Extracorporeal Life Support in Adult Out-of-Hospital Cardiac Arrest

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Disclosure

- No conflicts of interest

- Background
- VA ECMO
- ECMO CPR in Adult OHCA – current recommendations and evidence
- Patient Selection
- Complications
- Challenges
- Conclusion

OHCA

- Poor survival rates
- Treatment options
  - High quality CPR
  - Early defibrillation
  - Standard dose adrenaline
  - Anti-arryhthmics
- Refractory Cardiac Arrest requires prolonged resuscitative efforts
  - No fixed definitions on what constitutes refractory cardiac arrest

What is ECMO?

- 2 configurations
- Veno-venous, and Veno-arterial
- For ECPR – VA ECMO configuration is used
- Bridge to therapy / recovery / transplant

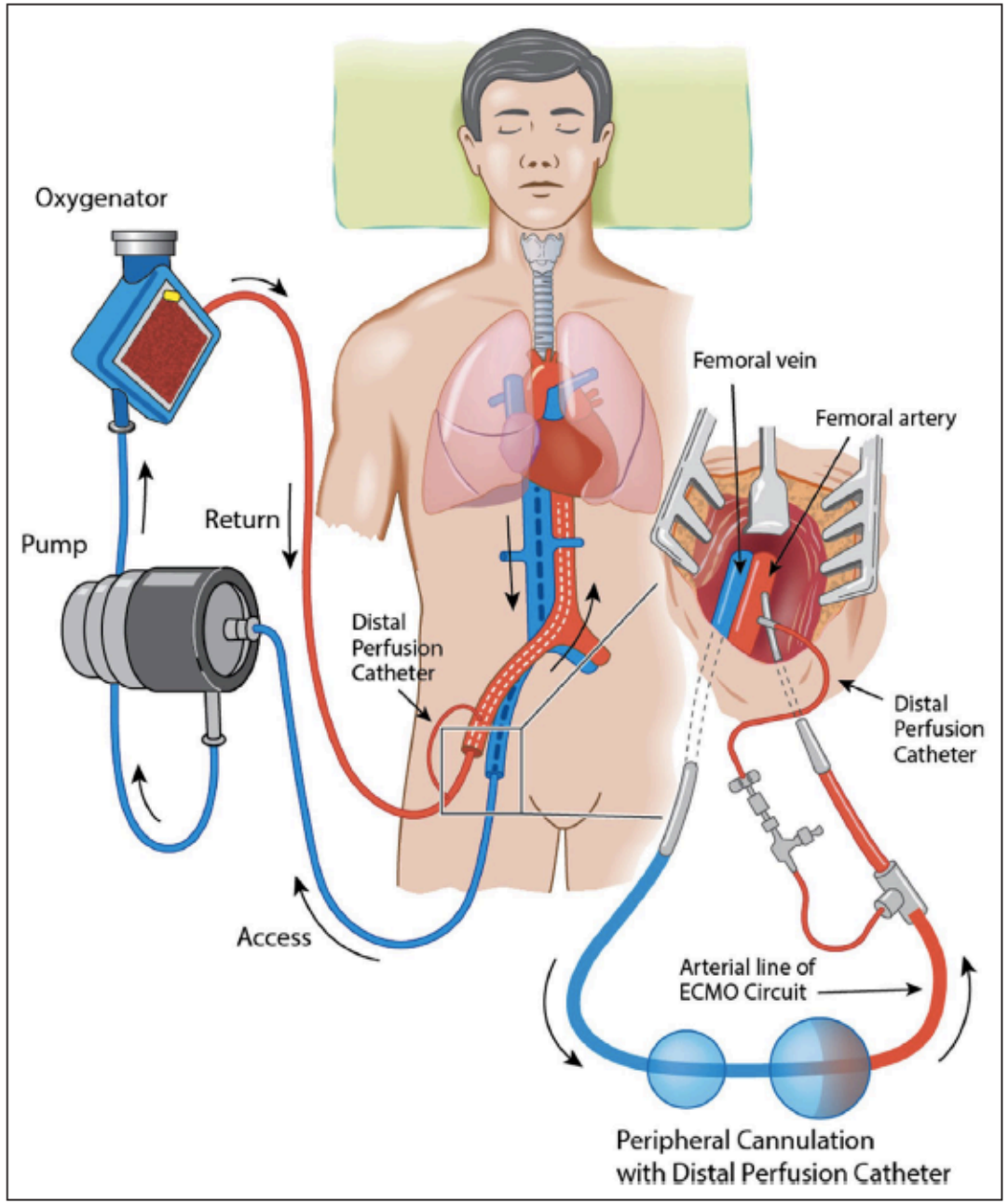
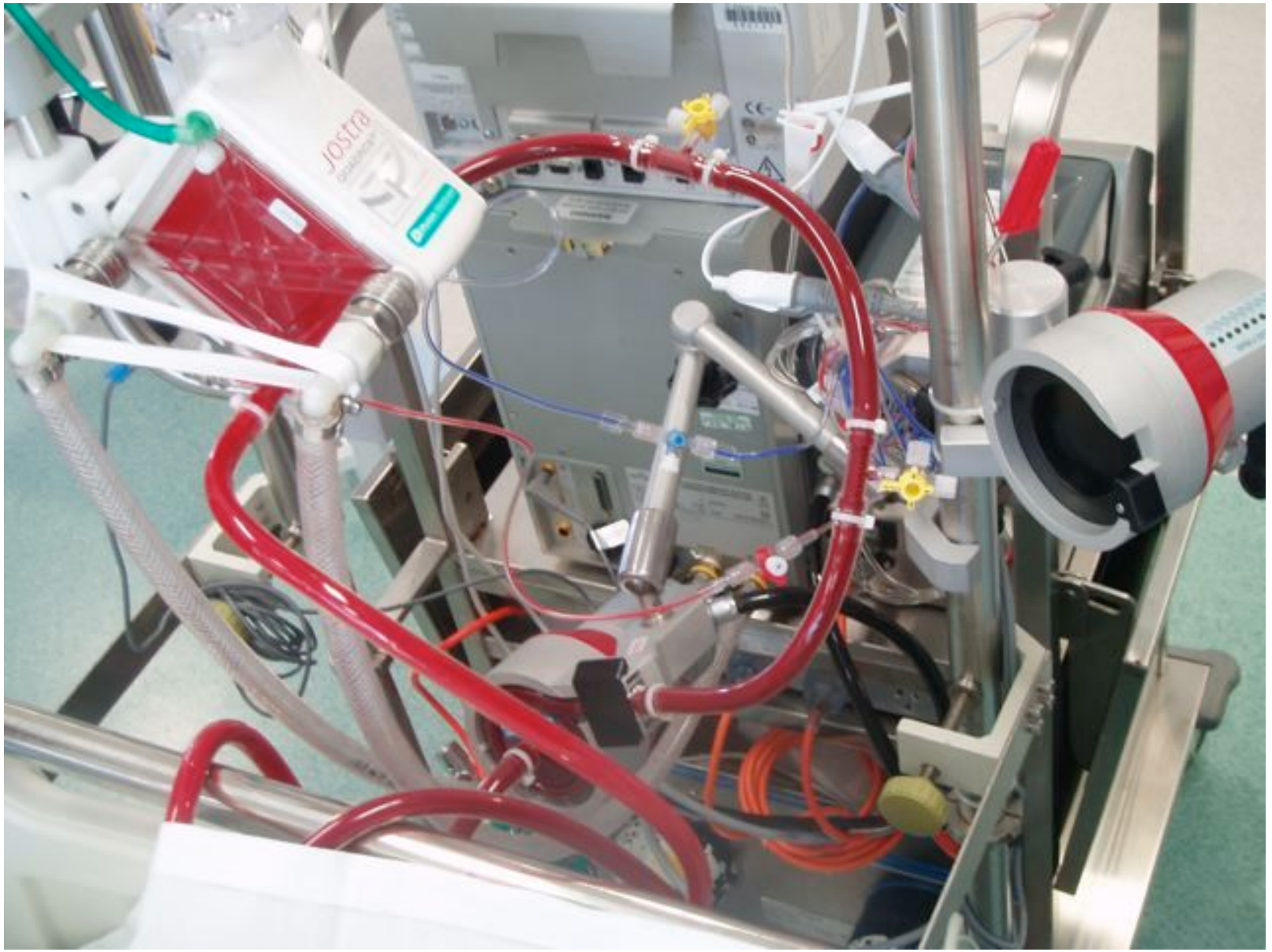


Fig 1. Dennis M, Lal S, Forrest P, Nichol A, Lamhaut L, Totaro RJ, Burns B, Sandroni C. In-Depth Extracorporeal Cardiopulmonary Resuscitation in Adult Out-of-Hospital Cardiac Arrest. J Am Heart Assoc. 2020 May 18;9(10):e016521


Jostra

Indications for ECMO

- VA ECMO
  - Decompensated cardiomyopathies / cardiogenic shock
  - Myocarditis
  - Pulmonary embolus
  - Post cardiac surgery
  - Post heart transplant
  - Bridge to transplant
  - Cardiotoxic drug overdose
  - *Cardiac arrest (ECPR in selected cases)*
- VV ECMO
  - ALI / ARDS
  - Pneumonia
  - Life-threatening asthma
  - Post lung transplant
  - Lung contusion
  - Neonatal and paediatric respiratory support
    - MAS, PPHN, CDH, HMD etc

What is ECMO CPR?

- Complex intervention
- Team work
- Time sensitive
- Resources
- Training

Image from https://www.jems.com/patient-care/how-physicians-perform-prehospital-ecmo-on-the-streets-of-paris/

General Contraindications

- DNR orders
- Traumatic cardiac arrest
- Uncontrolled bleeding
- Terminal conditions
- Severe brain injury
- Chronic end organ dysfunction
- Suspected aortic dissection, aortic valve incompetency
- Age > 65 – 80 (varies based on studies / local guidelines)

ECLS Registry Report

International Summary

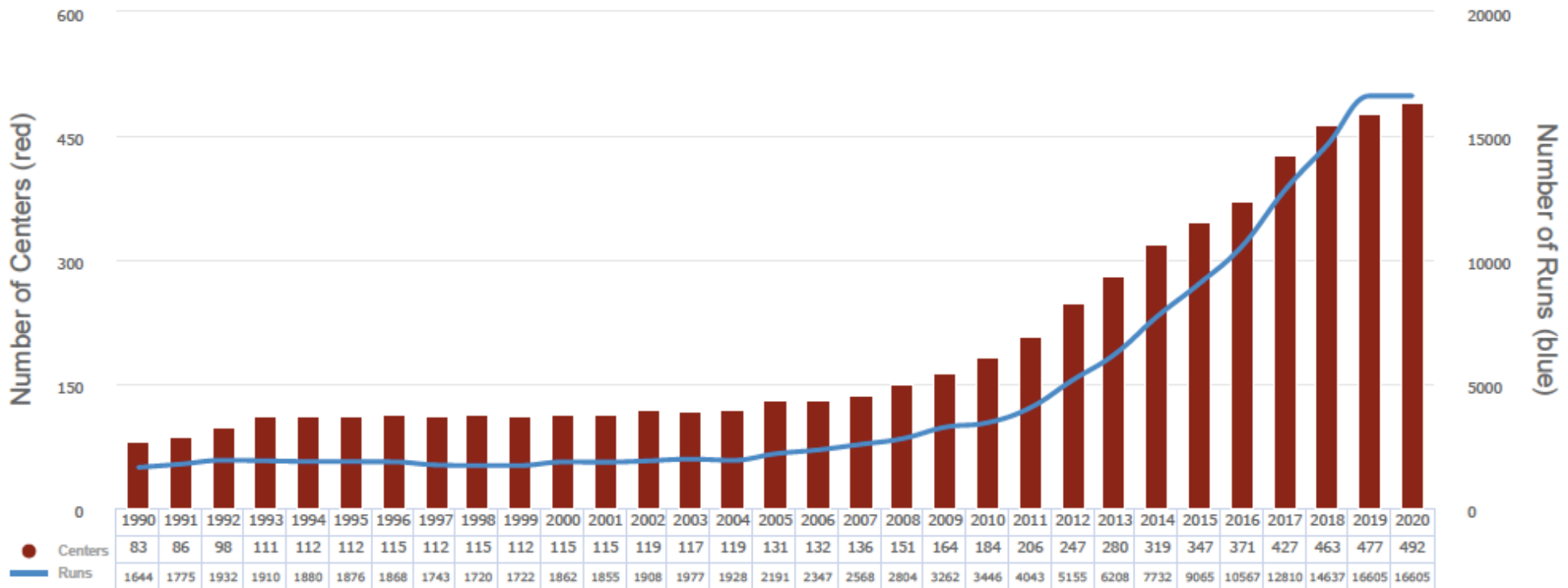
April, 2021

Report data through 2020

Extracorporeal Life Support Organization
3001 Miller Rd
Ann Arbor, MI 48103 USA

Centers

Centers by year



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Centers	83	86	98	111	112	112	115	112	115	112	115	115	119	117	119	131	132	136	151	164	184	206	247	280	319	347	371	427	463	477	492
Runs	1644	1775	1932	1910	1880	1876	1868	1743	1720	1722	1862	1855	1908	1977	1928	2191	2347	2568	2804	3262	3446	4043	5155	6208	7732	9065	10567	12810	14637	16605	16605

Overall Outcomes					
	Total Runs	Survived ECLS		Survived to DC or Transfer	
Neonatal					
Pulmonary	33,400	29,255	87%	24,398	73%
Cardiac	9,561	6,605	69%	4,186	43%
ECPR	2,244	1,574	70%	953	42%
Pediatric					
Pulmonary	11,168	8,084	72%	6,746	60%
Cardiac	13,945	10,103	72%	7,520	53%
ECPR	5,630	3,341	59%	2,388	42%
Adult					
Pulmonary	33,313	22,612	67%	19,734	59%
Cardiac	32,307	19,252	59%	14,378	44%
ECPR	10,115	4,213	41%	3,030	29%
Total	151,683	105,039	69%	83,333	54%

Resuscitation 85 (2014) 762–768

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical Paper

Extracorporeal cardiopulmonary resuscitation versus conventional cardiopulmonary resuscitation in adults with out-of-hospital cardiac arrest: A prospective observational study☆

Tetsuya Sakamoto, Naoto Morimura*, Ken Nagao, Yasufumi Asai, Hiroyuki Yokota, Satoshi Nara, Mamoru Hase, Yoshio Tahara, Takahiro Atsumi, SAVE-J Study Group[1]

The Japanese Scientific Research Group of the Ministry of Health, Labour and Welfare for Extracorporeal Cardiopulmonary Resuscitation: Study of Advanced Cardiac Life Support for Ventricular Fibrillation with Extracorporeal Circulation in Japan (SAVE-J), Japan

SAVE-J, 2014

- RCA cardiac arrest definition
- 454 patients in total
- Primary endpoints being favourable neurological outcomes at 6 months
- 11.2% vs 2.6% p=0.001, in ECPR vs CCPR

The study period was from September 8, 2008 to September 30, 2011. Inclusion criteria for this study were: (1) VF/VT on the initial ECG, (2) cardiac arrest on hospital arrival with or without pre-hospital ROSC, (3) within 45 min from reception of the emergency call (119) or the onset of cardiac arrest to the hospital arrival, and (4) no ROSC at least during the 15 min after hospital arrival (or after contact with a doctor) even though conventional CPR was performed. ROSC was defined as at least 1 min of continuing confirmation of pulsation, (5) and excluded patients with one or more of the following conditions: (a) under the age of 20 years or those aged 75 years or older, (b) poor level of activities of daily livings before the onset of cardiac arrest, (c) non-cardiac origin (e.g., external factors such as trauma and drug intoxication, primary cerebral disorders, acute aortic dissection diagnosed prior to the introduction of PCPS, and terminal phase of cancer), (d) core body temperature of less than 30 °C, and (e) no informed consent from the individuals representing patients.

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Resuscitation

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ILCOR Summary Statement

2019 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations☆,☆☆

Treatment recommendations

We suggest that ECPR may be considered as a rescue therapy for selected patients with cardiac arrest when conventional CPR is failing in settings in which it can be implemented (weak recommendation, very low certainty of evidence).

Justification and evidence to decision framework highlights

In making this weak recommendation, we have considered the extremely high mortality rate of patients with cardiac arrest, particularly when the arrest is refractory to standard advanced cardiac life support interventions (i.e., cardiac arrest when conventional CPR is failing). Therefore, the potential for benefit and the value of this intervention remain despite the overall low certainty of supporting evidence and lack of randomized trials.

Table 7 – Summary of adult ECPR studies.

Study, year	Country	Years of patient inclusion	IHCA vs OHCA	Inclusion criteria	Patients analyzed, n	Covariates included in adjusted analysis	Hospital discharge/1 mo		
							Exposed, n (%)	Unexposed, n (%)	Adjusted results, OR or RR (95% CI)
Agostinucci et al.[90] 2011	France	2005–2010	OHCA	Use of load-distributing band	285	NA	0/27 (0)	3/258 (1)	NR
Blumenstein et al.[91] 2015	Germany	2009–2013	IHCA	Cardiovascular admission, witnessed	353	Age, APACHE II score, CPR duration, obesity, dyslipidemia, coronary artery disease, lactate, creatine kinase, eGFR, creatinine, ICU, OR, dose of norepinephrine	14/52 (27)	9/52 (17)	1.76 (0.68–4.53) (calculated)
Cesana et al.[92] 2018	Italy	2011–2015	Combined	Age 18–75 y, witnessed, proven ischemic origin, absence of severe comorbidities that would have precluded ICU admission and conditioning in the short-term prognosis	148	NA	13/63 (21)	49/85 (58)	NR
Chen et al.[93] 2008	Taiwan	2004–2006	IHCA	Age 18–75 y, CPR for >10 min, cardiac origin, witnessed	92	Age, sex, initial cardiac rhythm, time point of CPR, CPR duration, comorbidities	15/46 (33)	8/46 (17)	2.30 (0.86–6.13) (calculated)
Cho et al.[94] 2014	Korea	2001–2013	IHCA	Pulmonary embolism	20	Hypertension, CPR duration	NR	NR	NR
Choi et al.[95] 2016	Korea	2011–2015	OHCA	Nontraumatic, age ≤75 y, witnessed cardiac arrest, bystander administration of CPR or no-flow time ≤5 min, prehospital low-flow time ≤30 min and refractory arrest >10 min of conventional CPR in the ED, known absence of severe comorbidities that preclude admission to the intensive care unit	60	NA	3/10 (30)	4/50 (8)	NR
Chou et al.[96] 2014	Taiwan	2006–2010	IHCA	Age >18 y, acute myocardial infarction in the ED, CPR for >10 min	66	NA	NR	NR	1.93 (0.60–6.23) (unadjusted)
Hase et al.[97] 2005	Japan	1999–2003	OHCA	Presumed cardiac cause	100	NA	13/38 (34)	27/62 (44)	NR
Kim et al.[98] 2014	Korea	2006–2013	OHCA	Age >18 y, not traumatic	104	Age, sex, comorbidity score, bystander CPR, witnessed cardiac arrest, first documented arrest rhythm, presumed cause of arrest, interval from arrest to CPR started by EMS provider, CPR duration, and therapeutic hypothermia	9/52 (17)	11/52 (21)	0.78 (0.29–2.08) (calculated)

(continued on next page)

Table 7 *(continued)*

Study, year	Country	Years of patient inclusion	IHCA vs OHCA	Inclusion criteria	Patients analyzed, n	Covariates included in adjusted analysis	Hospital discharge/1 mo		
							Exposed, n (%)	Unexposed, n (%)	Adjusted results, OR or RR (95% CI)
Lee et al.[89] 2015	Korea	2009–2014	Combined	NR	955	Age, main diagnosis, location, CPR duration, initial rhythm, hypertension, malignancy, stroke, chronic renal failure, cardiovascular disease	18/81 (22)	120/874 (14)	0.37 (0.13–1.06)
Lin et al.[90] 2010	Taiwan	2004–2006	IHCA	Age 18–75 y, cardiac origin, CPR duration >10 min, ROSC	54	Age, sex, initial rhythm, CPR duration, timing and location, comorbidities (diabetes mellitus, hypertension, dyslipidemia, malignancy, COPD, cardiovascular or cerebrovascular, abnormal liver function, dialysis)	8/27 (30)	5/27 (19)	1.85 (0.52–6.63) (calculated)
Maekawa et al.[91] 2013	Japan	2000–2004	OHCA	Presumed cardiac origin, age >16 y, witnessed, CPR duration >20 min	48	Not clear but probably age, sex, activities of daily living, location of OHCA, bystander CPR, initial rhythm, number of shocks, airway insertion, venous access, physician- staffed ambulance, ROSC during transport, times, TTM, IABP, PCI, CPR duration, time from arrest to ALS	9/24 (38)	3/24 (13)	4.20 (0.97–18.2) (calculated)
Poppe et al.[92] 2015	Austria	2013–2014	OHCA	Age >18 y, ongoing CPR	96	NA	2/12 (17)	8/84 (10)	NR
Sakamoto et al.[93] 2014	Japan	2008–2011	OHCA	Shockable rhythm, cardiac arrest on arrival, within 45 min from reception of the emergency call or the onset of cardiac arrest to the hospital arrival, no ROSC at least during the 15 min after hospital arrival	454	NA	69/260 (27)	12/193 (6)	NR
Schober et al.[94] 2017	Austria	2002–2012	OHCA	Cardiac origin, CPR duration >30 min	239	NA	NR	NR	NR
Shin et al.[95] 2011, Shin et al.[96] 2013	Korea	2003–2009	IHCA	Age 18–80 y, CPR duration >10 min, witnessed	120	Age, sex, comorbidities, clinical situation, cause of the arrest, location, year, time during day and week, initial rhythm, CPR duration, prearrest SOFA score, Deyo-Charlson score, post-CPR variables	19/60 (32)	6/60 (10)	4.17 (1.53–11.4) (calculated)

Table 7 *(continued)*

Study, year	Country	Years of patient inclusion	IHCA vs OHCA	Inclusion criteria	Patients analyzed, n	Covariates included in adjusted analysis	Hospital discharge/1 mo		
							Exposed, n (%)	Unexposed, n (%)	Adjusted results, OR or RR (95% CI)
Siao et al.[97] 2015	Taiwan	2011–2013	OHCA	Age 18–75 y, ventricular fibrillation, no-flow <5 min, refractory cardiac arrest	60	Age, CPR duration, defibrillation, female sex, use of therapeutic hypothermia	10/20 (50)	11/40 (28)	4.10 (0.79–21.3)
Tanno et al.[98] 2008	Japan	2000–2004	OHCA	Age >16 y, cardiac origin	398	NA	14/66 (21)	25/332 (8)	NR
Venturini et al.[99] 2017	United States	2011–2016	Combined	CPR in cardiac catheterization laboratory, mechanical chest compression	31	NA	1/14 (7)	3/17 (18)	NR
Yannapoulos et al.[100] 2016	United States	2015–2016	OHCA	Age 18–75 y, cardiac cause, initial shockable rhythm, minimum 3 direct-current shocks without ROSC, received amiodarone 300 mg, eligible for mechanical CPR, transfer time from scene to catheterization laboratory <30 min	188	NA	10/18 (53)	NR	NR
Yannapoulos et al.[101] 2017	United States	2015–2016	OHCA	Age 18–75 y, cardiac cause, initial shockable rhythm, minimum 3 direct-current shocks without ROSC, received amiodarone 300 mg, eligible for mechanical CPR, transfer time from scene to catheterization laboratory <30 min	232	NA	28/62 (45)	NR	NR

ALS indicates advanced life support; APACHE II, Acute Physiology, Age, Chronic Health Evaluation II; COPD, chronic obstructive pulmonary disorder; CPR, cardiopulmonary resuscitation; ECPR, extracorporeal cardiopulmonary resuscitation; ED, emergency department; eGFR, estimated glomerular filtration rate; EMS, emergency medical services; IABP, intra-aortal balloon pump; ICU, intensive care unit; IHCA, in-hospital cardiac arrest; NA, not applicable; NR, not reported; OHCA, out-of-hospital cardiac arrest; OR, odds ratio; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation; RR, relative risk; SOFA, sequential organ failure assessment; and TTM, targeted temperature management.

- Risk of bias critical for all studies, confounding being the primary source
- Heterogeneity was significant between studies, not suitable for meta-analysis
- Several studies reported unadjusted results
- Of the 15 studies that reported OHCA – 12 reported survival to discharge, 6 reported long term survival, 8 reported favourable neurological outcomes at hospital discharge, 6 reported long term favourable neurological outcomes

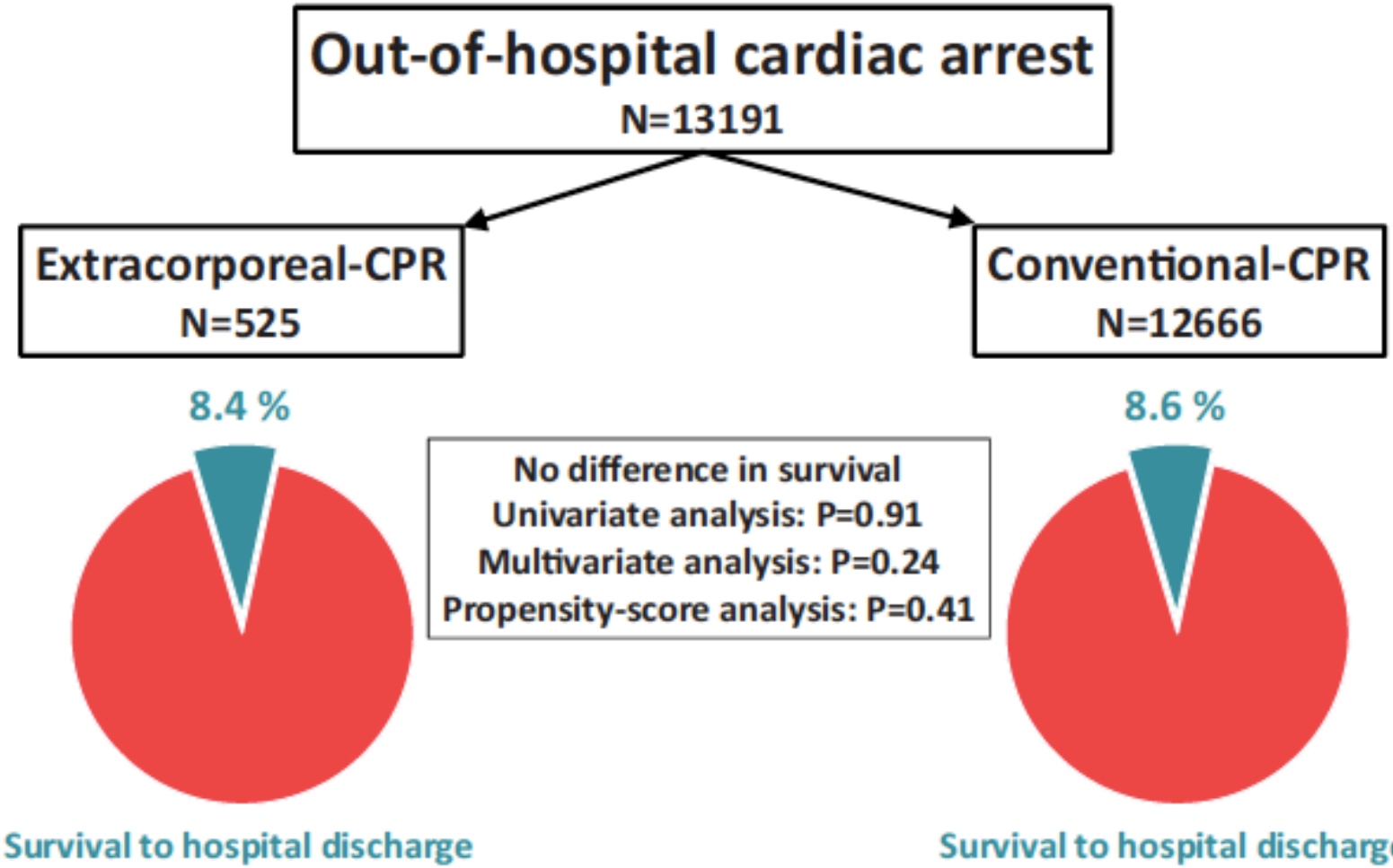
ESC European Society of Cardiology

European Heart Journal (2019) **0**, 1–11
doi:10.1093/eurheartj/ehz753

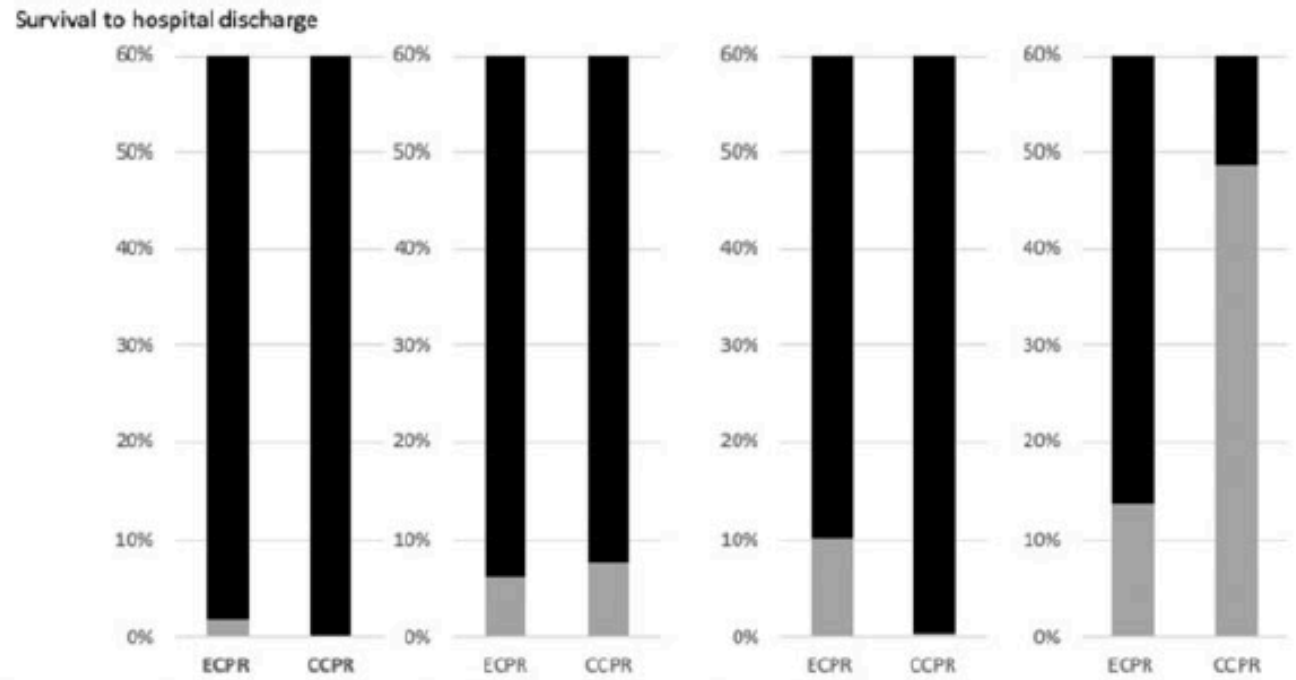
CLINICAL RESEARCH
Arrhythmia/electrophysiology

Extracorporeal cardiopulmonary resuscitation in out-of-hospital cardiac arrest: a registry study

Wulfran Bougouin [1,2,3,4], Florence Dumas[1,3,5,6], Lionel Lamhaut [1,3,4,5,7], Eloi Marijon[1,3,5,8], Pierre Carli [5,7], Alain Combes[9], Romain Pirracchio[5,10], Nadia Aissaoui[1,3,4,5,11], Nicole Karam [1,3,5,8], Nicolas Deye [4,12], Georgios Sideris[13], Frankie Beganton [1,3], Daniel Jost [1,3,14], Alain Cariou[1,3,4,5,15†], and Xavier Jouven[1,3,5,8*†]; On behalf of the Sudden Death Expertise Center investigators[‡]



Take home figure Among 13 191 out-of-hospital cardiac arrest, survival at hospital discharge did not differ between patients treated with extracorporeal-CPR and patients treated with conventional-CPR.



	Non shockable rhythm and no ROSC		Non shockable rhythm and ROSC		Shockable rhythm and no ROSC		Shockable rhythm and ROSC	
Survivors	2	0	3	208	28	3	11	844
Non survivors	110	6121	46	2558	247	1138	70	894

Figure 2 Survival to hospital discharge of patients treated with extracorporeal-CPR and conventional-CPR, according to initial rhythm and return of spontaneous circulation.

There was no difference in survival to discharge between the two groups (ECPR 8.4% vs. CCPR 8.6%, p = 0.91).

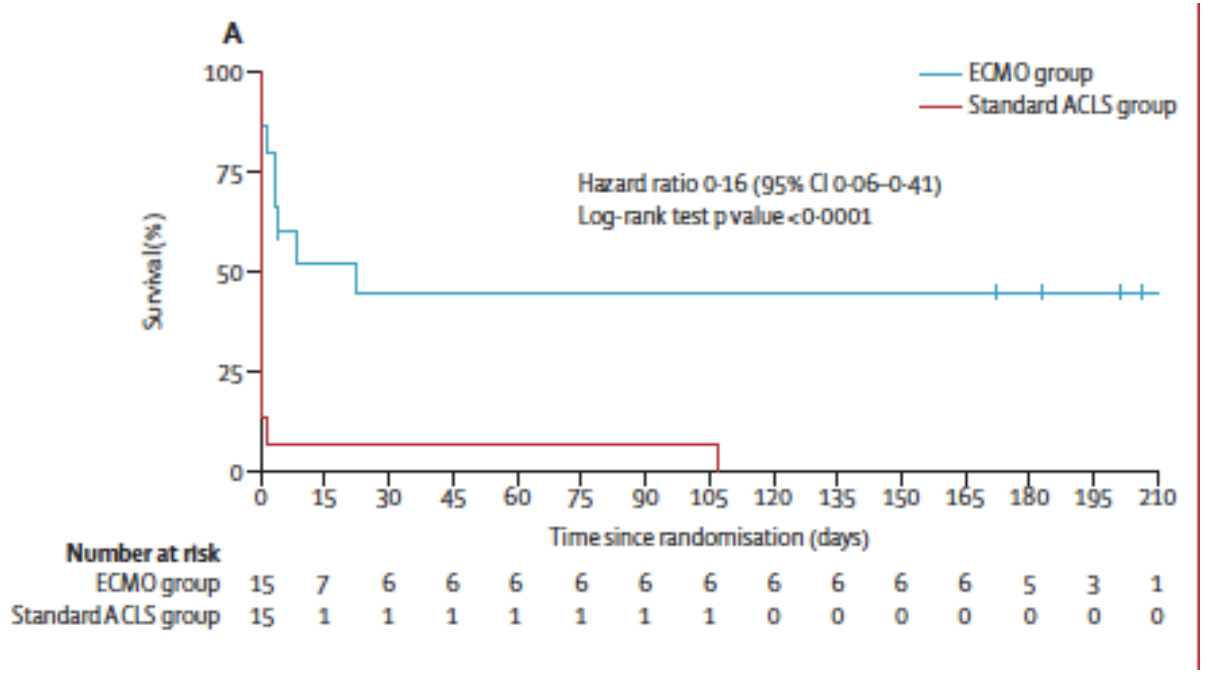
Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial

Demetris Yannopoulos, Jason Bartos, Ganesh Raveendran, Emily Walser, John Connett, Thomas A Murray, Gary Collins, Lin Zhang, Rajat Kalra, Marinos Kosmopoulos, Ranjit John, Andrew Shaffer, R J Frascone, Keith Wesley, Marc Conterato, Michelle Biros, Jakub Tolar, Tom P Aufderheide

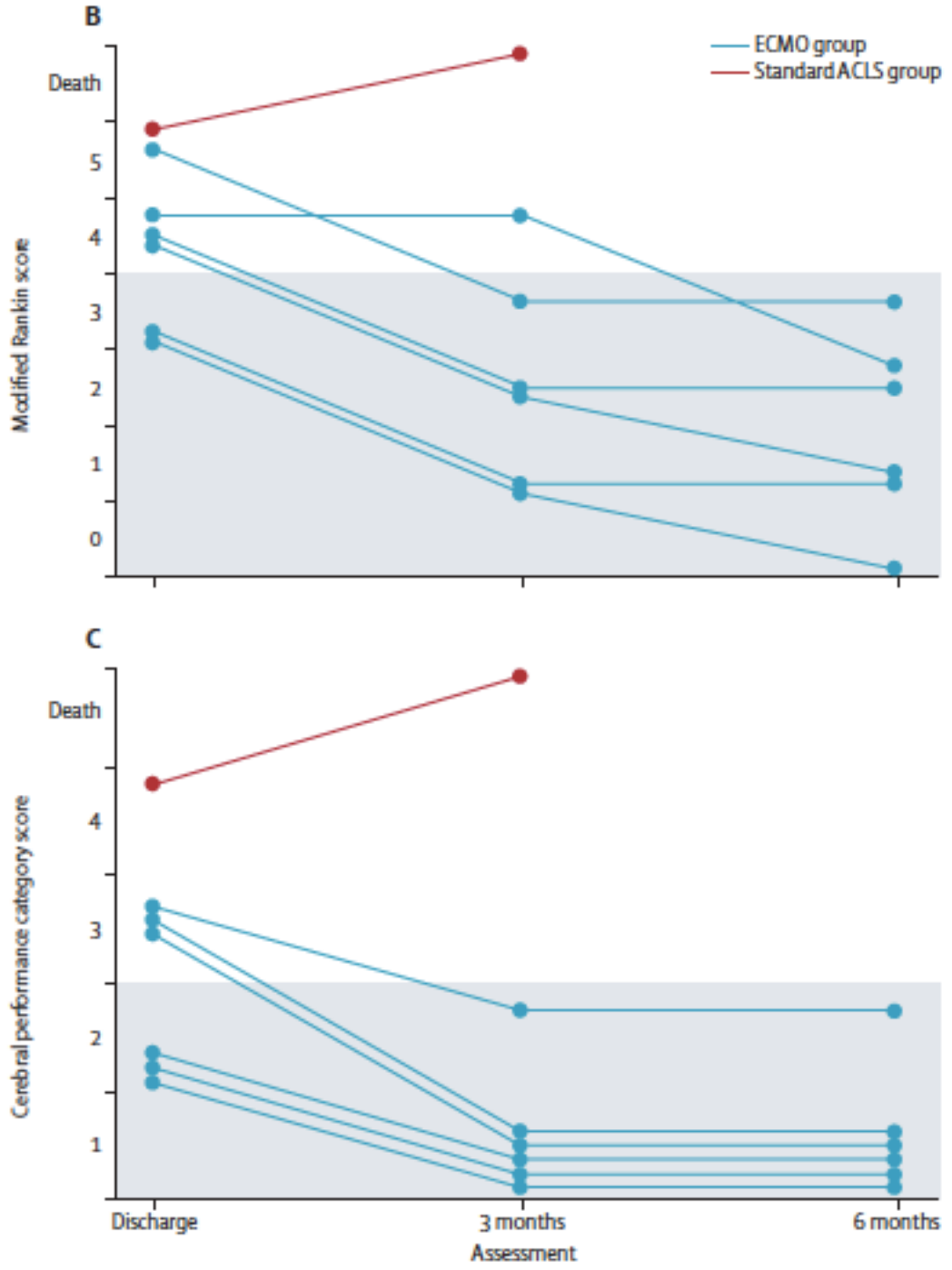
First RCT comparing ECPR vs CCPR for OHCA adult patients

We included all consecutive adults (presumed or known to be 18–75 years old) with an initial OHCA rhythm of ventricular fibrillation or pulseless ventricular tachycardia, no ROSC after three defibrillation shocks, body morphology able to accommodate a Lund University Cardiopulmonary Assist System, and an estimated transfer time to the emergency department shorter than 30 min. Exclusion criteria included valid do not resuscitate orders; blunt, penetrating, or burn-related injury; drowning; known overdose; known pregnancy; being a prisoner; being a nursing home resident; presence of an opt-out study bracelet; unavailability of the catheterisation laboratory; terminal cancer; absolute contraindications to emergent angiography; contrast allergies; and active gastrointestinal or internal bleeding. Sustainable ROSC within the first three shocks was an exclusionary criterion from the study, while ROSC achieved after the fourth shock did not exclude the patient because it was the main way that the standard ACLS group could achieve survival and it was a treatment goal of both groups.

- 6 survivors at 6months in ECPR group
- 0 in CCPR
- Study discontinued



- Most survivors in ECPR showed favourable neurological outcomes



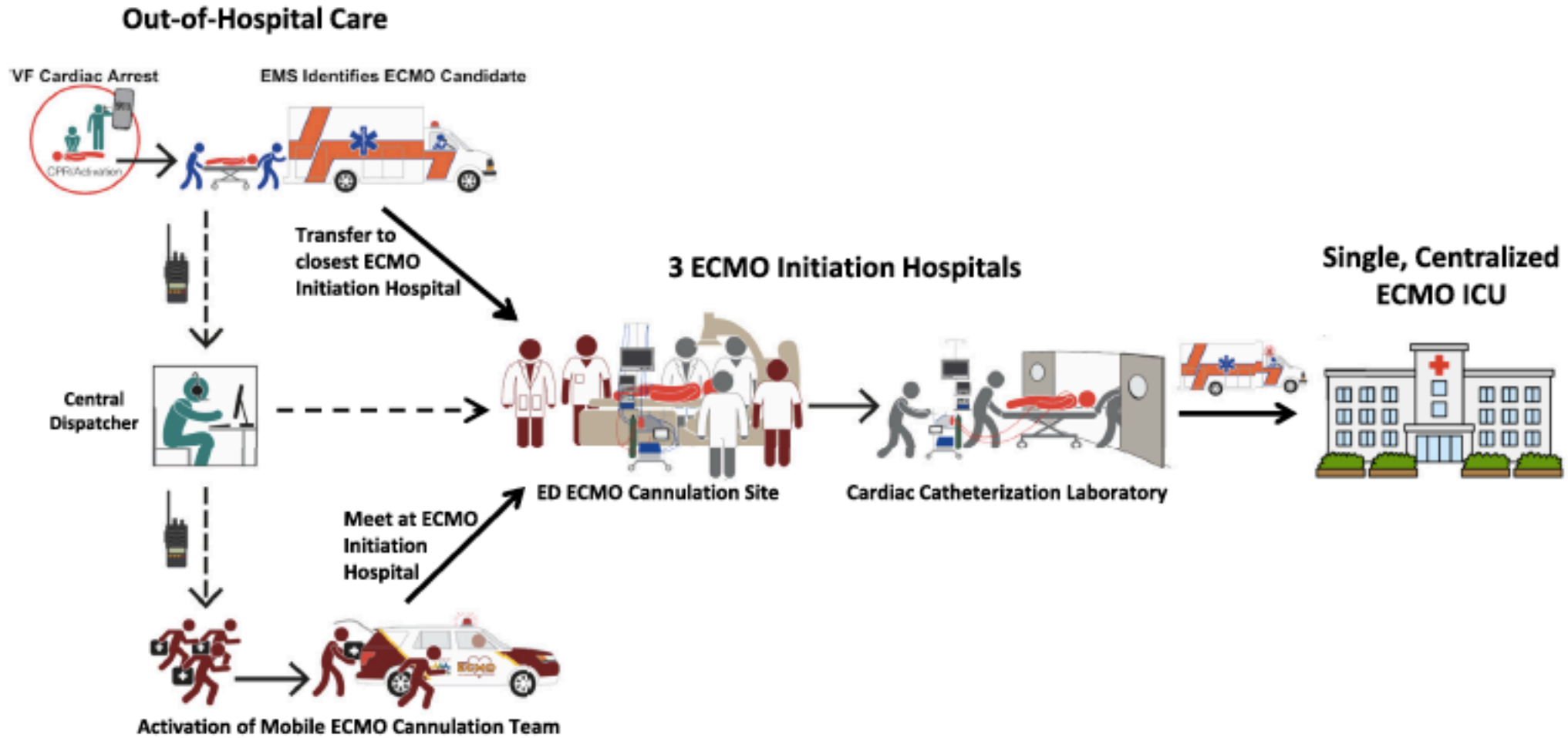


Fig. 2. Flow diagram of the ECMO Cannulation Team activation and patient stabilization process. A cardiac arrest is recognized and emergency medical services are activated. Paramedics arrive and begin ACLS. If the patient meets the MMRC VF/VT OHCA criteria, the central dispatcher is called who activates the mobile ECMO team and notifies the ED ECMO Cannulation Site. The mobile ECMO team and paramedics meet at one of 3 ECMO Initiation Hospital ED Cannulation Sites nearest to the patient and ECMO is initiated in the emergency department. Once ECMO-cannulated, the patient is taken to the cardiac catheterization laboratory for angiography and PCI, as indicated, at the ECMO Initiation Hospital. The patient is then transported to the single, centralized ECMO ICU for post-arrest care.

Patient Selection

- No clear consensus for ECPR
- Common inclusion criteria in ECPR for adult OHCA studies
  - Age between 18- 65 to 75 yrs
  - Cardiac arrest with bystander CPR
  - Initial shockable rhythm (VT/VF)
  - < 5 minutes of “no-flow time”
  - < 60 minutes of anticipated “low-flow time”
  - End tidal CO2 readings >10 mmHg
  - Signs of life

Complications of ECMO

- Bleeding is the commonest complication
- Also associated with high incidence of neurological complications

Table 10. Adverse Events During ECLS by Age and Indication

	Neonate (%)	Pediatric (%)	Adult (%)
Respiratory			
Mechanical: pump malfunction	1.6	2.2	1.5
Mechanical: oxygenator failure	5.7	10.6	9.1
Cannula hemorrhage	7.9	18.3	13.2
Surgical hemorrhage	6.3	12.6	10.5
Pulmonary hemorrhage	4.5	8.1	6.1
CNS hemorrhage	7.6	6.4	3.9
CNS infarction	6.8	4.2	2.0
Renal failure	7.8*	12.9*	9.3†
Hyperbilirubinemia	7.3	5.2	8.7
Infection	5.8	16.8	17.5
Cardiac			
Mechanical: pump malfunction	1.5	1.8	0.8
Mechanical: oxygenator failure	6.1	7.2	6.6
Cannula site hemorrhage	10.7	15.6	18.5
Surgical site hemorrhage	29.3	28.9	20.2
Pulmonary hemorrhage	5.2	5.3	3.1
CNS hemorrhage	11.3	5.3	2.2
CNS infarction	3.4	5.0	3.8
Renal failure	12.3*	7.2*	12.3†
Hyperbilirubinemia	4.9	7.2	12.2
Infection	7.1	11.0	13.0

Renal failure: serum creatinine *>1.5; †>3.0 mg/dl; hyperbilirubinemia: total bilirubin > 2 mg/dl or indirect bilirubin > 15 mg/dl.

CNS, central nervous system; ECLS, extracorporeal life support.

Take home messages

- Data is not definitive, but is compelling, with a positive signal seen
- There is a strong physiological basis for ECPR, and the current evidence base supports its use and ongoing development
- Patient selection is crucial to outcome determination
- ECPR on its own is not enough – quality of post-cardiac arrest care matters – ECMO bridges patients to care