Extracorporeal life support for acute myocardial infarction complicated by cardiogenic shock

ECLS-SHOCK

Holger Thiele on behalf of the ECLS-SHOCK Investigators

26th of August 2023

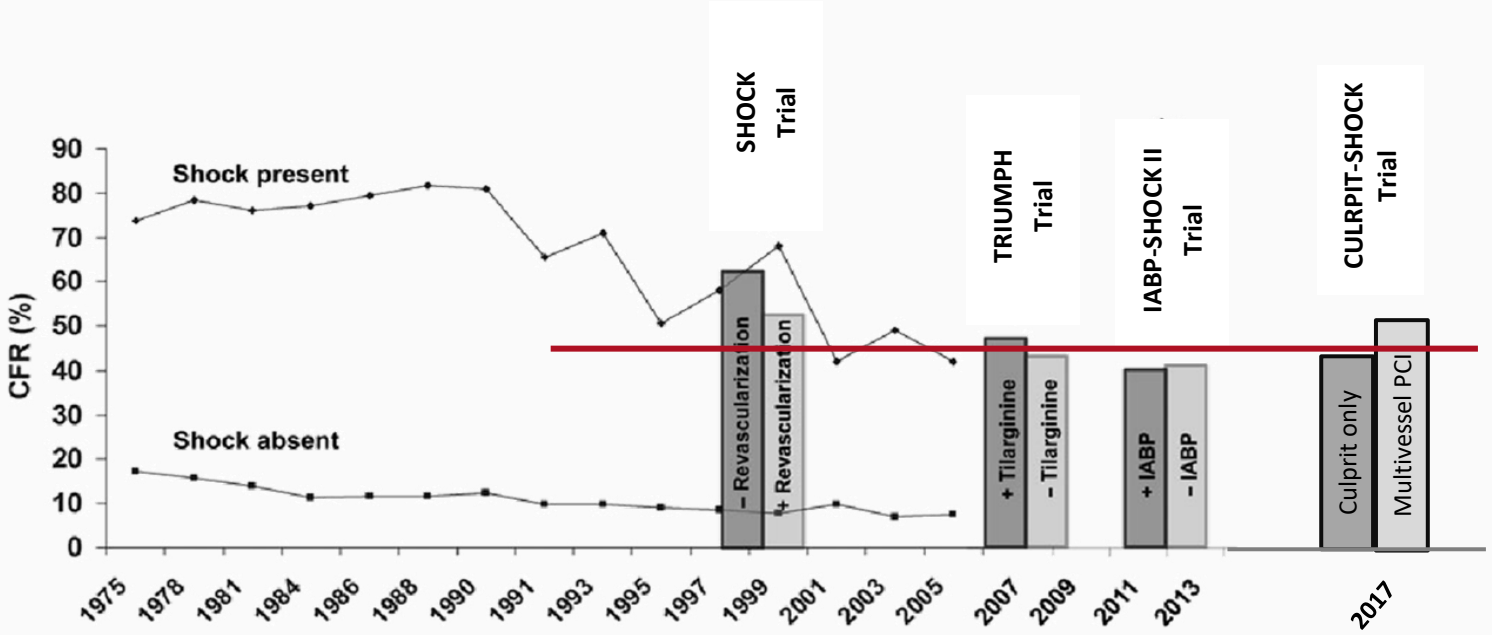
Conflict of Interest Statement

Funding:
German Research Foundation
German Heart Research Foundation
German Cardiac Society
European Union
Else-Kröner-Fresenius-Foundation
Schwiete-Foundation
Boston Scientific

Consulting:
None

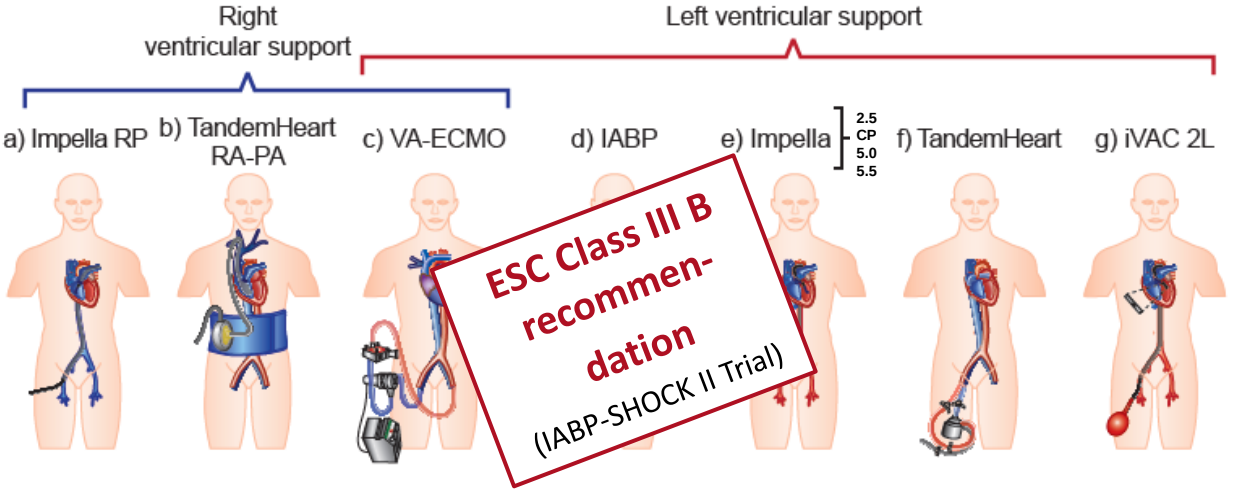
Speaker Honoraria:
None

Cardiogenic Shock - Mortality over Time



Adapted from Werdan et al. Eur Heart J 2014;35:156-167

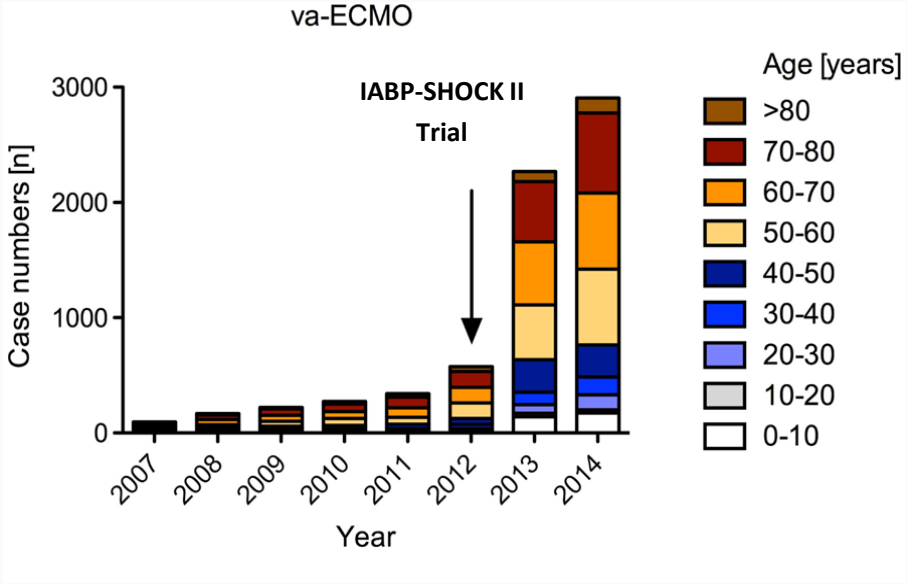
Currently Available MCS

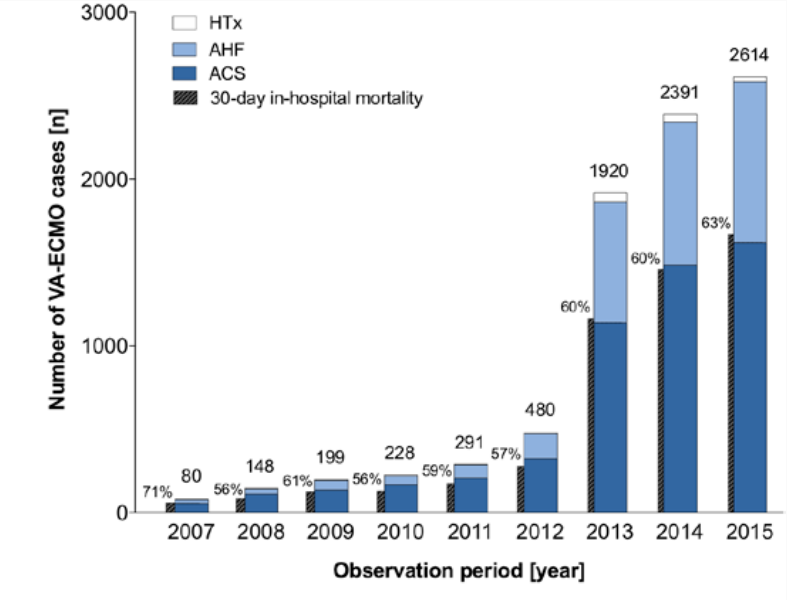


	a) Impella RP	b) TandemHeart RA-PA	c) VA-ECMO	d) IABP	e) Impella 2.5 CP 5.0 5.5	f) TandemHeart	g) iVAC 2L
Flow:	max. 4.0 L	max. 4.0 L	max. 7.0 L		2.5-5.5 L	max. 4.0 L	max. 2.8 L
Pump speed:	33.000 rpm	max. 7.500 rpm	max. 5000 rpm		max. 51.000 rpm	max. 7.500 rpm	40 ml/beat
Cannula size:	22 F	29 F	14-19 F arterial 17-21F venous	7-8 F	12-14 F	12-19 F arterial 21F venous	17 F
Insertion/ Placement	Femoral vein	Internal jugular vein	Femoral artery Femoral vein	Femoral artery	Femoral artery	Femoral artery Femoral vein for LA access	Femoral artery
LV Unloading	-	-	-	(+)	+ - ++	++	+
RV Unloading	+	+	++	-	-	-	-

Thiele et al. Eur Heart J 2019:40:2671-2683
Byrne/Ibanez et al. Eur Heart J 2023;epub

Increase in VA-ECMO (ECLS) Over Time





Karagiannidis et al. Intensive Care Med.2016;42:889–896
Becher et al. Circulation 2018;138:2298-2300

Endpoints/Statistical Methodology

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Primary endpoint

30-day all-cause mortality

Secondary endpoints

- Time to hemodynamic stabilization
- Duration of catecholamine therapy
- Serial creatinine-level and creatinine-clearance until hemodynamic stabilization
- Mean and area under the curve of arterial lactate during 48 hours after PCI
- Peak release of myocardial enzymes
- Serial SAPS II
- Length of mechanical ventilation
- Length of ICU stay
- Length of hospital stay
- Acute renal failure requiring renal replacement therapy within 30 days
- Recurrent myocardial infarction within 30 days
- Need for repeat revascularization (PCI and/or CABG) within 30-days
- Rehospitalization for heart failure within 30 days
- Cerebral performance category (CPC) at 30 days

Sample size

- **Estimated event rate** for primary endpoint**:**
  - **49%** in **control group** versus
  - **35%** in **ECLS group**
- 1 interim analysis (50% of patients)
- 2-sided Chi^2-test; power: 80%, alpha=0.048 for final analysis → **390 patients**
- To compensate for losses in follow-up → **420 patients**

Thiele et al. Am Heart J 2021;234: 1-1

In- and Exclusion Criteria

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Inclusion Criteria	Exclusion Criteria
• Cardiogenic shock complicating AMI (STEMI or NSTEMI) plus obligatory: 1. Planned revascularization 2. SBP <90 mmHg >30 min or catecholamines required to maintain SBP >90 mmHg 3. Signs of impaired organ perfusion with at least one of the following criteria: ➢ Altered mental status ➢ Cold, clammy skin and extremities ➢ Oliguria with urine output <30 ml/h 4. Arterial lactate >3 mmol/l • Informed consent	• Resuscitation >45 minutes • Mechanical cause of cardiogenic shock • Onset of shock >12 h • Severe peripheral artery disease with impossibility to insert ECLS cannulae • Age <18 years or >80 years • Shock of other cause (bradycardia, sepsis, hypovolemia, etc.) • Other severe concomitant disease with limited life expectancy <6 months • Pregnancy • Participation in another trial

Thiele et al. Am Heart J 2021;234: 1-1

Trial Flow

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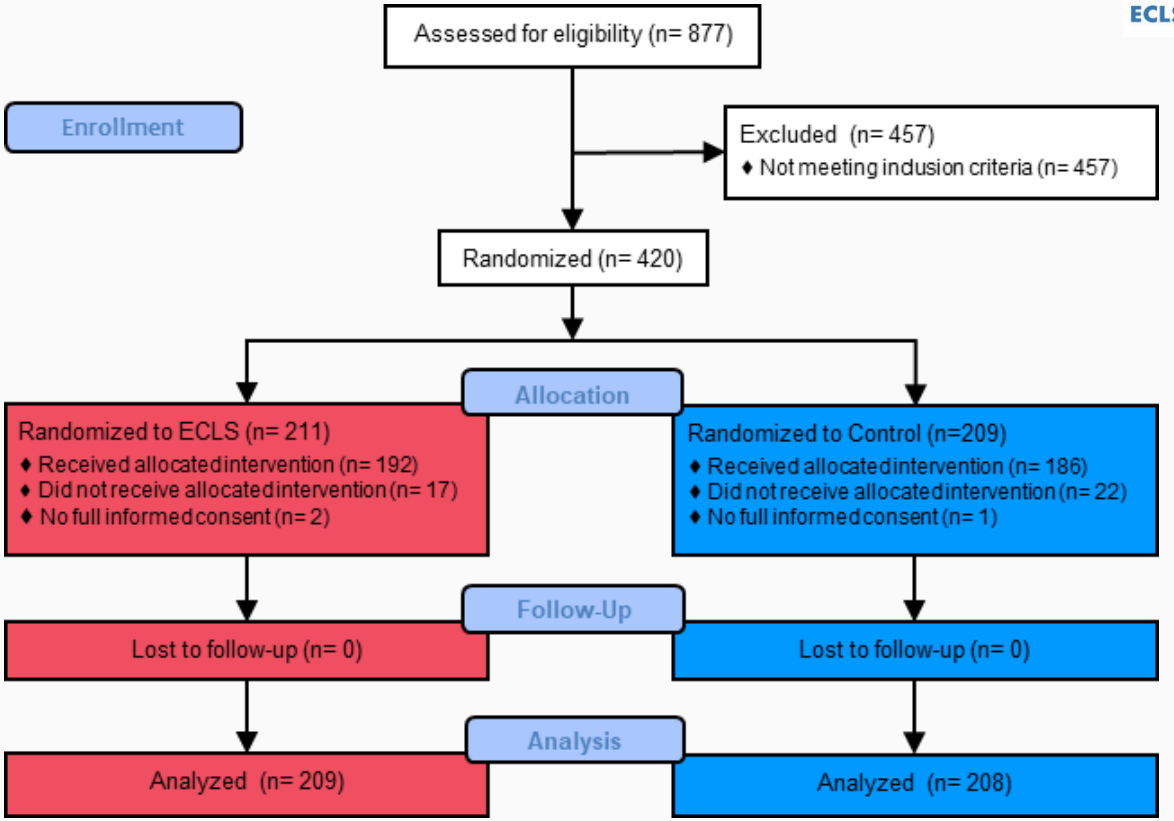
44 study sites



Thiele et al. Am Heart J 2021;234: 1-1

Baseline Characteristics

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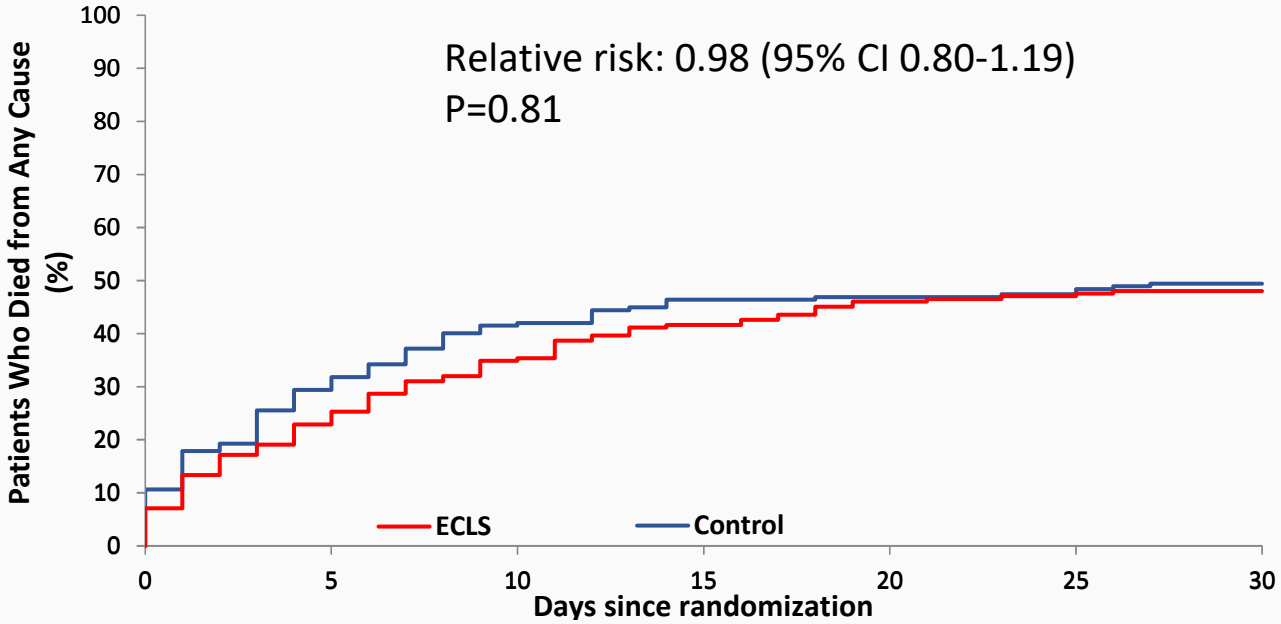
	ECLS (n=209)	Control (n=208)
Age (years); median (IQR)	62 (56 - 69)	63 (57 - 71)
Male sex; n/total (%)	170/209 (81.3)	169/208 (81.3)
Signs of impaired organ perfusion; n/total (%)		
Altered mental status	200/209 (95.7)	198/208 (95.2)
Cold, clammy skin and extremities	202/209 (96.7)	204/208 (98.1)
Oliguria	150/209 (71.8)	150/208 (72.1)
Mean blood pressure (mmHg); median (IQR)	71 (61 - 87)	72 (60 - 88)
STEMI; n/total (%)	135/204 (66.2)	141/207 (68.1)
Resuscitation before randomization; n/total (%)	162/209 (77.5)	162/208 (77.9)
No. of diseased vessels; n/total (%)		
1	71/203 (35.0)	63/200 (31.5)
2	71/203 (35.0)	53/200 (26.5)
3	61/203 (30.0)	84/200 (42.0)
LVEF (%); median (IQR)	30 (20 - 35)	30 (20 - 40)
Laboratory values on admission		
pH; median (IQR)	7.2 (7.1 - 7.3)	7.2 (7.1 - 7.3)
Lactate (mmol/L); median (IQR)	6.8 (4.5 – 9.6)	6.9 (4.6 – 10.0)

Treatment

ECLS-SHOCK

	ECLS (n=209)	Control (n=208)
Type of inital revascularization; n/total (%)		
PCI	199/208 (95.7)	199/204 (97.5)
CABG	1/208 (0.5)	0/204
PCI with emergent transfer to CABG	2/208 (1.0)	0/204
ECLS therapy; n/total (%)	192/209 (91.8)	26/208 (12.5)
Initiation in catheterization laboratory		
Prior revascularization	42/192 (21.9)	4/26 (15.4)
During revascularization	50/192 (26.0)	8/26 (30.8)
After revascularization	100/192 (52.1)	7/26 (26.9)
Initiation after catheterization laboratory		
<24 hours	0/192	3/26 (11.5)
≥24 hours	0/192	4/26 (15.4)
Duration of ECLS therapy (days); median (IQR)	2.7 (1.5 - 4.8)	2.7 (2.2 – 3.8)
Peripheral antegrade perfusion sheath; n/total (%)	183/192 (95.3)	16/19 (84.2)
Active left ventricular unloading in ECLS; n/total (%)	11/191 (5.8)	6/19 (31.6)
Other MCS in patients without ECLS; n/total (%)	0/17	28/182 (15.4)
Invasive mechanical ventilation; n/total (%)	183/203 (90.1)	177/202 (87.6)

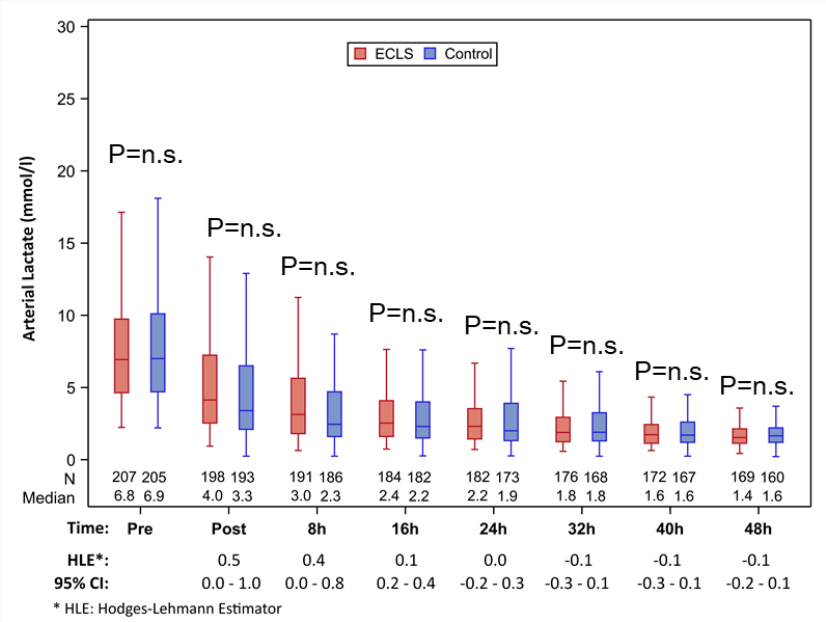
Primary Endpoint – 30-Day All-Cause Mortality



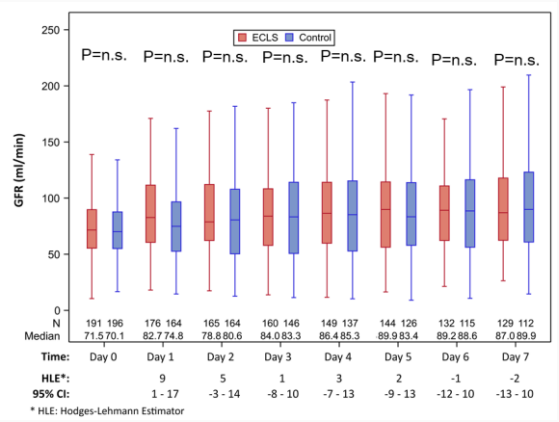
No. at Risk							
Control	208	146	120	109	105	104	100

Key Secondary Endpoints

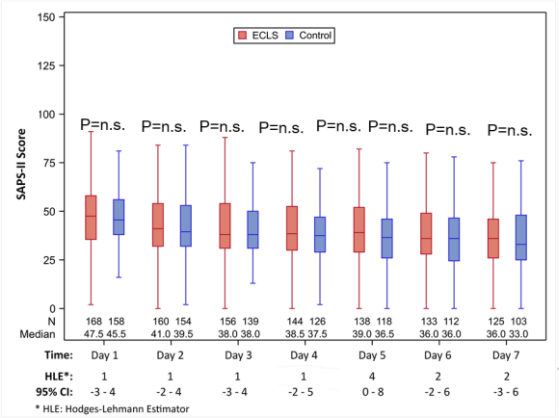
Arterial Lactate



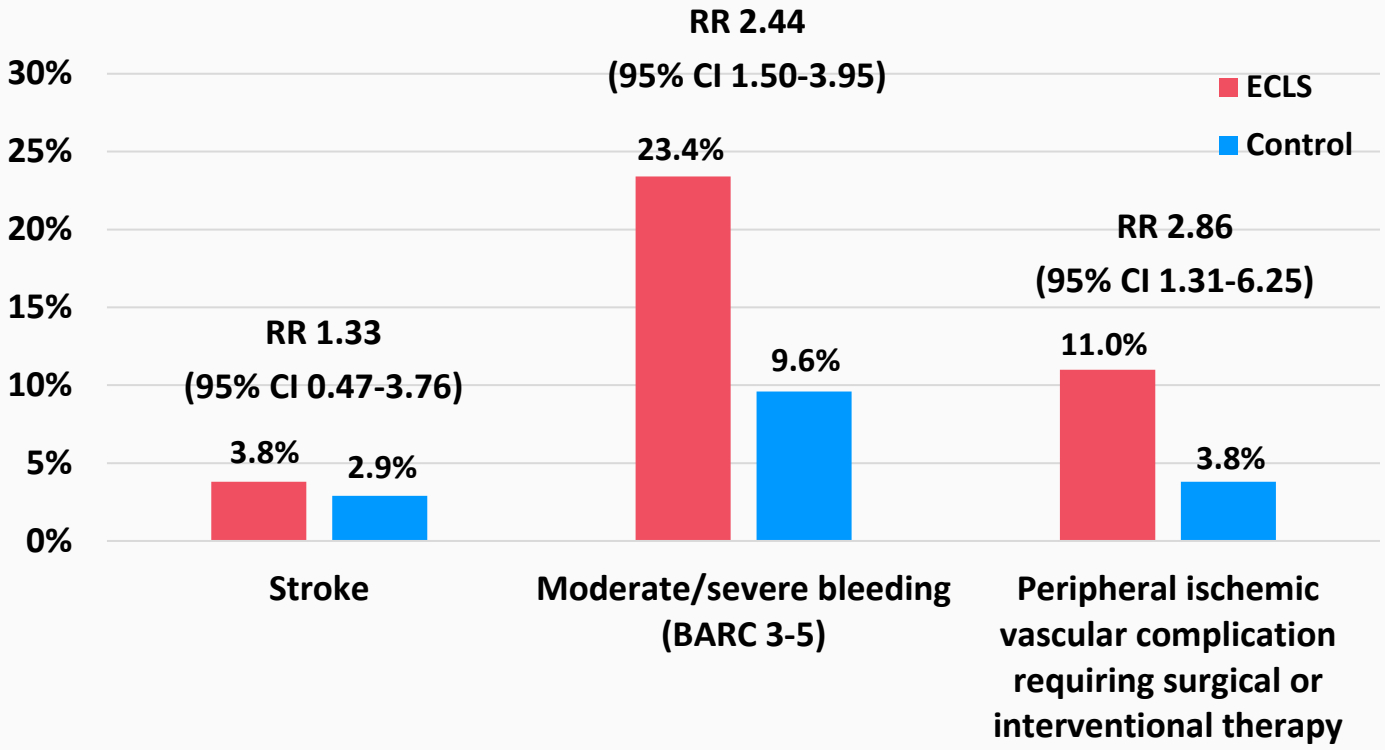
Renal Function - eGFR



SAPS-II



Safety


RR 2.44
(95% CI 1.50-3.95)
30%
25%
20%
15%
10%
5%
0%
ECLS
Control
23.4%
RR 2.86
(95% CI 1.31-6.25)
11.0%
RR 1.33
(95% CI 0.47-3.76)
9.6%
3.8%
2.9%
3.8%
Stroke
Moderate/severe bleeding (BARC 3-5)
Peripheral ischemic vascular complication requiring surgical or interventional therapy

30-Day All-Cause Mortality - Subgroups

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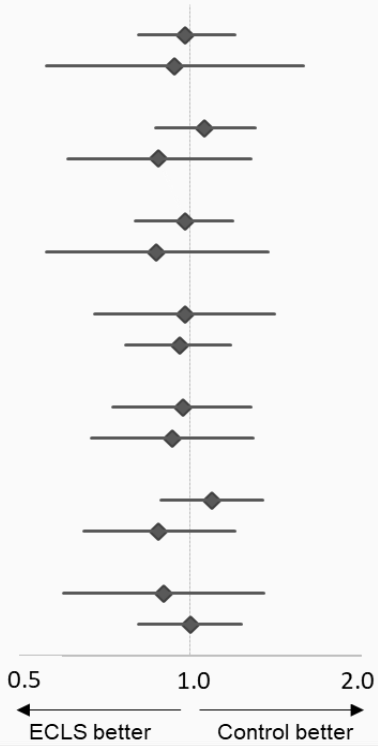
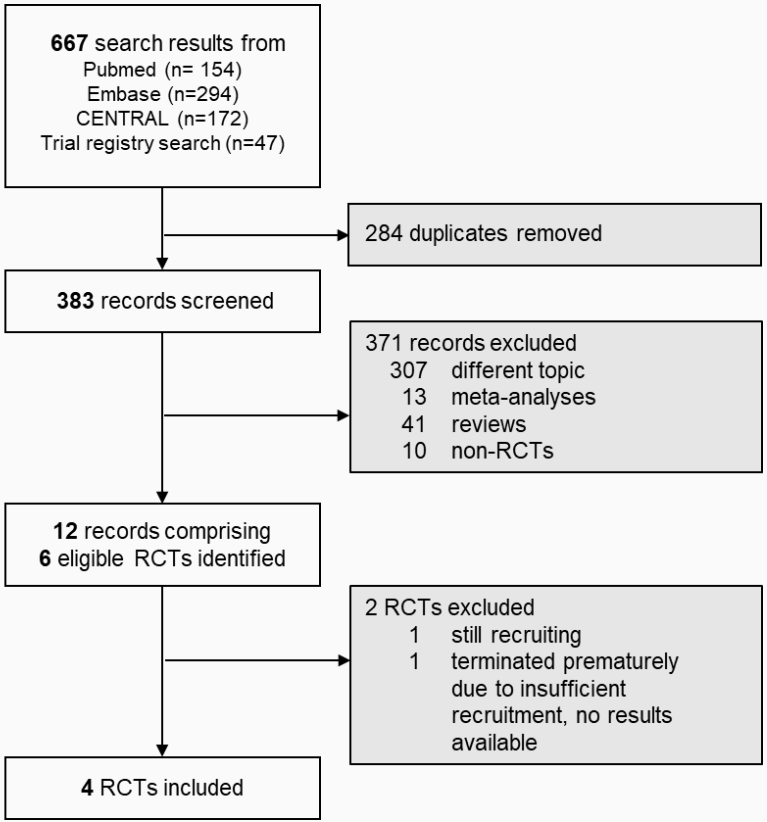
	30-day all-cause mortality (%) Control No. of patients with event/total no. of patients (%)	ECLS (%)	Relative Risk (95%)
Sex			
Male	79/169 (46.7)	78/170 (45.9)	0.98 (0.81-1.20)
Female	23/39 (59.0)	22/39 (56.4)	0.94 (0.56-1.58)
Age			
<65 years	41/112 (36.6)	50/124 (40.3)	1.06 (0.87-1.30)
>= 65 years	61/96 (63.5)	50/85 (58.8)	0.88 (0.61-1.28)
Diabetes			
No	62/146 (42.5)	57/138 (41.3)	0.98 (0.80-1.19)
Yes	39/60 (65.0)	42/70 (60.0)	0.87 (0.56-1.37)
Type of infarction			
NSTEMI	36/66 (54.5)	37/69 (53.6)	0.98 (0.68-1.41)
STEMI	65/141 (46.1)	59/135 (43.7)	0.96 (0.77-1.18)
STEMI type			
Anterior infarction	39/85 (45.9)	33/75 (44.0)	0.97 (0.73-1.28)
Non-anterior infarction	26/56 (46.4)	25/59 (42.4)	0.93 (0.67-1.29)
Arterial lactate			
<= 6 mmol/l	24/85 (28.2)	30/87 (34.5)	1.09 (0.89-1.34)
> 6 mmol/l	75/120 (62.5)	69/120 (57.5)	0.88 (0.65-1.20)
CPR			
No	24/46 (52.2)	22/47 (46.8)	0.90 (0.60-1.35)
Yes	78/162 (48.2)	78/162 (48.2)	1.00 (0.81-1.23)

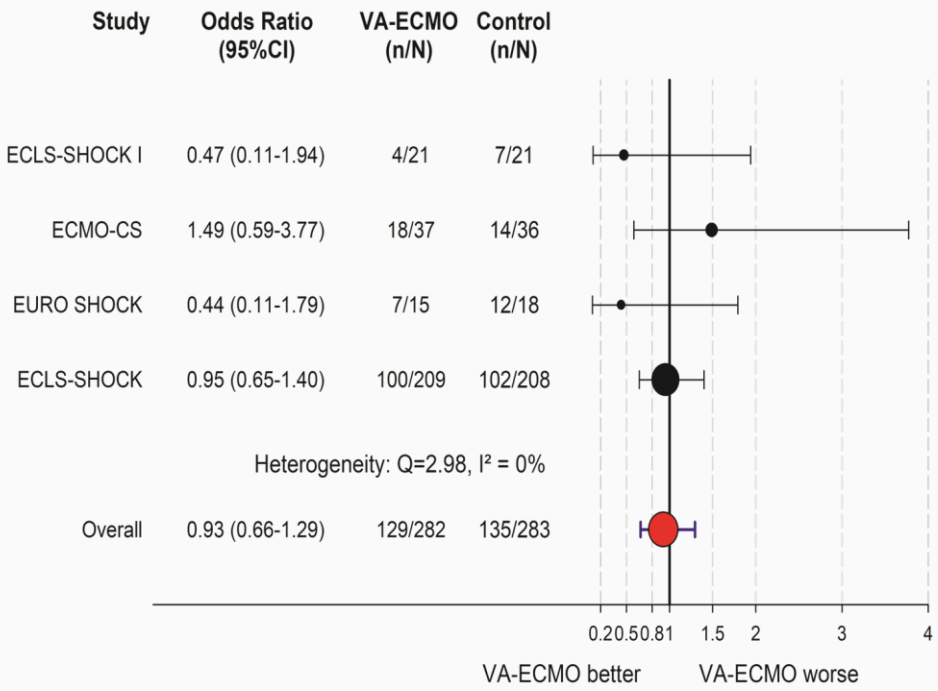


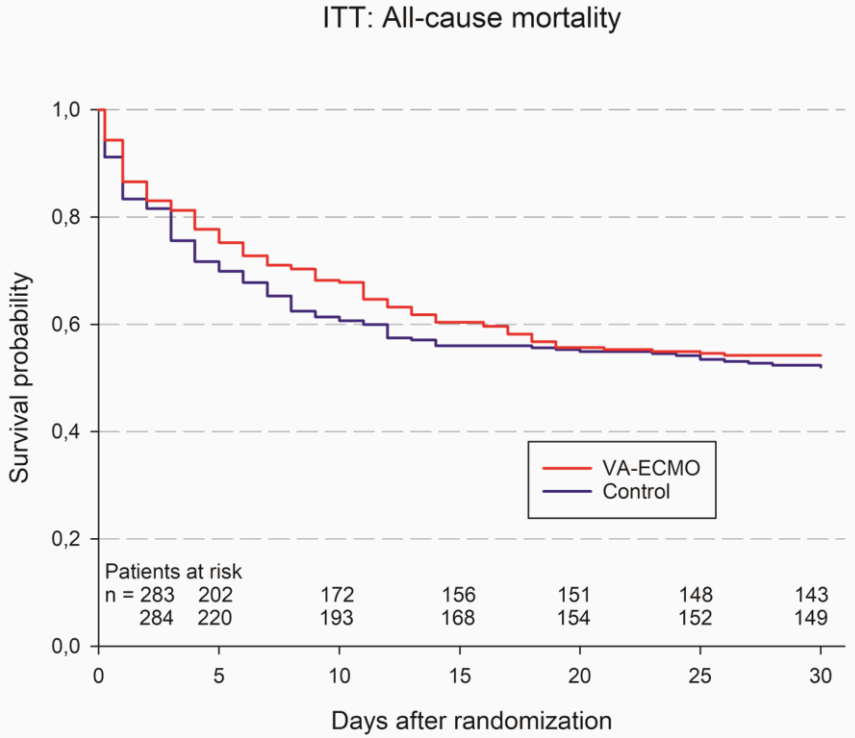
IPD Meta-Analysis VA-ECMO vs No VA-ECMO



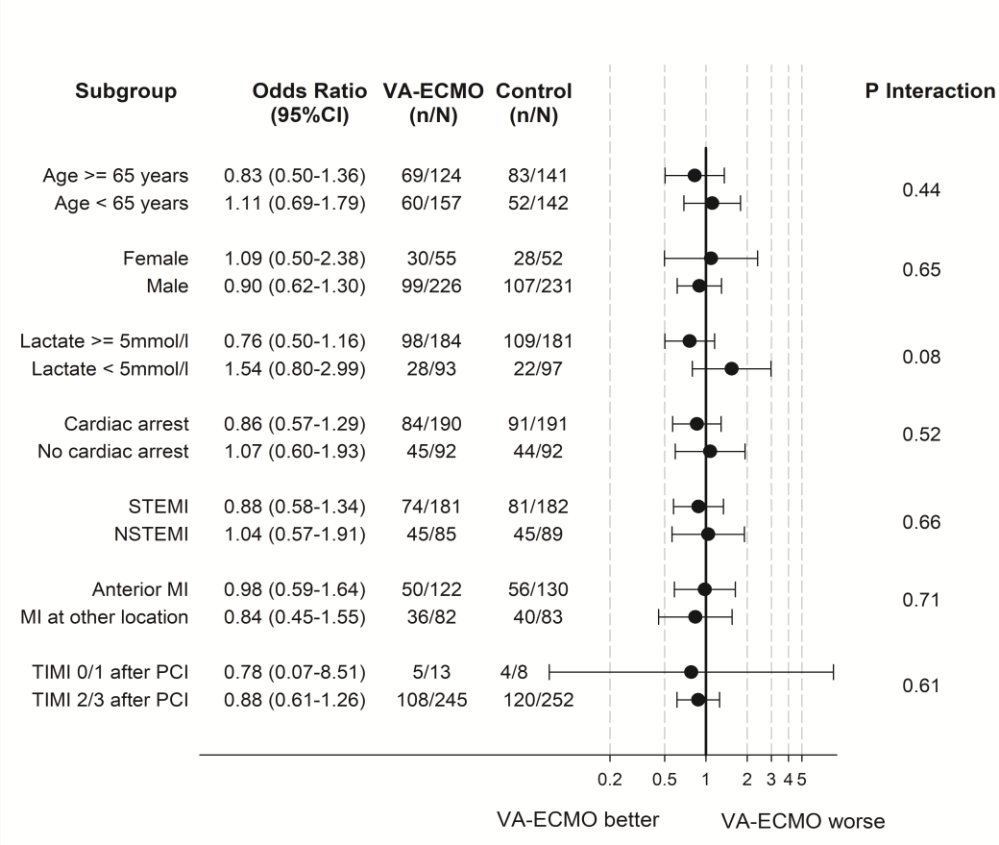
Results

IPD Metaanalysis – 30-Day All-Cause Mortality





IPD Metaanalysis – 30-Day Mortality - Subgroups

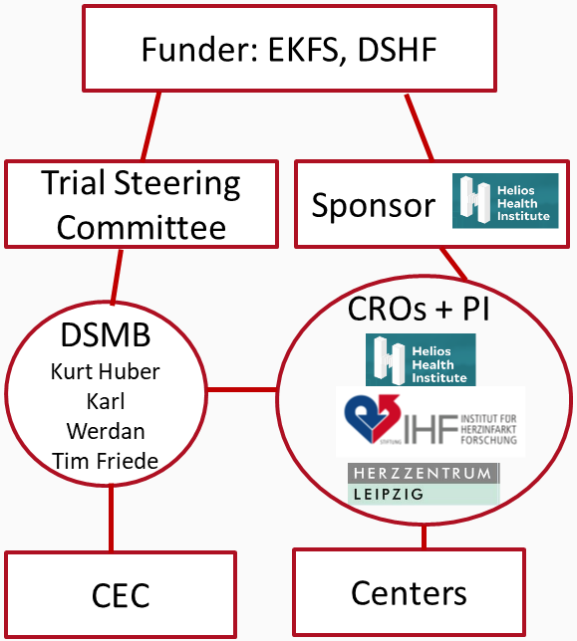


Summary and Conclusions

ECLS-SHOCK

- In patients with acute myocardial infarction and cardiogenic shock with planned revascularization ECLS (VA-ECMO) versus control does not reduce 30-day all-cause mortality.
- This lack of mortality benefit is supported by an IPD metaanalysis of all 4 RCTs comparing ECLS vs control.
- This lack of mortality benefit is further supported by the fact that there were no differences in the secondary endpoints (e.g. lactate, renal function, duration of catecholamines, etc.).
- ECLS is associated with higher rates of moderate or severe BARC bleeding and peripheral ischemic complications requiring intervention.
- The findings challenge current guideline recommendations and clinical practice with increasing rates of mechanical circulatory support in cardiogenic shock.

Acknowledgments and Thank You



Our greatest thanks go to the patients and relatives.

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