

The Role of ECMO in Resuscitation

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Disclosure Information

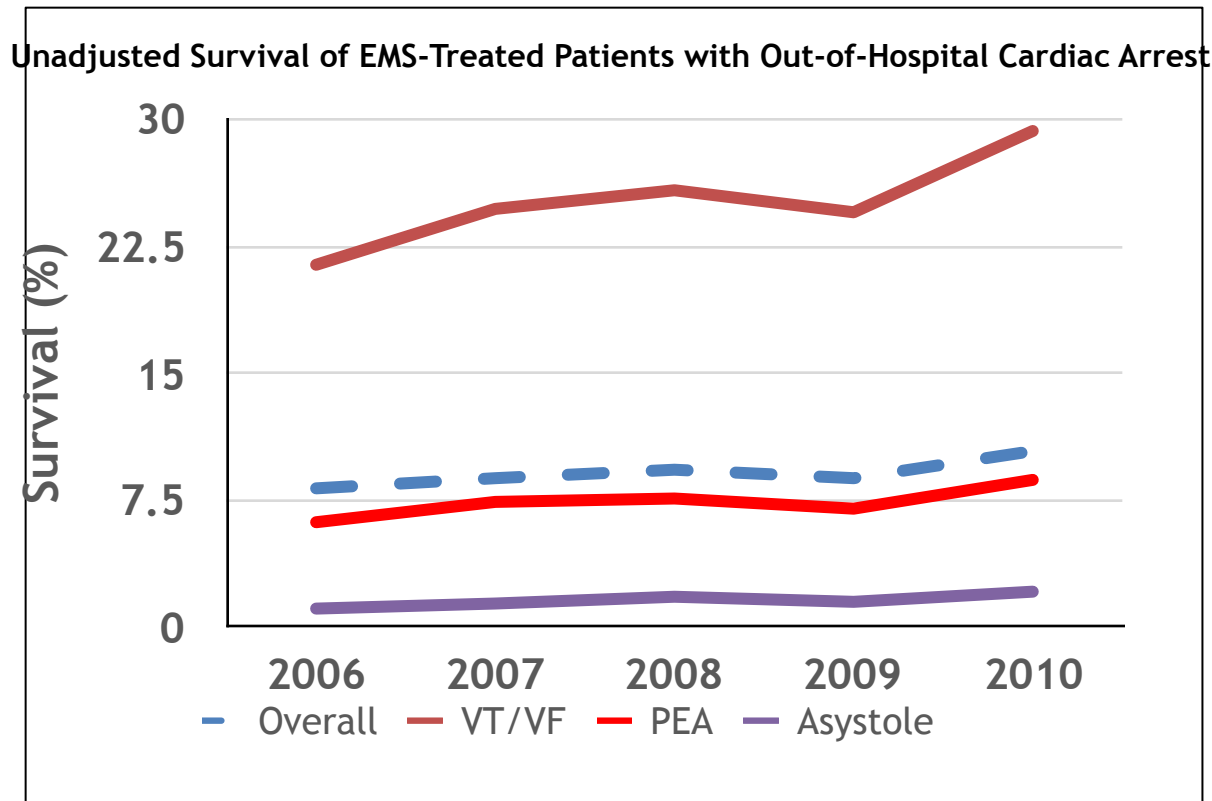
- **Disclosure of Relevant Financial Relationships**
 - I have no financial relationships to disclose.
- **Disclosure of Off-Label and/or investigative Uses**
 - I will discuss the following off label use and/or investigational use in my presentation:
 - ECMO for > 6Hrs for refractory out-of-hospital VF cardiac arrest

Outline

- Cardiac arrest epidemiology and pathophysiology
- Current approach to resuscitation
- ECMO for patients with refractory VF arrest
- Recovery of patients after refractory VF

Cardiac Arrest: Epidemiology

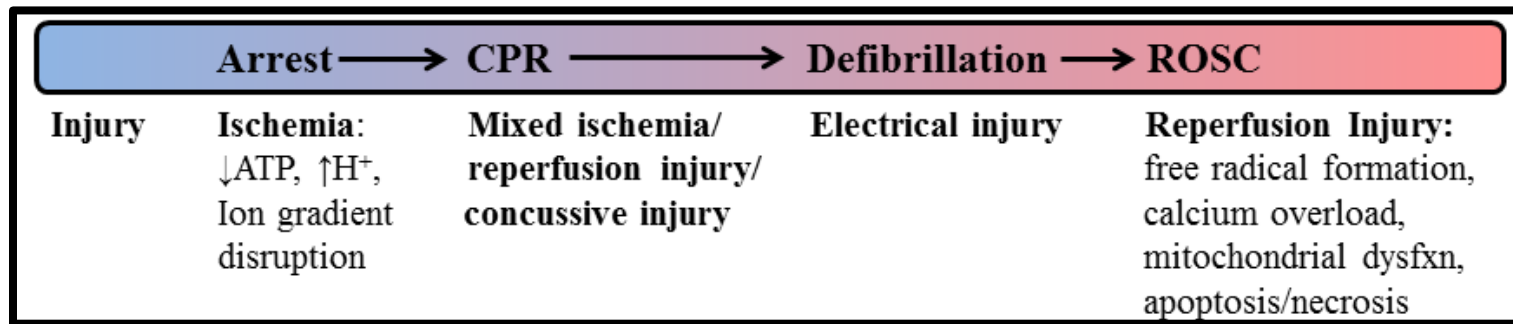
- 600,000 cardiac arrests in the US each year; 400,000 are OHCA
- 3rd leading cause of death in the US
- 80% of all survivors present with VT/VF



Adapted from Daya et al, Resuscitation, 2015

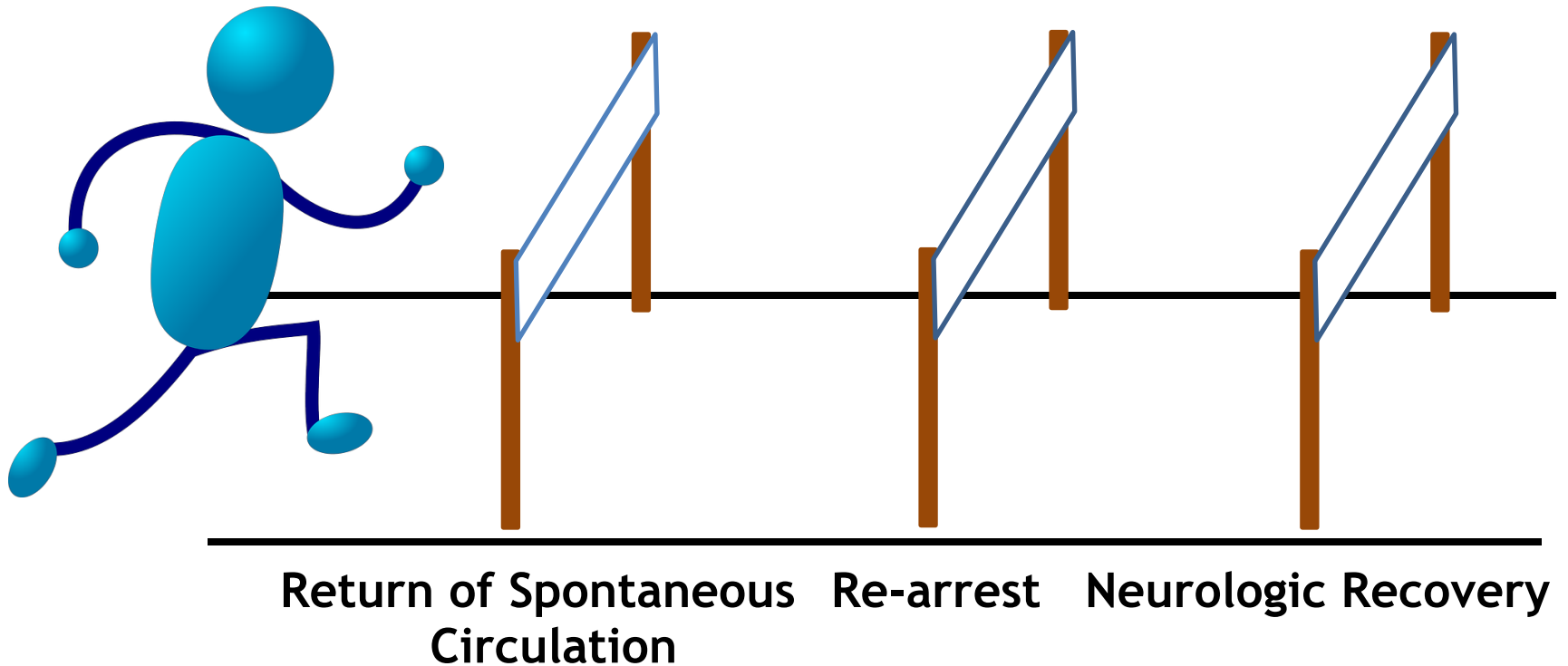
Cardiac Arrest: The Injury

- Injury occurs at each stage of resuscitation



Bartos and Yannopoulos. COCC, 2013

Barriers to Survival



Pre-hospital/Early Resuscitation

- CPR/Defibrillation

- History:

- 1740: Paris Academy of Sciences recommended mouth-to-mouth for drowning victims
 - 1891: Dr. Friedrich Maass performed the first documented chest compressions in humans
 - 1960: CPR was coined. Public training began in 1980's
 - 1979: ACLS was developed
 - 1990's: Paramedics began using defibrillators



Fig 2.—Position of hands during massage of adult.

Kouwenhoven et al. JAMA, 1960

Pre-hospital Resuscitation

Basic Life Support

- Bystander CPR (OR 2.0)
- Active Compression/ Decompression and Impedance threshold device (OR 1.5)
- Early Bystander Defibrillation (OR 2.6)



Gilmore et al. Am J Cardiol, 2006
Aufderheide et al., Lancet, 2011
Pollack et al. Circulation, 2018

Pre-hospital Resuscitation

Advanced Cardiac Life Support

- Epinephrine
 - Perkins et al., NEJM, 2018
- Vasopressin
 - Wenzel et al., NEJM, 2004; Gueugniaud et al., NEJM, 2008
- Amiodarone/Lidocaine
 - Dorian et al., NEJM, 2002, Kudenchuk et al., NEJM, 2016
- Sodium bicarbonate
 - NCT01377337
- Intubation
 - Jabre et al., JAMA 2018

Pre-hospital Resuscitation

Advanced Cardiac Life Support

– Epinephrine

- ROSC 36% vs. 12%, Survival to hospital discharge 3.2% vs. 2.3%
- No difference in neurologically intact survival: 2.2% vs. 1.9%
- Time to drug = 22 min from arrest; 15 min from CPR

– Vasopressin

- ROSC 25% (37% for VF), Survival to hospital discharge 2-10% (18-19% for VF)
- Time to drug = 20 min from arrest; 10-13 min from CPR

– Amiodarone/Lidocaine

- ROSC 36%, Survival to hospital discharge 24% (VF only)
- Time to drug = 16 min from arrest; 10 min from CPR

– Sodium bicarbonate: ?

– Intubation

- Did not meet non-inferiority or superiority compared to BVM

What Remains

Basic Life Support

- Bystander CPR
- Active Compression/
Decompression and Impedance
threshold device
- Early Bystander Defibrillation

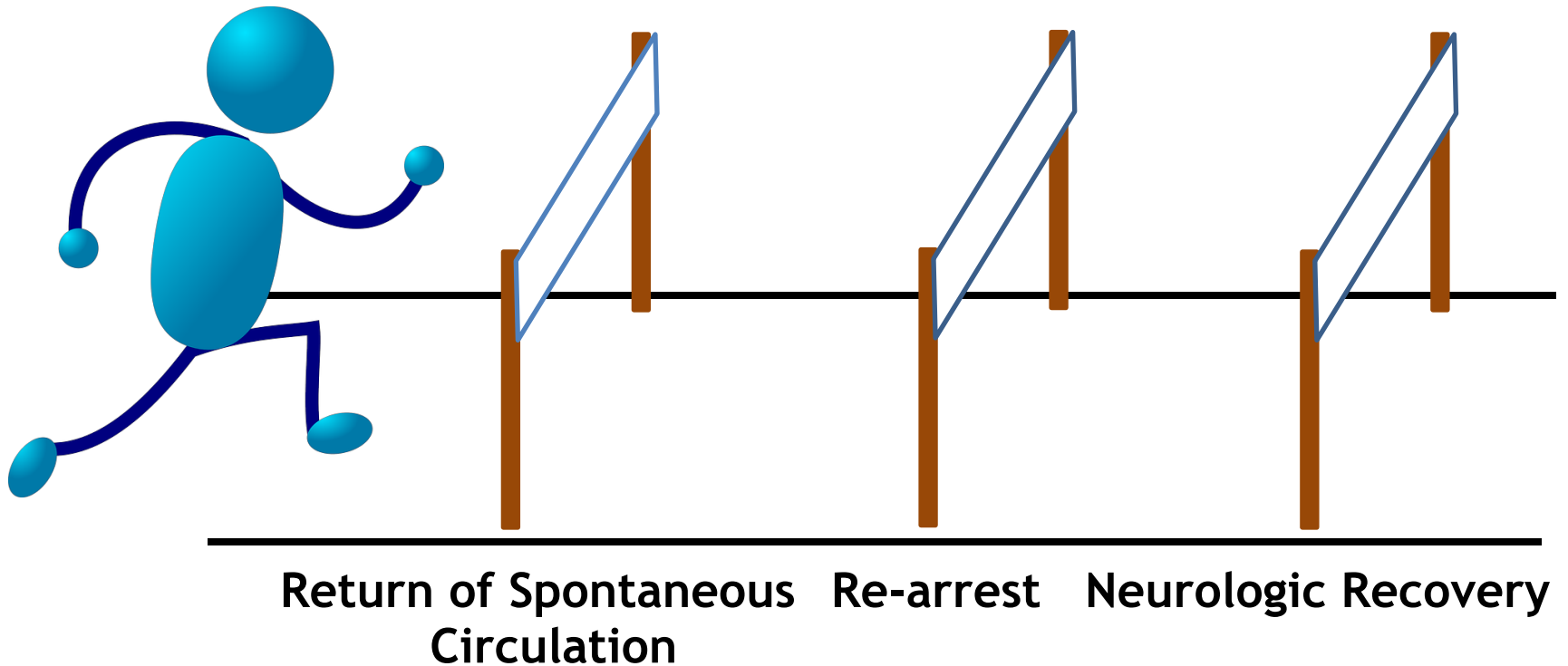
Advanced Cardiac Life Support

- Epinephrine ?
- Vasopressin
- Amiodarone/Lidocaine ?
- Sodium bicarbonate?
- Intubation?

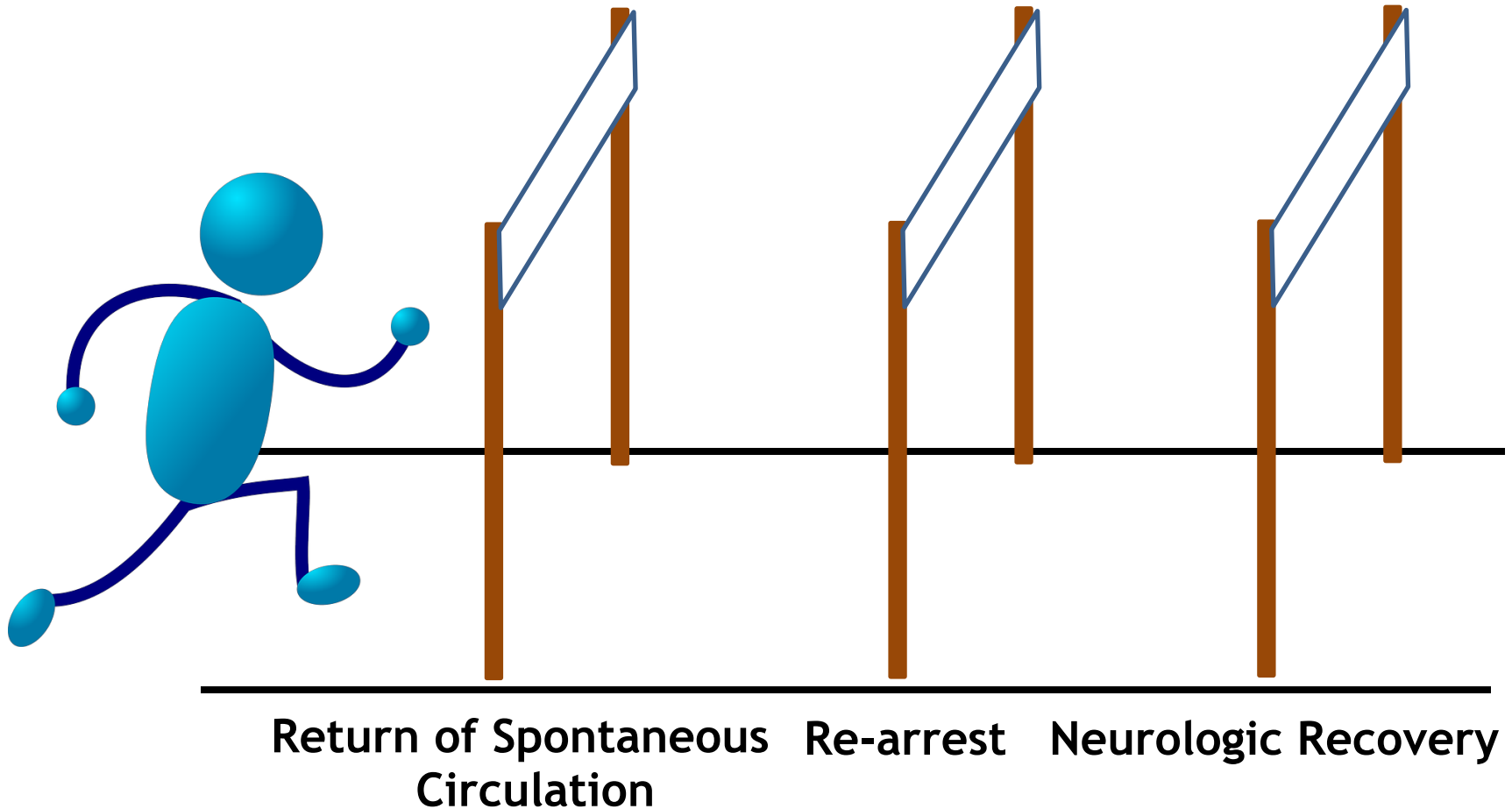


Fig 2.—Position of hands during massage of adult.

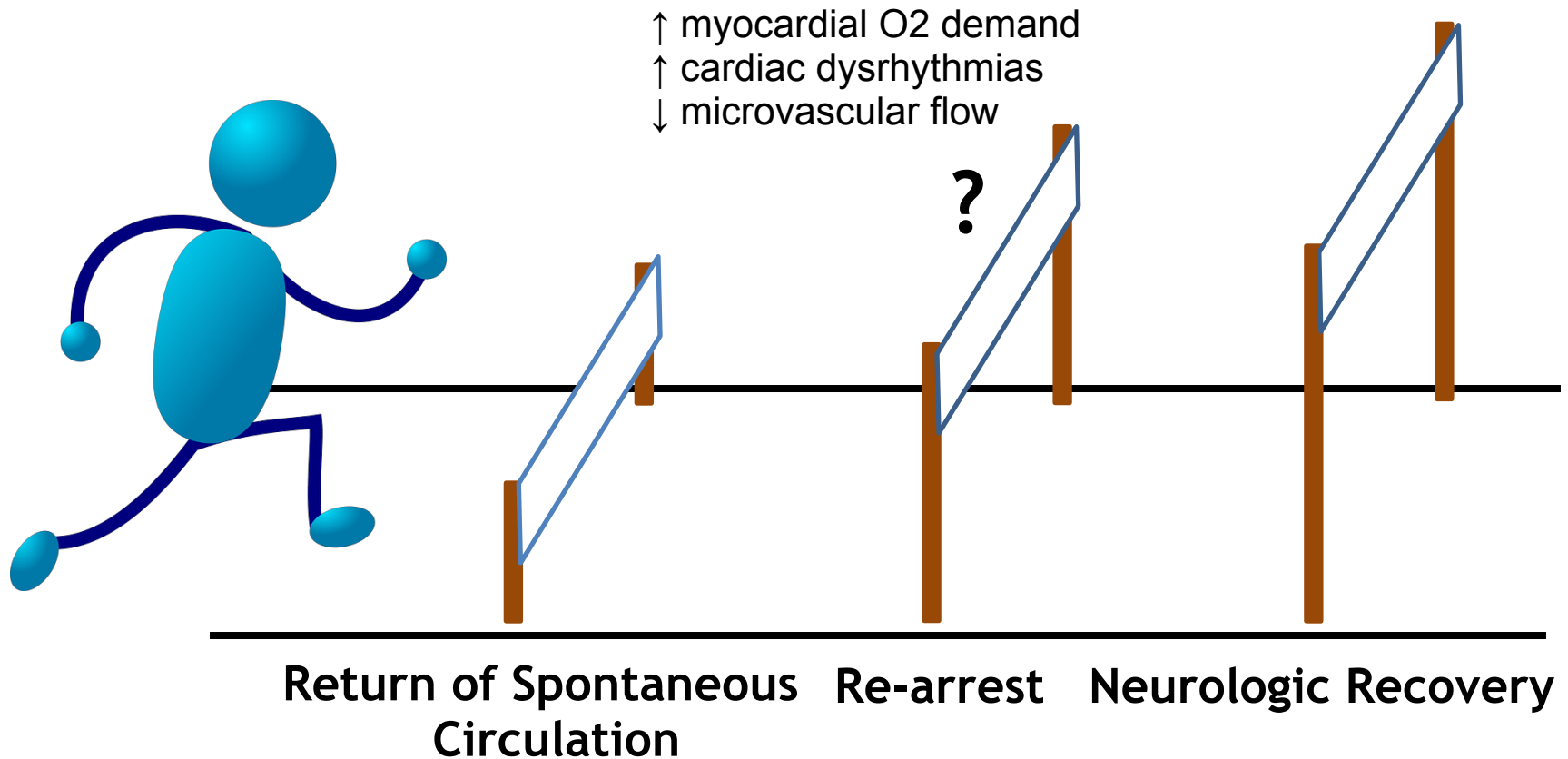
Barriers to Survival



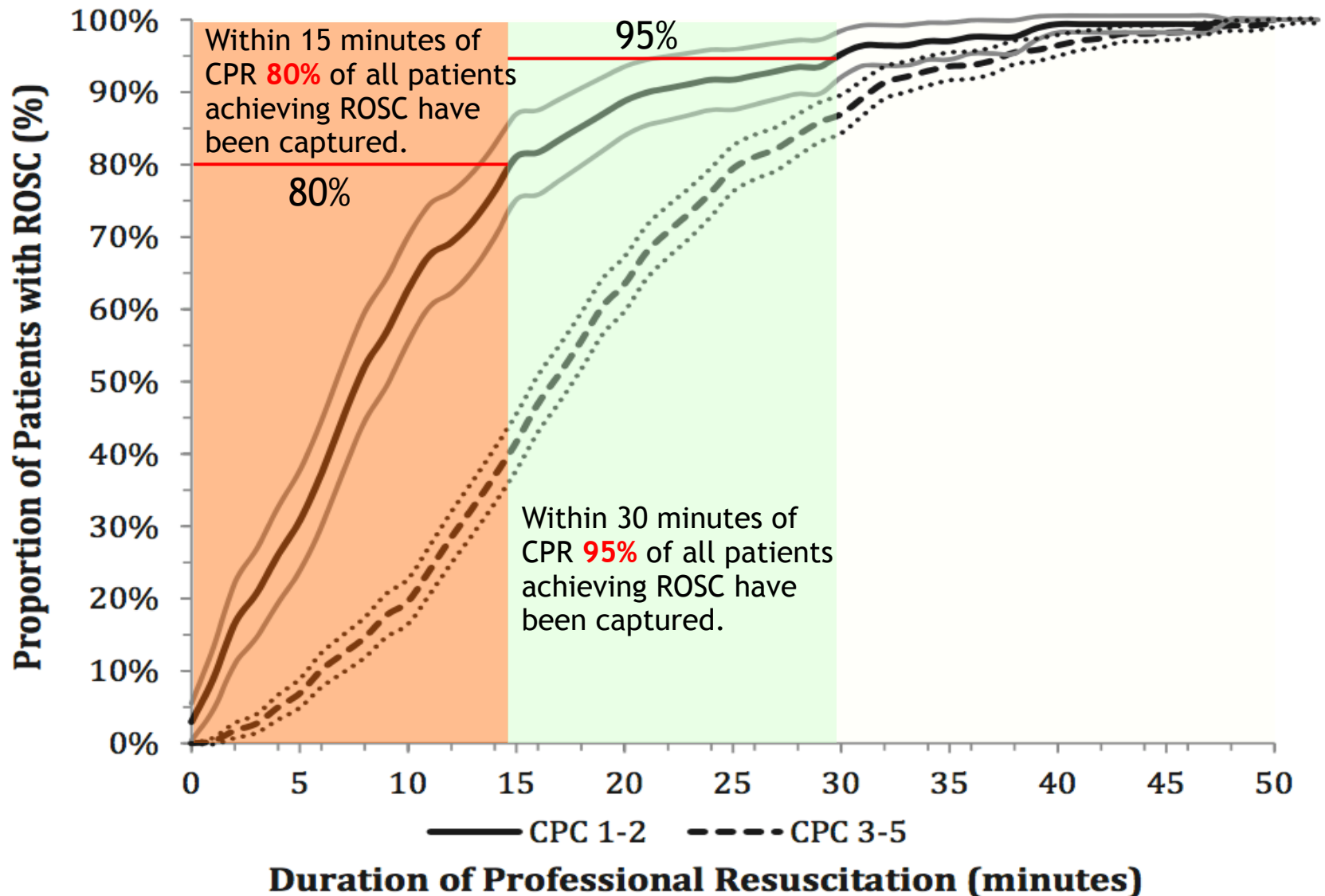
Barriers to Survival - Without BLS



Barriers to Survival - Epinephrine

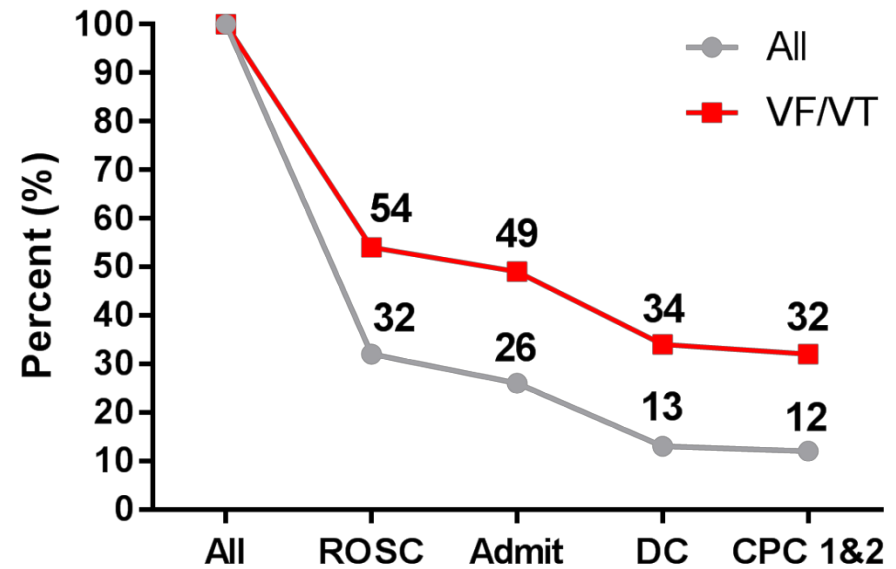
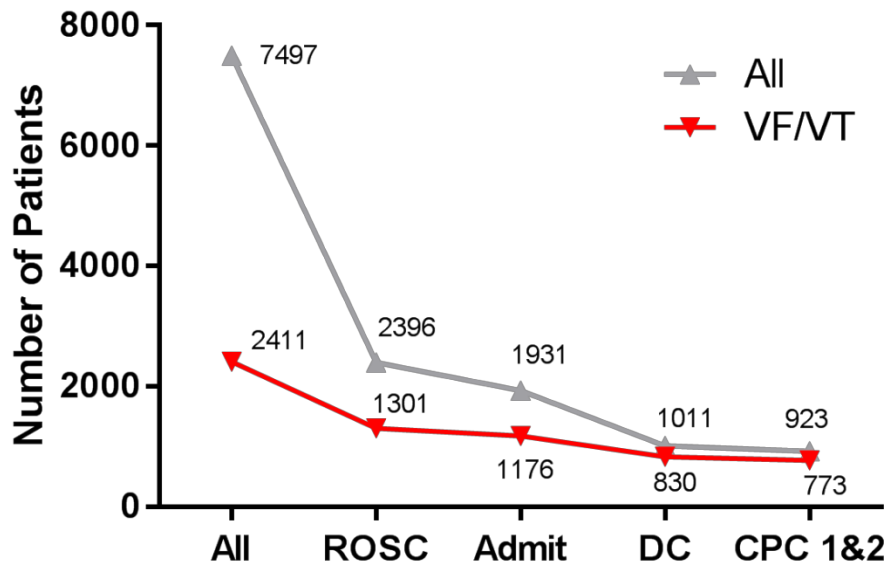


Duration of CPR and Likelihood of ROSC



Minnesota Epidemiology

2011-2016 Minnesota OHCA ages 18-75



Yannopoulos et al., Circulation, 2018

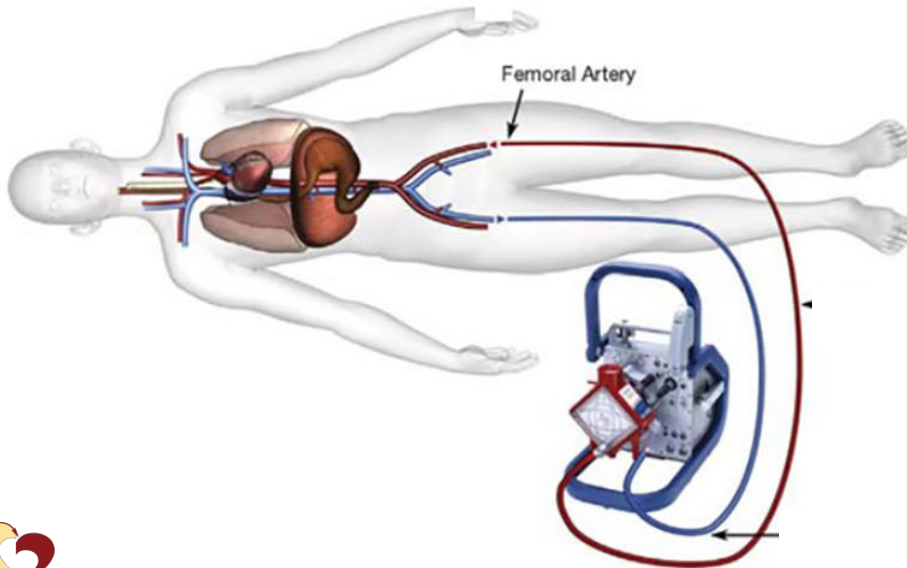
66% of VF patients who achieve hospital admission are discharged neurologically intact

Extracorporeal membrane oxygenation

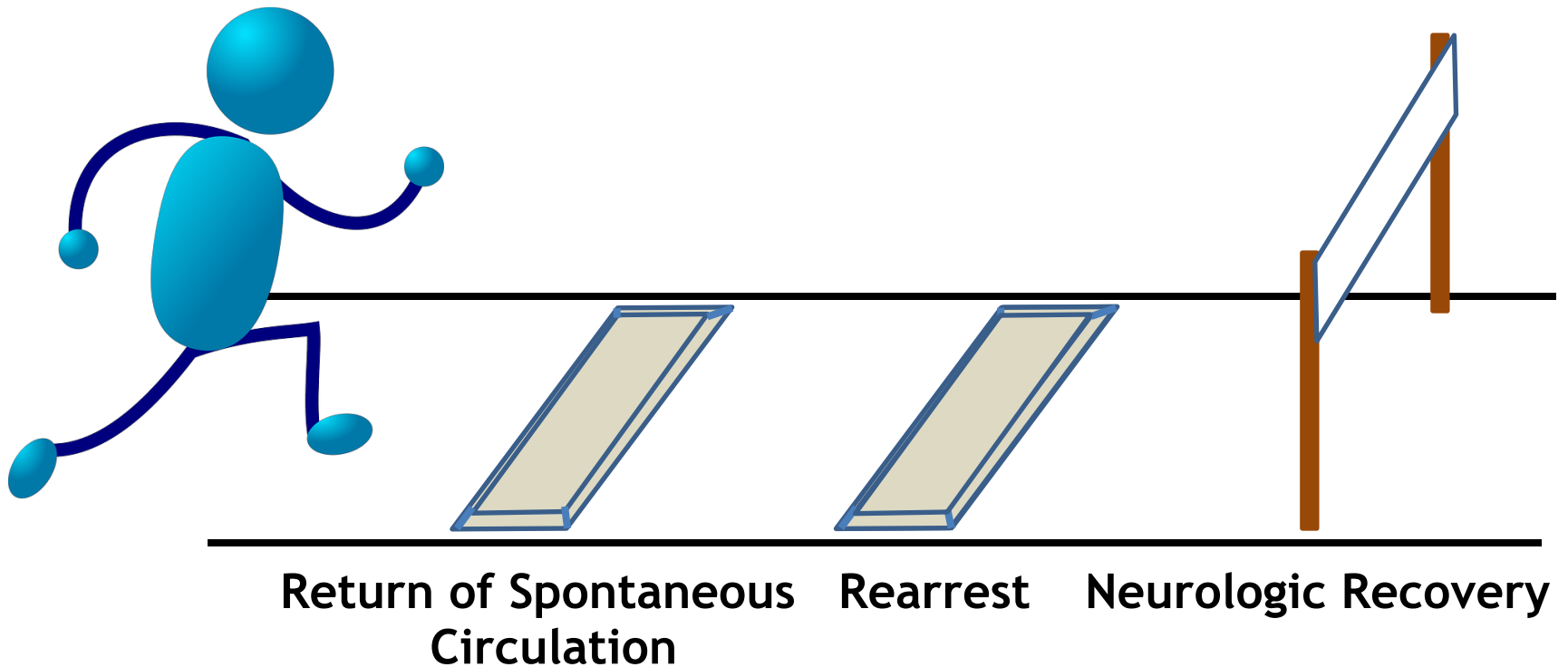
- Peripherally cannulated veno-arterial ECMO
- Hemodynamic effects: ↑ systemic blood flow with flows 3-5L/min, afterload, may ↑ myocardial oxygen demand
- Provides oxygenation and CO₂ removal and blood flow
- Independent of RV function and rhythm
- Typical cannula sizes: Arterial – 15-17Fr; Venous – 25 Fr

↑

V-A ECMO



Barriers to Survival - ECMO



Minnesota Resuscitation Consortium

Advanced Perfusion and Reperfusion Cardiac Life Support Strategy
for Out-of-Hospital Refractory Ventricular Fibrillation

Three Priorities

- Early mobilization from the field
- Achieve and maintain hemodynamic stability with support devices initiated on arrival to the cardiac catheterization lab
- Treat the underlying etiology of the cardiac arrest including coronary revascularization

Hemodynamic Support

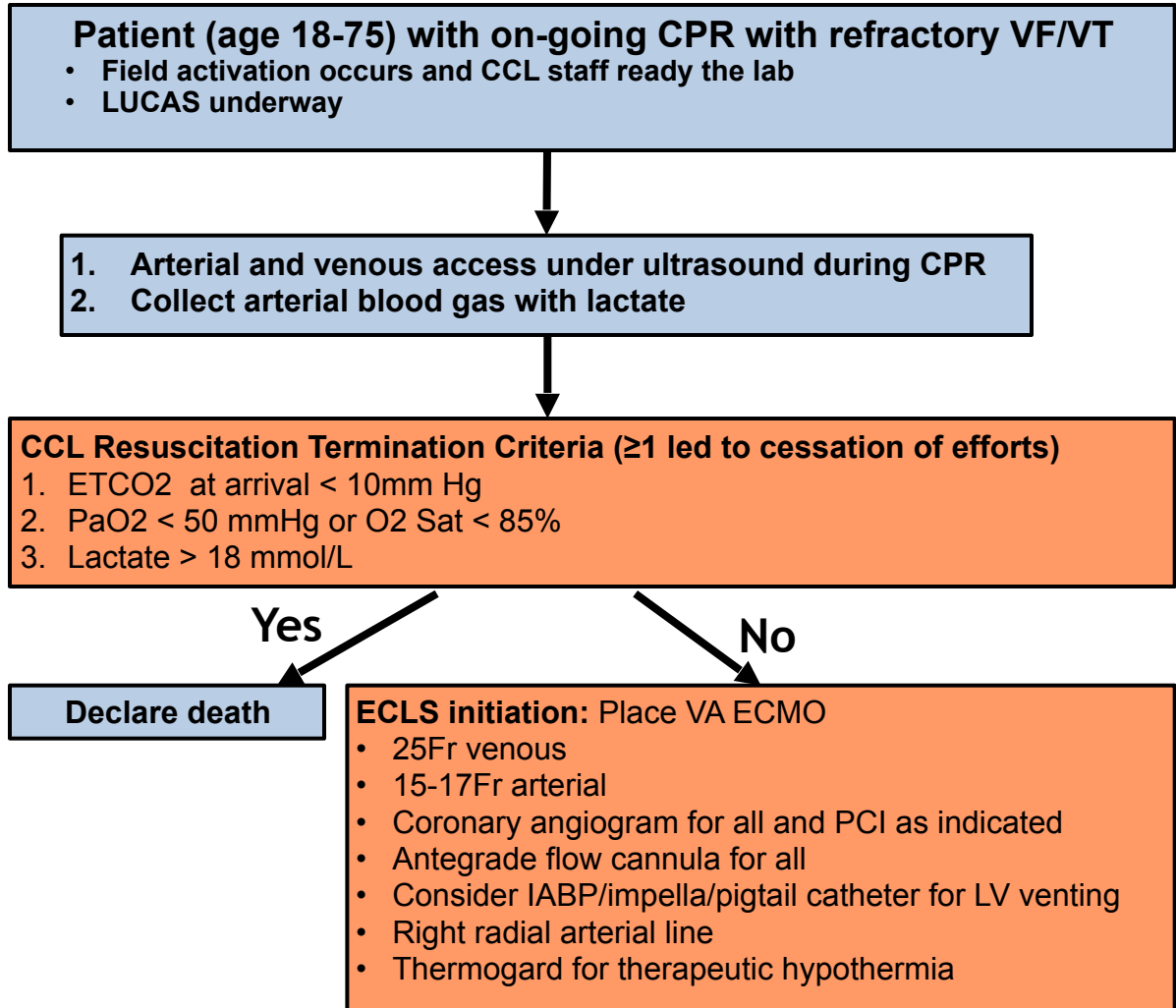
Field Criteria

Inclusion:

- Ages 18-75
- VT/VF as the presenting rhythm
- Refractory cardiac arrest with VT/VF after ≥ 3 EMS-delivered shocks and 300mg of amiodarone or refractory PEA/asystole
- LUCAS CPR
- Estimated transfer time from scene to CCL < 30 min

Exclusion:

- DNR/DNI status or known terminal illness
- Nursing home residents
- Clear non-cardiac etiology
- Pregnancy



Resuscitation Goals

- Perfuse the vital organs
 - CPR
- Achieve return of spontaneous circulation
 - Defibrillation
- Address the underlying etiology
 - Cath lab/ICU admission

Refractory Cardiac Arrest

- Perfuse the vital organs
 - CPR → VA ECMO
- Address the underlying etiology
 - Cath lab → PCI
- Achieve return of spontaneous circulation
 - Defibrillation

ECLS Registry Report

International Summary

July, 2018



Extracorporeal Life Support Organization
2800 Plymouth Road
Building 300, Room 303
Ann Arbor, MI 48109

Overall Outcomes

	Total Runs	Survived ECLS		Survived to DC or Transfer	
Neonatal					
Pulmonary	30,934	25,990	84%	22,662	73%
Cardiac	7,794	5,063	64%	3,281	42%
ECPR	1,718	1,140	66%	708	41%
Pediatric					
Pulmonary	8,820	5,953	67%	5,131	58%
Cardiac	10,462	7,177	68%	5,447	52%
ECPR	3,946	2,262	57%	1,675	42%
Adult					
Pulmonary	16,337	10,857	66%	9,649	59%
Cardiac	15,942	8,865	55%	6,747	42%
ECPR	4,952	1,896	38%	1,443	29%

Extracorporeal Cardiopulmonary Resuscitation

Table 1: Survival in patients with refractory OHCA treated with advanced perfusion techniques (ECMO and PCI)

	Enrollment years	ECMO cannulation	Number of patients		Survival rates		
			OHCA n	V fib/V tach n (%)	All OHCA n (%)	CPC 1-2 n (%)	V fib/V tach n (%)
Kagawa et al 2012	7.5	ED	42	23 (55)	7 (17) ^a	6 (14) ^a	17/46 (37) ^c
Avali et al 2012	5	ED/ICU/CCL	18	16 (89)	1 (5.5) ^a	1 (5.5) ^a	—
Haneya et al 2012	5	ED	26	12 (46.2)	4 (15) ^b	27/85 (32) ^c	—
Leick et al 2013	2	CCL	28	8 (28.6)	11 (39) ^a	8 (28.5) ^a	—
Maekawa et al 2013	4.5	ED	53	32 (60.4)	17 (32.1) ^b	8 (15.1) ^b	—
Wang et al 2014	5.5	ED	31	15 (48.4)	12 (38.7) ^b	8 (25.8) ^b	—
Johnson et al 2014	7	ED	15	11/26 (42) ^a	1 (6.6) ^b	3/26 (11.5) ^{bc}	—
Sakamoto et al 2014	3	ED	234	234 (100)	68 (29) ^{ad}	32 (13.7) ^{ad}	68 (29) ^{ad}
Kim et al 2014	7.5	ED	55	31 (56.4)	9 (16.4) ^b	8 (14.5) ^b	—
Stub et al 2015	3	ED	11	11 (100)	5 (45) ^b	5 (45) ^b	5 (45) ^b
Pozzi et al 2016	4	ED	68	19 (28)	6 (8.8) ^b	3 (15.8) ^b	6 (31.5) ^b
Lee et al 2016	4	ED	23	20 (87)	10 (43.5) ^a	7 (30.4) ^a	8 (40) ^a
Fjølner et al 2017	3.5	CCL	21	9 (43)	7 (33) ^b	7 (33) ^b	5 (55.6) ^b
Lamhaut et al 2017	4	Field vs. ED	156	81 (58) ^e	21 (13.5) ^b	21 (13.5) ^b	21 (25.9) ^b
Schober et al 2017	10	ED	7	4/7 (57)	1 (14) ^f	—	—
Yannopoulos et al 2017	1	CCL	62	62 (100)	28 (45) ^b	26 (42) ^b	28 (45) ^b

^a Thirty-day survival ^b Survival to hospital discharge. ^c Percentage includes OHCA and IHCA.

^d This is per protocol analysis. Intention-treat-analysis was 32/260 (12.3%). ^e 139 patients with available data. ^f Six-month survival.

Yannopoulos D, JEMS, 2017





Patient and Arrest Characteristics

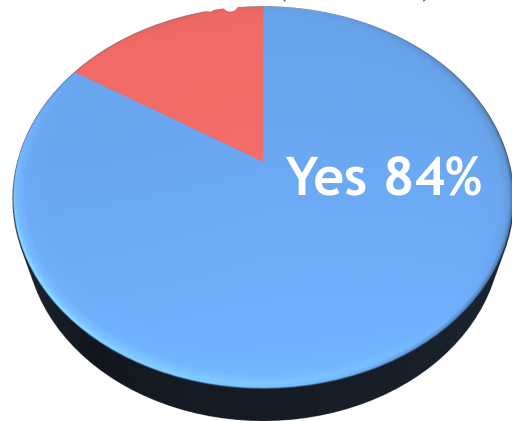
Patient and Arrest Characteristics		(n = 83)
Sex, No. (%)	Male	64 (77%)
	Female	19 (23%)
Age, No. (%), y	<40	10 (12%)
	40-60	43 (52%)
	>60-75	30 (36%)
Ethnicity, No. (%)	White	67 (81%)
	Black	9 (11%)
	Other	7 (8.4%)
	Diabetes	19 (23%)
	Hypertension	37 (45%)
	Hyperlipidemia	25 (30%)
	Smoking	21 (25%)
Known Comorbidities, No. (%)	Coronary artery disease	18 (22%)
	Prior coronary artery stent	10 (12%)
	Coronary artery bypass grafting	7 (8.4%)
	Congestive heart disease	12 (14%)
	Chronic Renal Failure	2 (2.4%)
	Hemodialysis	2 (2.4%)
	Alcoholism	5 (6.0%)
	History of Stroke or Dementia	4 (4.8%)

Patient and Arrest Characteristics		(n = 83)
Arrest Location, No. (%)	Home	45 (54%)
	Public Place	38 (46%)
Initial Cardiac Rhythm, No. (%)	VF/VT	83 (100%)
	Other	0 (0%)
Bystander CPR, No. (%)	Yes	60 (72%)
	No	23 (28%)
Time, mean (SEM), min	911 to first responder	7.6 (1.2)
	911 to CCL arrival	56.7 (1.8)
	CCL arrival to ECMO support	8 (0.5)

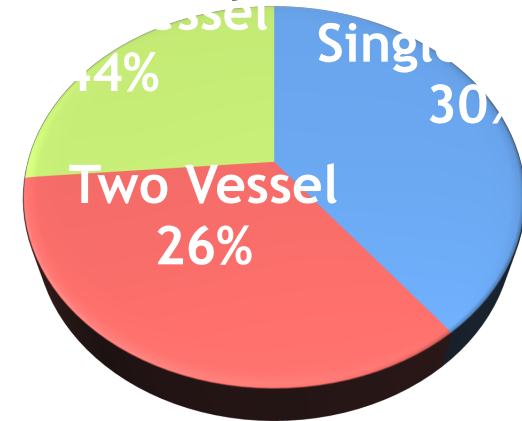
Bartos et al, Resuscitation, 2018

Coronary Artery Disease

Significant Coronary Disease ($\geq 70\%$)



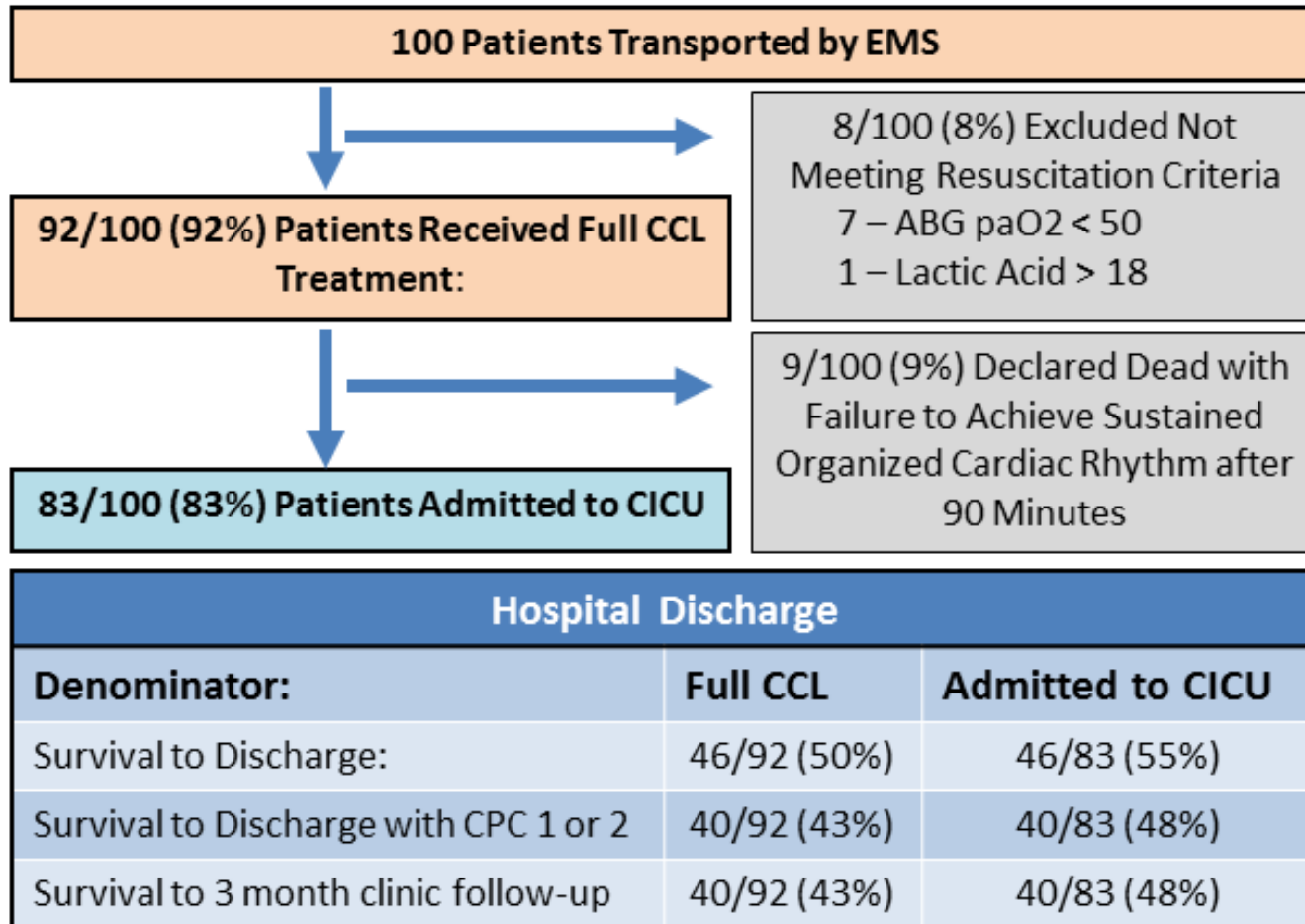
Extent of Coronary Artery Disease



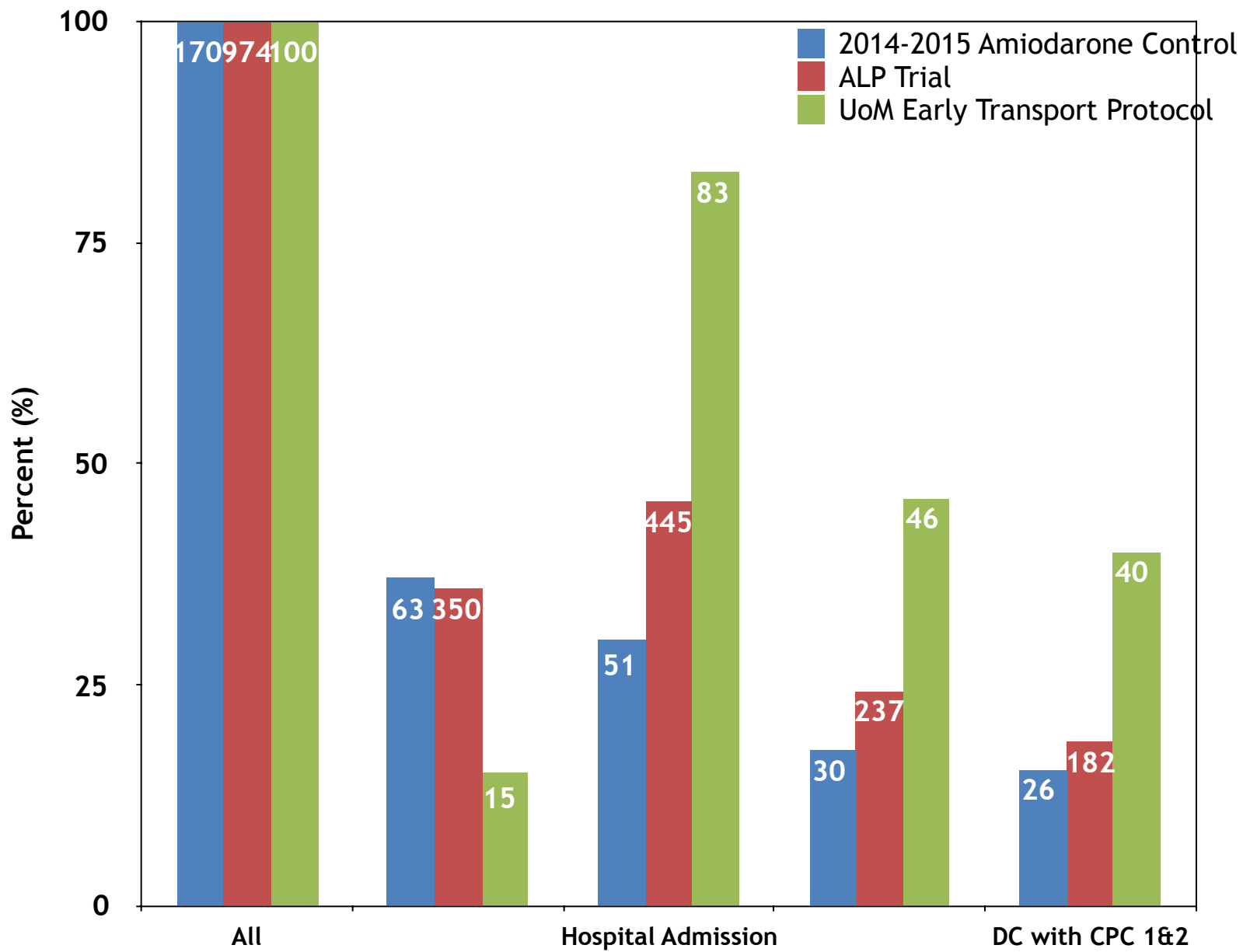
Lesion Complexity	Value
Prior Coronary Artery Bypass Grafts	5 (9%)
Chronic Total Occlusion Present	18 (33%)
Patients with Acute Thrombotic Lesions	35 (64%)
SYNTAX Score	29.4 $\pm$ 13.9

Yannopoulos et al., JACC, 2017

Overall Survival

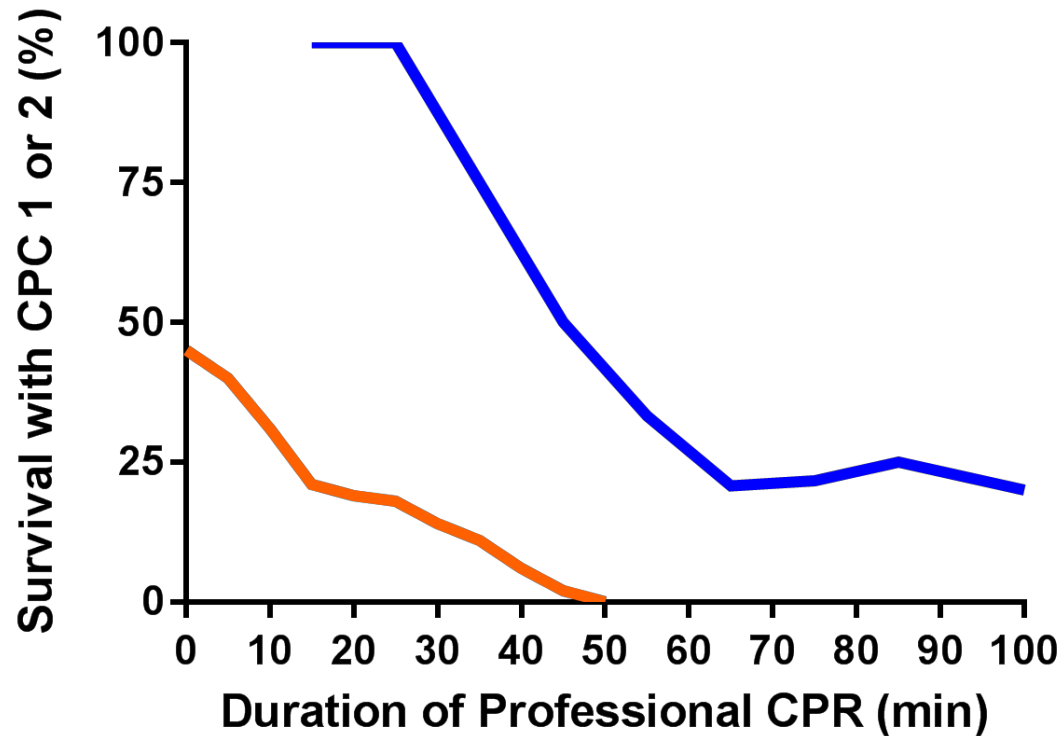


Bartos et al, Resuscitation, 2018



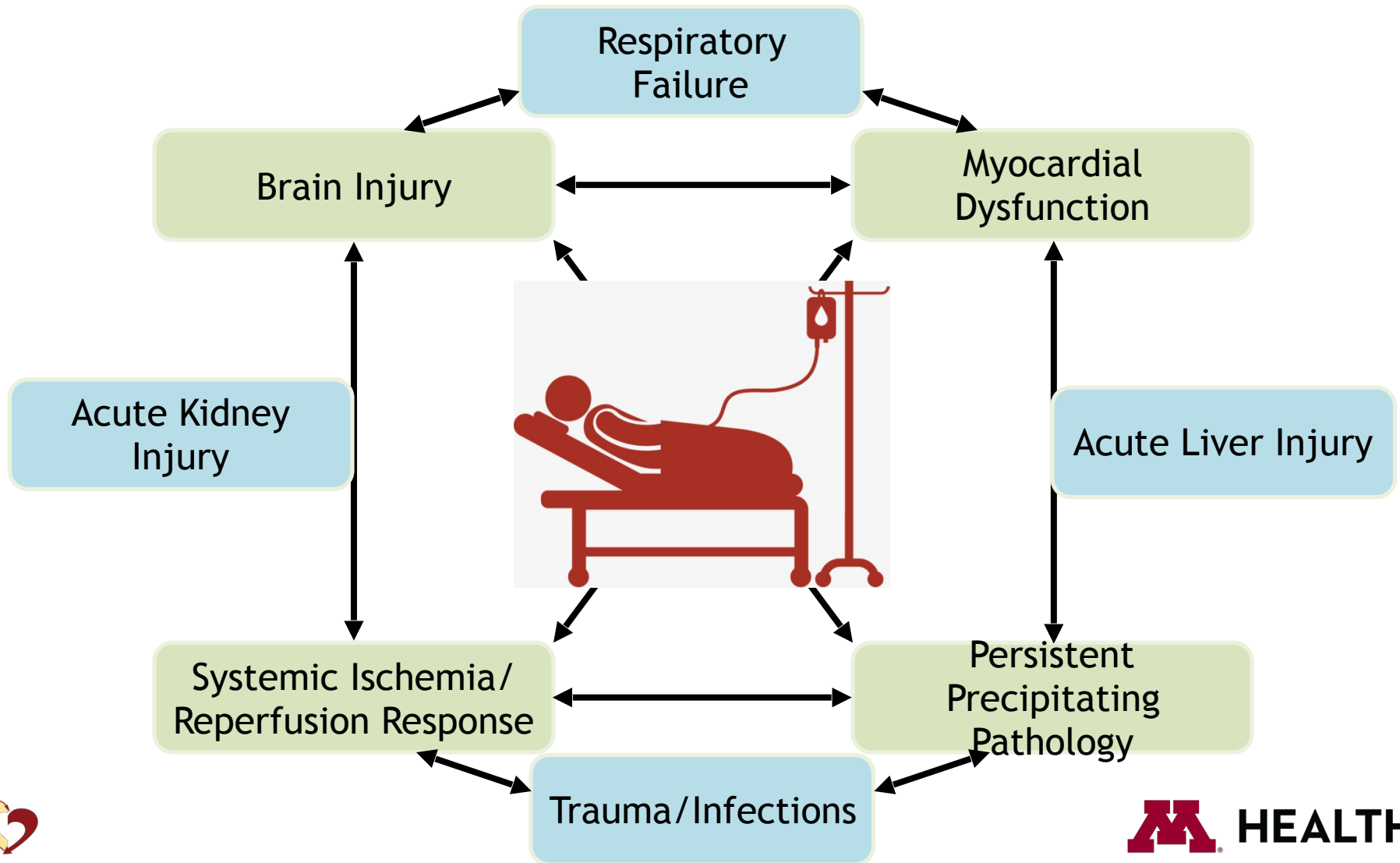
Yannopoulos et al., JACC, 2017; Kudenchuk, et al., NEJM, 2016; Bartos et al, Resuscitation, 2018

CPR Duration and Neurologically Intact Survival



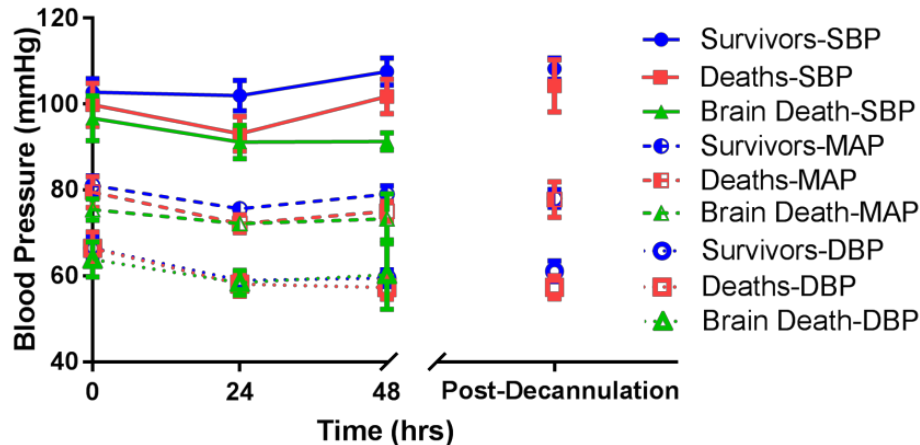
— Standard ACLS: Adapted from Grunau et al. 2016
— MRC ECPR Protocol

Post-Cardiac Arrest Syndrome in Refractory Cardiac Arrest

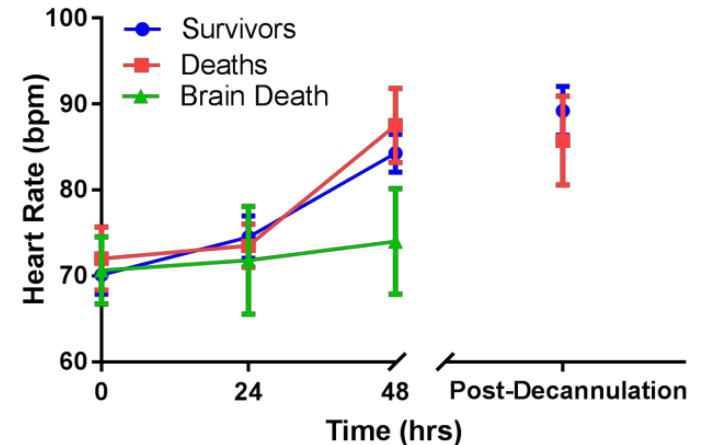


Hemodynamic Stabilization

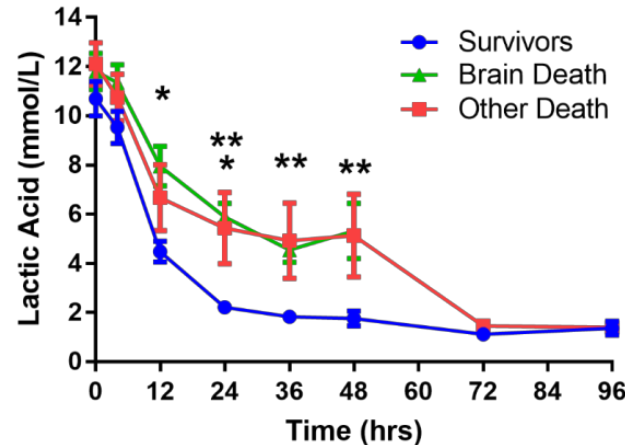
Blood Pressure



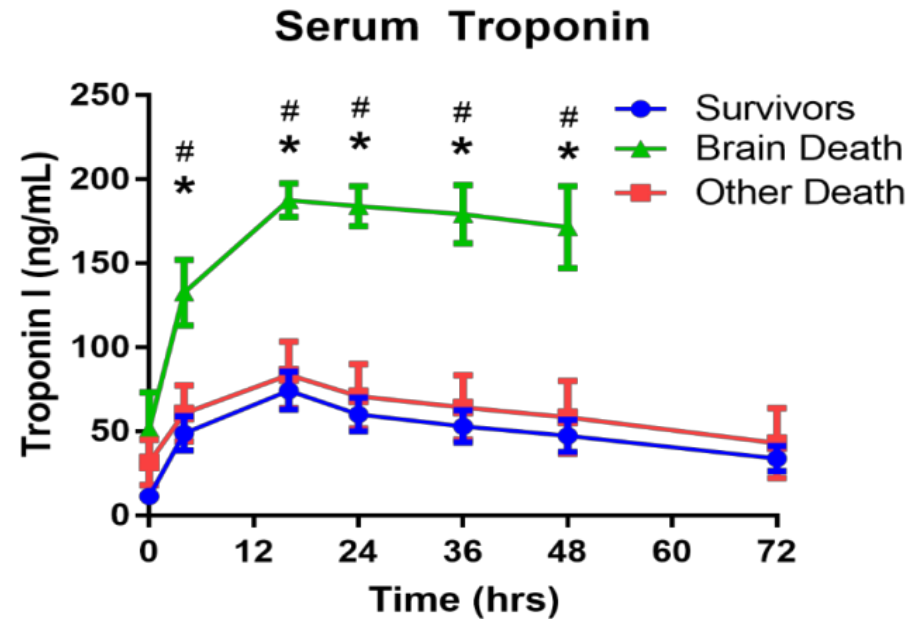
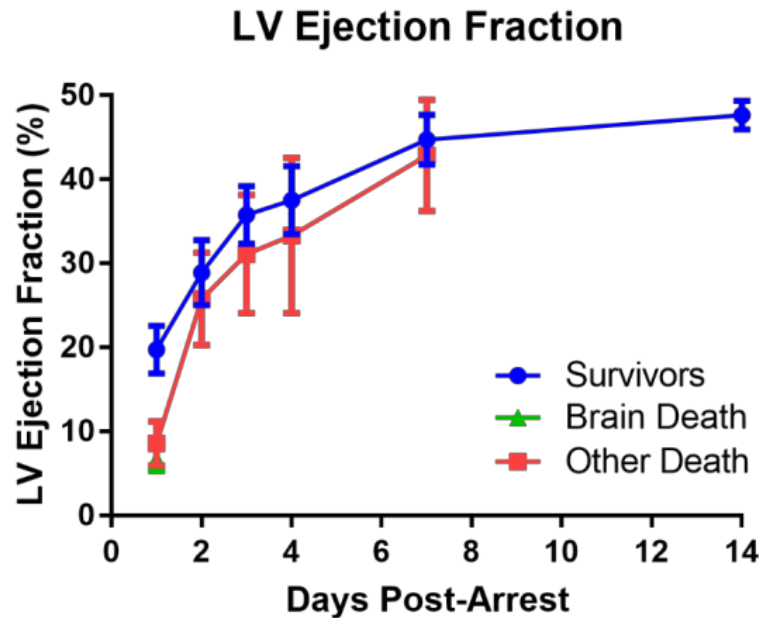
Heart Rate



Arterial Lactic Acid Level

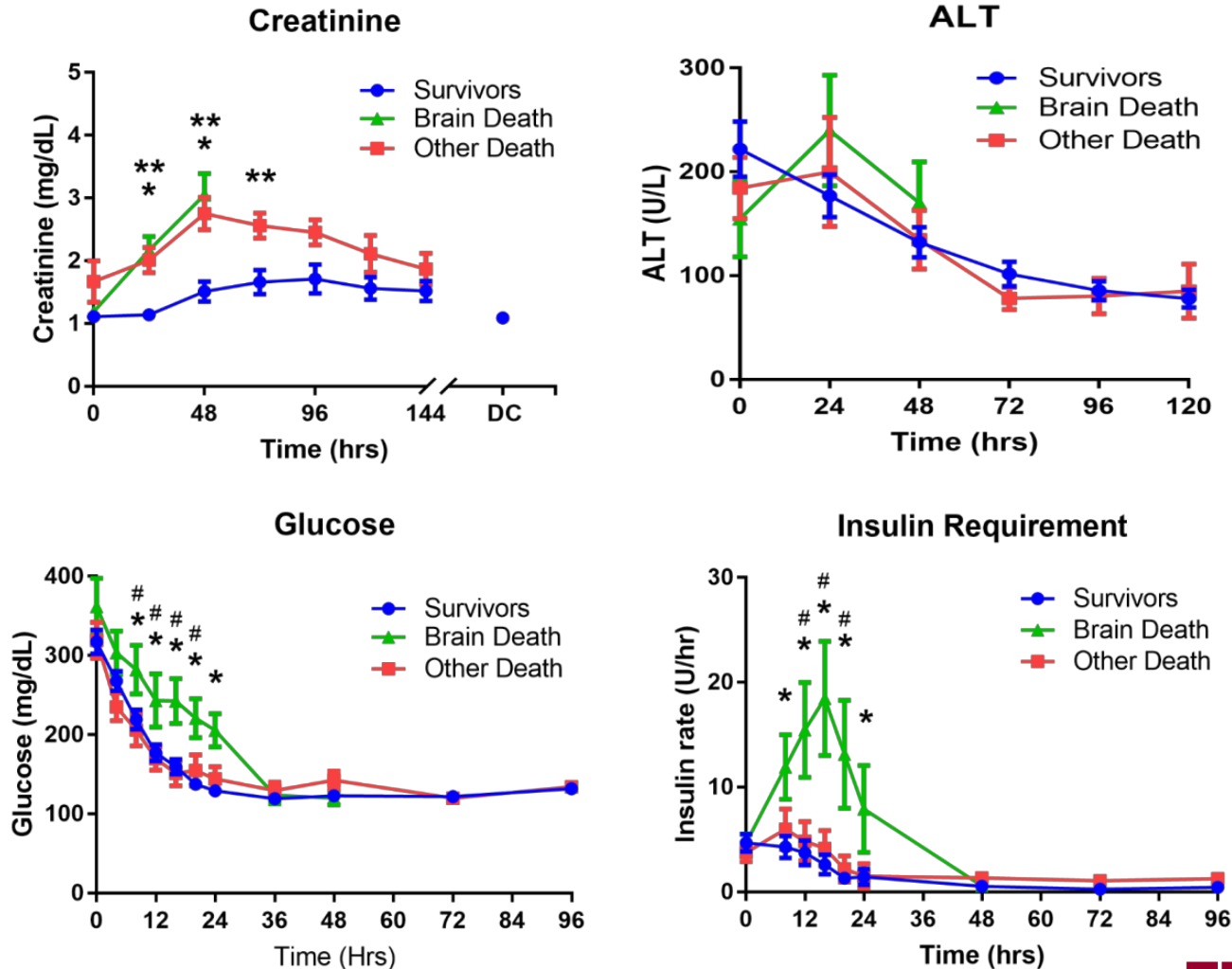


Cardiac Injury and Recovery



Bartos et al, Resuscitation, 2018

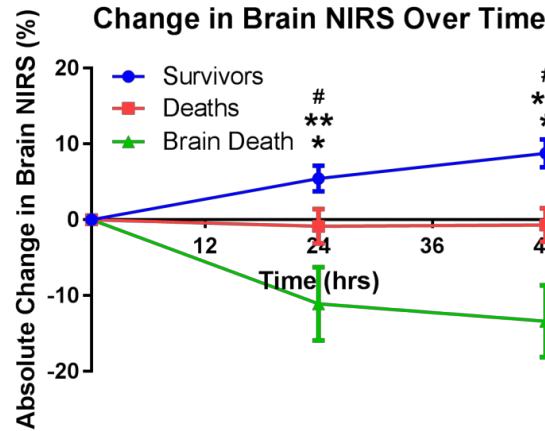
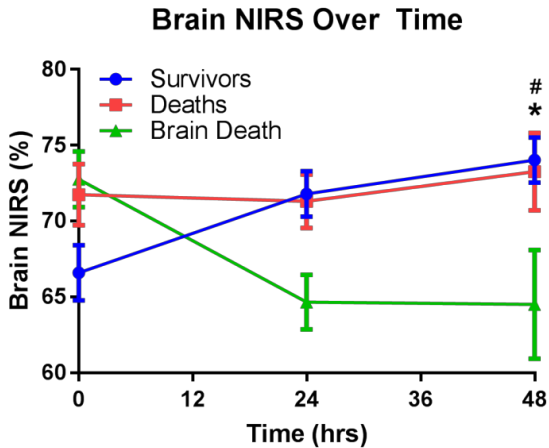
End-organ Damage



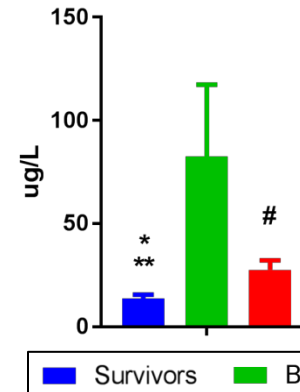
Neurologic Injury

Refractory VT/VF patients Admitted to ICU		Overall	Survivors (46)	Deaths (23)	Brain Death (14)
Initial Head CT	Anoxic Injury	17/83 (20%)	3/46 (6.5%)	5/23 (22%)	9/14 (64%)
	Edema	14/83 (17%)	0%	6/23 (26%)	8/14 (57%)
	Intracranial Hemorrhage	0%	0%	0%	0%
	Acute Ischemic Stroke	1/83 (1.2%)	0%	1/23 (4.3%)	0%
Follow-up CT or MRI	Anoxic Injury	14/69 (20%)	6/46 (13%)	8/23 (35%)	NA
	Edema	6/69 (8.7%)	1/46 (2.1%)	5/23 (22%)	NA
	Intracranial Hemorrhage	1/69 (1.4%)	1/46 (2.1%)	0%	NA
	Acute Ischemic Stroke	9/69 (13%)	5/46 (11%)	4/23 (17%)	NA

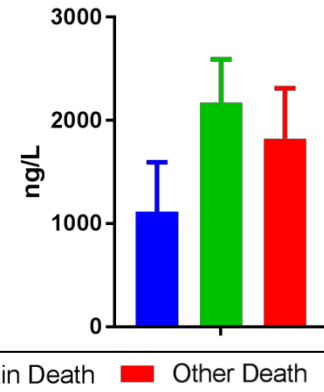
Monitoring Brain Injury



Neuron Specific Enolase



S100b

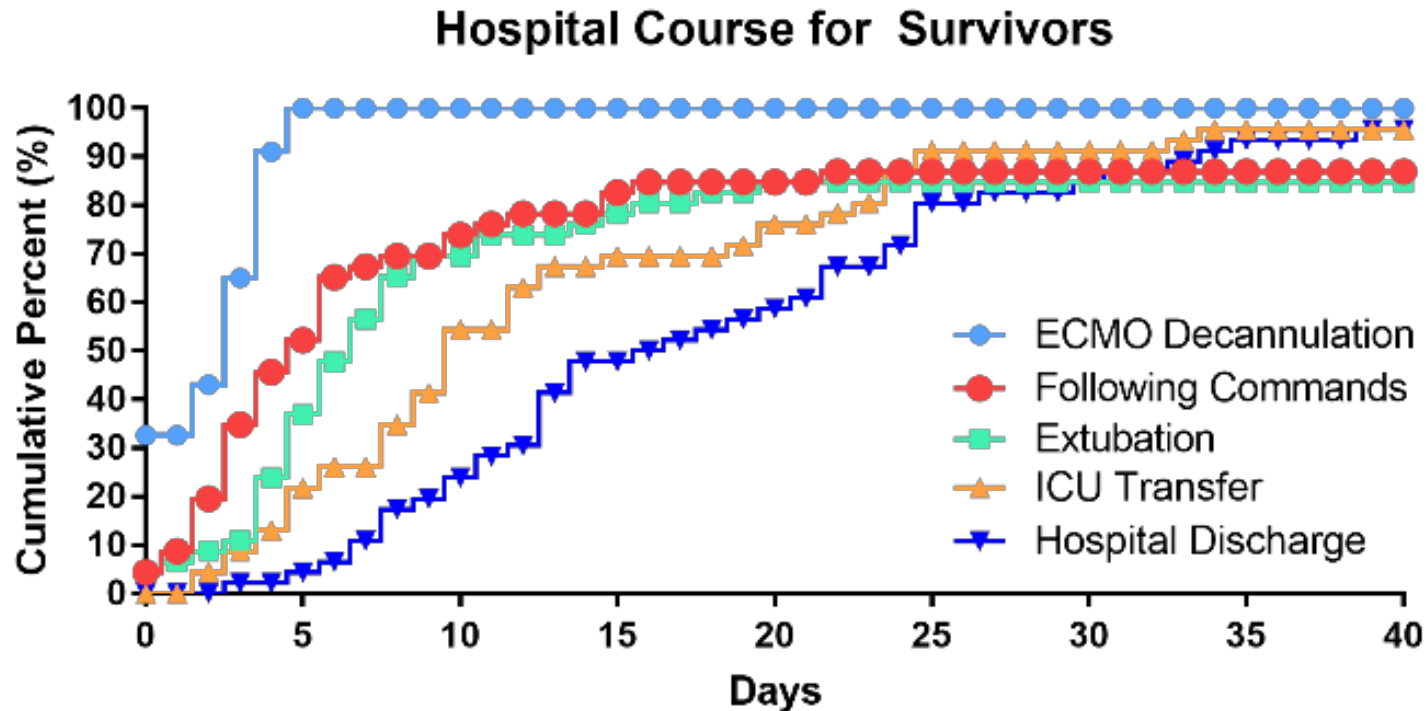


Refractory VT/VF patients Admitted to ICU		Overall (83)	Survivors (46)	Deaths (23)	Brain Death (14)
Continuous EEG	Convulsive Seizures	1/83 (1.2%)	2/46 (4.3%)	0%	0%
	Non-convulsive Status Epilepticus	11/83 (13%)	4/46 (8.7%)	7/23 (30%)	0%

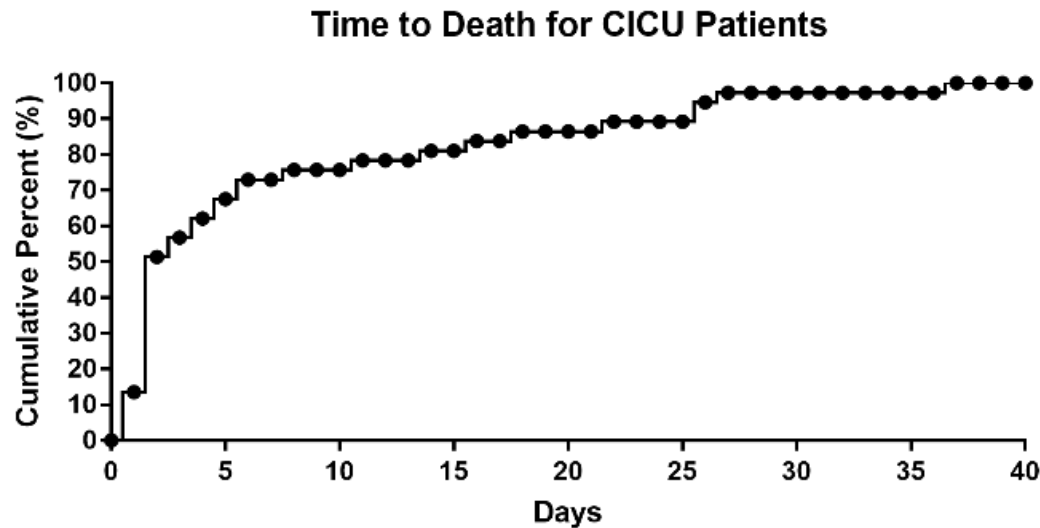
Trauma

Refractory VT/VF patients Admitted to ICU		Overall (83)	Survivors (46)	Deaths (23)	Brain Death (14)
CT Chest	Rib Fractures	37/83 (45%)	17/46 (37%)	12/23 (52%)	8/14 (57%)
	Lung Injury	64/83 (77%)	33/46 (72%)	20/23 (87%)	11/14 (79%)
	Pneumothorax	6/83 (7.2%)	4/46 (8.7%)	0%	2/14 (14%)
	Pneumothorax Requiring Chest tube	2/83 (2.4%)	2/46 (4.3%)	0%	0%
	Thoracic/Pericardial Bleed	11/83 (13%)	6/46 (13%)	3/23 (13%)	2/14 (14%)
CT Abd/ Pelvis	Abdominal Bleed	6/83 (7.2%)	3/46 (6.5%)	3/23 (13%)	0%
	Pancreatitis	4/83 (4.8%)	2/46 (4.3%)	2/23 (8.7%)	0%
	RP Bleed	3/83 (3.6%)	2/46 (4.3%)	1/23 (4.3%)	0%

Patient Recovery Benchmarks



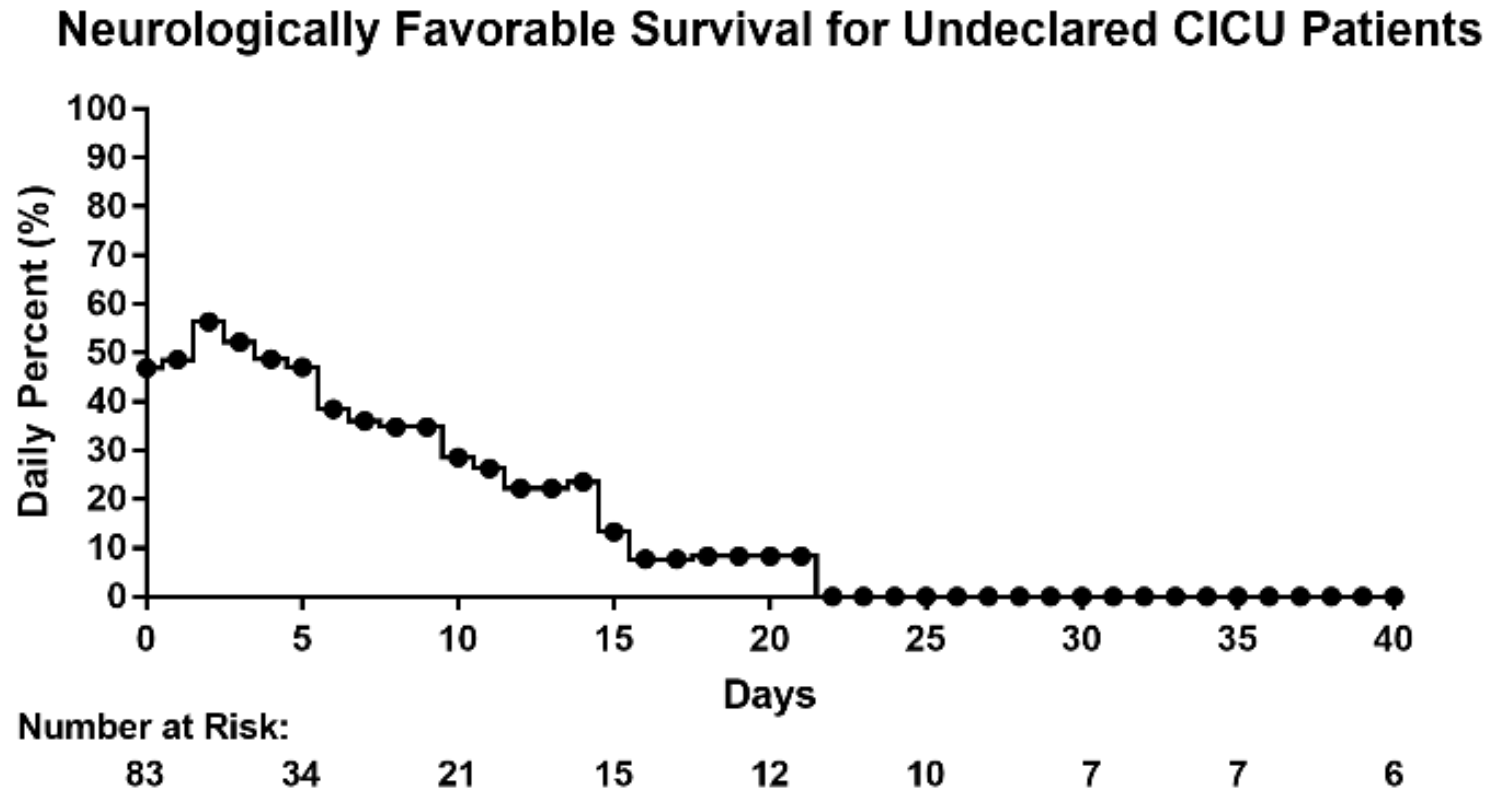
Cause and Timing of Death



Causes of Death (N=37)	N (%)
Recurrent VF Cardiac Arrest	3/37 (8.1%)
Brain Death	14/37 (38%)
Anoxic Brain Injury	12/37 (32%)
Acute Hemorrhagic Shock Due to Intra-Abdominal Bleeding	2/37 (5.4%)
Refractory Shock	4/37 (11%)
	4/37

Bartos et al, Resuscitation, 2018

Odds of Survival Over Hospital Course



The Most Common Cause of Death after Admission for Cardiac Arrest is Withdrawal of Care

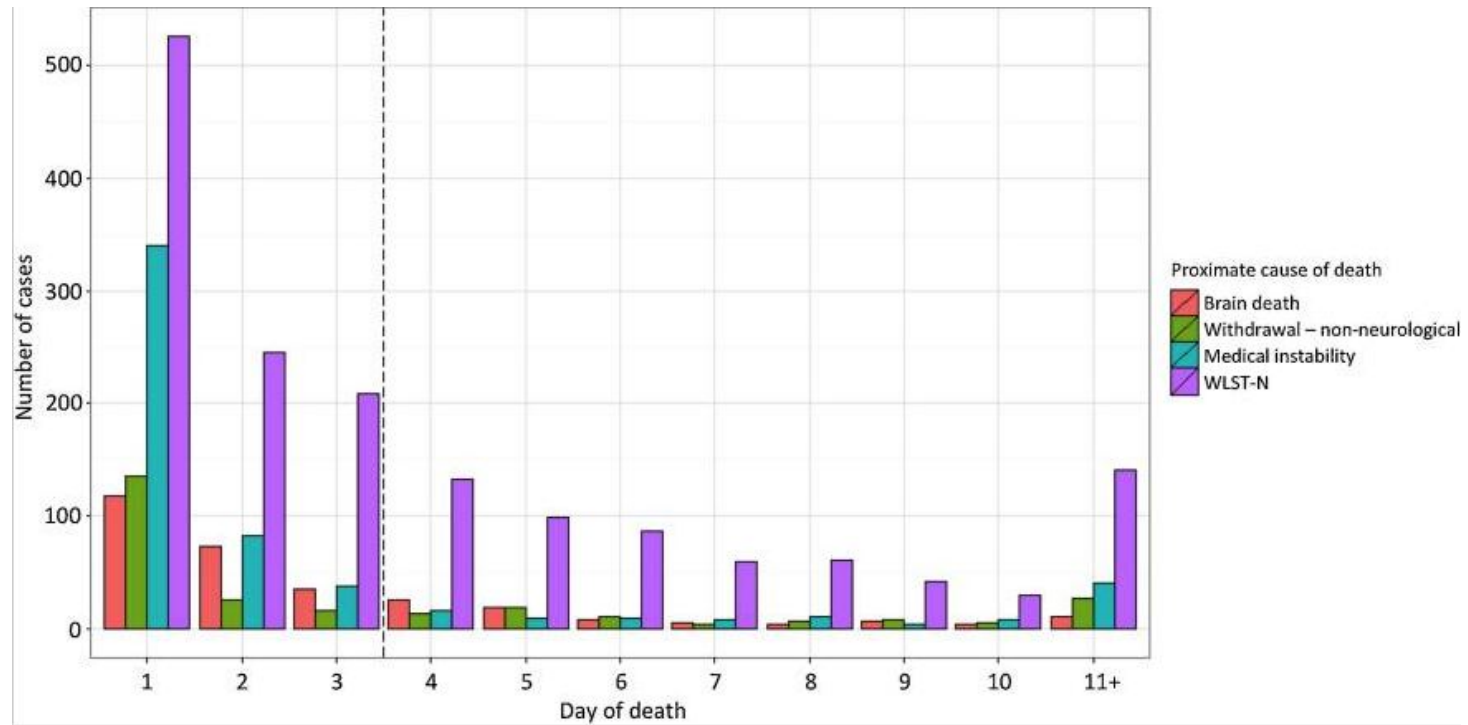
Outcome	Epinephrine	Placebo
Median length of stay in ICU (IQR) — days		
Patients who survived	7.5 (3.0–15.0)	7.0 (3.5–12.5)
Patients who died	2.0 (1.0–5.0)	3.0 (1.0–5.0)

Perkins et al., NEJM, 2018

Prognostication

AHA 2015 Guideline: The earliest time for prognostication using clinical examination in patients treated with TTM may be 72 hours after return to normothermia (Class IIb).

- 22% of all subjects had withdrawal of support before 72 hrs
- Up to 64% may survive



Elmer, Resuscitation, 2016

Conclusions

We are in a new era of resuscitation

- We have new tools to save lives
 - The previous science may not pertain (treatments and prognosis)
 - We need new prognostic tools to decide when good outcomes are possible
 - High quality comprehensive critical care is mandatory for the survival of these patients.
- Patience is survival.

Contact Information

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