Studie, které ovlivnily moji praxi
Mechanické podpory

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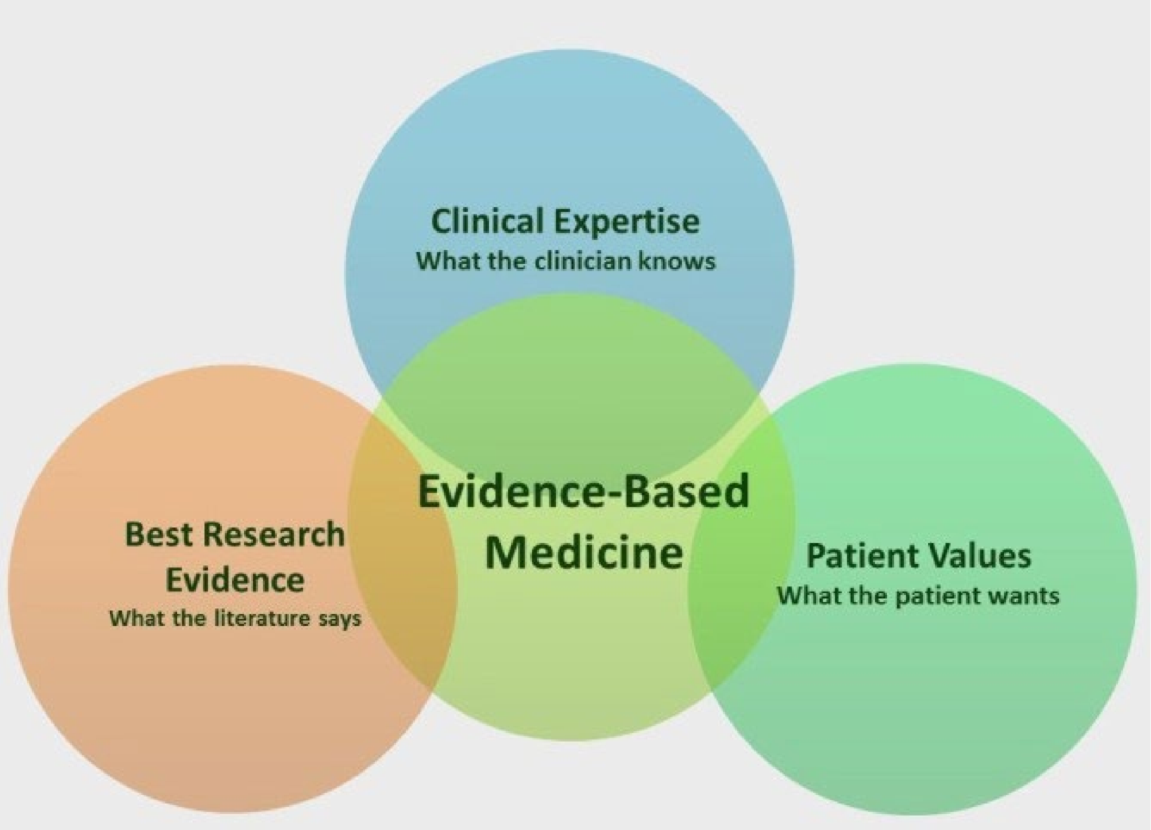
VFN PRAHA

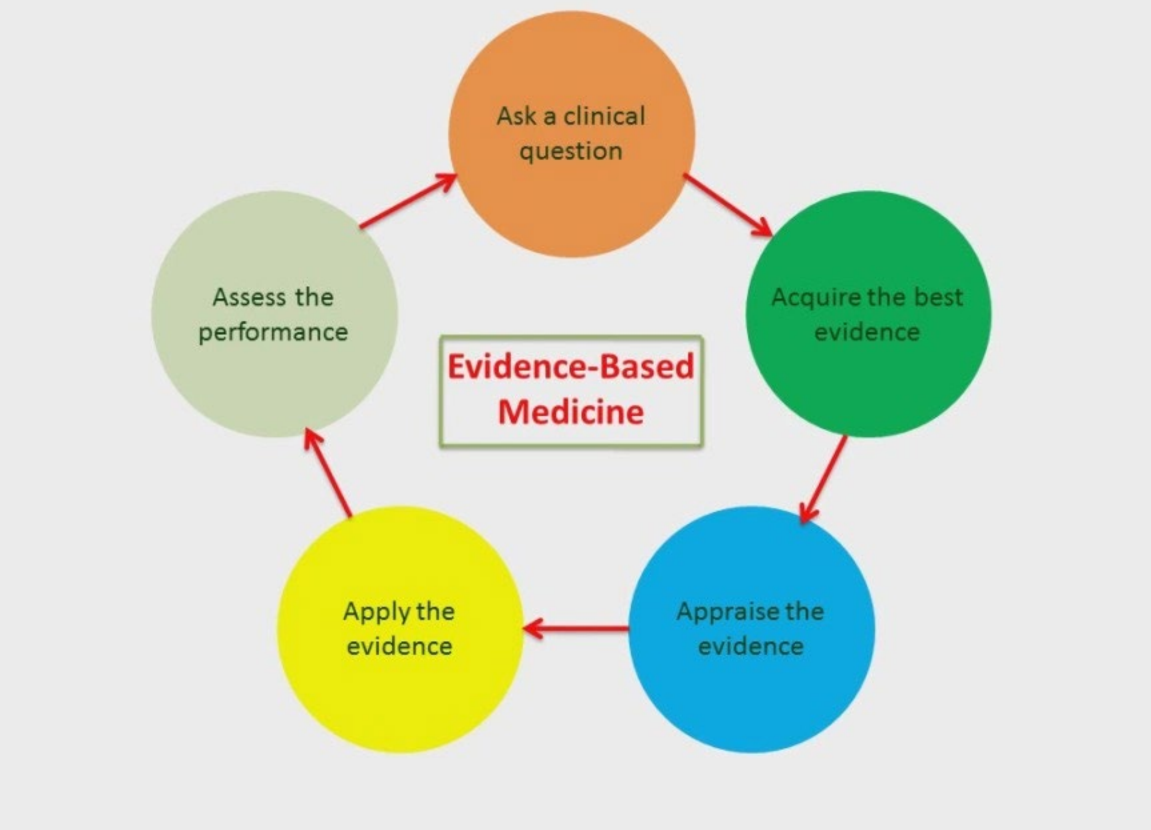
Disclosures

- PI of Prague OHCA study
- Proctor, lecturer for Getinge
- Proctor, lecturer for Abiomed
- Advisory board member and lecturer for Medtronic, Fresenius, AstraZeneca, Novartis, Boehringer Ingelheim, Amgen

Evidence based medicine

…a way to achieve improved quality (survival), improved patient satisfaction, and reduced costs.





Step 1: Ask a clinical question to identify a key problem
Step 2: Acquire the best evidence (medical knowledge) possible
Step 3: Appraise the evidence (make sure it's applicable to the population and the question asked)
Step 4: Apply the evidence to daily clinical practice
Step 5: Assess your performance

Randomized evidence?

- VV – ECMO in adults
  - one positive RCT (Cesar)
  - one negative RCT (Eolia) + individual patients data metaanalysis - positive

- VA – ecmo in adults
  - ECMO-CS RCT (Czech Republic) completed – presented at AHA November 2022
  - ongoing randomized trials (ECLS Shock, EuroShock, Anchor)
  - Danger Shock – Impella vs. Rescue ECMO – ongoing

- ECPR
  - ARREST RCT (30 patients) – positive results
  - Prague OHCA study (mixed results)
  - Metaanalysis of both to be presented at RESS AHA November 2022
  - Inception to be published

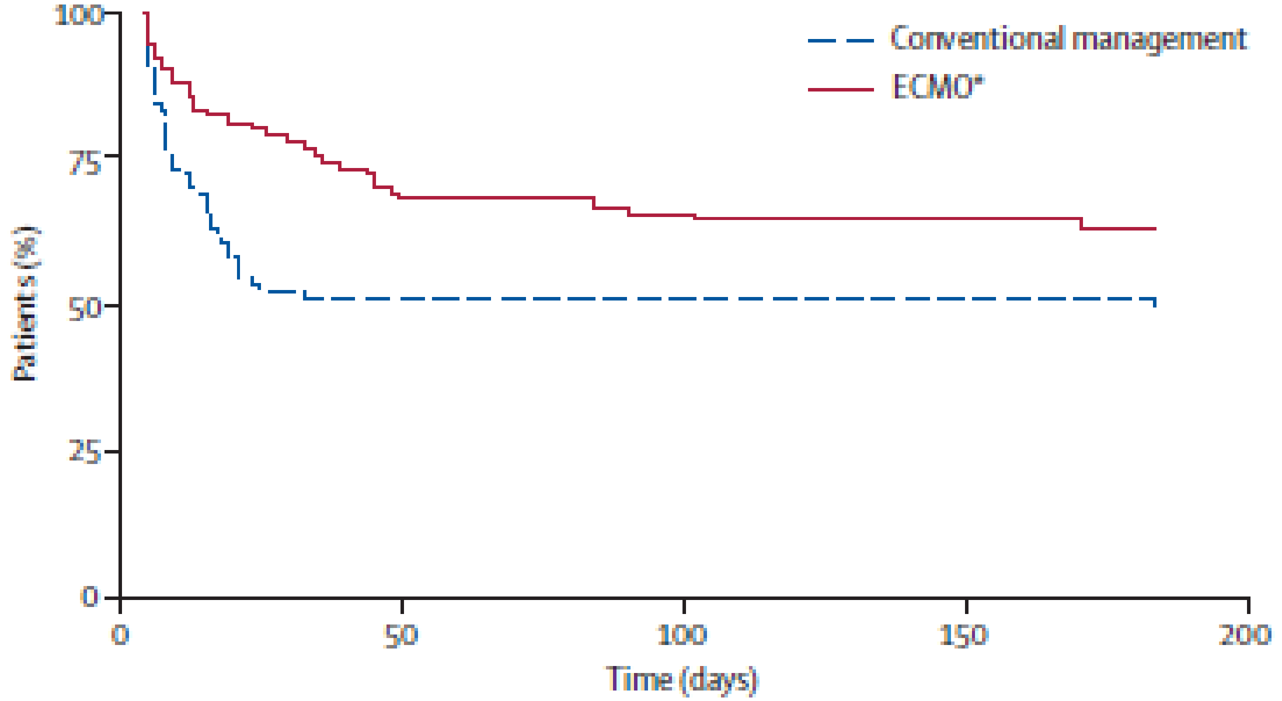
- Unloading

- Translational research

ECMO in ARDS

Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Giles J Peek, Miranda Mugford, Ravindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalanany, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration



Patients at risk					
Conventional management	90	45	44	44	0
ECMO*	90	61	59	58	0

Figure 2: Kaplan-Meier survival estimates
ECMO=extracorporeal membrane oxygenation. *Patients were randomly allocated to consideration for treatment by ECMO, but did not necessarily receive this treatment.

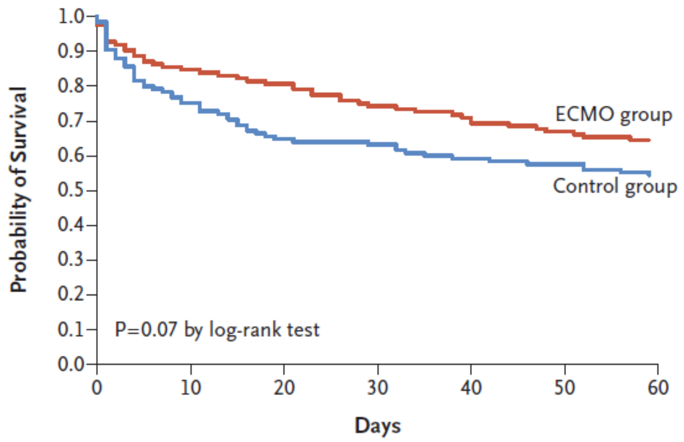
Lancet 2009; 374: 1351–63

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 24, 2018 VOL. 378 NO. 21

Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome

A. Combes, D. Hajage, G. Capellier, A. Demoule, S. Lavoué, C. Guervilly, D. Da Silva, L. Zafrani, P. Tirot, B. Veber, E. Maury, B. Levy, Y. Cohen, C. Richard, P. Kalfon, L. Bouadma, H. Mehdaoui, G. Beduneau, G. Lebreton, L. Brochard, N.D. Ferguson, E. Fan, A.S. Slutsky, D. Brodie, and A. Mercat, for the EOLIA Trial Group, REVA, and ECMONet*



No. at Risk							
ECMO	124	105	100	92	88	83	80
Control	125	94	81	79	74	72	69

Figure 2. Kaplan–Meier Survival Estimates in the Intention-to-Treat Population during the First 60 Days of the Trial.

Intensive Care Med (2020) 46:2048–2057
https://doi.org/10.1007/s00134-020-06248-3

ORIGINAL

ECMO for severe ARDS: systematic review and individual patient data meta-analysis

Alain Combes[1,2*], Giles J. Peek[3], David Hajage[4], Pollyanna Hardy[5], Darryl Abrams[6,7], Matthieu Schmidt[1,2], Agnès Dechartres[4] and Diana Elbourne[8]

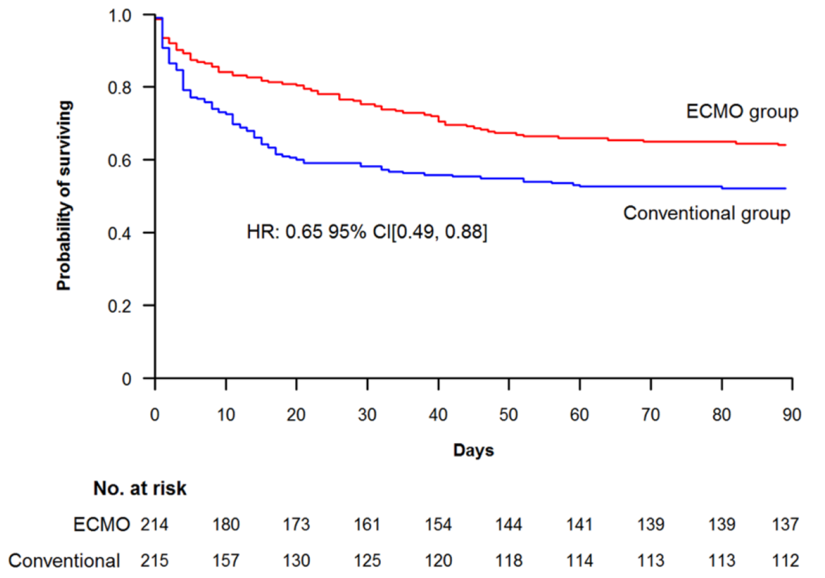


Fig. 2 Kaplan–Meier survival estimates in the intention-to-treat population of the time to death within the first 90 study days

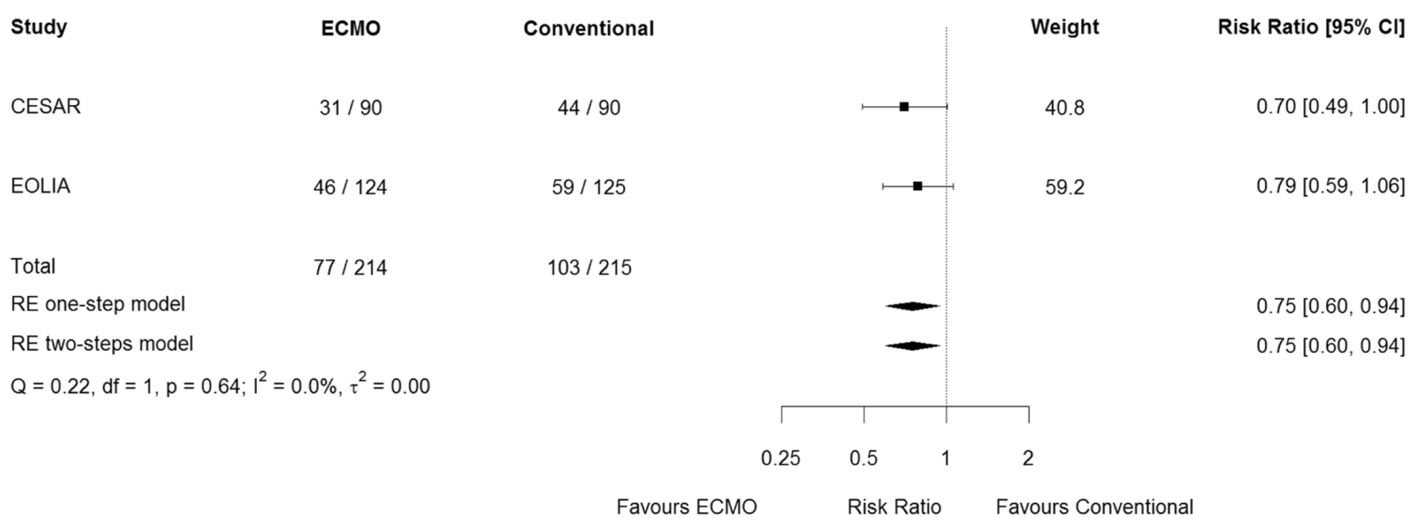
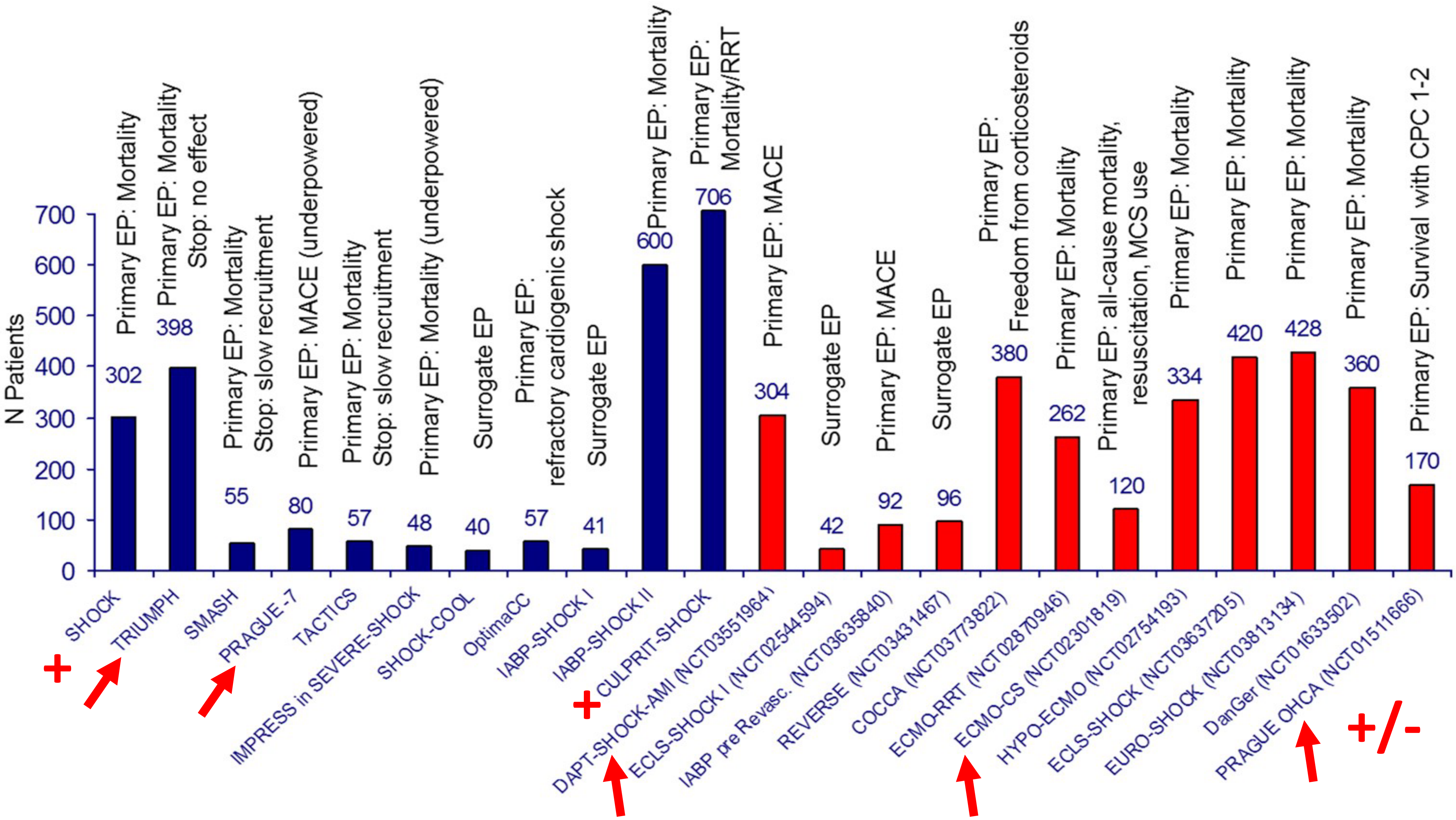


Fig. 1 Forest plot of 90-day mortality in the intention-to-treat population

Cardiogenic shock – cardiac arrest

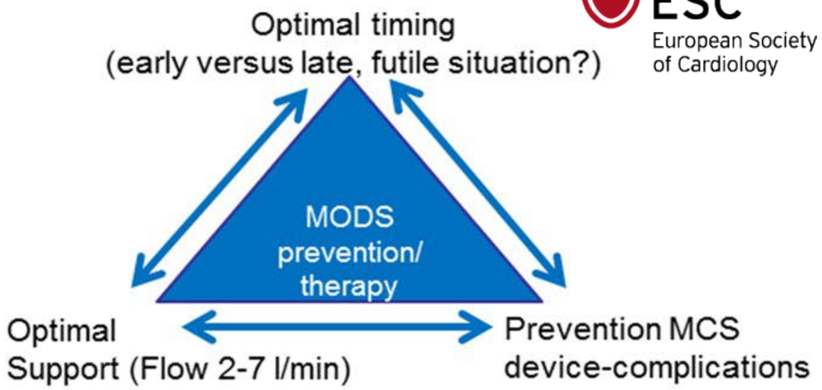
Devices work…but how to prove it?

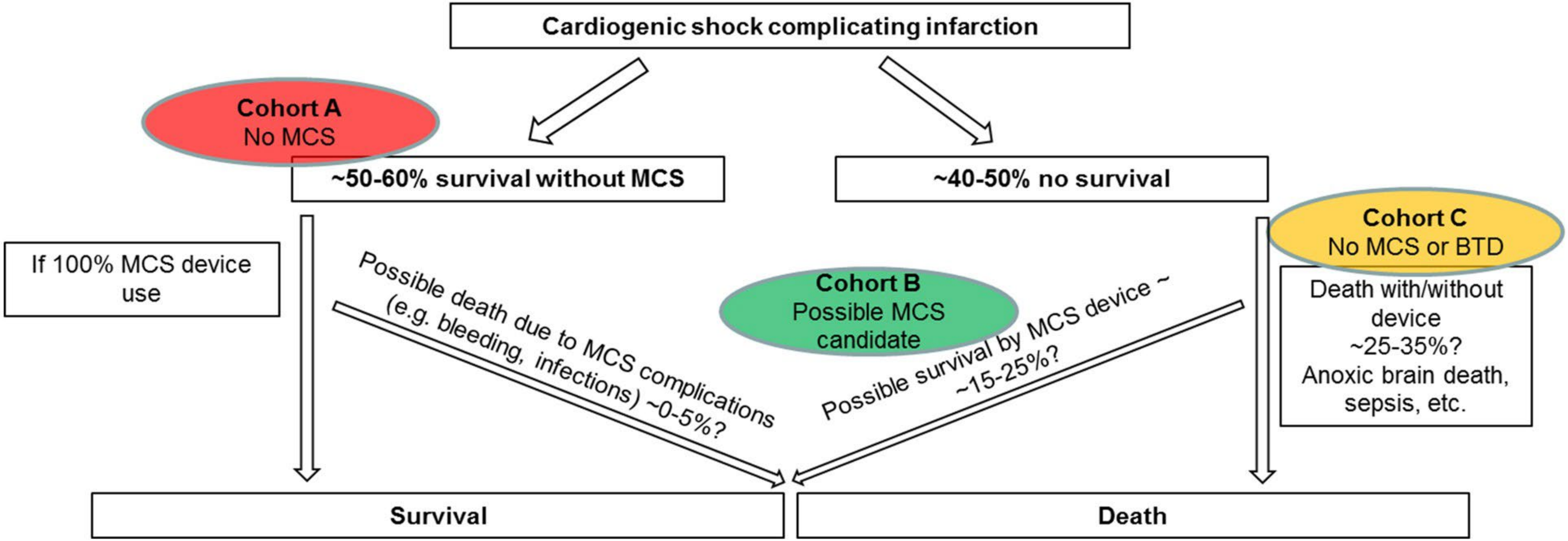
CS trials past and ongoing



Eur Heart J, Volume 40, Issue 32, 21 August 2019, Pages 2671–2683, https://doi.org/10.1093/eurheartj/ehz363

Considerations on use of mechanical circulatory support for MODS prevention and therapy





Eur Heart J, Volume 40, Issue 32, 21 August 2019, Pages 2671–2683, https://doi.org/10.1093/eurheartj/ehz363

Appropriate CS population?

Appropriate CS device?

FIGURE 1 The pyramid of CS classification [Color figure can be viewed at wileyonlinelibrary.com]

SCAI definition 2019

Interactive CardioVascular and Thoracic Surgery 30 (2020) 711–714
doi:10.1093/icvts/ivaa015 Advance Access publication 22 February 2020

BRIEF COMMUNICATION

Cite this article as: Vasin S, Philipp A, Floerchinger B, Rastogi P, Lunz D, Mueller T *et al.* Increasing use of the Impella®-pump in severe cardiogenic shock: a word of caution. Interact CardioVasc Thorac Surg 2020;30:711–4.

Increasing use of the Impella®-pump in severe cardiogenic shock: a word of caution

Sergey Vasin[a], Alois Philipp[a], Bernhard Floerchinger[a], Priyank Rastogi[a], Dirk Lunz[b], Thomas Mueller[c], Christof Schmid[a] and Daniele Camboni[a,*]

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[b] Department of Anesthesiology, University Medical Center Regensburg, Regensburg, Germany
[c] Department of Internal Medicine II, University Medical Center Regensburg, Regensburg, Germany

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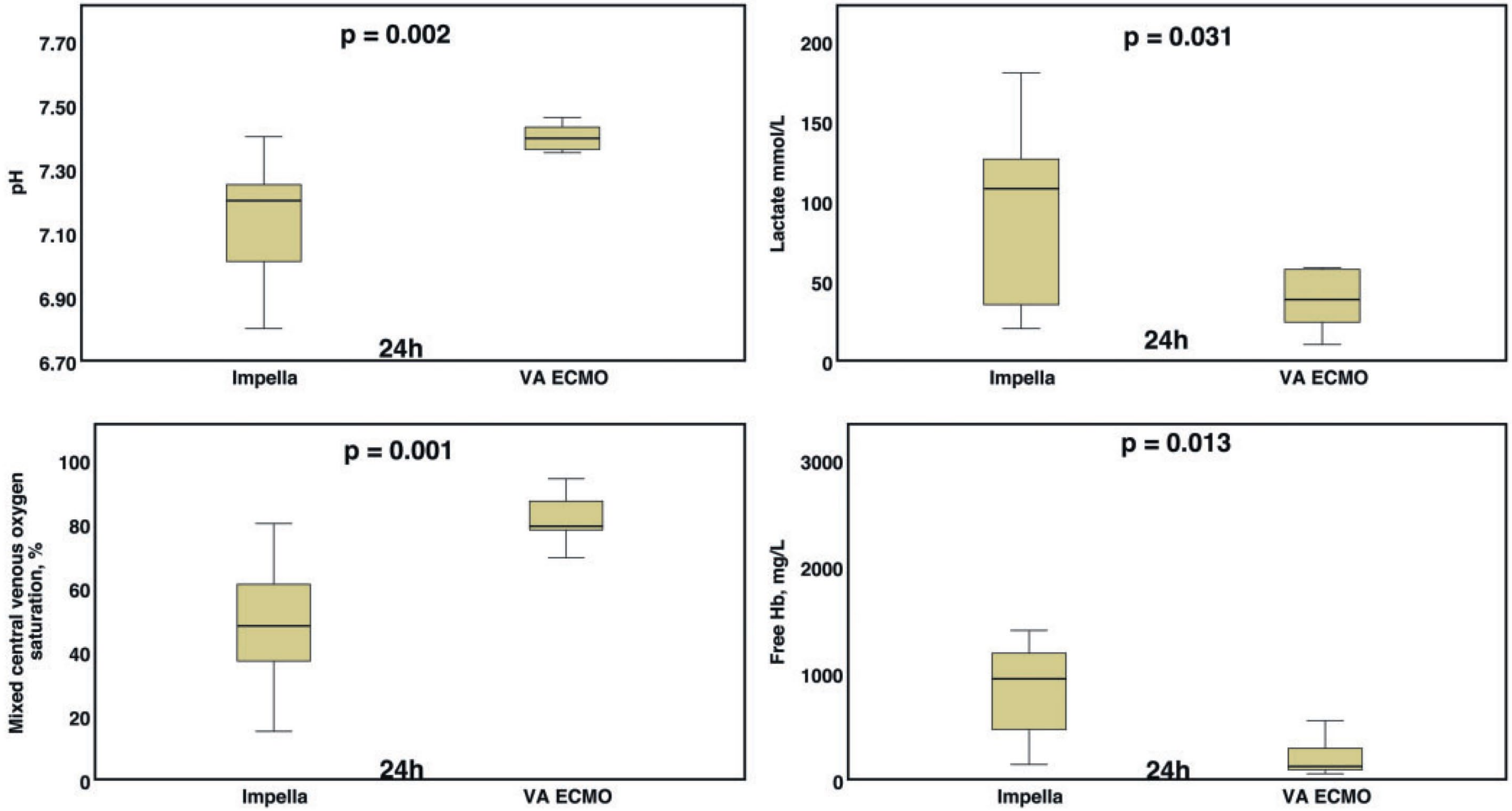


Figure 1: Laboratory data after switch from Impella support to VA ECMO. VA ECMO: venoarterial extracorporeal membrane oxygenation.

These data indicate that the Impella 2.5$_{VR}$ and CP$_{VR}$ might not be sufficient in profound cardiogenic shock.

ECMO CS trial

10.1161/CIRCULATIONAHA.122.062949

Extracorporeal Membrane Oxygenation in the Therapy of Cardiogenic Shock: Results of the ECMO-CS Randomized Clinical Trial

Running title: *Ostadal et al.; ECMO in cardiogenic shock*

Petr Ostadal, MD, PhD[1]; Richard Rokyta, MD, PhD[2]; Jiri Karasek, MD, PhD[3,4]; Andreas Kruger, MD, PhD[1]; Dagmar Vondrakova, MD, PhD[1]; Marek Janotka, MD[1]; Jan Naar, MD, PhD[1]; Jana Smalcova, MD[4]; Marketa Hubatova, MSc[4]; Milan Hromadka, MD, PhD[3]; Stefan Volovar, MD[3]; Miroslava Seyfrydova, MD[3]; Jiri Jarkovsky, PhD[5]; Michal Svoboda, MSc[6]; Ales Linhart, MD, PhD[4]; Jan Belohlavek, MD, PhD[4]; for the ECMO-CS Investigators

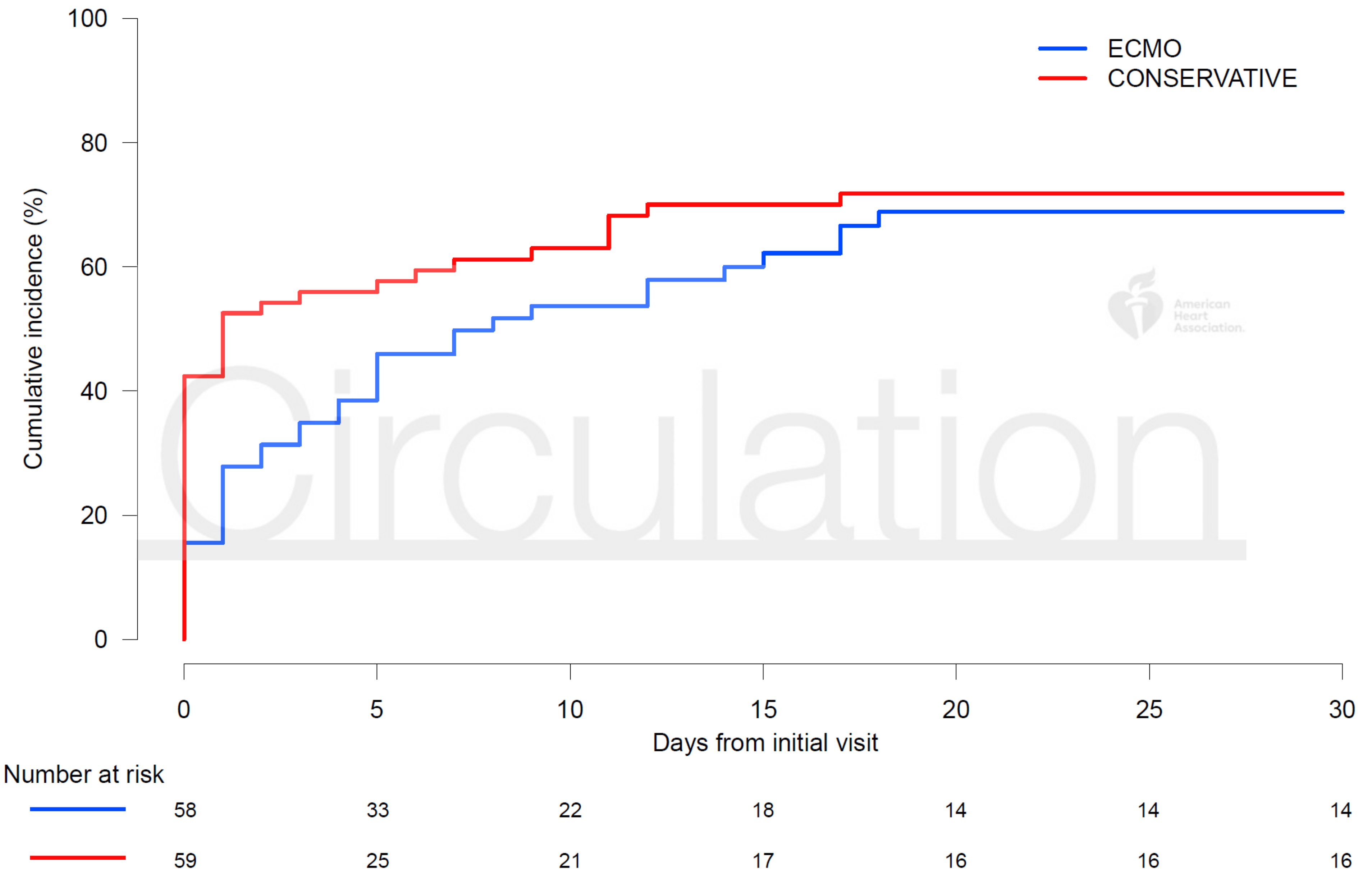
Table 2. Baseline characteristics

Characteristic	All	VA-ECMO	Conservative	P-value
	N = 117	N = 58	N = 59	
Sex - no. (%)				
Male	86 (73.5 %)	43 (74.1 %)	43 (72.9 %)	0.878
Female	31 (26.5 %)	15 (25.9 %)	16 (27.1 %)	
Age - years (IQR)	66 (59; 73)	67 (60; 74)	65 (58; 71)	0.356
Medical history - no. (%)				
Chronic coronary syndrome	39 (34.2 %)	21 (37.5 %)	18 (31.0 %)	0.467
Chronic heart failure	27 (23.7 %)	14 (25.0 %)	13 (22.4 %)	0.745
Dilated cardiomyopathy	15 (13.3 %)	6 (10.9 %)	9 (15.5 %)	0.471
Chronic renal failure	16 (14.2 %)	7 (12.5 %)	9 (15.8 %)	0.616
Periphery artery disease	10 (8.8 %)	3 (5.5 %)	7 (11.9 %)	0.324
Hypertension	73 (64.0 %)	35 (62.5 %)	38 (65.5 %)	0.737
Diabetes	37 (32.5 %)	16 (28.6 %)	21 (36.2 %)	0.384
Current smoker	41 (36.9 %)	14 (25.9 %)	27 (47.4 %)	0.019
Clinical parameters at randomization - median (IQR)				
Blood lactate (mmol/L)	5.0 (3.2; 8.0)	5.3 (3.1; 8.4)	4.7 (3.3; 7.4)	0.960
Systolic blood pressure (mmHg)	85.0 (80.0; 100.0)	84.0 (80.0; 95.0)	89.0 (79.5; 105.0)	0.282
Mean arterial pressure (mmHg)	63.3 (55.3; 72.0)	63.3 (56.7; 68.7)	64.5 (54.3; 75.3)	0.289
Heart rate (beats/min)	102.0 (84.0; 120.0)	110.0 (86.5; 130.0)	100.0 (82.0; 110.0)	0.076
Therapy at randomization - no. (%)				
Intra-aortic balloon pump	15 (13.3 %)	6 (10.9 %)	9 (15.5 %)	0.471
Mechanical ventilation	81 (72.3 %)	41 (74.5 %)	40 (70.2 %)	0.605
Renal replacement therapy	7 (6.2 %)	4 (7.3 %)	3 (5.2 %)	0.712
Norepinephrine	100 (85.5 %)	50 (86.2 %)	50 (84.7 %)	
Norepinephrine dose [µg/kg/min]	0.50 (0.23; 1.24)	0.48 (0.23; 1.36)	0.50 (0.27; 1.19)	0.741
Epinephrine	4 (3.4 %)	1 (1.7 %)	3 (5.1 %)	

10.1161/CIRCULATIONAHA.122.062949

Epinephrine dose [µg/kg/min]	0.26 (0.14; 0.80)	0.21 (0.21; 0.21)	0.30 (0.07; 1.30)	0.999
Dobutamine	64 (54.7 %)	31 (53.4 %)	33 (55.9 %)	
Dobutamine dose [µg/kg/min]	5.1 (4.9; 8.0)	6.1 (5.0; 9.7)	5.1 (4.7; 7.6)	0.492
Milrinone	38 (32.5 %)	22 (37.9 %)	16 (27.1 %)	
Milrinone dose [µg/kg/min]	0.40 (0.30; 0.50)	0.40 (0.30; 0.50)	0.40 (0.37; 0.51)	0.389
Vasopressin	41 (35.0 %)	19 (32.8 %)	22 (37.3 %)	
Vasopressin dose [U/kg/min]	0.0017 (0.0010; 0.0025)	0.0020 (0.0010; 0.0030)	0.0017 (0.0012; 0.0022)	0.824
Levosimendan	32 (29.4 %)	20 (37.0 %)	12 (21.8 %)	0.081
Vasoactive-inotropic score - median (IQR)	61.0 (30.0; 124.0)	59.9 (32.8; 121.5)	61.0 (28.0; 124.9)	0.976
Cause of cardiogenic shock				
ST-elevation myocardial infarction	59 (50.4 %)	30 (51.7 %)	29 (49.2 %)	0.854
Non-ST-elevation myocardial infarction	14 (12.0 %)	7 (12.1 %)	7 (11.9 %)	0.999
Decompensation of chronic heart failure	27 (23.1 %)	14 (24.1 %)	13 (22.0 %)	0.829
Mechanical complications of myocardial infarction	3 (2.6 %)	1 (1.7 %)	2 (3.4 %)	0.999
Other	14 (12.0 %)	6 (10.3 %)	8 (13.6 %)	0.777

Other causes of cardiogenic shock include myocarditis, aortic stenosis and mitral regurgitation. IQR, interquartile range



ECMO
CONSERVATIVE
Cumulative incidence (%)
100
80
60
40
20
0
0
5
10
15
20
25
30
Days from initial visit
Number at risk
58 33 22 18 14 14 14
59 25 21 17 16 16 16

ASAIO J. 2019 Nov/Dec;65(8):819-826.

Improving Outcomes in INTERMACS Category 1 Patients with Pre-LVAD, Awake Venous-Arterial Extracorporeal Membrane Oxygenation Support.

Mori M et al.

19 z 83 pacientů pro durable LVAD

Artificial Organs

N=23

Main Text Article

Cardiac Awake Extracorporeal Life Support—Bridge to Decision?

Wiebke Sommer, Georg Marsch, Tim Kaufeld, Philipp Röntgen, Gernot Beutel, Joern Tongers, Gregor Warnecke, Igor Tudorache, Bernhard Schieffer, Axel Haverich, Christian Kühn

First published: 16 January 2015 | https://doi.org/10.1111/aor.12396 |

Interactive CardioVascular and Thoracic Surgery 20 (2015) 755–760
doi:10.1093/icvts/ivv057 Advance Access publication 21 March 2015

ORIGINAL ARTICLE – ADULT CARDIAC

Cite this article as: Mohite PN, Kaul S, Sabashnikov A, Rashid N, Fatullayev J, Zych B *et al*. Extracorporeal life support in patients with refractory cardiogenic shock: keep them awake. Interact CardioVasc Thorac Surg 2015;20:755–60.

Extracorporeal life support in patients with refractory cardiogenic shock: keep them awake

Prashant N. Mohite*, Sundeep Kaul, Anton Sabashnikov, Naufal Rashid, Javid Fatullayev, Bartlomiej Zych, Aron-Frederik Popov, Olaf Maunz, Nikhil P. Patil, Diana Garcia-Saez, Fabio DeRobertis, Toufan Bahrami, Mohamed Amrani, Nicholas R. Banner and Andre R. Simon

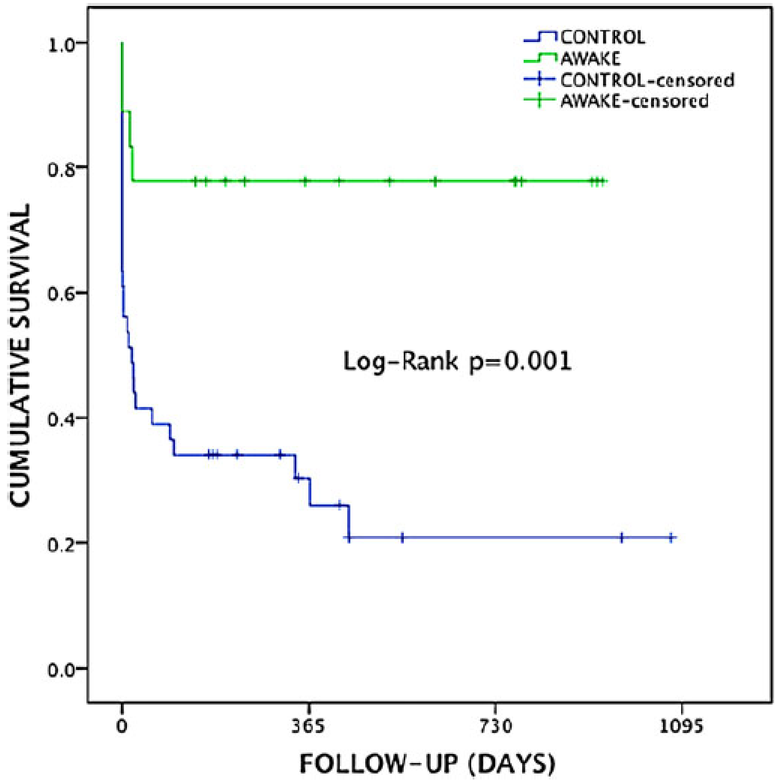
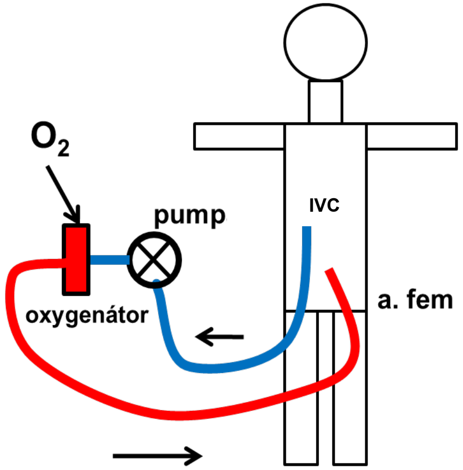


Figure 1: Kaplan–Meier survival estimate for awake and control groups ($P = 0.001$)

ECPR

Extracorporal CPR

- continuation in CPR using mechanical circulatory support
- VA-ECMO – other devices?

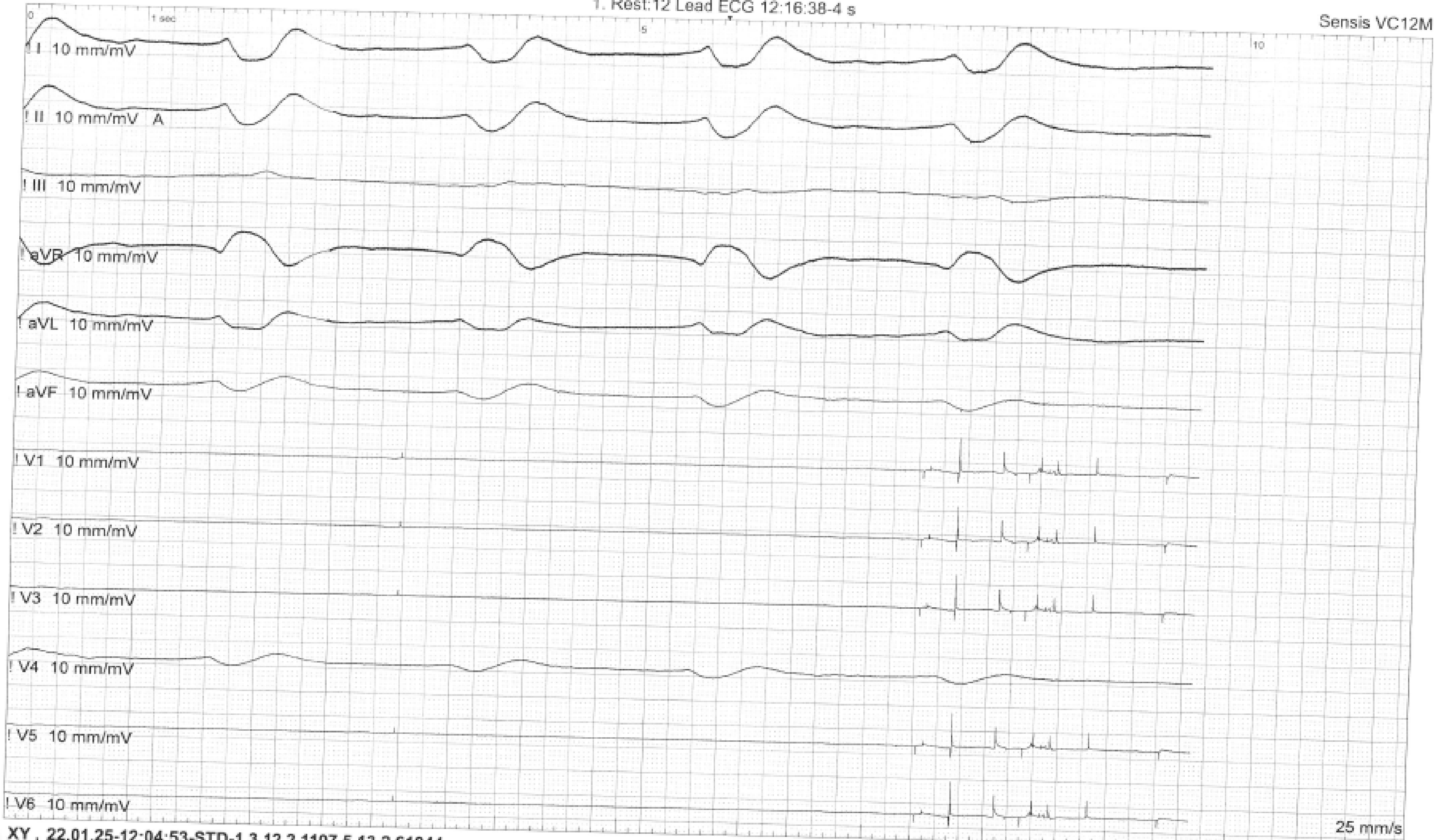


Bělohlávek et al. Interv Acute Cardiol 2010; 9(3): 121–128

SIEMENS

1. Rest:12 Lead ECG 12:16:38-4 s

Sensis VC12M



25 mm/s

XY , 22.01.25-12:04:53-STD-1.3.12.2.1107.5.13.2.61044

Study: Coronary^Diagnostic ...

Date: 25-Jan-22

SIEMENS

1. Rest:12 Lead ECG 12:17:42-4 s

Sensis VC12M

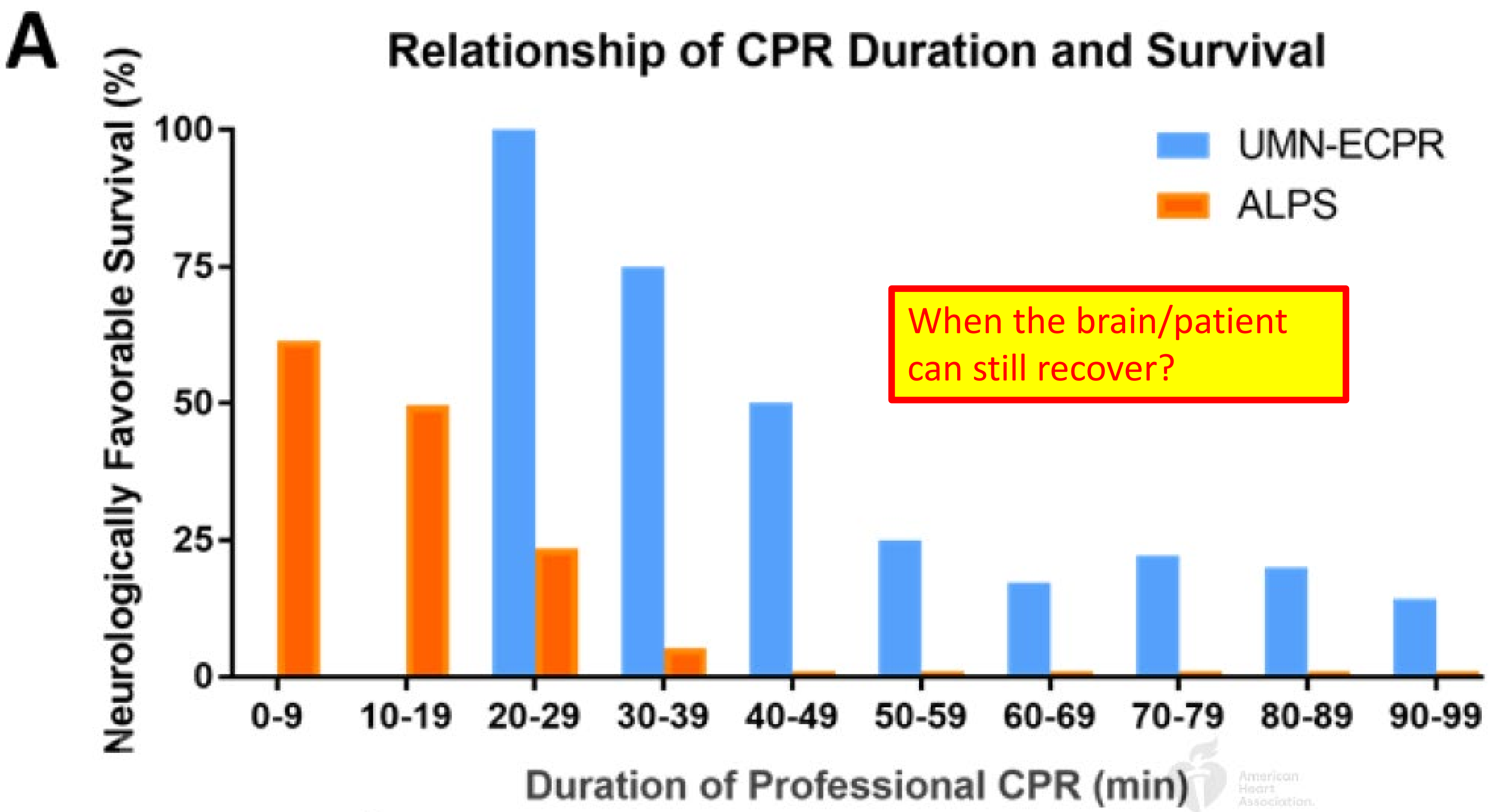
XY , 22.01.25-12:04:53-STD-1.3.12.2.1107.5.13.2.61044

Study: Coronary^Diagnostic ...

Date: 25-Jan-22

CPR for 72 mins

Provided informed consent



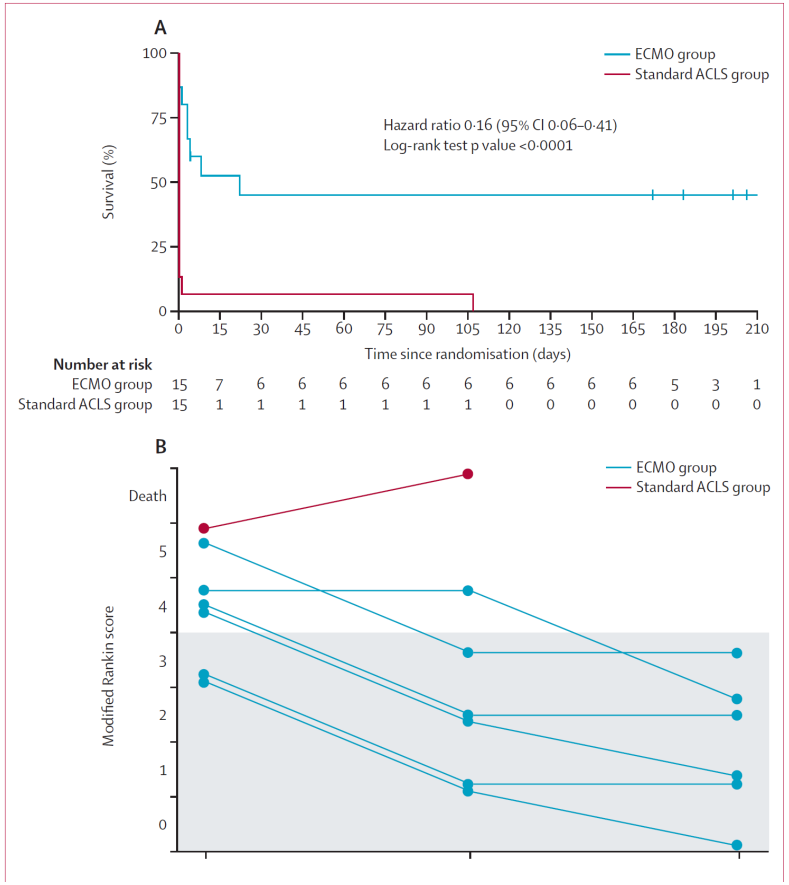
Patients at Risk

Time (min)	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	Total
UMN-ECPR	0	0	8	12	20	36	35	27	15	7	160
ALPS	70	151	102	95	99	69	29	11	3	7	636

BartosJA….Yannopoulus D et al. Circulation 2020

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



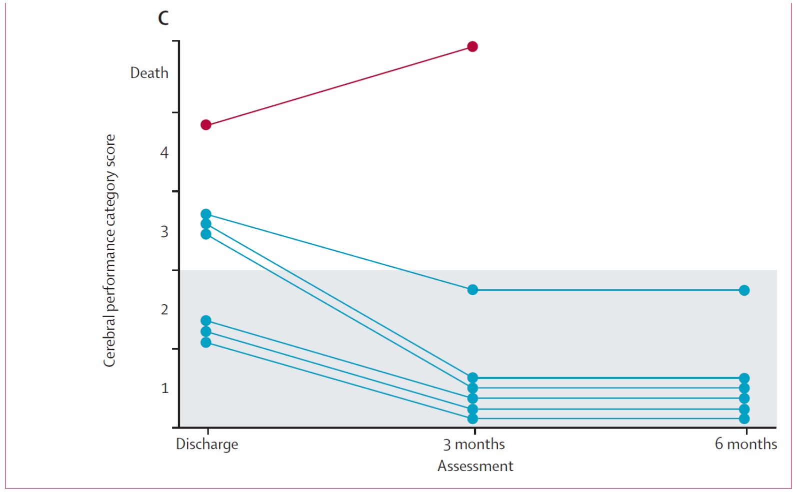


Figure 2: **Cumulative survival after randomisation (A) and functional scores in all survivors at hospital discharge and at 3 months and 6 months after discharge (B, C)**
(A) Kaplan-Meier plot showing cumulative survival of patients from the index cardiac arrest to 6 months after discharge. Blinded modified Rankin scale (B) and cerebral performance category scale (C) scores in survivors at hospital discharge and 3 months and 6 months after hospital discharge. Neurological function was mainly preserved, and functional status scores were significantly improved after physical therapy and rehabilitation. Grey shading denotes the favourable range of neurological survival scores. ECMO=extracorporeal membrane oxygenation. ACLS=advanced cardiac life support.

www.thelancet.com **Published online November 13, 2020 https://doi.org/10.1016/S0140-6736(20)32338-2**

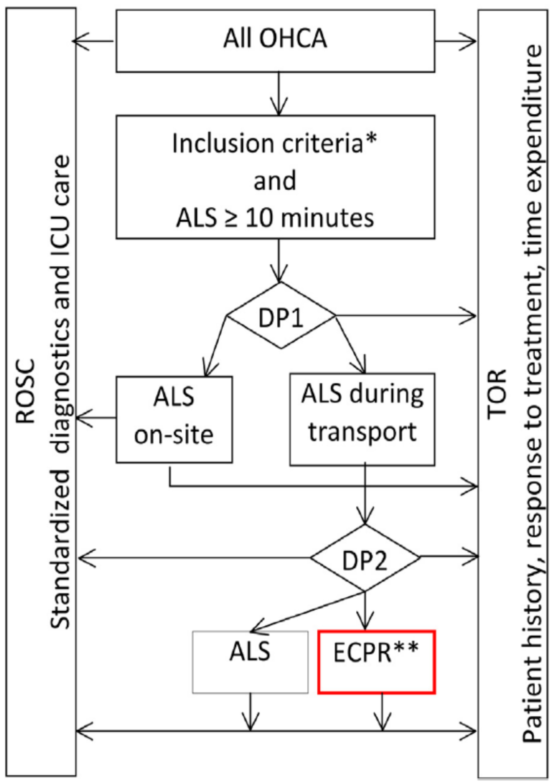


Fig. 1 – Flow diagram for selection of patients eligible for ECPR. *Inclusion criteria see Table 1. **ECPR was only available to selected patients after protocol implementation. DP1—prehospital anesthesiologist decides if patient meets criteria, and decide further treatment based on patient history, response to treatment and expected evacuation time.
DP2—Emergency room team reconsider if patient still meets criteria, supported by patient journal, response to treatment and time expenditure. ROSC—return of spontaneous circulation, ICU—intensive care unit, OHCA—out-of-hospital cardiac arrest, ALS—advanced life support, DP—decision point, ECPR—extracorporeal cardiopulmonary resuscitation, TOR—Termination of resuscitation.

RESUSCITATION 162 (2021) 35 –42

Available online at www.sciencedirect.com

Resuscitation

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

EUROPEAN RESUSCITATION COUNCIL

Clinical paper

Outcome in refractory out-of-hospital cardiac arrest before and after implementation of an ECPR protocol

Kristin Alm-Kruse[a,b,*], *Gro Sørensen*[c], *Svein Are Osbakk*[d], *Kjetil Sunde*[b,e], *Bjørn Bendz*[b,c], *Geir Øystein Andersen*[f], *Arnt Fiane*[b,c], *Ove Andreas Hagen*[c], *Jo Kramer-Johansen*[b,d]

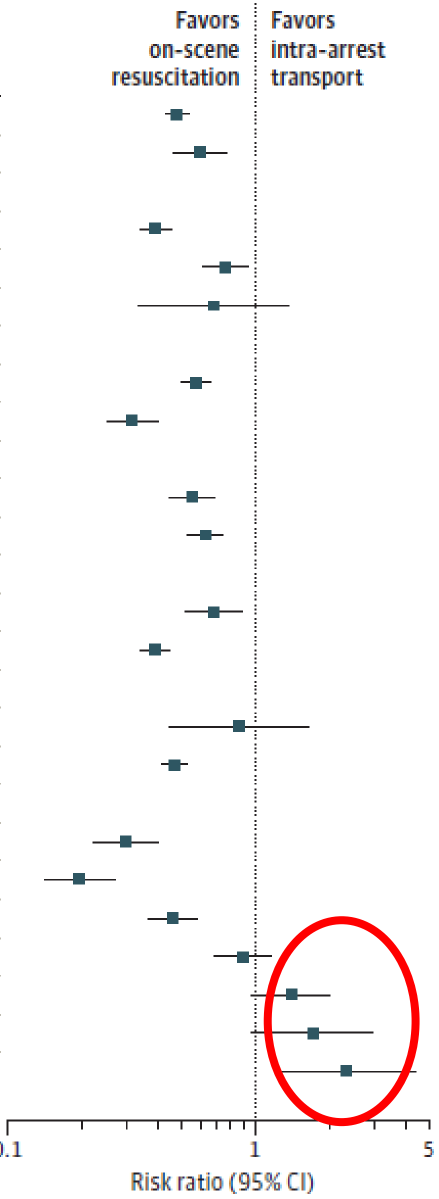
	ECPR candidates		
Outcome	Before n = 48	After n = 100	p-value
Sustained ROSC* (%)	30 (63)	50 (50)	0.2
24 -h survival (%)	29 (60)	52 (52)	0.3
30 days survival (%)	21 (44)	37 (37)	0.4
CPC score 1–2** (%)	21 (100)	30 (81)	0.03
ALS during transport and on arrival to hospital (%)	7 (15)	26 (26)	0.1
Time from CA to arrival at hospital			0.3
≤40 min	2	14	
41–59 min	2	8	
≥60 min	3	4	

Conclusions

The implementation of the ECPR protocol did not increase survival after OHCA in our system. Quality in the chain of survival might be equally important to increase the chance of ROSC and survival even in patients with prolonged cardiac arrest duration.

Figure 3. Adjusted Analyses Examining the Association of Intra-arrest Transport and Survival Among the Full Propensity-Matched Cohort and Subgroups

	No. of events/patients On-scene resuscitation	No. of events/patients Intra-arrest transport	Risk ratio (95% CI)	Interaction P value
Full cohort	1557/18 299	372/9406	0.48 (0.43-0.54)	
Neurological outcome	733/10 317	148/5066	0.60 (0.47-0.76)	
EMS level of care				.001
ALS first	936/9709	213/5603	0.40 (0.34-0.46)	
ALS second	599/8355	143/3353	0.75 (0.61-0.93)	
BLS only	22/235	16/450	0.68 (0.34-1.35)	
EMS witnessed				.001
Yes	313/2021	98/1557	0.58 (0.50-0.66)	
No	1244/16 278	274/7849	0.32 (0.25-0.41)	
Initial shockable rhythm				.38
Yes	1101/4045	230/2401	0.55 (0.45-0.68)	
No	456/14 254	142/7005	0.63 (0.53-0.74)	
EMS witnessed or shockable				.001
Yes	1272/5727	293/3753	0.68 (0.52-0.89)	
No	285/12 572	79/5653	0.39 (0.34-0.45)	
Mechanical chest compressions				.08
Yes	47/832	19/505	0.85 (0.45-1.62)	
No	1510/17 467	353/8901	0.47 (0.42-0.53)	
Time-based epochs, min				.001
0-5	490/1319	49/411	0.30 (0.22-0.41)	
5-10	472/2013	45/849	0.20 (0.14-0.27)	
10-15	341/3619	96/1757	0.47 (0.37-0.59)	
15-20	145/3815	86/2031	0.90 (0.69-1.17)	
20-25	65/3322	51/1837	1.40 (0.97-2.01)	
25-30	27/2112	25/1220	1.70 (0.97-2.98)	
>30	17/2099	20/1301	2.31 (1.22-4.38)	



JAMA. 2020;324(11):1058-1067. doi:10.1001/jama.2020.14185

Belohlavek et al. Journal of Translational Medicine 2012, 10:163
http://www.translational-medicine.com/content/10/1/163

JOURNAL OF TRANSLATIONAL MEDICINE

PROTOCOL Open Access

Hyperinvasive approach to out-of hospital cardiac arrest using mechanical chest compression device, prehospital intraarrest cooling, extracorporeal life support and early invasive assessment compared to standard of care. A randomized parallel groups comparative study proposal. "Prague OHCA study"

Jan Belohlavek[1*], Karel Kucera[2], Jiri Jarkovsky[3], Ondrej Franek[2], Milana Pokorna[2], Jiri Danda[2], Roman Skripsky[2], Vit Kandrnal[3], Martin Balik[4], Jan Kunstyr[4], Jan Horak[1], Ondrej Smid[1], Jaroslav Valasek[2], Vratislav Mrazek[1], Zdenek Schwarz[2] and Ales Linhart[1]

Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Intra-arrest Transport, Extracorporeal Cardiopulmonary Resuscitation, and Immediate Invasive Assessment and Treatment on Functional Neurologic Outcome in Refractory Out-of-Hospital Cardiac Arrest
A Randomized Clinical Trial

Jan Belohlavek, MD, PhD; Jana Smalcova, MD; Daniel Rob, MD; Ondrej Franek, MD; Ondrej Smid, MD; Milana Pokorna, MD, PhD; Jan Horák, MD; Vratislav Mrazek, MD; Tomas Kovarnik, MD, PhD; David Zemanek, MD, PhD; Ales Kral, MD, PhD; Stepan Havranek, MD, PhD; Petra Kavalkova, PhD; Lucie Kompelentova, MD; Helena Tomková, MD; Alan Mejstrik, MSc; Jaroslav Valasek, MD; David Peran, MSc; Jaroslav Pekara, MSc; Jan Rulisek, MD, PhD; Martin Balik, MD, PhD; Michal Huptych, PhD; Jiri Jarkovsky, PhD; Jan Malik, MD, PhD; Anna Valerianova, MD, PhD; Frantisek Mlejnsky, MSc, PhD; Petr Kolouch, MD; Petra Havrankova, MD, PhD; Dan Romportl, MD; Arnost Komarek, PhD; Ales Linhart, MD, PhD; for the Prague OHCA Study Group

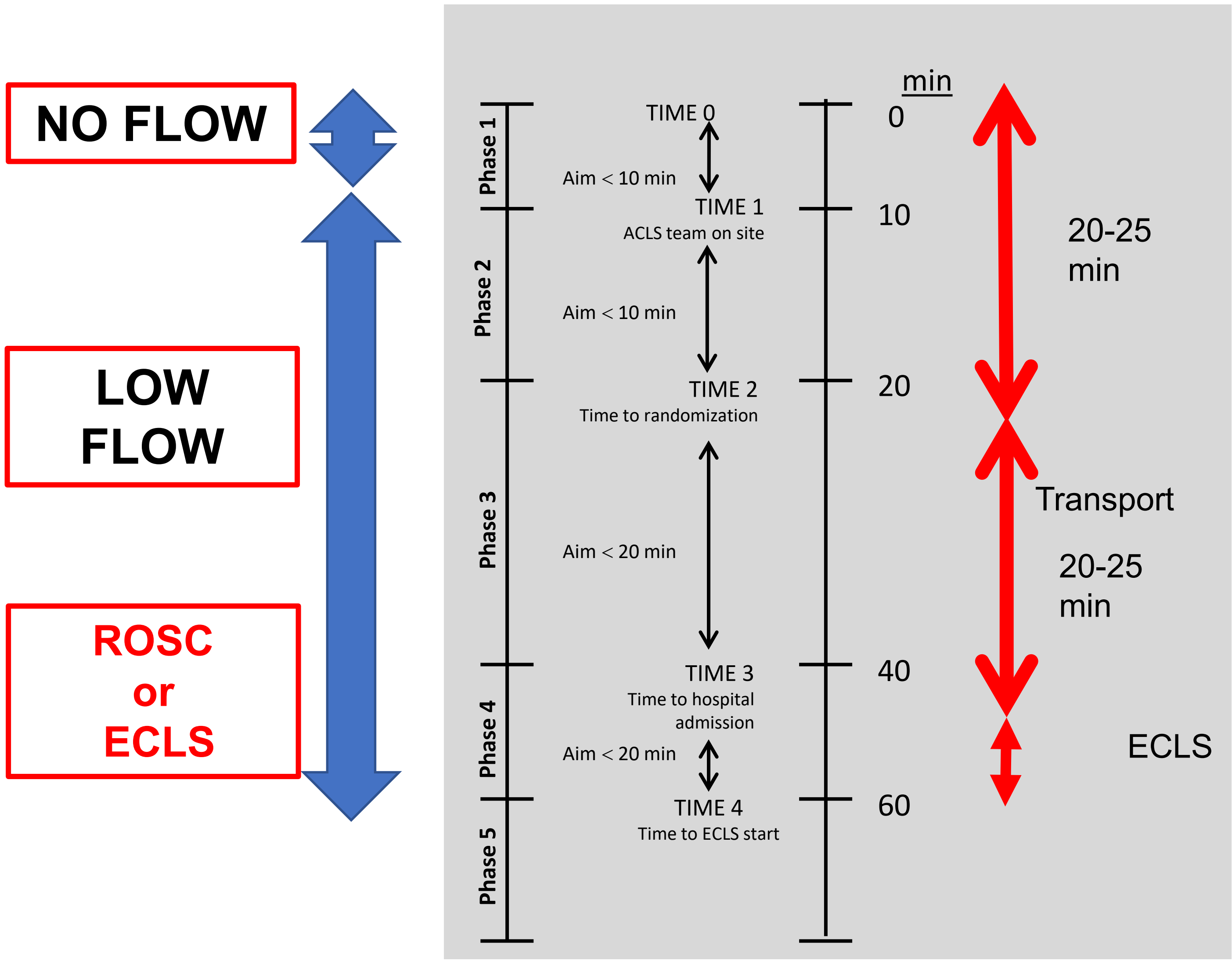
IMPORTANCE Out-of-hospital cardiac arrest (OHCA) has poor outcome. Whether intra-arrest transport, extracorporeal cardiopulmonary resuscitation (ECPR), and immediate invasive

Visual Abstract

Supplemental content

JAMA, in press, Feb 22, 2022

Prague OHCA proposed and real time outlines



Telephone bystander CPR
3 (2-5) mins

Decision – 24 (21-30) mins

Transport – 26 (19-33) mins

Admission 49 (44-60) mins

Time to ECLS **61** (44-60) mins

12 mins cannulation

Belohlavek J. et al., J Transl Med, 2012

Belohlavek J. et al., JAMA, Feb 22, 2022

Results

10% presumed

Table 2. Primary and Secondary Outcomes in a Study of Intra-arrest Transport, Extracorporeal Cardiopulmonary Resuscitation, and Immediate Invasive Assessment and Treatment in Refractory Out-of-Hospital Cardiac Arrest

	No. (%)			
	Invasive strategy (n = 124)	Standard strategy (n = 132)	Absolute difference, % (95% CI)	*P* value
Primary outcome				
Survival with minimal or no neurologic impairment at 180 d[a]	39 (31.5)	29 (22.0)	9.5 (−1.3 to 20.1)	.09
Secondary outcomes				
Survival with minimal or no neurologic impairment at 30 d[a]	38 (30.6)	24 (18.2)	12.4 (1.9 to 22.7)	.02
Cardiac recovery at 30 d[b]	54 (43.5)	45 (34.1)	9.4 (−2.5 to 21)	.12

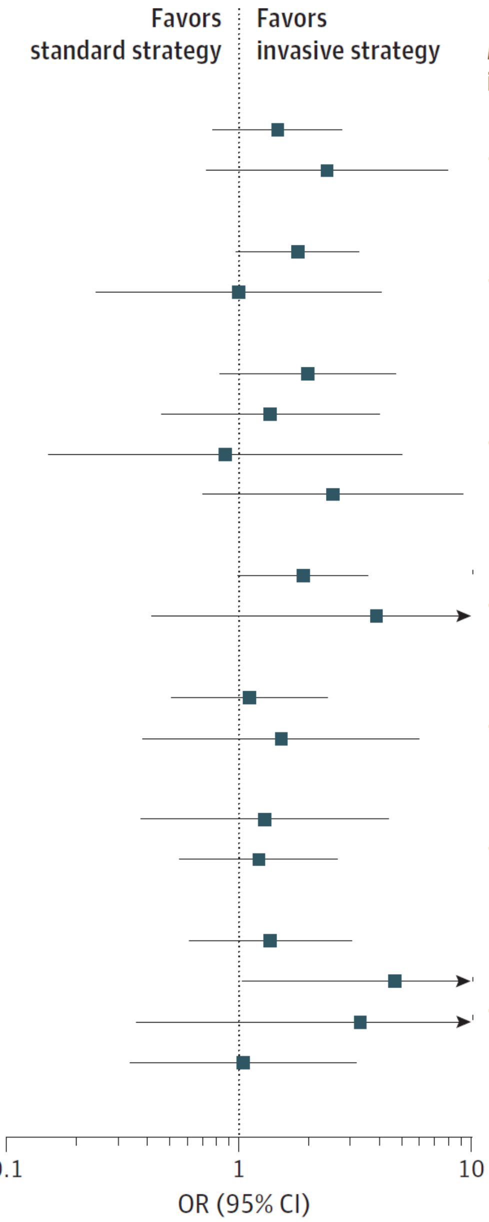
[a] Defined as Cerebral Performance Category 1 or 2. The Cerebral Performance Category schema ranges from 1 (defined as conscious, alert, able to work), 2 (conscious, sufficient cerebral function for independent activities of daily life, able to work in sheltered environment), 3 (conscious, dependent on others for daily support), 4 (comatous, vegetative state) to 5 (defined as brain death). All patients observed to death or 180 days.

[b] Defined as absence of both pharmacological and mechanical cardiac support for at least 24 hours.

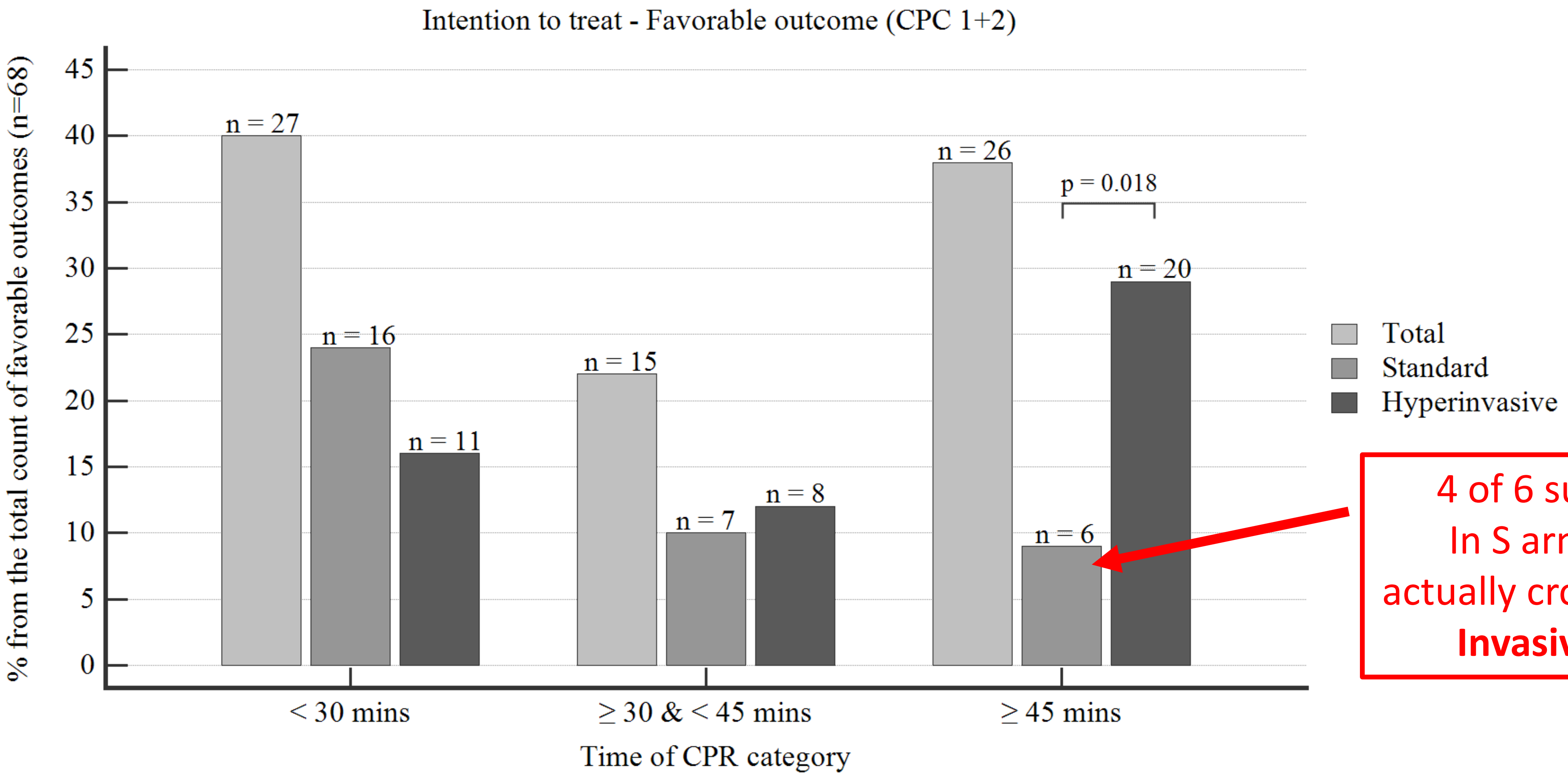
Subgroup analysis

Figure 2. Post Hoc Analysis, Primary Outcome According to Subgroups in a Study of Intra-arrest Transport, Extracorporeal Cardiopulmonary Resuscitation, and Immediate Invasive Assessment and Treatment in Refractory Out-of-Hospital Cardiac Arrest

	Survival with minimal or no neurologic impairment at 180 d, No./total No. (%)				
	Invasive strategy	Standard strategy	Difference, % (95% CI)	OR (95% CI)	*P* value for interaction
Age, y					
<65	29/89 (32.6)	24/97 (24.7)	7.8 (-5.1 to 20.8)	1.47 (0.78-2.79)	.48
≥65	10/35 (28.6)	5/35 (14.3)	14.3 (-4.6 to 33.2)	2.40 (0.72-7.95)	
Sex					
Men	34/102 (33.3)	24/110 (21.8)	11.5 (-0.5 to 23.5)	1.79 (0.97-3.30)	.46
Women	5/22 (22.7%)	5/22 (22.7)	0.0 (-24.8 to 24.8)	1.00 (0.24-4.10)	
Place of cardiac arrest					
Public	17/44 (38.6)	13/54 (24.1)	14.6 (-3.8 to 32.9)	1.99 (0.83-4.74)	.41
Home	11/42 (26.2)	7/34 (20.6)	5.6 (-13.4 to 24.6)	1.37 (0.47-4.03)	
EMS	3/19 (15.8)	3/17 (17.6)	-1.9 (-26.3 to 22.6)	0.88 (0.15-5.05)	
Other	8/19 (42.1)	6/27 (22.2)	19.9 (-7.3 to 47.1)	2.55 (0.70-9.21)	
Initial rhythm					
Shockable	35/72 (48.6)	28/84 (33.3)	15.3 (0.0 to 30.6)	1.89 (0.99-3.62)	.54
Nonshockable	4/52 (7.7)	1/48 (2.1)	5.6 (-2.7 to 13.9)	3.92 (0.42-36.35)	
pH[a]					
≥6.95	29/54 (53.7)	25/49 (51.0)	2.7 (-16.6 to 22.0)	1.11 (0.51-2.42)	.70
<6.95	10/69 (14.5)	3/30 (10.0)	4.5 (-9.1 to 18.1)	1.53 (0.39-5.99)	
Lactate[a]					
≥11.6 mmol/L	12/70 (17.1)	4/29 (13.8)	3.3 (-12.0 to 18.7)	1.29 (0.38-4.40)	.94
<11.6 mmol/L	27/52 (51.9)	23/49 (46.9)	5.0 (-14.5 to 24.5)	1.22 (0.56-2.67)	
Cardiac arrest cause					
ACS	18/64 (28.1)	14/63 (22.2)	5.9 (-9.2 to 21.0)	1.37 (0.61-3.07)	.12
CAD	9/14 (64.3)	5/18 (27.8)	36.5 (4.0 to 69.0)	4.68 (1.04-21.04)	
CHF	5/8 (62.5)	2/6 (33.3)	29.2 (-21.3 to 79.6)	3.33 (0.36-30.70)	
Other	7/38 (18.4)	8/45 (17.8)	0.6 (-16.0 to 17.3)	1.04 (0.34-3.20)	



Survival related to time of CPR



4 of 6 survivors
In S arm were
actually crossovers to
Invasive arm

Prague OHCA and ARREST comparison

	Prague OHCA	ARREST
N of patients	256	30
Invasive arm/ECPR	124	15
Age (years)	58.5	59
Male	82%	93%
Bystander CPR	99%	87%
Rhythm	All	VF
VF	58%	100%
Randomization	On the scene	ER - on admission
Time to rando (min)	25	49
Transport time (min)	26	19
Time to ROSC/ECMO (min)	58	59
Survival (180 days)	31.5%	43%
Survival VF (180 days)	49%	43%

Intrarrest Transport, Extracorporeal Cardiopulmonary Resuscitation and Early Invasive Management in Refractory Out-of-hospital Cardiac Arrest. An Individual Patient Data Meta-analysis.

Jan Belohlavek, MD, PhD[1*], Demetris Yannopoulos[2*], Jana Smalcova, MD[1], Daniel Rob, MD[1]; Jason Bartos[2], Michal Huptych, PhD[3]; Petra Kavalkova, PhD[1], Brian Grunau MD, MHSc[4], Fabio Silvio Taccone[5]

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■**Question:** Does an invasive approach (intra-arrest transport, in-hospital extracorporeal cardiopulmonary resuscitation, and early invasive management) improve outcomes for refractory out-of-hospital cardiac arrest, compared to continued standard advanced cardiac life support?

■**Findings** In this individual patient data meta-analysis of two randomized trials of 286 patients with refractory out-of-hospital cardiac arrest, neurologically favorable outcome at 6-months occurred in 32.4% patients in the invasive and 19.7% in the standard arm, a difference that was statistically significant.

■**Meaning** An invasive approach demonstrated statistically significant improvement in neurologically favorable survival in 180 days in patients with refractory out-of-hospital cardiac arrest of presumed cardiac cause.

Introduction/Importance

Refractory out of hospital cardiac arrest (OHCA) has dismal outcome. Whether intraarrest transport, in-hospital extracorporeal cardiopulmonary resuscitation (ECPR) and immediate invasive management improves outcome remains uncertain.

Purpose

To assess the effect of intraarrest transport, in-hospital ECPR and immediate coronary angiography +/- percutaneous intervention (invasive approach) compared to continued standard advanced cardiac life support on neurologically favorable survival in refractory OHCA of presumed cardiac cause.

Methods

An individual patient data meta-analysis of two randomized controlled trials (RCTs, ARREST and Prague OHCA study). The primary outcome was 180-day survival with favorable neurological outcome defined as cerebral performance

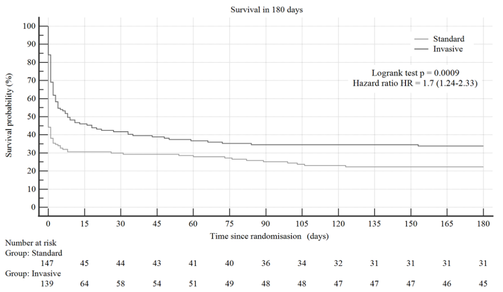
Results

The two RCTs enrolled 286 patients, 147 in the standard and 139 in the invasive arm, the median age 57 (IQR 47.3-65) and 58 (IQR 48-66) years, and 82 and 84% were males, respectively. The median duration of resuscitation was 49 (IQR 33-71) and 58 (IQR 43-69) minutes (p=0.17), in the standard and invasive arms, respectively. In an intention to treat analysis, 29 (19.7%) in the standard and 45 (32.4%) patients in the invasive arm survived to 180 days with a good neurological outcome (OR: 1.95 [95% CI 1.14-3.34]; p=0.016). At 30 days 24 (16.3 %) and 44 (31.7 %) patients (OR: 2.37 [95% CI 1.35-4.18]; p=0.003) had favorable neurological outcome, and 46 (31.3 %) and 60 (43.2 %) patients (OR: 1.67 [95% CI 1.03-2.71]; p=0.04) had cardiac recovery, in the standard and invasive arms, respectively. Patients in the invasive arm had worse metabolic status on admission and suffered more bleeding complications.

Demographic and baseline data	Invasive (N = 139)	Standard (N = 147)	P value
Age (years)	58 (48-66)	57 (47.3-65)	0.58
Sex			
Women	23 (16.5 %)	26 (17.7 %)	0.88
Men	116 (83.5 %)	121 (82.3 %)	
Medical history			
Hypertension	49 (39.8 %)	47 (48 %)	0.27
Coronary artery disease	19 (16 %)	21 (21.4 %)	0.38
Chronic heart failure	12 (9.9 %)	5 (5.3 %)	0.31
Diabetes	22 (18.5 %)	20 (20.4 %)	0.73
Chronic kidney disease	3 (2.5 %)	4 (4.3 %)	0.7
COPD	9 (7.5 %)	3 (3.2 %)	0.24
ICD implanted	3 (2.5 %)	0 (0.0 %)	0.26
Location of cardiac arrest			
Home	48 (34.5 %)	41 (27.9 %)	0.41
Public place	52 (37.4 %)	61 (41.5 %)	
EMS	19 (13.7 %)	17 (11.6 %)	
Health facility	2 (1.4 %)	1 (0.7 %)	
Car	8 (5.8 %)	7 (4.8 %)	
Hotel	4 (2.9 %)	6 (4.1 %)	
Workplace	5 (3.6 %)	14 (9.5 %)	
Initial rhythm			
VF	87 (62.6 %)	99 (67.3 %)	0.44
Asystole	31 (22.3 %)	24 (16.3 %)	
PEA	21 (15.1 %)	24 (16.3 %)	
Bystander CPR	137 (98.6 %)	143 (97.3 %)	0.68
Time from collapse to EMS arrival (min)	8 (7–10.3)	9 (6–11)	0.63
Time from collapse to randomization (Prague)	24 (21-30)	26 (20-35)	0.17
Time from collapse to randomization (ARREST)	52.5 (42-60.5)	58 (44-66)	0.57
Number of epinephrine doses prehospitally (mg)	4 (2-5)	5 (2.3-7)	**0.003**
Number of defibrillations prehospitally	4 (3-6)	4 (2-7)	0.97
Intermittent ROSC	41 (29.5 %)	45 (34.1 %)	0.7

Procedural characteristics	Invasive (N = 139)	Standard (N = 147)	P value
Admitted to hospital	138 (99.3 %)	102 (69.4 %)	**< 0.0000001**
Time to hospital admission (min)	49 (44-60)	59 (49-68.3)	**< 0.0001**
Declared dead	13 (9.4 %)	78 (53.1 %)	**< 0.0001**
Prehospitally	1 (7.7 %)	46 (59.0 %)	**0.0006**
Within 1 hour from admission	12 (92.3 %)	32 (41.0 %)	
Time of CPR (time to death/ROSC or ECLS) (min)	58 (43.2-68.5)	49 (33-71)	0.17
Time of CPR subgroups			
< 30 min	14 (10.7 %)	26 (18.3 %)	**0.02**
≥ 30 and < 45 min	20 (15.3 %)	33 (23.2 %)	
≥ 45 min	97 (74.0 %)	83 (58.5 %)	
Sustained ROSC on admission	34 (24.5 %)	59 (40.1 %)	**0.005**
TTM used	129 (93.5 %)	63 (61.8 %)	**<0.0001**
ECLS			
ECLS implanted	94 (68.6 %)	10 (6.8 %)	**< 0.0001**
Time to ECLS (min)	61 (55-70)	62 (51-73)	0.9
Time of implantation (door to ECLS) (min)	12 (9-15)	15.5 (11-17)	0.055
Invasive assessment			
Coronary angiography	128 (94.1 %)	68 (81.9 %)	**0.006**
Emergency invasive interventions			
PCI (both for ACS and CAD)			
Successful	62 (91.2 %)	26 (81.2 %)	0.19
Unsuccessful	6 (8.8 %)	6 (18.8 %)	
Laboratory values on admission			
pH	6.94 (6.8-7.1)	7.03 (6.9-7.2)	**0.003**
pH ≤ 6.85 and CPC 1+2	9 (6.5 %)	1 (1.1 %)	0.05
pH ≤ 6.80 and CPC 1+2	4 (2.9 %)	1 (1.1 %)	0.65
Lactate (mmol/L)	12.4 (9.4-15.9)	10.2 (7.6-13.5)	**0.006**

Outcomes	Invasive (N = 124)	Standard (N = 132)	P value
Primary outcome			
Survival with CPC at 180 days			
1 or 2	45 (32.4 %)	29 (19.7 %)	0.015
≥3	94 (67.6 %)	118 (80.3 %)	
Secondary outcomes			
Survival with CPC at 30 days			
1 or 2	44 (31.7 %)	24 (16.3 %)	0.003
≥3	95 (68.3 %)	123 (83.7 %)	
Cardiac recovery at 30 days			
Yes	60 (43.2 %)	46 (31.3 %)	0.04
No	79 (56.8 %)	101 (68.7 %)	



ClinicalTrials.gov identifier: NCT01511666 (Prague OHCA trial) and NCT03880565 (ARREST

Conclusions and Relevance

In this meta-analysis of individual patient data, the invasive approach demonstrated significant improvement in neurologically favorable survival at 180 days in patients with refractory out-of-hospital cardiac arrest of presumed cardiac cause.

Intrarrest Transport, Extracorporeal Cardiopulmonary Resuscitation and Early Invasive Management in Refractory Out-of-hospital Cardiac Arrest. An Individual Patient Data Meta-analysis.

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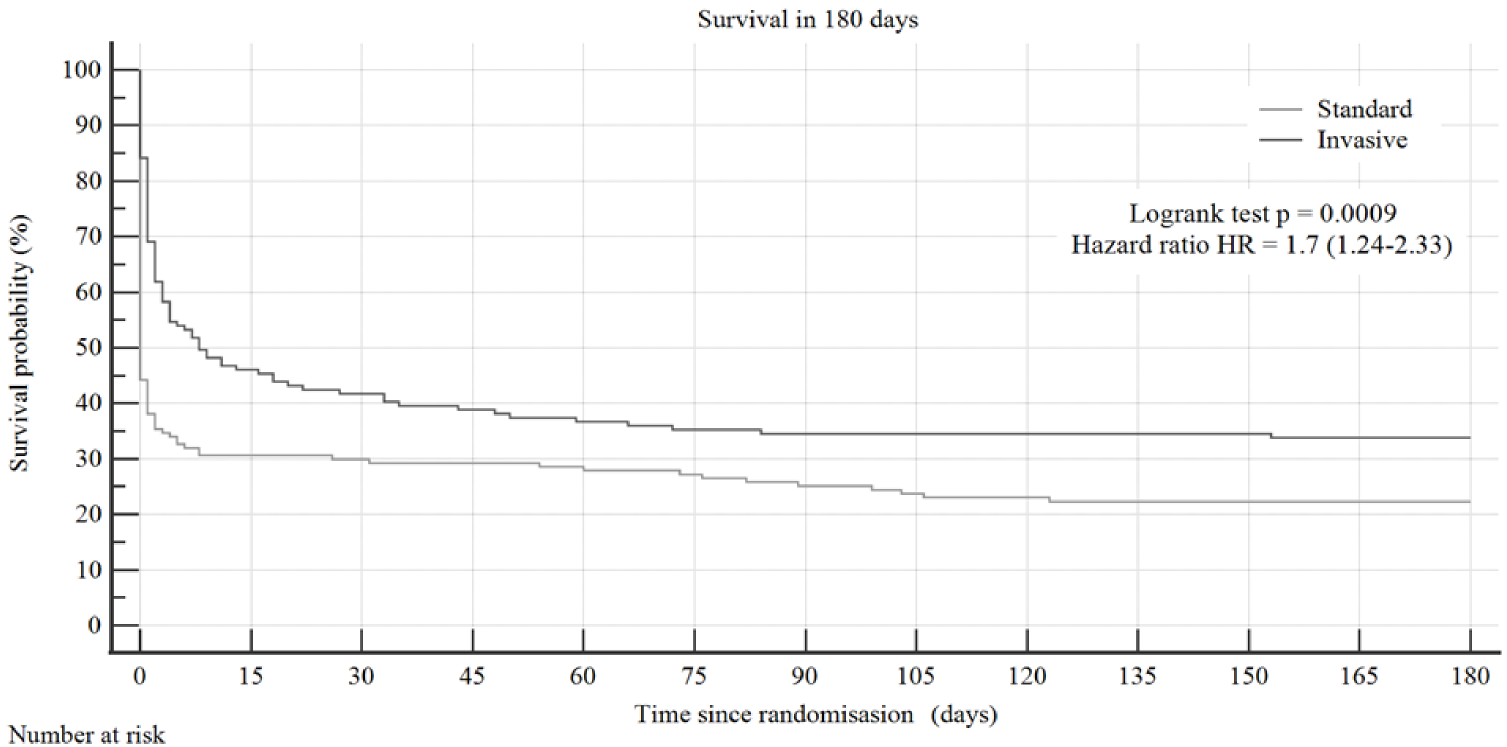

Number at risk

Group	0	15	30	45	60	75	90	105	120	135	150	165	180
Group: Standard	147	45	44	43	41	40	36	34	32	31	31	31	31
Group: Invasive	139	64	58	54	51	49	48	48	47	47	47	46	45

Intrarrest Transport, Extracorporeal Cardiopulmonary Resuscitation and Early Invasive Management in Refractory Out-of-hospital Cardiac Arrest. An Individual Patient Data Meta-analysis.

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Yes	60 (43.2 %)	46 (31.3 %)	**0.04**
No	79 (56.8 %)	101 (68.7 %)	

Rob *et al. Critical Care* _###################_
https://doi.org/10.1186/s13054-022-04199-3

Critical Care

RESEARCH **Open Access**

Extracorporeal versus conventional cardiopulmonary resuscitation for refractory out-of-hospital cardiac arrest: a secondary analysis of the Prague OHCA trial

Daniel Rob[1], Jana Smalcova[1], Ondrej Smid[1], Ales Kral[1], Tomas Kovarnik[1], David Zemanek[1], Petra Kavalkova[1], Michal Huptych[2], Arnost Komarek[3], Ondrej Franek[4], Stepan Havranek[1], Ales Linhart[1] and Jan Belohlavek[1*]

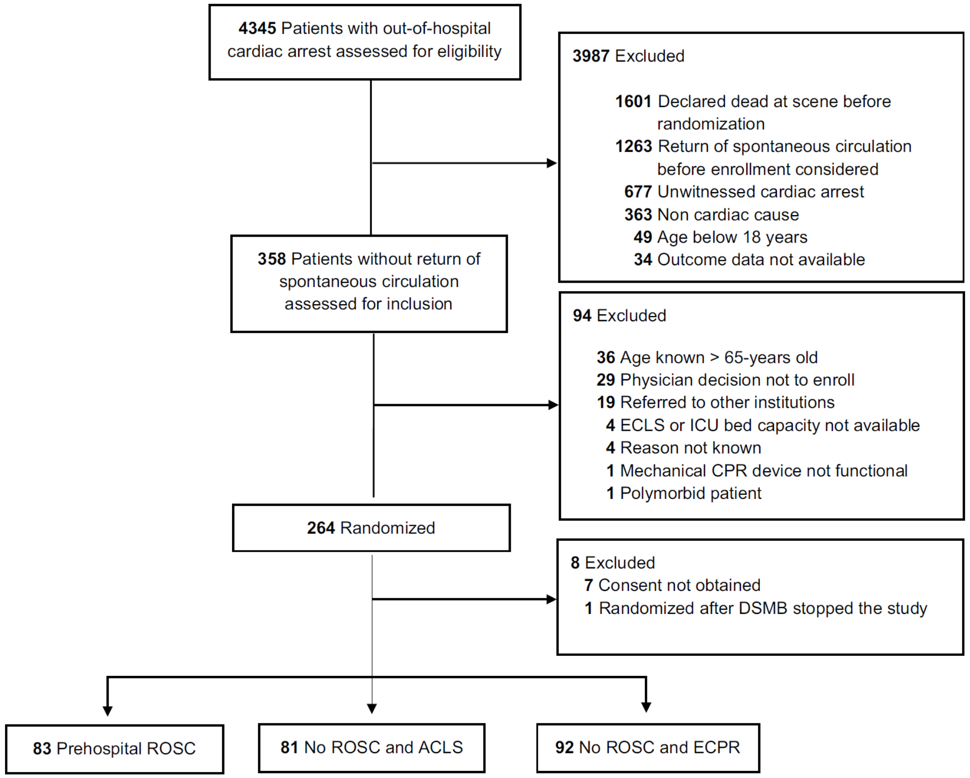


Fig. 1 Modified consort flow diagram of the Prague OHCA study. *ACLS* advanced cardiac life support, *CPR* cardiopulmonary resuscitation, *DSMB* data safety monitoring board, *ICU* intensive care unit, *ECLS* extracorporeal life support, *ECPR* extracorporeal membrane resuscitation, *ROSC* return of spontaneous circulation

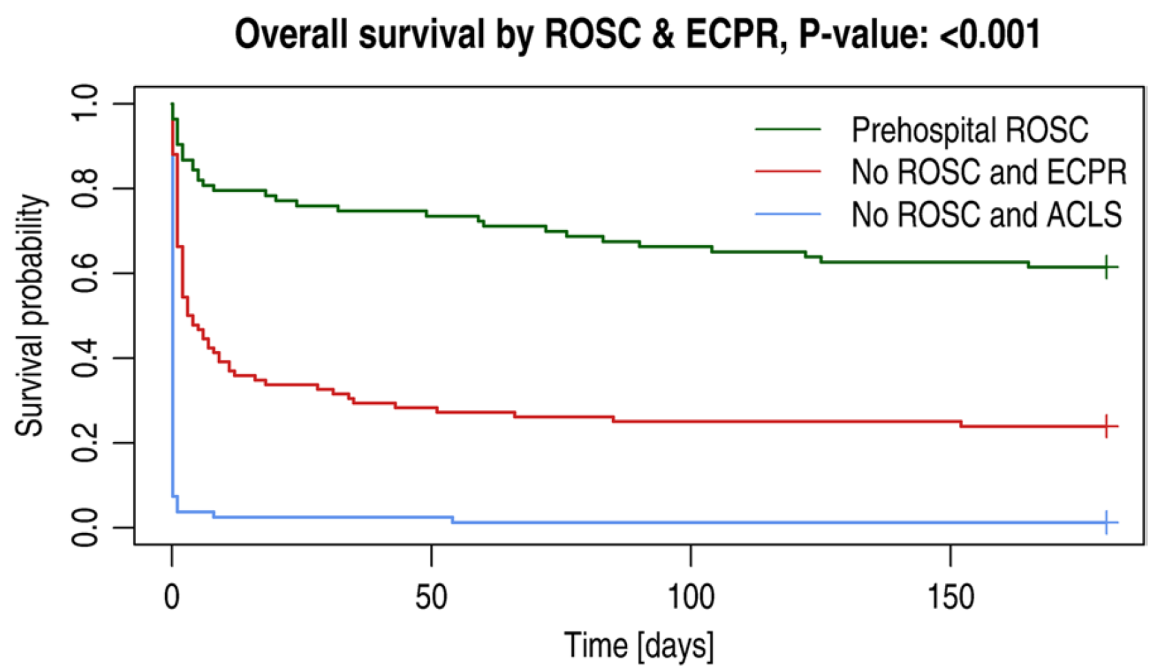


Fig. 2 Kaplan–Meier survival curve in the study according to ROSC and ECPR status

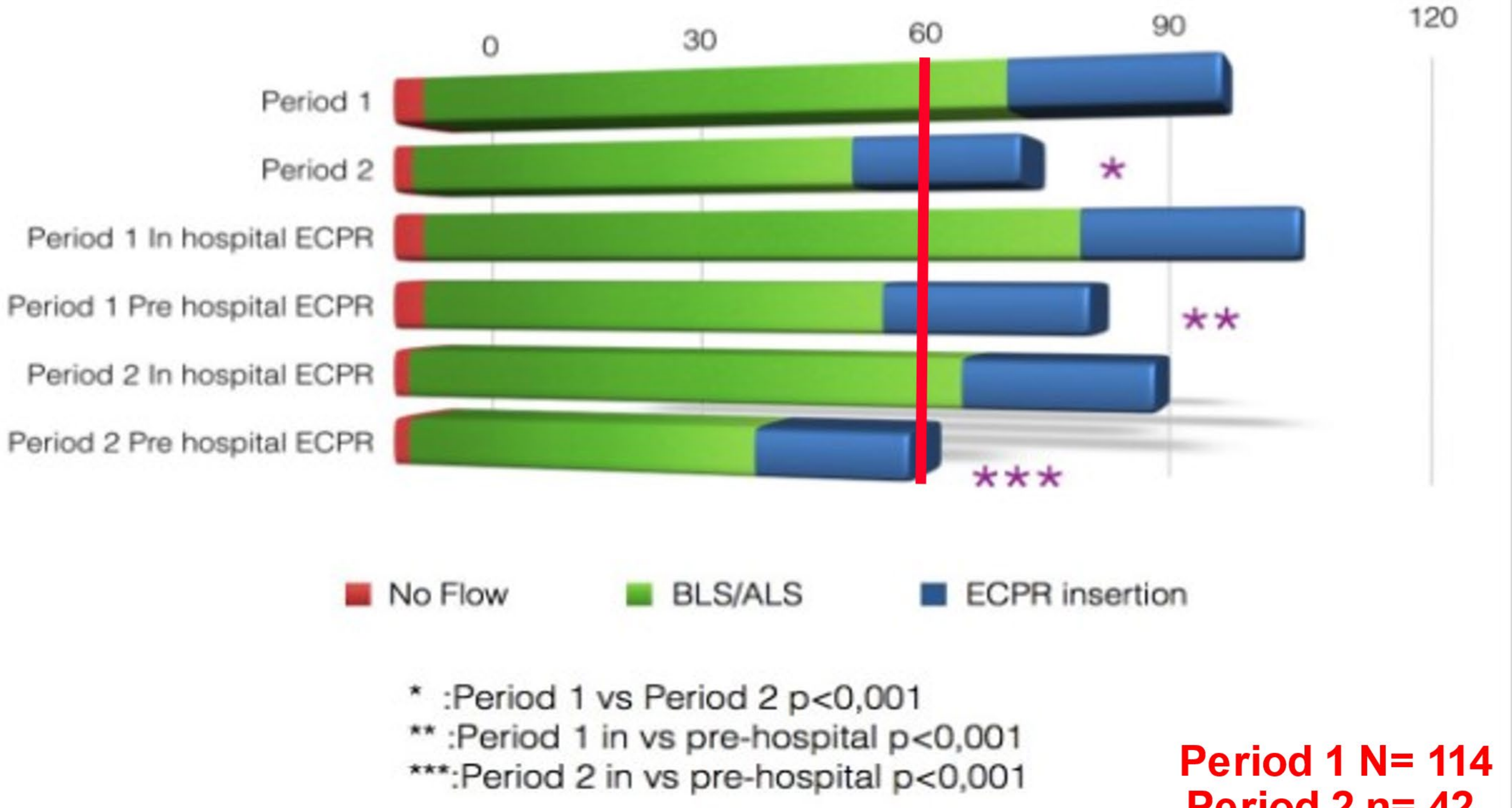
In this secondary analysis of the randomized r-OHCA trial, **ECPR was associated with improved 180-day survival** in patients without prehospital ROSC.

Initial **shockable rhythm, younger age and shorter time of resuscitation were all associated with better 180-day survival** in r-OHCA.

Majority of r-OHCA survivors treated by ECPR had good neurological outcome at 180 days.

ECPR should become a standard of care for selected patients with refractory cardiac arrest

« Global E-CPR strategy »



Period 1 N= 114
Period 2 n= 42

15680 OHCA in Paris – 156 included!!! Less than 1%!!!

Lamhaut et coll Resuscitation . 2017 Apr 14

Unloading

Circulation

ORIGINAL RESEARCH ARTICLE

Left Ventricular Unloading Is Associated With Lower Mortality in Patients With Cardiogenic Shock Treated With Venoarterial Extracorporeal Membrane Oxygenation

Results From an International, Multicenter Cohort Study

668 patients, propensity matching registry study

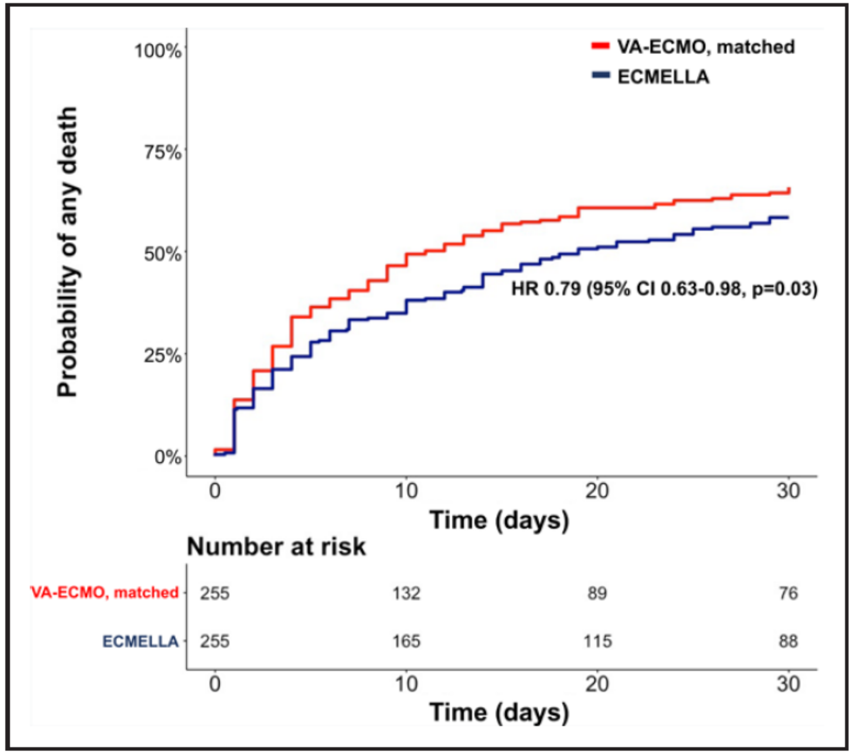


Figure 2. Kaplan-Meier curve of the matched study cohort.
ECMELLA indicates Impella+extracorporeal membrane oxygenation; HR, hazard ratio; and VA-ECMO, venoarterial extracorporeal membrane oxygenation.

B. Schrage…D. Westermann, Circulation 2020

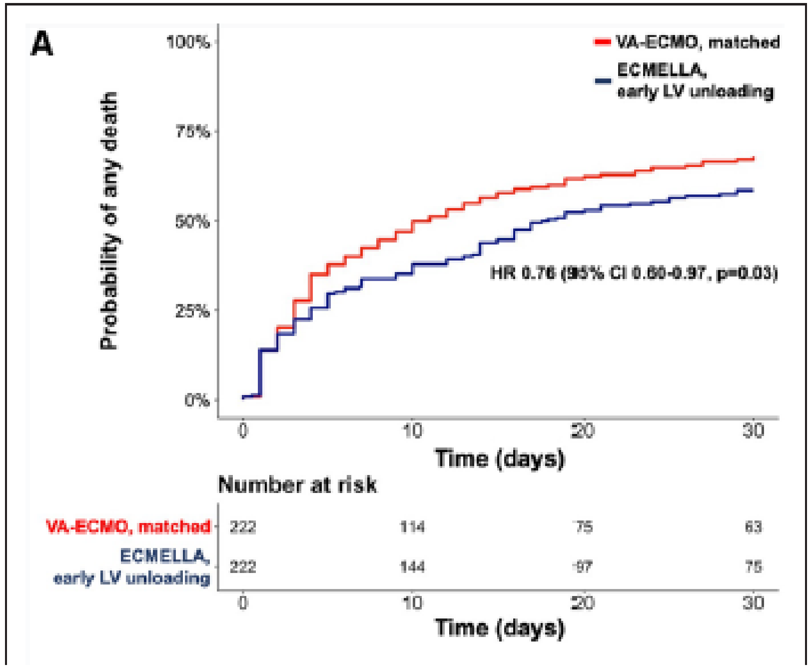
Circulation

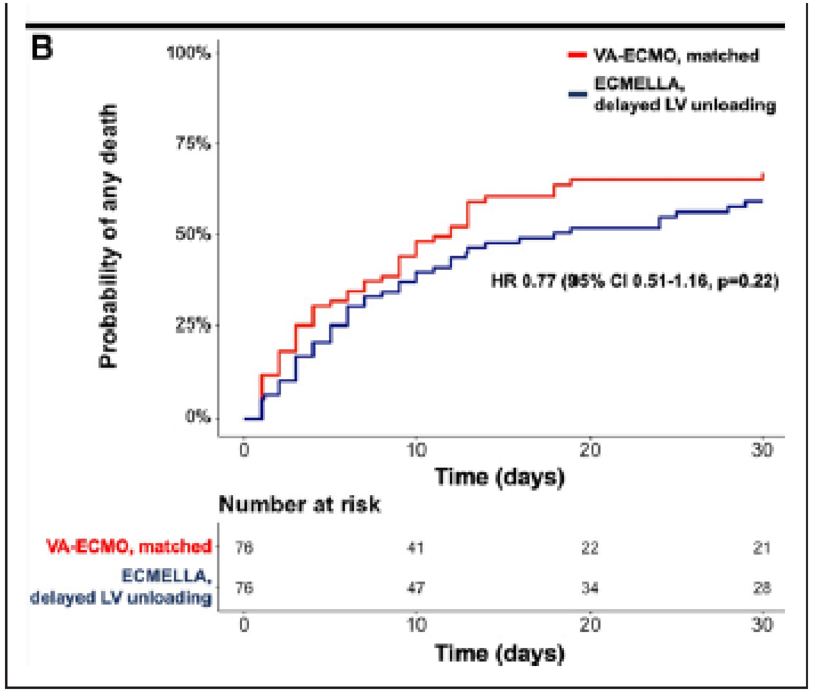
ORIGINAL RESEARCH ARTICLE

Left Ventricular Unloading Is Associated With Lower Mortality in Patients With Cardiogenic Shock Treated With Venoarterial Extracorporeal Membrane Oxygenation

Results From an International, Multicenter Cohort Study

Early (within 2 hours) vs. Delayed unloading





B. Schrage…D. Westermann, Circulation 2020

Translational research

Bělohlávek et al. Critical Care 2012, 16:R50
http://ccforum.com/content/16/2/R50

CRITICAL CARE

RESEARCH Open Access

Coronary versus carotid blood flow and coronary perfusion pressure in a pig model of prolonged cardiac arrest treated by different modes of venoarterial ECMO and intraaortic balloon counterpulsation

Jan Bělohlávek[1*], Mikuláš Mlček[2], Michal Huptych[3], Tomáš Svoboda[2], Štěpán Havránek[1], Petr Ošťádal[4], Tomáš Bouček[1], Tomáš Kovárník[1], František Mlejnský[5], Vratislav Mrázek[1], Marek Bělohlávek[6], Michael Aschermann[1], Aleš Linhart[1] and Otomar Kittnar[2]

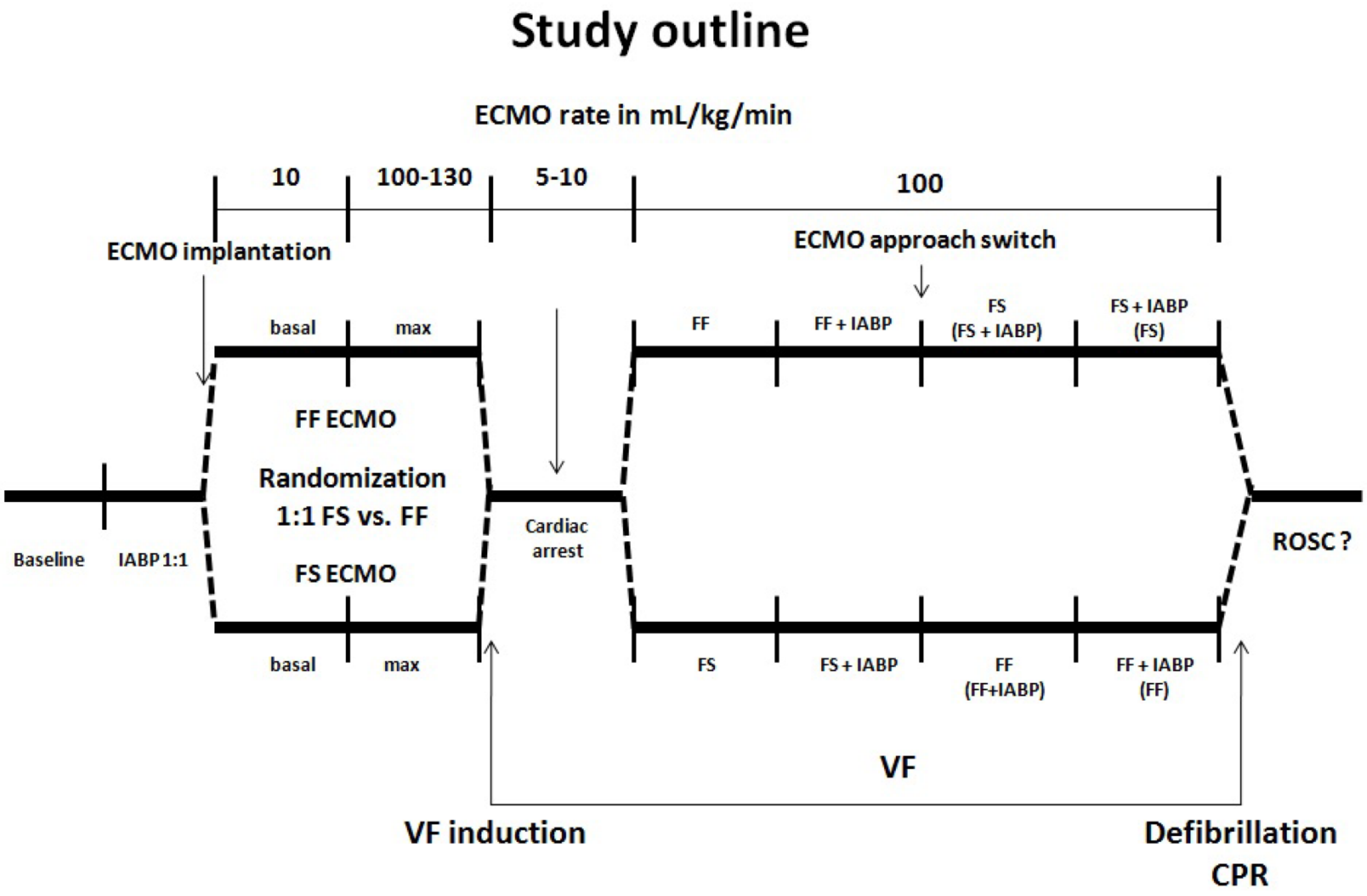
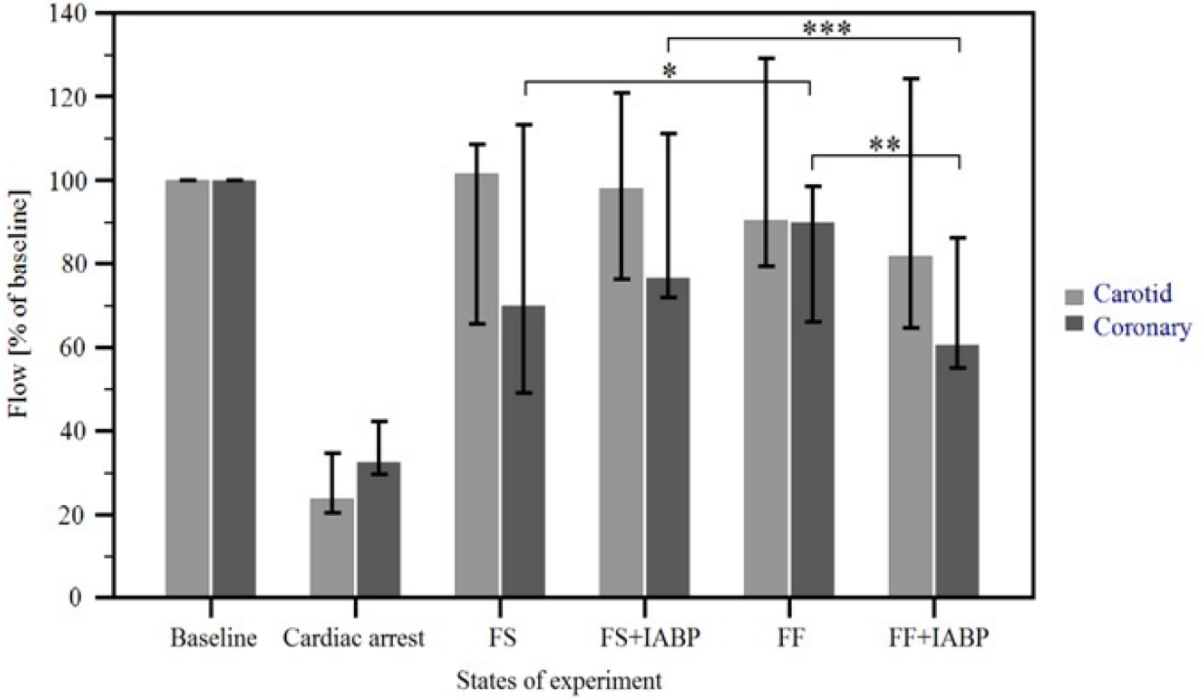


Figure 1 Outline of the study protocol. For an explanation see text. Vertical bars represent 15-minute intervals for respective measurement periods. CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; FF, femoro-femoral; FS, femoro-subclavian; IABP, intraaortic balloon countepulsation; VF, ventricular fibrillation; ROSC, return of spontaneous circulation.

Experimental lab
Dept. of Physiology, 1st Medical School, Charles University in Prague



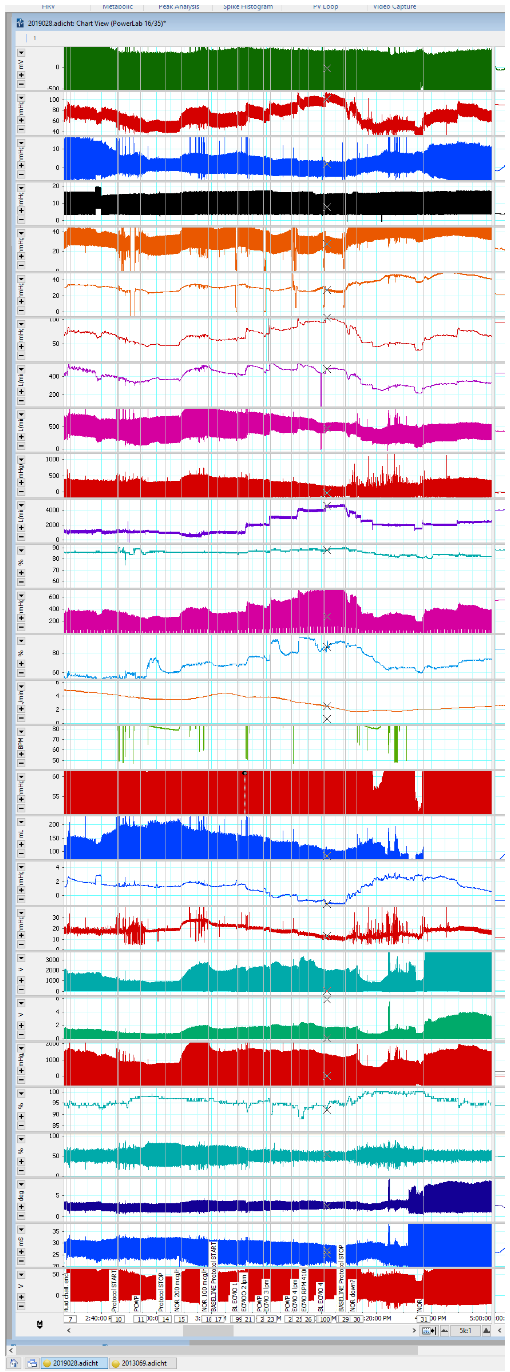
	P-values			
N = 11	FS vs. FF	FS vs. FS+IABP	FF vs. FF+IABP	FS+IABP vs. FF+IABP
Flow Velocity				
Carotid	0.095	0.87	0.16	0.87
Coronary	**0.039** *	0.16	**0.004** **	**0.026** ***

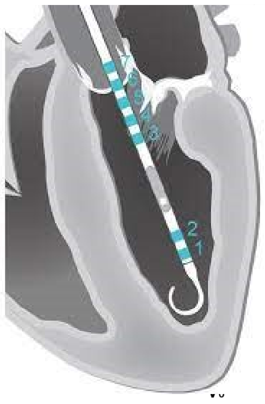
Figure 2 Carotid and coronary blood flow velocities relative to baseline. Values are expressed as median percentages of baseline with 25- and 75-percentiles represented by the vertical bars (for actual values see Table 1) along with *P*-values for respective comparisons at the bottom. Statistically significant differences in bold. Cardiac arrest values are significantly different to all other values, comparisons not shown.

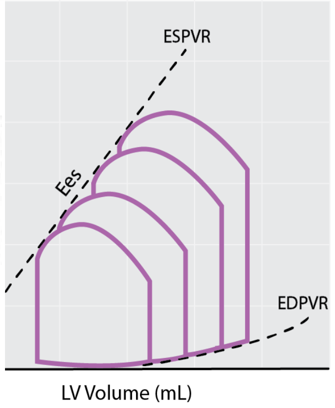
Lessons learned:

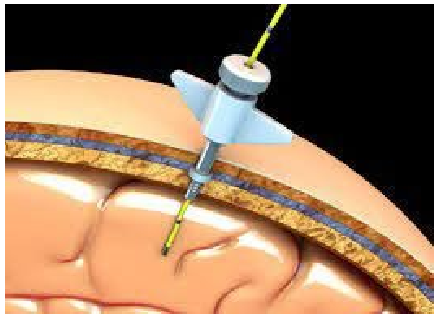
- randomized
- robust and clinically relevant design
- power analysis
- pilot training
- Reproducible measurements used
- Advanced data integration

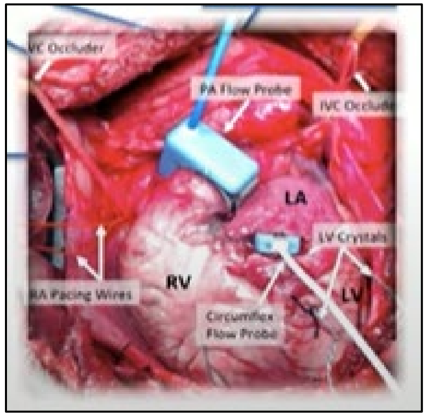
DATA Integration











Seminars in Thoracic and Cardiovascular Surgery, 2020

Transaortic or Pulmonary Artery Drainage for Left Ventricular Unloading in Venoarterial Extracorporeal Life Support: A Porcine Cardiogenic Shock Model

Paolo Meani, MD,[,†,a] Mikulas Mlcek, MD, PhD,[‡,§,a] Mariusz Kowalewski, MD,[*] Giuseppe Maria Raffa, MD, PhD,[*] Michaela Popkova, DVM,[§] Michele Pilato, MD,[¶] Antonio Arcadipane, MD,[¶] Jan Belohlavek, MD, PhD,[§,‖] and Roberto Lorusso, MD, Pl*

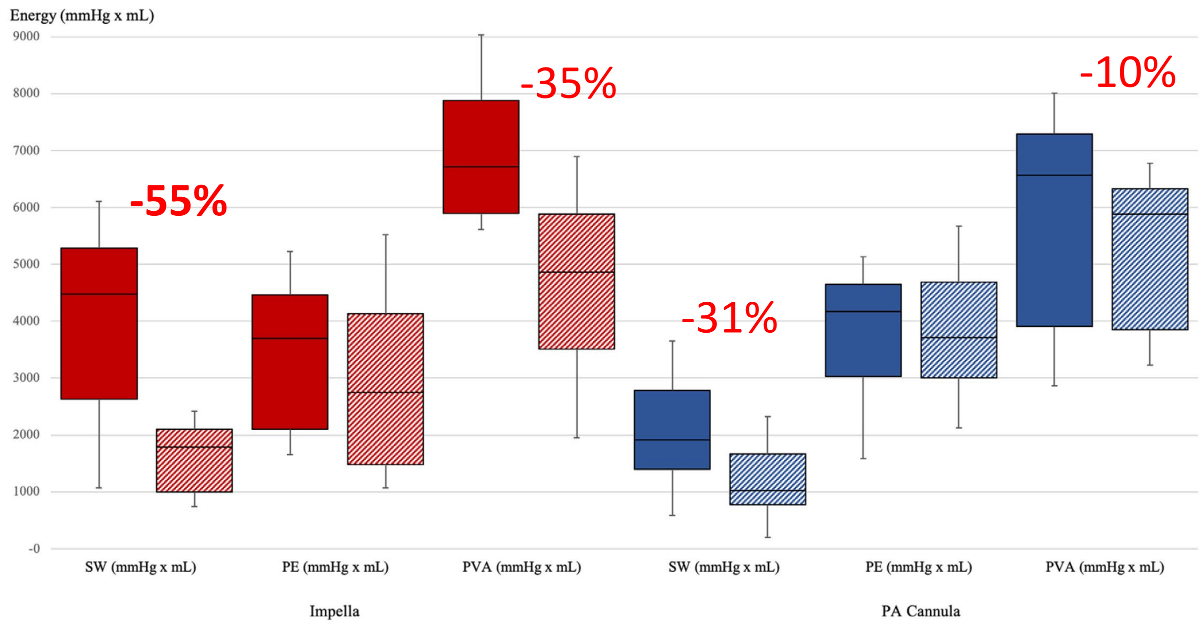
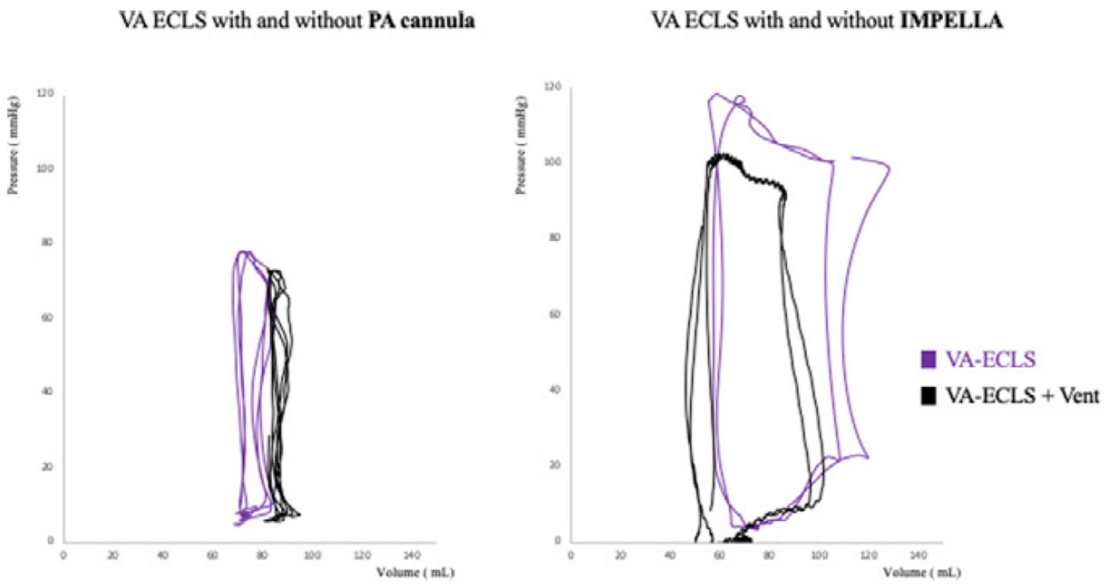


Figure 3. Energy Changes occurred with PA cannula or Impella in association with venoarterial extracorporeal life support during cardiogenic shock. Impella reduces either the stroke work (SW) or the potential energy (PE), thus the Pressure Volume Area (PVA) decrease resulted higher compared with pulmonary artery drainage. The upper and lower borders of the box represent the first and



Impella is more effective in terms of LV unloading than PA cannula during V-A ECLS.

Central Message

The Impella and pulmonary artery cannula, in association with venoarterial extracorporeal life support, provided effective left ventricle unloading maintaining adequate end-organ perfusion. However, Impella seemed to guarantee a stronger left ventricle unloading effect.

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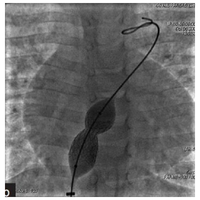
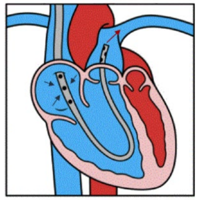
Atrial Septostomy for Left Ventricular Unloading During Extracorporeal Membrane Oxygenation for Cardiogenic Shock

Animal Model

Mikulas Mlcek, MD, PhD,[a,*] Paolo Meani, MD,[b,c,*] Mauro Cotza, CCP,[b] Mariusz Kowalewski, MD,[c] Giuseppe Maria Raffa, MD, PhD,[c,d] Eduard Kuriscak, MD, PhD,[a] Michaela Popkova, DVM, PhD,[a] Michele Pilato, MD,[e] Antonio Arcadipane, MD,[e] Marco Ranucci, MD, PhD,[b] Roberto Lorusso, MD, PhD,[b,f,*] Jan Belohlavek, MD, PhD[a,g,*]

LV Unloading Compared - Results





Method	O.D.	Flow	LV work reduction	Notes
LV pump (Impella)	14 F	~ 3.5 LPM	~35%	Most powerful
Atrial Septostomy	9mm		~ 22 %	Preferred in Ao regurgitation
PA Venting	19 F	~ 1.7 LPM	~10%	Preferred in RV overload/PAH

Meani..Belohlavek et al 2020, Seminars in Thoracic & Cardiovascular Surgery 33 (3)
Mlcek..Belohlavek et al 2021, JACC: Cardiovascular Interventions 14 (24)