardiopulmonary resuscitation (CPR), initial cardiac rhythm other than asystole, and a CPR-to-ECMO interval < 60 min. However, deviation from these is permitted at the discretion of individual physicians.

The ECMO circuit is primed and managed by surgical ICU nurses for the first hour after initiation. Designated nurses undergo monthly training sessions to assure delivery of the primed circuit to any needed location in the hospital within 10 min of notification. We store two machines using Quadrox oxygenators and Rotaflow pumps (Maquet, Rastatt, Germany) in our surgical ICU that are rapidly mobilized to the ED.

Initiation and cannulation are performed primarily by EPs in the location of the subject's acute event (e.g., ED, ICU, trauma bay, cardiac catheterization suite). If immediately available, other ECMO-trained specialties are incorporated into the resuscitation (Figure 1). Ideally, the resuscitation team comprises three clinicians. The first ('initiator') manages the overall resuscitation and is ultimately responsible for the decision to initiate ECMO. The second ('cannulator #1') cannulates the femoral artery, and the third ('cannulator #2') cannulates the femoral vein. After ECMO initiation, subjects move to the cardiac catheterization suite or interventional radiology for some combination of left heart catheterization, pulmonary artery catheter placement, left heart decompression, or distal leg perfusion. Multidisciplinary inpatient care utilizes Cardiothoracic Surgery, Cardiology, Critical Care, Neurology, and Social Services. Prognostication and weaning strategies are collectively formulated by this multidisciplinary team that has been managing critically ill subjects on ECMO for more than 30 years (12).

Study Definitions and Outcomes

The primary outcome was survival to hospital discharge. Secondary outcomes included cerebral performance category (CPC) at hospital discharge and long-term survival. We recorded ECMO indication, age, sex, comorbidities, initial blood pH, ECMO duration, and hospital length of stay for all ECMO subjects. For ECPR cases, we additionally recorded Utstein variables (event location, witnessed collapse, bystander CPR, and initial cardiac rhythm, CPR duration). Initial pH was recorded using first arterial or venous blood gas obtained either during or immediately after cardiac arrest.

Statistical Analyses

Analyses were performed with R 3.5 (R Foundation, Vienna, Austria) and SPSS v. 22.0 (IBM, Armonk, New York). We tabulated subject characteristics and clinical features, stratifying them by survival to hospital discharge and comparing them with chi-squared or rank-sum test. We also tabulated the annual number of

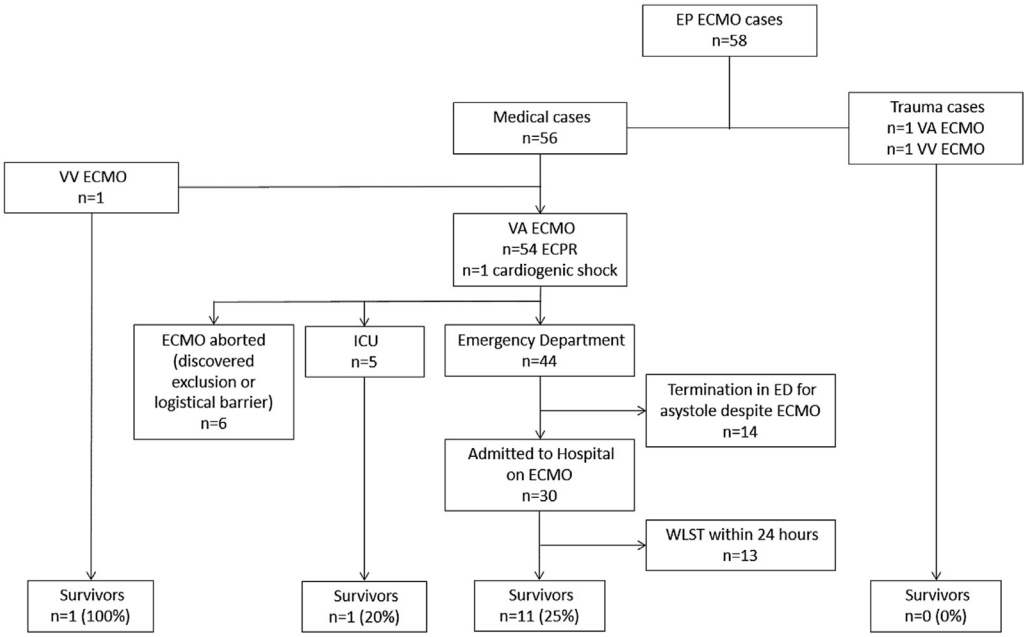

Figure 1. Patient Flow for Emergency Physician (EP) initiated extra-corporeal membrane oxygenation (ECMO). VA = venoarterial; VV = venovenous; EPCR = extracorporeal cardiopulmonary resuscitation; ED = emergency department; ICU = intensive care unit; WLST = withdrawal of life sustaining therapy.

EP-initiated ECMO cases and the particular roles assumed by EPs. Finally, we used several models to compare clinical outcomes of ED ECPR cases from 2010–2013 to a concurrent control group of cardiac arrest subjects that were eligible for ECPR but did not receive it. Beyond 2013, the penetration of EP-ECMO was sufficiently high that ECPR-eligible subjects not treated with ECPR were rare. We performed adjusted logistic regression to test the association between ECPR and survival to hospital discharge with both the concurrent control group and a subset with CPR duration > 30 min during those years. No patients who received ECPR in 2010–2013 had < 30 min of chest compressions prior to initiation.

Propensity score analysis matched the 29 treated (ECMO) patients over 2010–2013 with the n = 188 untreated (no ECMO) patients using a preselected host of covariates (age, duration, out of hospital collapse, witnessed collapse, bystander CPR, and initial cardiac rhythm) (13). After analysis with the fuzzy algorithm, a replacement using a tolerance of 0.10, there were n = 28 matched pairs, with one incomplete match that did not meet the tolerance levels.

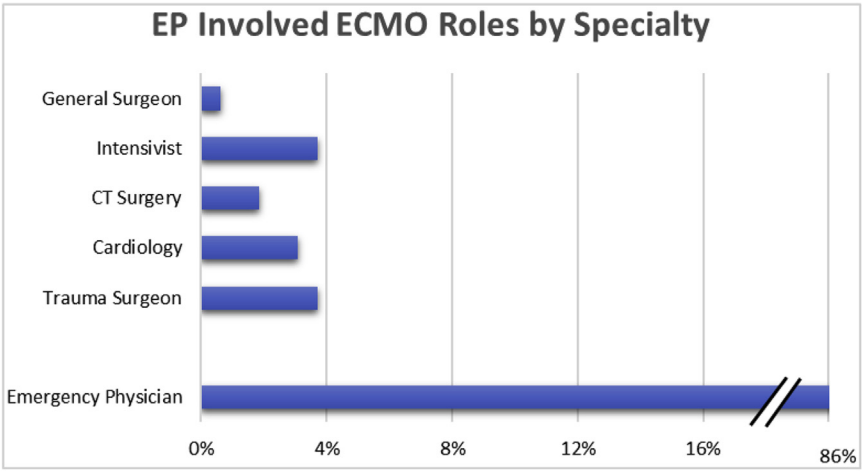

Figure 2. Percent of ECMO (extra-corporeal membrane oxygenation) roles completed by specialty. Three roles per patient (1 initiator, 2 cannulators), all initiations done by emergency physicians (EP).

RESULTS

A total of 58 subjects had EP-initiated ECMO over 7 years (Figure 2). The vast majority of the 56 medical cases (98%) entailed venoarterial ECMO for cardiac arrest (ECPR); most of them (91%) occurred in the ED. Six subjects had cannulation commenced but not initiated on ECMO. Discovery of exclusion criterion or logistical barriers to successful cannulation led to a cessation of further resuscitative efforts.

Table 1 summarizes clinical features of the 43 ECPR cases initiated in the ED. Most had a witnessed (93%) out-of-hospital collapse (63%) with an initial shockable cardiac rhythm (51%) and bystander CPR (84%). Average chest compression duration was 52 min. Survivors had a shorter duration of chest compressions (30 vs. 58 min) and longer hospital lengths of stay (16 [IQR: 12–39] vs. 0 [IQR: 0–1] days). Eleven (25%) ED venoarterial ECMO subjects (43 ECPR, one cardiogenic shock) survived to hospital discharge (nine of those with CPC 1). Two subjects had CPC 3 after suffering ischemic strokes during their hospitalizations. Fourteen patients (32%) had ECMO initiated but failed to have a return of mechanical heart activity post ECMO. These patients were pronounced in the ED. Consequently, survival to hospital discharge was 37% among patients who were admitted and 65% among subjects surviving 24 h. Most patients who died were pronounced within the first 24 h (Figure 3). Figure 4 displays survival over several clinical milestones beyond hospital discharge.

Table 2 contains the clinical features and outcomes of ECPR subjects from 2010–2013 compared with the concurrent ECPR-eligible control group and a subset of those with prolonged resuscitation efforts. More ECPR subjects survived to hospital discharge compared with both control groups. Adjusting for known covariates, ECPR subjects were more likely to survive than concurrent controls treated with traditional CPR (odds ratio [OR] 8.4, 95% confidence interval [CI] 1.2–60.4), and a nonsignificant trend in those with chest compression durations of > 30 min (OR 6.6, 95% CI 0.8–55.7). Propensity-adjusted comparisons showed a nonsignificant trend (OR 2.0, 95% CI 0.5–7.8) in favor of the use of ECMO.

DISCUSSION

We observed promising clinical outcomes (Figure 2) after EP-initiated ECMO in our study. Reynolds et al. and Grunau et al. both estimated the natural history of subjects meeting typical ECPR selection criteria and found that expected survival would be < 5% after 30 min of conventional resuscitation (14,15). Our institutional selection criteria are less restrictive than those used in these estimates as well as other reported ECMO cohorts (1,2,6,7). We allow subjects up to 75 years of age, longer durations of cardiac arrest, pulseless electrical activity as an initial rhythm, and occasional subjects with asystole. Still, nearly one-quarter of ED ECPR cases had good neurologic outcome at hospital discharge, and the vast majority were still alive after 1 year. Selection

Table 1. Clinical Features of ED ECPR Subjects Stratified by Survival

	Survivors (n = 10)	Nonsurvivors (n = 33)	*p* Value
Age (years)	55.5 ± 14.5	56.3 ± 14.4	0.81
Male sex	7 (70%)	27 (81%)	0.41
Comorbidities			
Heart failure	1 (10%)	4 (12%)	1.00
Coronary artery disease	1 (10%)	4 (12%)	1.00
Diabetes	2 (20%)	5 (15%)	0.66
Dyslipidemia	2 (20%)	4 (12%)	0.62
Hypertension	5 (50%)	13 (39%)	0.71
Witnessed collapse	10 (100%)	30 (90%)	1.00
Out-of-hospital collapse	4 (40%)	23 (70%)	0.14
Bystander CPR	10 (100%)	26 (79%)	0.17
Initial cardiac rhythm			
Shockable	6 (60%)	16 (48%)	0.72
PEA	3 (30%)	12 (36%)	1.00
Asystole	1 (10%)	5 (15%)	1.00
Duration of CPR (minutes)	30 (22–44)	58 (44–64)	< 0.001
Prehospital CPR for OHCA (minutes)	8 (5–14)	40 (19–37)	0.04
Initial pH	7.03 ± 0.19	6.98 ± 0.24	0.60
Time on ECMO (hours)	25.4 (4.4–48.6)	6.3 (1.8–24.6)	0.08
Hospital length of stay (days)	16 (12–39)	0 (0–1)	< 0.001

ED = emergency department; ECPR = extracorporeal cardiopulmonary resuscitation; CPR = cardiopulmonary resuscitation; PEA = pulseless electrical activity; ECMO = extracorporeal membrane oxygenation; OHCA = out-of-hospital cardiac arrest.
Continuous variables are median (interquartile range) or mean ± standard deviation. Categorical variables are count (%).

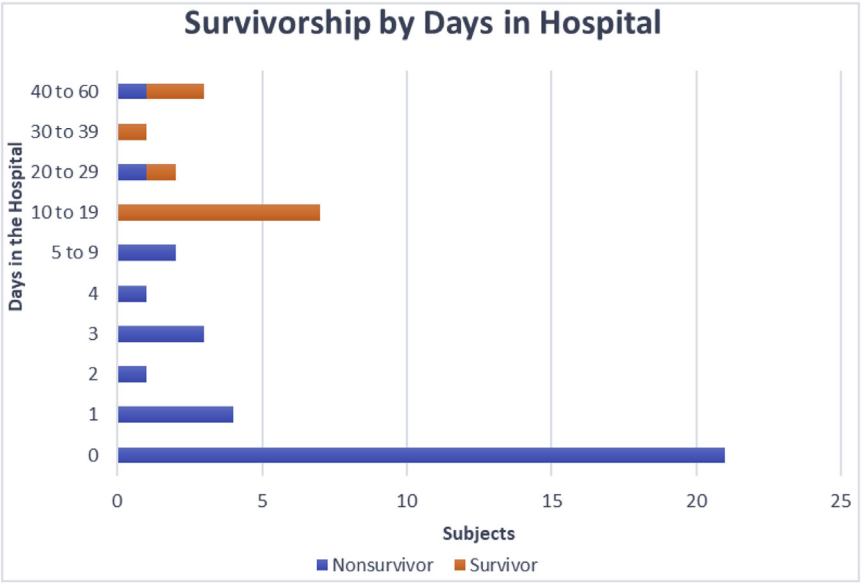

Figure 3. Number of days each subject survived after ECMO (extra-corporeal membrane oxygenation) initiation. Survivors were subjects who survived to discharge. Non-Survivors died prior to discharge.

bias notwithstanding, this approaches fivefold the expected survival rate of similar subjects treated without ECPR. Likewise, the subset of ED ECPR cases was between two and eight times more likely to survive to hospital discharge than concurrent controls eligible for ECPR, depending on the precise control group utilized. Taken together, these data support the notion that EP-initiated ECPR offers potential benefit to eligible subjects. Prospective validation in a controlled trial is urgently needed.

Our data suggest that the expansion of resuscitative ECMO does not have to be limited to large academic centers. We utilize ECMO-trained cardiologists and cardiothoracic surgeons if available, but over 80% of the ECMO initiations were performed without involvement of these specialists. It also demonstrates the feasibility of expansion of EP-initiated ECMO beyond the confines of the ED. This is potentially important in hospitals like ours, which do not have a dedicated ECMO/ECPR team within the hospital. Each system of care will need to define their optimal strategy utilizing their available resources.

One critique of ECPR is the concern for prolonged ICU lengths of stay. We did not observe this in our cohort. Our ED ECMO program yielded 30 subjects admitted to the hospital over 7.5 years who may otherwise have died in

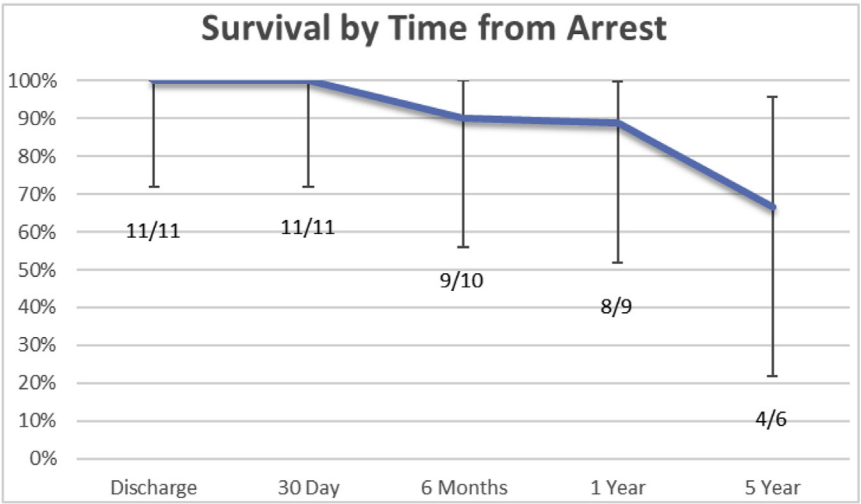

Figure 4. Proportion (with 95% confidence intervals) of ED VA-ECMO (emergency department venoarterial extra-corporeal membrane oxygenation) subjects remaining alive at successive clinical milestones (survivors/subjects remaining alive). Five patients have yet to reach 5 year mark from arrest.

Table 2. Clinical Features and Outcomes of ECPR Subjects From 2010–2013 Compared With Two Different Temporally Matched Control Groups: ECPR-Eligible Without Available Personnel to Initiate ECMO Treated With Traditional CPR, and ECPR-Eligible Subjects Without Available Personnel to Initiate ECMO Treated With Traditional CPR and Resuscitation Efforts > 30 Min

	ECPR (n = 25)	ECPR Eligible (n = 183)	*p*-Value	ECPR Eligible with CPR > 30 Min (n = 99)	*p*-Value
Clinical Features					
Age (years)	57.9 ± 13.7	68.7 ± 17.0	0.003	66.2 ± 17.8	0.03
Male sex	22 (88%)	109 (60%)	0.002	68 (67%)	0.02
Witnessed collapse	20 (80%)	135 (74%)	0.33	65 (66%)	0.09
Out-of-hospital collapse	17 (68%)	134 (73%)	0.82	92 (93%)	0.006
Bystander CPR	19 (76%)	103 (56%)	0.10	46 (46%)	0.004
Shockable initial cardiac rhythm	14 (56%)	51 (28%)	0.01	30 (30%)	0.009
Duration of CPR (minutes)	62 (50–75)	36 (17–50)	< 0.001	47 (40–60)	0.003
Outcomes					
Survival to discharge (%)	6 (24%)	26 (14%)	0.23	4 (4%)	0.004
Odds ratios of survival for ECPR compared with group					
Unadjusted (95% CI)	Reference	2.0 (0.7–5.5)	0.18	7.9 (2.0–30.9)	0.003
Adjusted (95% CI)	Reference	8.4 (1.2–60.4)	0.03	6.6 (0.8–55.7)	0.08

ECPR = extracorporeal cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; CPR = cardiopulmonary resuscitation; CI = confidence interval.
Continuous variables are mean median ± standard deviation or median (interquartile range). Categorical variables are count (%).

the ED. This relatively small impact on ICU census is partially due to our practice of withdrawing circulatory support in the ED for subjects with persistent asystole despite ECMO. Furthermore, two-thirds of ultimate nonsurvivors admitted to the hospital had life-sustaining therapy withdrawn within 24 h. We acknowledge that this brief hospital length of stay among nonsurvivors in our cohort may indicate a self-fulfilling prophecy, where early prognostication leads to premature withdrawal of life-sustaining therapy. Although the recommended neurologic prognostication process after resuscitation from cardiac arrest is reasonably defined, it remains unknown what modalities translate to ECMO subjects (16).

Survivors after ED ECPR tended to have more favorable clinical features, a finding that is consistent with other cohorts (16,17). Upon review, 75% of subjects met our institutional consensus selection criteria for ECMO, and those that met consensus criteria (30%) were more likely to survive to hospital discharge than those that did not (9%). This comparison did not achieve statistical significance, but it does raise the question of how strictly clinicians should follow the selection criteria for ECPR. We did observe a survivor with good neurologic outcome whose initial rhythm was asystole. Ordinarily, this subject would have been disqualified from ECPR, and we presume (s)he would have died. However, observational data suggest a stepwise decline in favorable outcomes with deviation from ideal clinical features in ECPR candidates (10). This raises intertwining issues of risk, benefit, cost, resource utilization, and clinician judgment that need to be further defined in a prospective trial.

Additional centers in the United States now utilize ED-driven ECMO programs with various levels of EP involvement (18). Others have provided innovative examples of ECPR application outside the ED. Yannopoulos et al. describe an ECPR program in which out-of-hospital cardiac arrest cases with refractory ventricular fibrillation are brought from the prehospital setting directly to the cardiac catheterization suite for rapid ECMO initiation and left heart catheterization (1). This program reports a typical arrival-to-ECMO initiation of 6 min and survival rates > 40%, suggesting that training and systems optimization contribute to ECMO success. Although not directly measured, we believe that our ECMO cannulation and initiation intervals have shortened over the last 2 years by incorporating several of the techniques described in Yannopolous et al. (1). In Paris, France, Lamhaut et al. utilize prehospital ECMO in an attempt to minimize CPR duration prior to initiation as much as possible (6). Both of these models offer potential advantages over our institutional model, but it remains to be determined whether they can be duplicated in a community hospital setting such as ours.

Limitations

Other than the inherent limitations of a single-center retrospective cohort, our data set includes a heterogeneous set of experiences because we have modified our resuscitation strategy over time and gained considerable experience with the use of ECMO. We also had difficulty defining unsuccessful cannulation. Subjects did not

complete ECMO initiation for a variety of reasons, including prolonged cardiac arrest, exclusion criteria elucidated during resuscitation, physician skill, and patient anatomy. Additionally, the absence of cannulation does not necessarily mean that the relevant vessel was not accessed with a place-holder guidewire or catheter. Thus, true cannulation success is difficult to calculate. A final limitation is the lack of a control group beyond 2013, but this merely reflects the penetration of ECPR in our ED over the study period.

CONCLUSIONS

In our single-center community hospital, EPs initiated and managed the majority of ED ECPR cases. Our ED ECPR program demonstrates promising clinical outcomes with limited downstream inpatient resource utilization. Institution-specific factors should influence the optimal logistics surrounding the clinicians and location utilized for emergent ECMO. Prospective trials are needed to address the remaining knowledge gaps.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jemermed.2019.02.004.

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ARTICLE SUMMARY

1. Why is this topic important?

Advanced resuscitative strategies like extracorporeal membrane oxygenation (ECMO) are being used with increasing frequency worldwide. The emergency physician's (EP) role in the initiation of ECMO is not yet fully elucidated.

2. What does this study attempt to show?

This study attempts to show that EPs in a nonacademic hospital can initiate ECMO with reasonable clinical outcomes.

3. What are the key findings?

Of 43 ECMO cases initiated in the Emergency Department (ED) and primarily managed by EPs, 25% survived and nearly all survivors had favorable neurologic recovery. Adjusting for known covariates, extracorporeal cardiopulmonary resuscitation (ECPR) subjects were more likely than concurrent controls to survive to hospital discharge. Propensity-adjusted comparisons revealed a nonsignificant trend favoring ECPR. The study also shows that EPs were able to initiate venovenous ECMO and in patients outside of the ED.

4. How is patient care impacted?

Survival with meaningful neurologic recovery is the primary goal after cardiac arrest. We demonstrate that EPs can institute ECPR outside the traditional academic center with promising clinical outcomes.