Mechanical Unloading Trials

Critical appraisal of rationale & evidence

Dirk Donker MD PhD • Cardiologist - Intensivist

UNIVERSITY OF TWENTE. | TECHMED CENTRE

Universitair Medisch Centrum Utrecht

Conflicts of interest

Research cooperation & consultancy

- Getinge Maquet Critical Care AB
- Abiomed
- Hbox GmbH
- Sonion BV

Importance of nomenclature, definitions & understanding

Importance of nomenclature, definitions & understanding

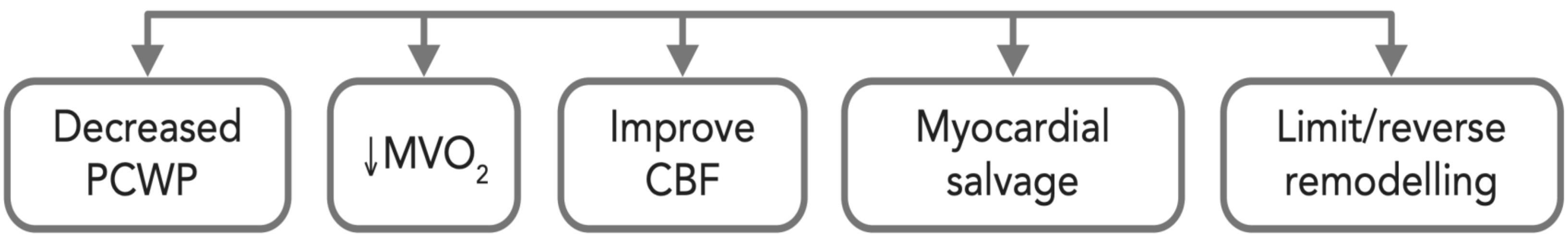
Unload, offload …

Importance of nomenclature, definitions & understanding

Unload, offload … NOT OFFSIDE – simply a GOAL !?

x.com/ESPNFC 21. June 2024

Cardiac unloading



Burkhoff D. Interventional Cardiology Review 2019

Journal of the American College of Cardiology
Vol. 41, No. 7, 2003

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ISSN 0735-1097/03/$30.00
doi:10.1016/S0735-1097(03)00084-6

Left Ventricular Support by Catheter-Mounted Axial Flow Pump Reduces Infarct Size

Bart Meyns, MD, PHD, Jarek Stolinski, MD, Veerle Leunens, Erik Verbeken, MD, PHD, Willem Flameng, MD, PHD

Leuven, Belgium

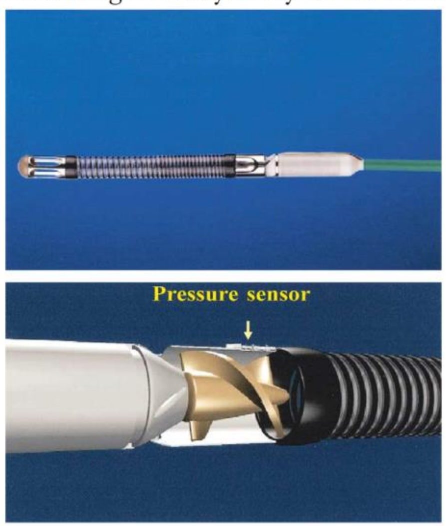
OBJECTIVES We sought to investigate the effect of a catheter-mounted microaxial blood pump (Impella, Aachen, Germany) on myocardial infarct size.

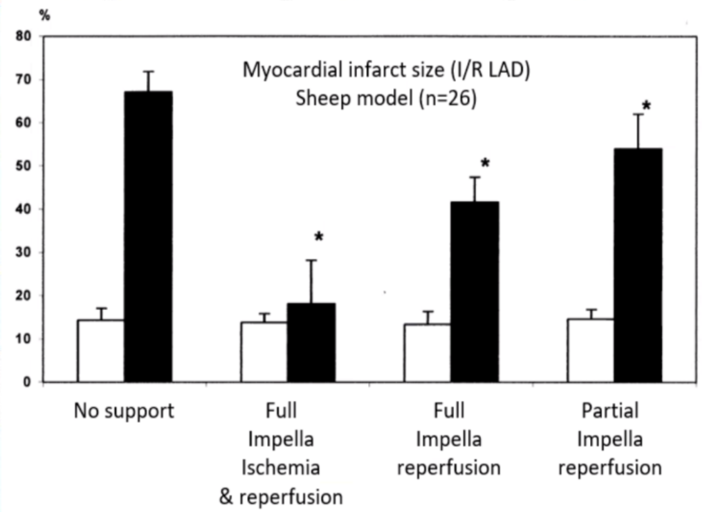
BACKGROUND The small rotary blood pump Impella provides unloading of the left ventricle and is introducible via the femoral artery.

METHODS Myocardial infarction was induced by occlusion of major branches of the left anterior descending coronary artery for 60 min followed by 120 min of reperfusion in 26 sheep. The

RESULTS

CONCLUSIONS





Special Issue: EuroELSO 2024

Perfusion

Perfusion
2024, Vol. 39(1S) 5S–12S

DOI: 10.1177/02676591241237639
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The physiology of venoarterial extracorporeal membrane oxygenation - A comprehensive clinical perspective

Libera Fresiello,[1] Jeannine A.J. Hermens,[2] Lara Pladet,[2] Christiaan L. Meuwese[3,4] and Dirk W. Donker[1,2]

- **Unloading or decompressing strategies:**
  to reduce mechanical (over-)load on the LV
  depends on LV cavity pressures & geometry (Laplace's law)

- **Venting strategies:**
  to assure transpulmonary & transcardiac blood flow
  to prevent LV cavity & aortic root thrombosis

- **Combined MCS strategies:**
  VA ECMO & adjunct device
  to increase total systemic blood flow >> VA ECMO alone

ESC European Society of Cardiology

European Journal of Heart Failure (2023) **25**, 2037–2046
doi:10.1002/ejhf.3014

RESEARCH ARTICLE

Early left atrial venting versus conventional treatment for left ventricular decompression during venoarterial extracorporeal membrane oxygenation support: The EVOLVE-ECMO randomized clinical trial

Hanbit Park[1,2], Jeong Hoon Yang[3], Jung-Min Ahn[1], Do-Yoon Kang[1], Pil Hyung Lee[1], Tae Oh Kim[1], Ki Hong Choi[3], Pil Je Kang[4], Sung-Ho Jung[4], Sung-Cheol Yun[5], Duk-Woo Park[1], Seung-Whan Lee[1], Seung-Jung Park[1], and Min-Seok Kim[1]*

[1]Division of Cardiology, Department of Internal Medicine, Asan Medical Center Heart Institute, University of Ulsan College of Medicine, Seoul, Republic of Korea; [2]Division of Cardiology, Department of Medicine, Gangneung Asan Hospital, University of Ulsan College of Medicine, Gangneung, South Korea; [3]Division of Cardiology, Department of Internal Medicine, Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [4]Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; and [5]Department of Clinical Epidemiology and Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

ESC
European Society of Cardiology

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RESEARCH ARTICLE

Early left atrial venting versus conventional treatment for left ventricular decompr... during venoarterial extraco... oxygenation su... ECMO ran...

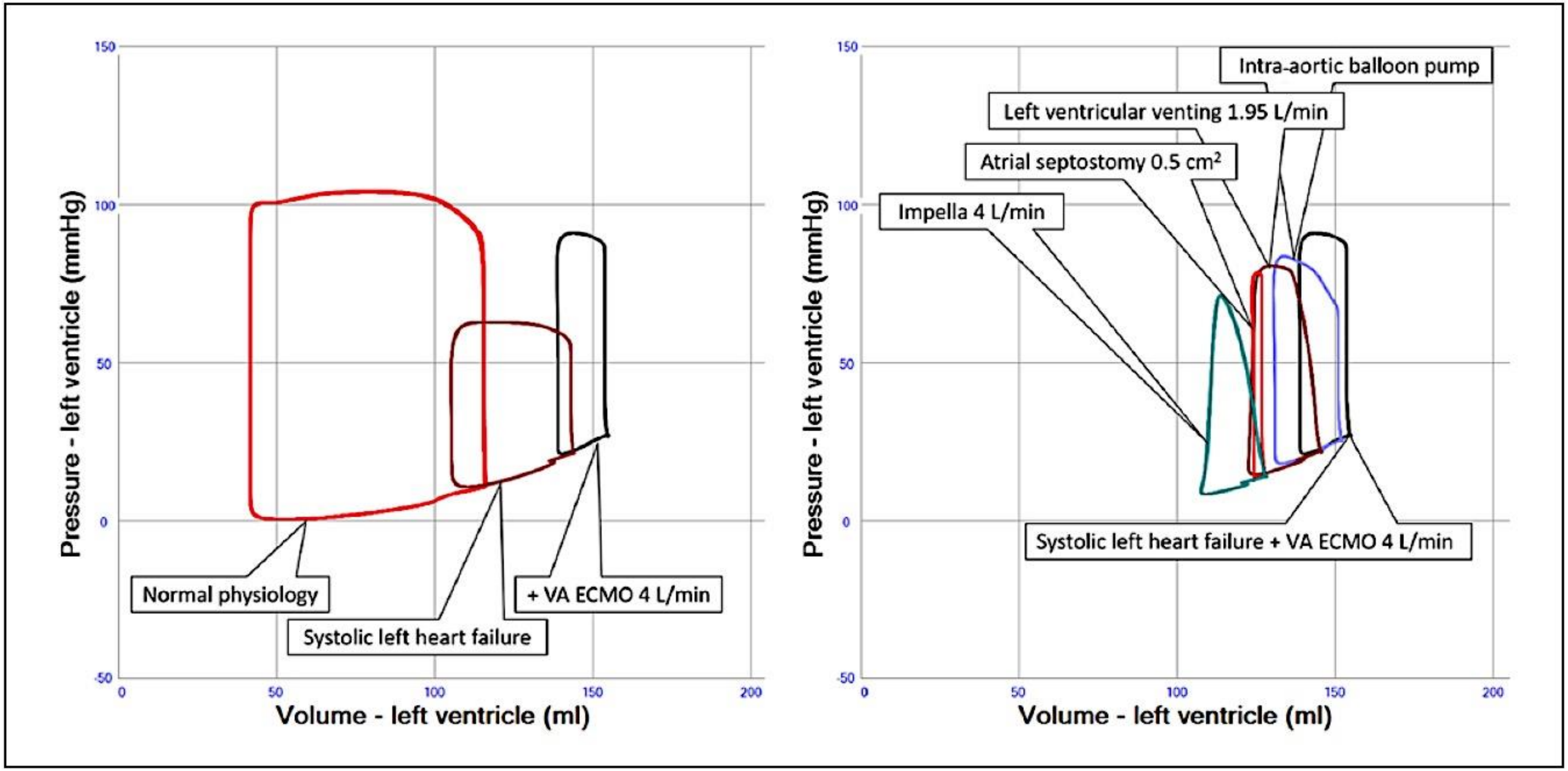
LV unloading using percutaneous transseptal left atrial cannulation via the femoral vein into the ECMO venous circuit.

...ng Hoon Yang[3], Jung-Min Ahn[1], Do-Yoon Kang[1], Pil Hyung Lee[1], ...Kim[1], Ki Hong Choi[3], Pil Je Kang[4], Sung-Ho Jung[4], Sung-Cheol Yun[5], Duk-Woo Park[1], Seung-Whan Lee[1], Seung-Jung Park[1], and Min-Seok Kim[1]*

[1]Division of Cardiology, Department of Internal Medicine, Asan Medical Center Heart Institute, University of Ulsan College of Medicine, Seoul, Republic of Korea; [2]Division of Cardiology, Department of Medicine, Gangneung Asan Hospital, University of Ulsan College of Medicine, Gangneung, South Korea; [3]Division of Cardiology, Department of Internal Medicine, Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [4]Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; and [5]Department of Clinical Epidemiology and Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

LV Unloading During Veno-Arterial ECMO

comparison of LV unloading interventions



Donker DW et al. Perfusion 2019

Left Ventricular Unloading During Veno-Arterial ECMO: A Simulation Study

Dirk W. Donker,* Daniel Brodie,† José P. S. Henriques,‡ and Michael Broomé§¶‖

Table 1. Hemodynamic Data for Normal Physiology, Isolated Left Ventricular (LV) Failure and LV Failure Supported With VA ECMO and Various Adjunct Therapies

		ECMO Flow (L/min)	Heart Rate (/min)	MAP (mm Hg)	MPAP (mm Hg)	LV EDV (mL)	LV ESV (mL)	LV SV (mL)	LV EF (%)	LV PVA (mm Hg mL)	PCWP (mm Hg)	RAP (mm Hg)	LV Coronary Flow (mL/min)	Qp/Qs`	Comment
1	Normal	0	100	101	17	121	51	70	58%	11,470	7	4	164	99%	
2	LV heart failure	0	100	61	33	158	127	31	20%	5946	30	11	67	97%	
3	+VA ECMO 4 L/min	4	100	85	36	173	161	12	7%	8076	35	10	106	21%	Increase in LV loading
4	+Afterload ↓	4	100	65	33	161	134	27	17%	6294	30	10	74	38%	
5	+800 mL blood volume ↓ + afterload ↓	4	100	65	25	153	135	18	12%	5945	22	3	85	30%	
6	+Inotropic support + afterload ↓	4	100	65	22	138	103	36	26%	6305	17	3	90	46%	
7	+IABP (no inotropic support)	4	100	65	24	149	125	24	16%	5343	21	3	121	36%	Increase in coronary flow
8	+Impella 2.5 L/min	4	100	72	23	143	131	13	9%	5600	20	3	106	40%	
9	+Impella 5.0 L/min	4	100	89	19	118	100	18	16%	3775	13	3	159	55%	
10	+Impella 5.0 L/min + afterload ↓	4	100	65	19	118	100	18	16%	3811	13	3	106	55%	
11	+ASD 0.5 cm^2	4	100	58	20	123	114	9	7%	4133	14	4	85	105%	
12	+ASD 1.0 cm^2	4	100	54	19	107	102	4	4%	3158	10	5	84	150%	
13	+ASD 1.5 cm^2	4	100	52	18	98	95	2	2%	2683	8	5	83	175%	Risk of LV thrombus
14	+ASD 1.5 cm^2 + afterload ↑	4	100	65	18	98	97	1	1%	2740	8	5	112	177%	Risk of LV thrombus
15	+Pulmonary artery venting 1.50 L/min	4	100	63	22	146	130	15	11%	5490	20	3	77	26%	
16	+Left atrial venting 1.25 L/min	4	100	63	23	145	130	15	11%	5477	20	3	77	49%	
17	+Left ventricular venting 1.90 L/min	4	100	61	23	142	119	23	16%	5120	19	4	74	58%	

ESC European Society of Cardiology

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RESEARCH ARTICLE

Early left atrial venting versus conventional treatment for left ventricular decompression during venoarterial extracorporeal membrane oxygenation support: The EVOLVE-ECMO randomized clinical trial

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The EVOLVE-ECMO randomized controlled trial

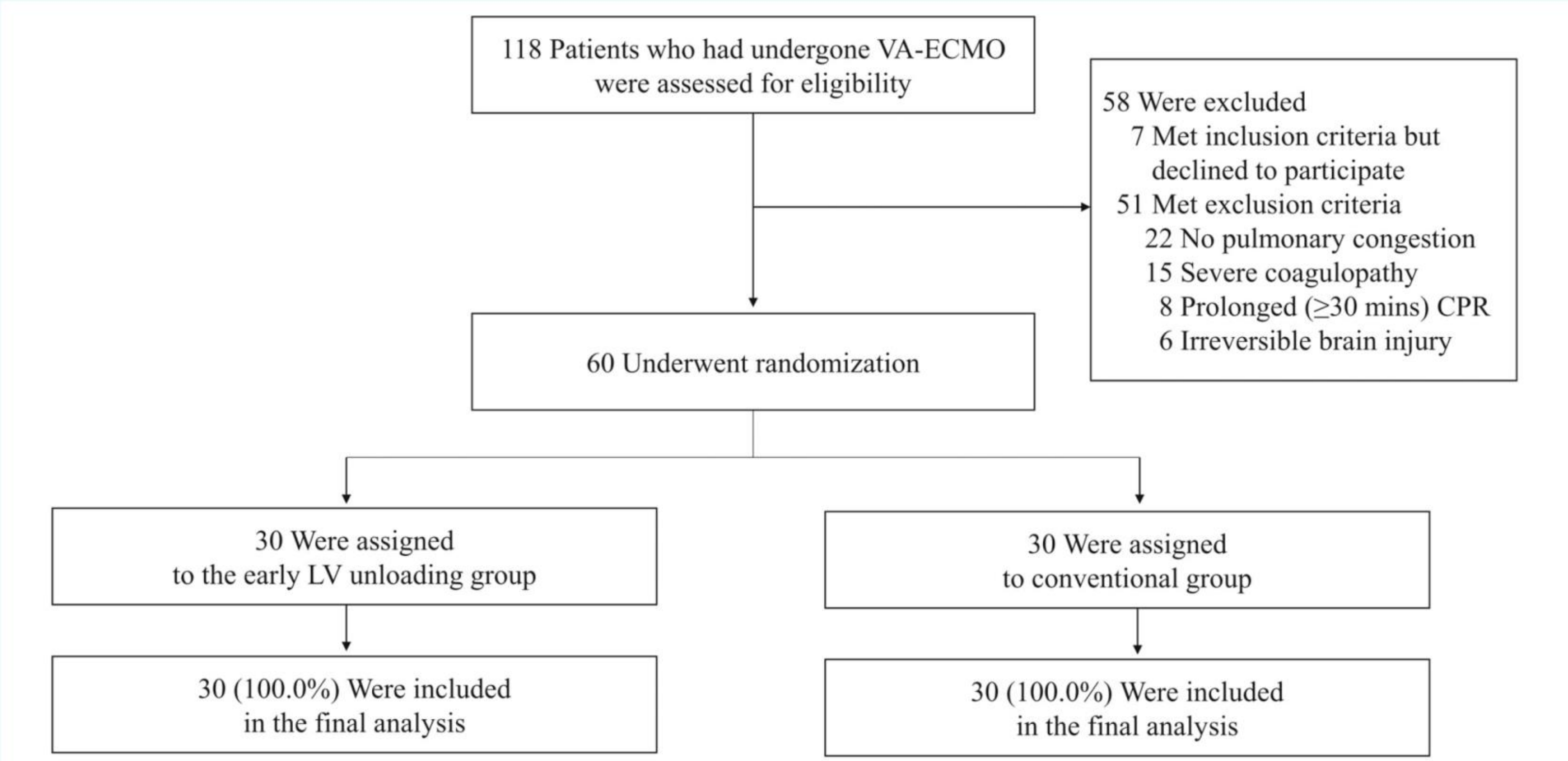
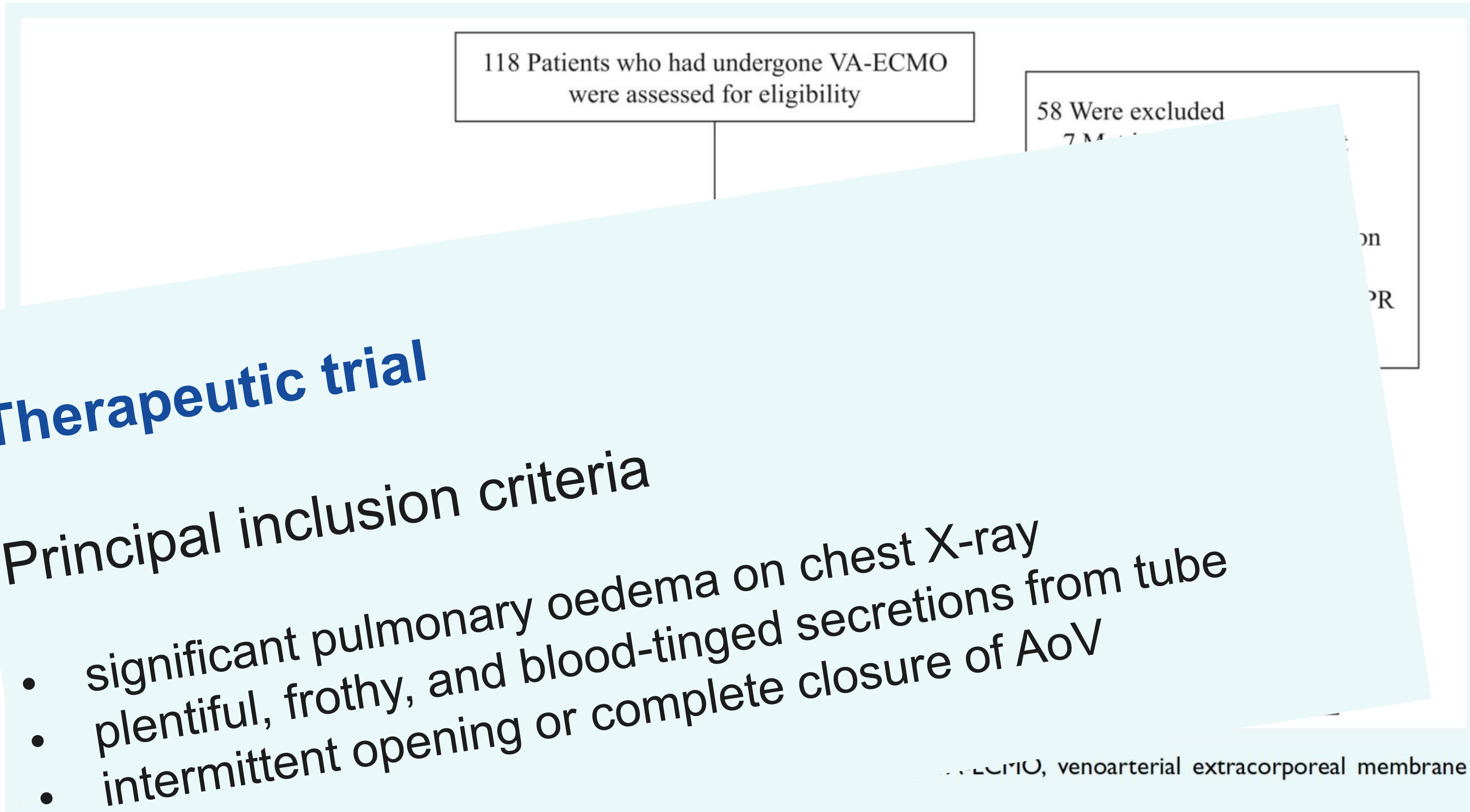


Figure 1 Study flow-chart. CPR, cardiopulmonary resuscitation; LV, left ventricular; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

Park H et al. Eur Heart J 2023

The EVOLVE-ECMO randomized controlled trial



Therapeutic trial

Principal inclusion criteria

- significant pulmonary oedema on chest X-ray
- plentiful, frothy, and blood-tinged secretions from tube
- intermittent opening or complete closure of AoV

Park H et al. Eur Heart J 2023

The EVOLVE-ECMO randomized controlled trial

Early versus late LV unloading

LV unloading during VA-ECMO - 86.7% of all cases !

- 29 (96.7%) cases - **early** LV unloading
  LV unloading after VA-ECMO initiation; median **2.4 h** (1.2-7.9 h)

- 23 (76.7%) cases - **conventional** LV unloading group
  LV unloading after VA-ECMO initiation; median **48.4 h** (47.8-96.5 h)

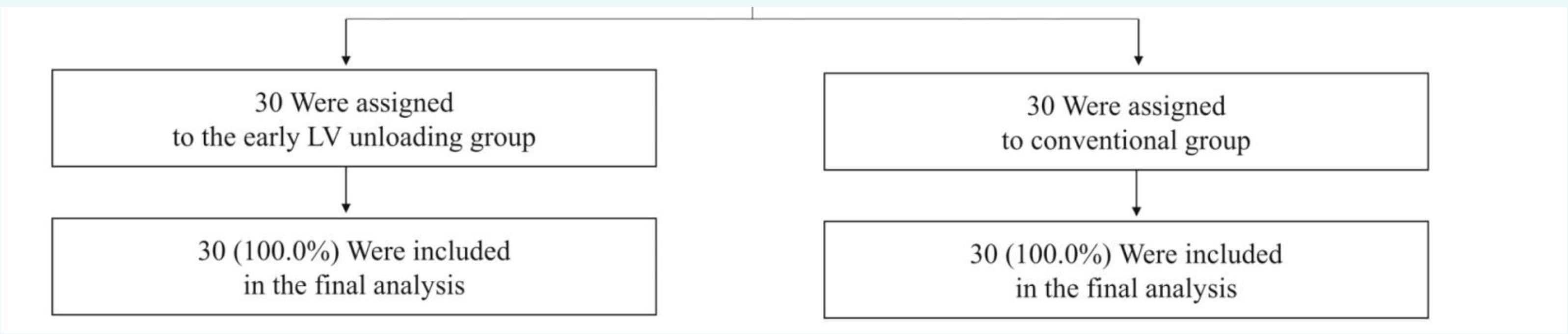


Figure 1 Study flow-chart. CPR, cardiopulmonary resuscitation; LV, left ventricular; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

Park H et al. Eur Heart J 2023

The EVOLVE-ECMO randomized controlled trial

Table 2 Medication, vital signs, and laboratory data at randomization

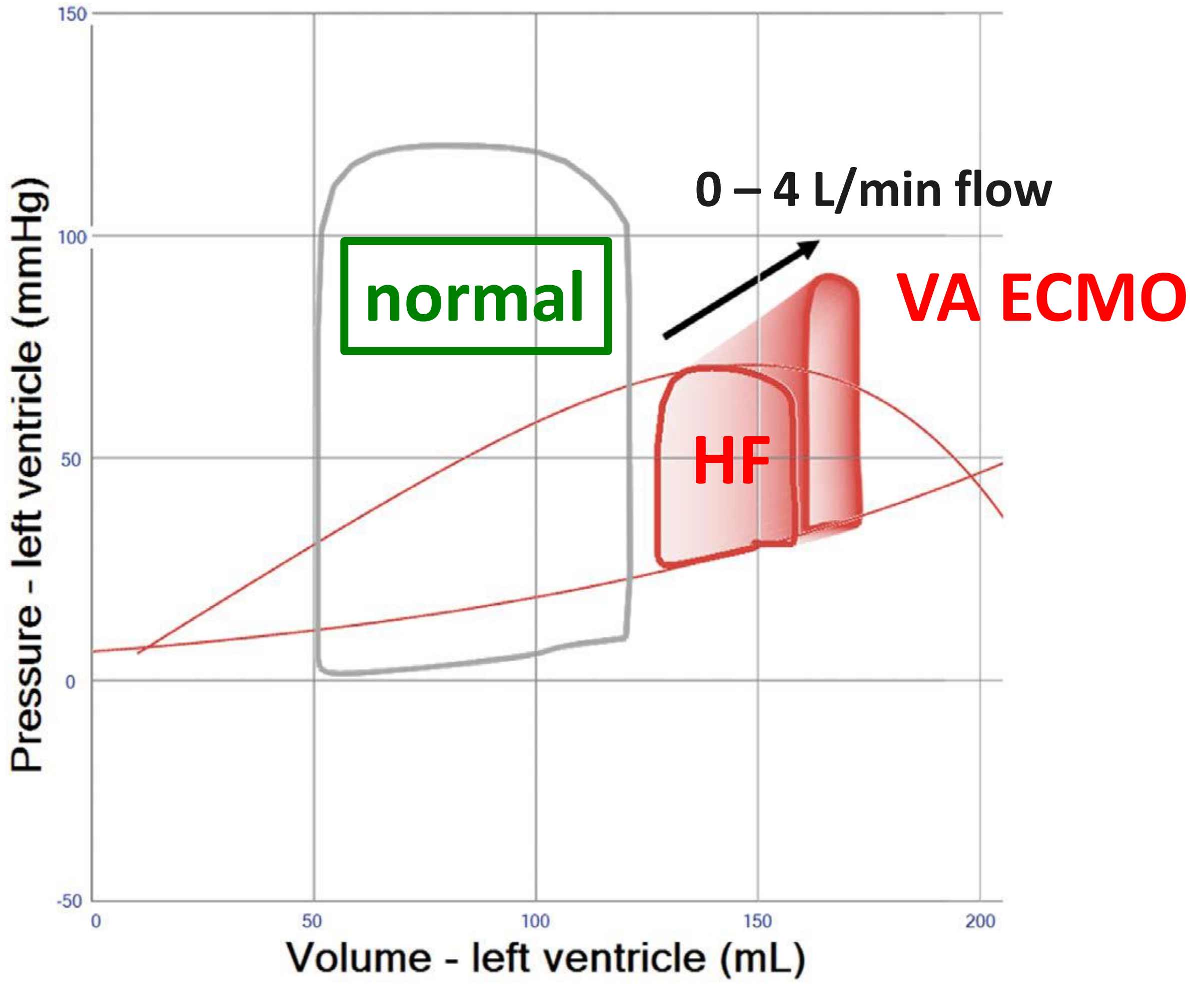
	Early LV unloading group ($n = 30$)	Conventional LV unloading group ($n = 30$)	p-value
Medication at randomization, n (%)			
IV dobutamine	12 (40.0)	9 (30.0)	0.417
IV dopamine	7 (23.3)	7 (23.3)	0.999
IV norepinephrine	26 (86.7)	26 (86.7)	0.999
IV milrinone	1 (3.3)	1 (3.3)	0.999
IV vasopressin	15 (50.0)	10 (33.3)	0.190
IV furosemide	9 (30.0)	9 (30.0)	0.999
Vital signs at randomization			
Systolic blood pressure, mmHg	95.8 ± 25.2	86.3 ± 17.2	0.099
Diastolic blood pressure, mmHg	69.0 ± 20.5	63.7 ± 17.0	0.288
Mean blood pressure, mmHg	77.9 ± 20.4	71.9 ± 15.1	0.206
Heart rate, bpm	82.2 ± 28.0	93.8 ± 29.2	0.124

Figure 1 Study flow-chart. CPR, cardiopulmonary resuscitation; LV, left ventricular; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

Park H et al. Eur Heart J 2023

LV Unloading During Veno-Arterial ECMO

simulation study



Donker DW et al. ASAIO 2018

LV Unloading During Veno-Arterial ECMO

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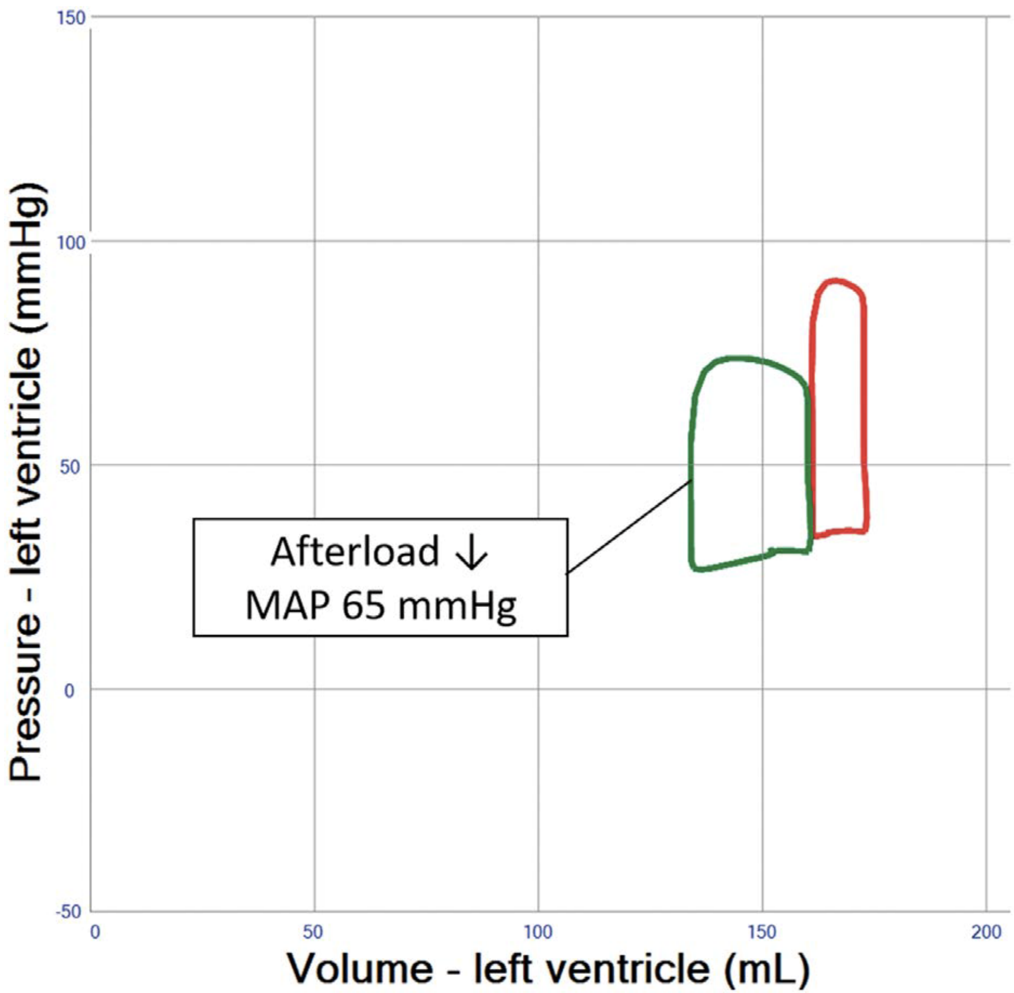

Donker DW et al. ASAIO 2018

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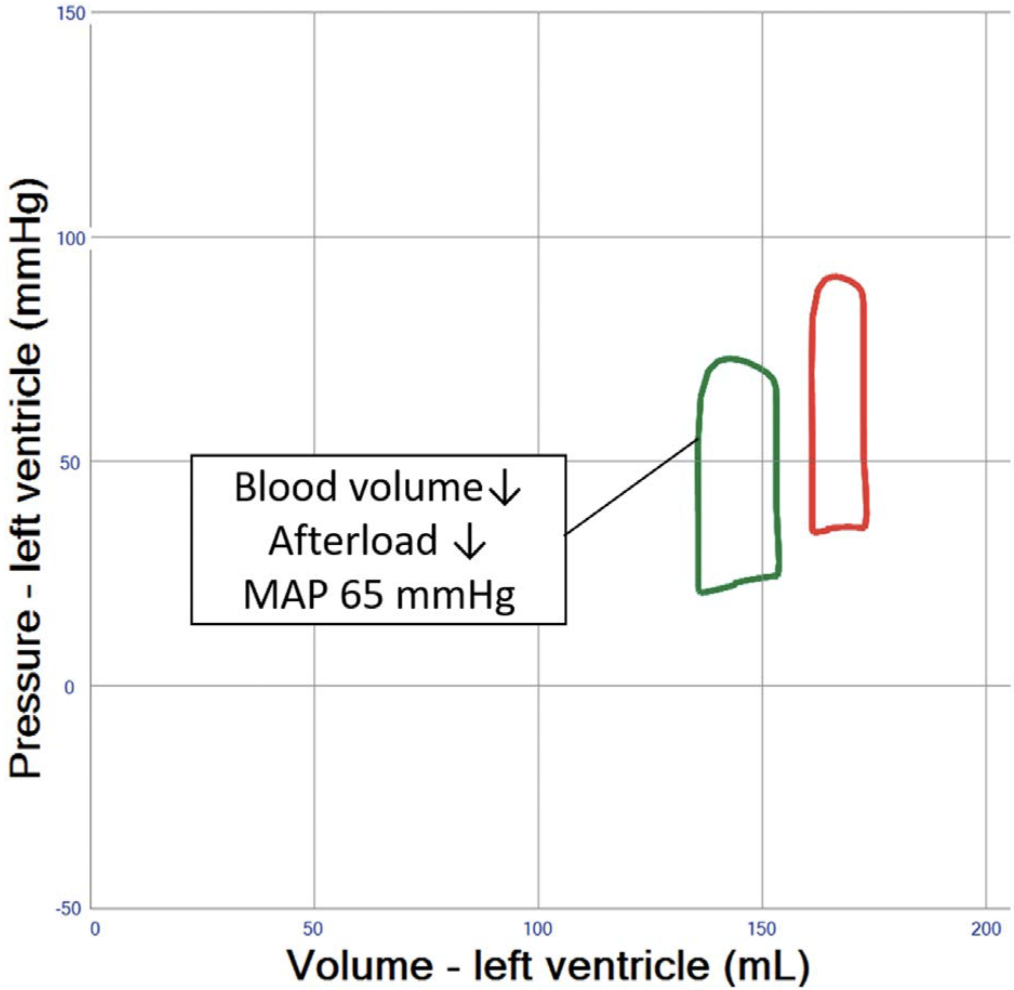

Donker DW et al. ASAIO 2018

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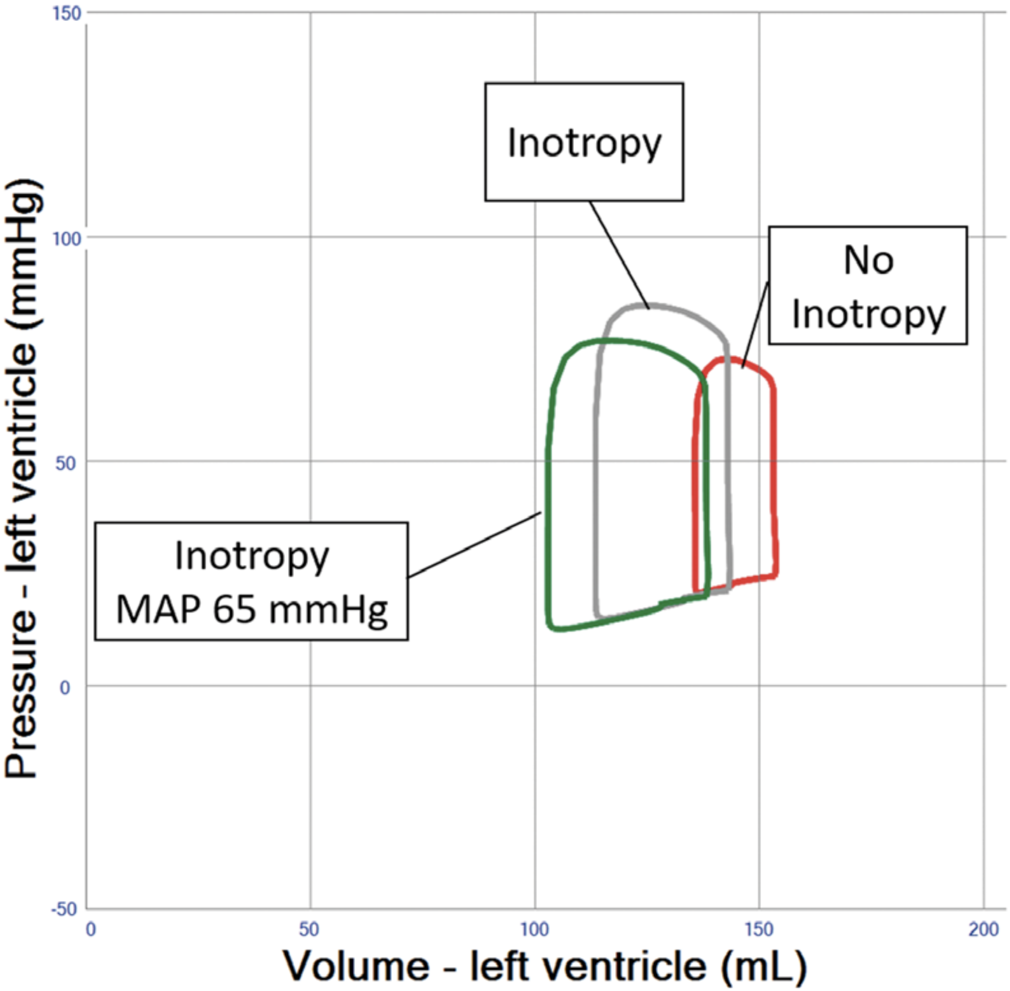
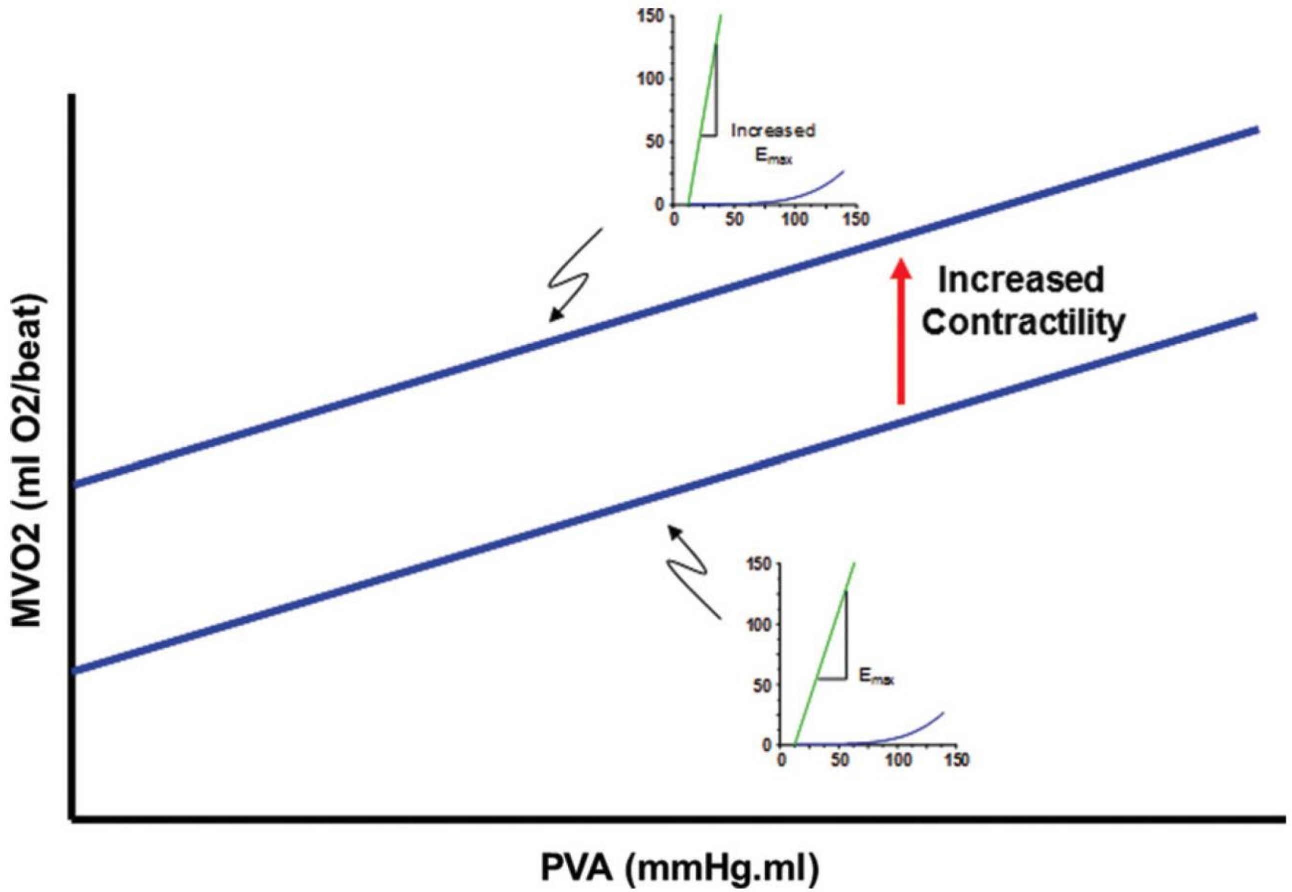


Donker DW et al. ASAIO 2018

Cardiac energetics *physics meets biology !?*

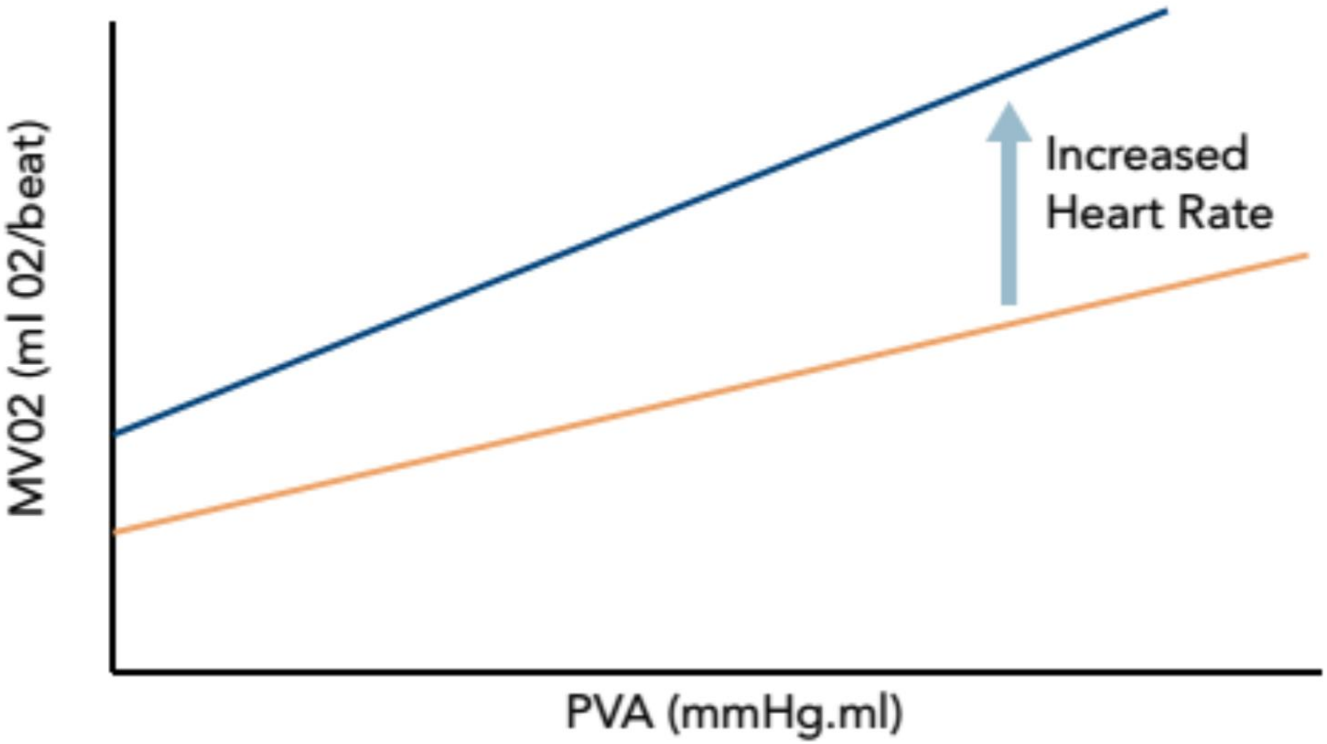
Effect of contractility on oxygen consumption



Burkhoff D. et al. Catheterization and Cardiovascular Interventions 2012

Cardiac energetics in physics

Pressure volume loop area and heart rate



Burkhoff D. RadcliffCardiology 2021

The EVOLVE-ECMO randomized controlled trial

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Heart rate, bpm	82.2 ± 28.0	93.8 ± 29.2	0.124
Pulmonary oedema on chest radiography, n (%)	29 (96.7)	29 (96.7)	0.999
LA pressure on catheterization, mmHg	17.9 ± 10.2	21.9 ± 11.9	0.449

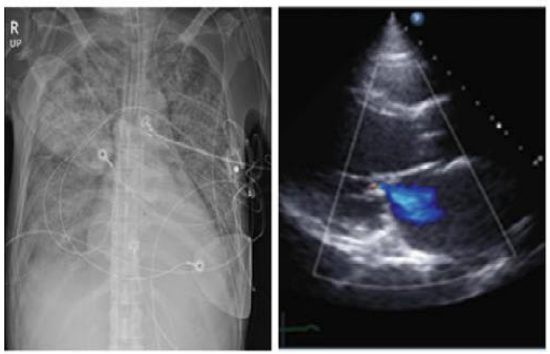
Figure 1 Study flow-chart. CPR, cardiopulmonary resuscitation; LV, left ventricular; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

Park H et al. Eur Heart J 2023

The EVOLVE-ECMO randomized controlled trial

Therapeutic trial - early versus late LV unloading

Significant pulmonary oedema or AV closure during VA-ECMO



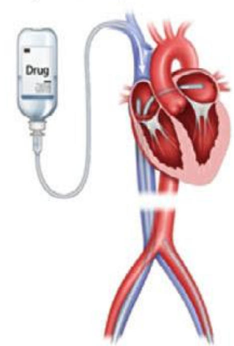
Randomization 1:1

Early LV unloading strategy

LV unloading performed at the time of VA-ECMO insertion

Conventional strategy

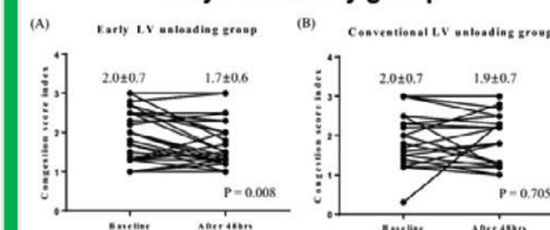
LV unloading performed when medically refractory pulmonary oedema identified



No difference in clinical outcomes

	Early Group (n=30)	Conventional group (n=30)	P
VA-ECMO Weaning	70.0%	76.7%	ns
Survival to discharge	53.5%	50.0%	ns
In-hospital CV mortality	16.7%	16.7%	ns
Bridge to HT or LVAD	40.0%	36.7%	ns
Duration of mechanical ventilation	12.9days	36.4days	ns
Length of ICU stay	23.3days	31.3days	ns
Adverse events	53.3%	76.7%	ns

Improvement of pulmonary congestion only in the early group



Park H et al. Eur Heart J 2023

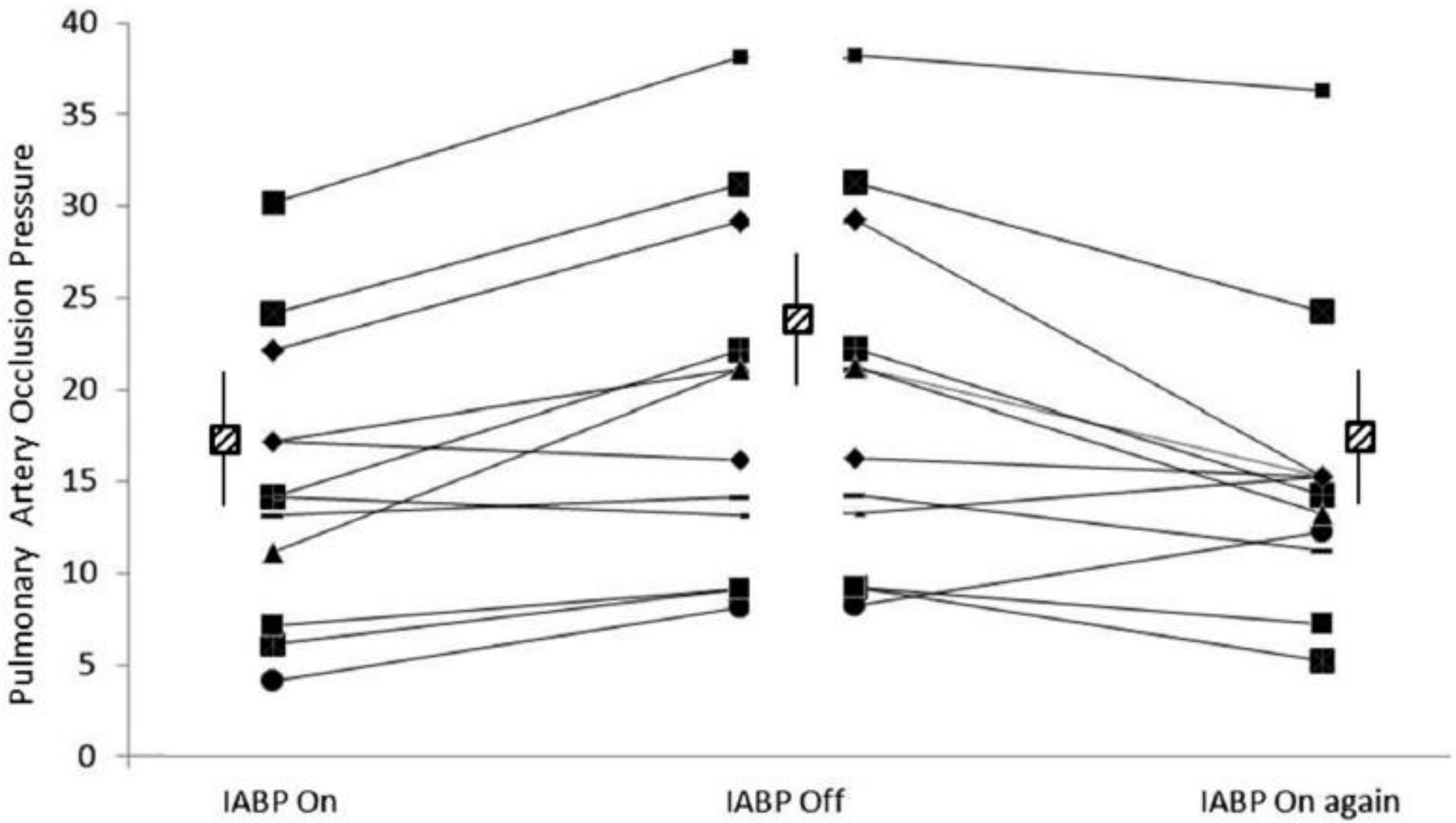
Clinical intuition driven LV unloading …

Intra-Aortic Balloon Pump Effects on Macrocirculation and Microcirculation in Cardiogenic Shock Patients Supported by Venoarterial Extracorporeal Membrane Oxygenation*

Thibaut Petroni, MD[1]; Anatole Harrois, MD, PhD[2]; Julien Amour, MD, PhD[3]; Guillaume Lebreton, MD[4]; Nicolas Brechot, MD, PhD[1]; Sébastien Tanaka, MD[2]; Charles-Edouard Luyt, MD, PhD[1]; Jean-Louis Trouillet, MD[1]; Jean Chastre, MD[1]; Pascal Leprince, MD, PhD[4]; Jacques Duranteau, MD, PhD[2]; Alain Combes, MD, PhD[1]

Petroni T et al. Crit Care Med. 2014

PCWP with/ without *IABP* during ECMO



Petroni T et al. Crit Care Med. 2014

European Heart Journal
Acute Cardiovascular Care
EUROPEAN SOCIETY OF CARDIOLOGY®

Original scientific paper

European Heart Journal: Acute Cardiovascular Care
1–8

DOI: 10.1177/2048872617711169
journals.sagepub.com/home/acc
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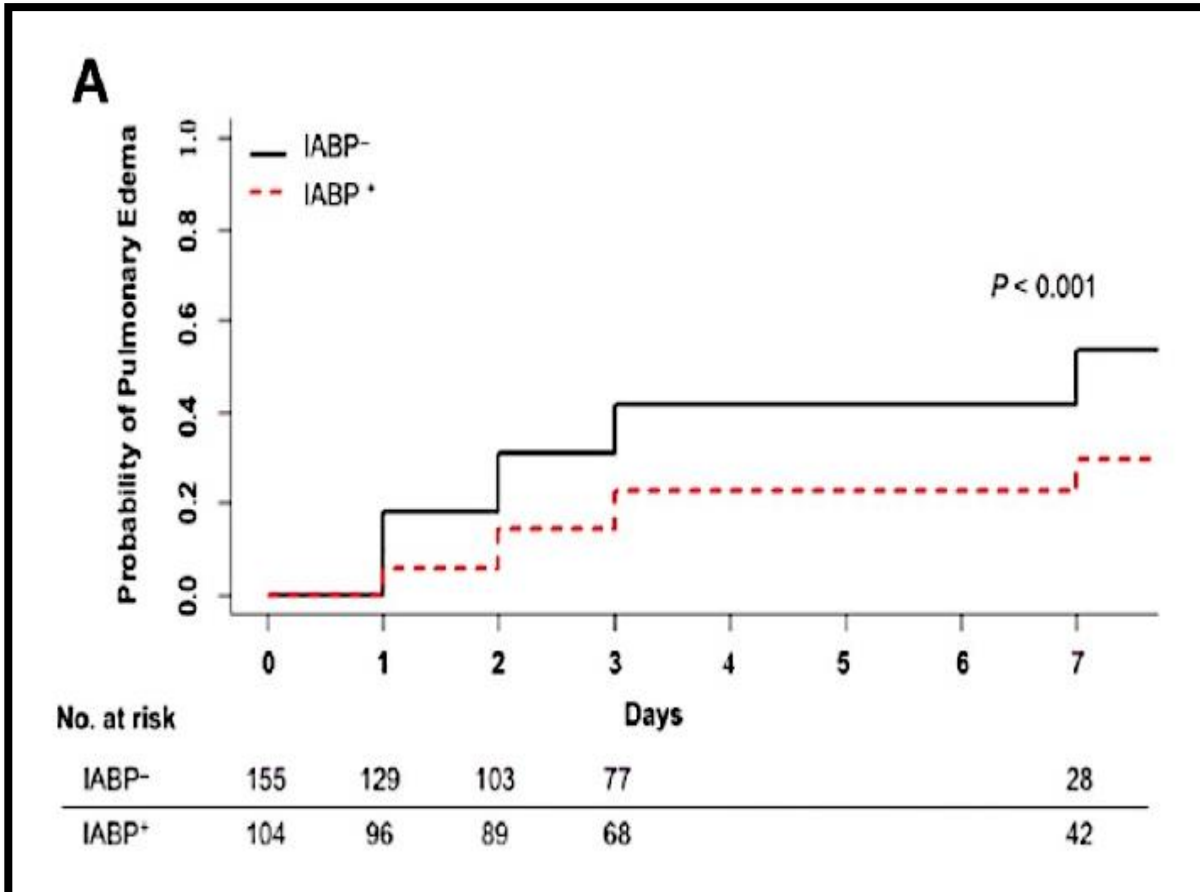
Intra-aortic balloon pump protects against hydrostatic pulmonary oedema during peripheral venoarterial-extracorporeal membrane oxygenation

Nicolas Bréchot[1,2], Pierre Demondion[3,4], Francesca Santi[3], Guillaume Lebreton[3,4], Tai Pham[5,6], Apostolos Dalakidis[7], Laetitia Gambotti[8], Charles-Edouard Luyt[1,4], Matthieu Schmidt[1,4], Guillaume Hekimian[1,4], Philippe Cluzel[4,7], Jean Chastre[1,4], Pascal Leprince[3,4] and Alain Combes[1,4]

IABP protects against hydrostatic pulmonary edema during peripheral VA ECMO



Bréchot N et al. Eur Heart J: Acute Cardiovasc Care 2017

ORIGINAL RESEARCH ARTICLE

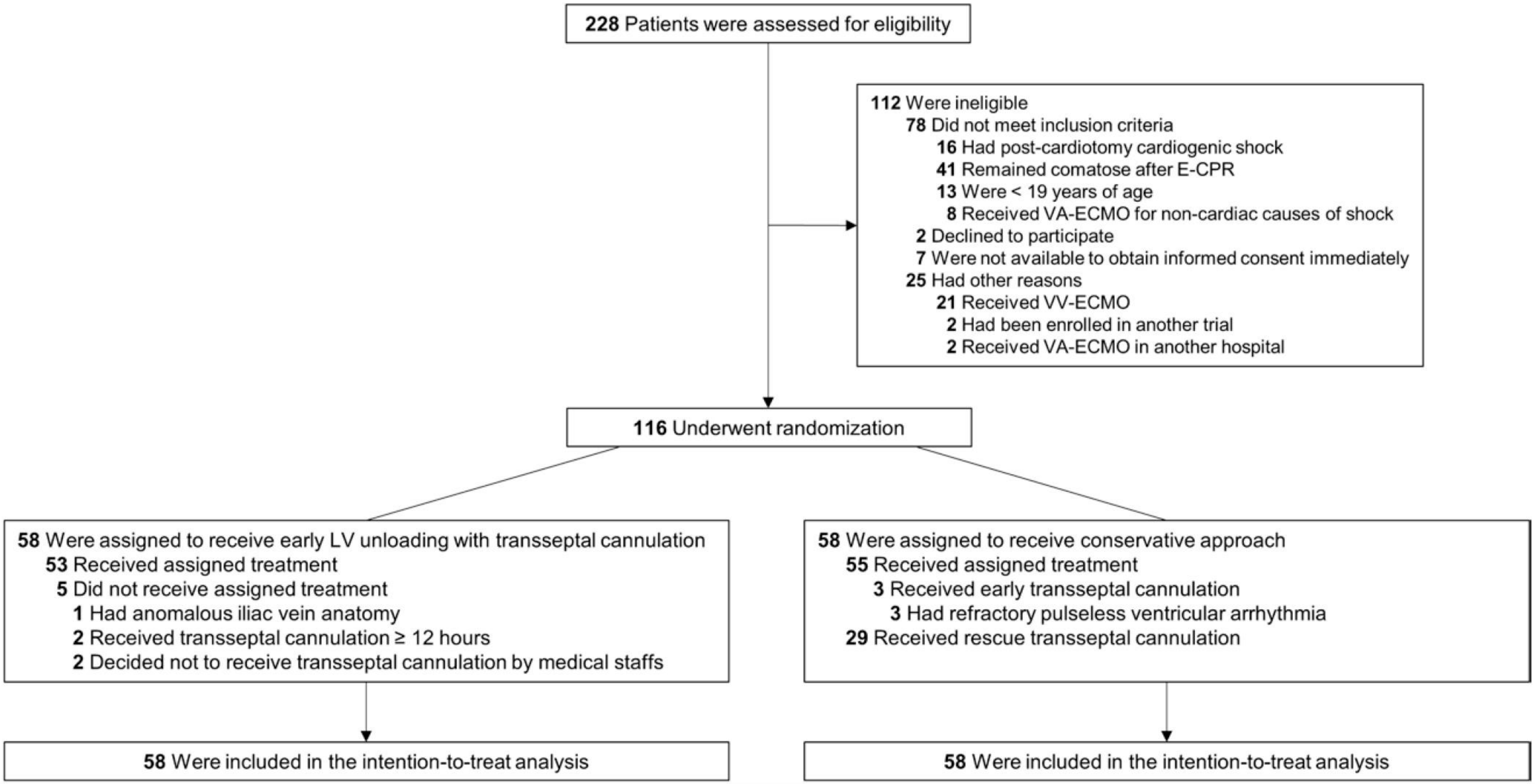
Early Left Ventricular Unloading or Conventional Approach After Venoarterial Extracorporeal Membrane Oxygenation: The EARLY-UNLOAD Randomized Clinical Trial

Min Chul Kim, MD, PhD; Yongwhan Lim, MD; Seung Hun Lee, MD, PhD; Yoonmin Shin, MD; Joon Ho Ahn, MD, PhD; Dae Young Hyun, MD, PhD; Kyung Hoon Cho, MD, PhD; Doo Sun Sim, MD, PhD; Young Joon Hong, MD, PhD; Ju Han Kim, MD, PhD; Myung Ho Jeong, MD, PhD; Yong Hun Jung, MD, PhD; In-Seok Jeong, MD, PhD; Youngkeun Ahn, MD, PhD

Circulation 2023

Early LV unloading versus Conventional VA ECMO

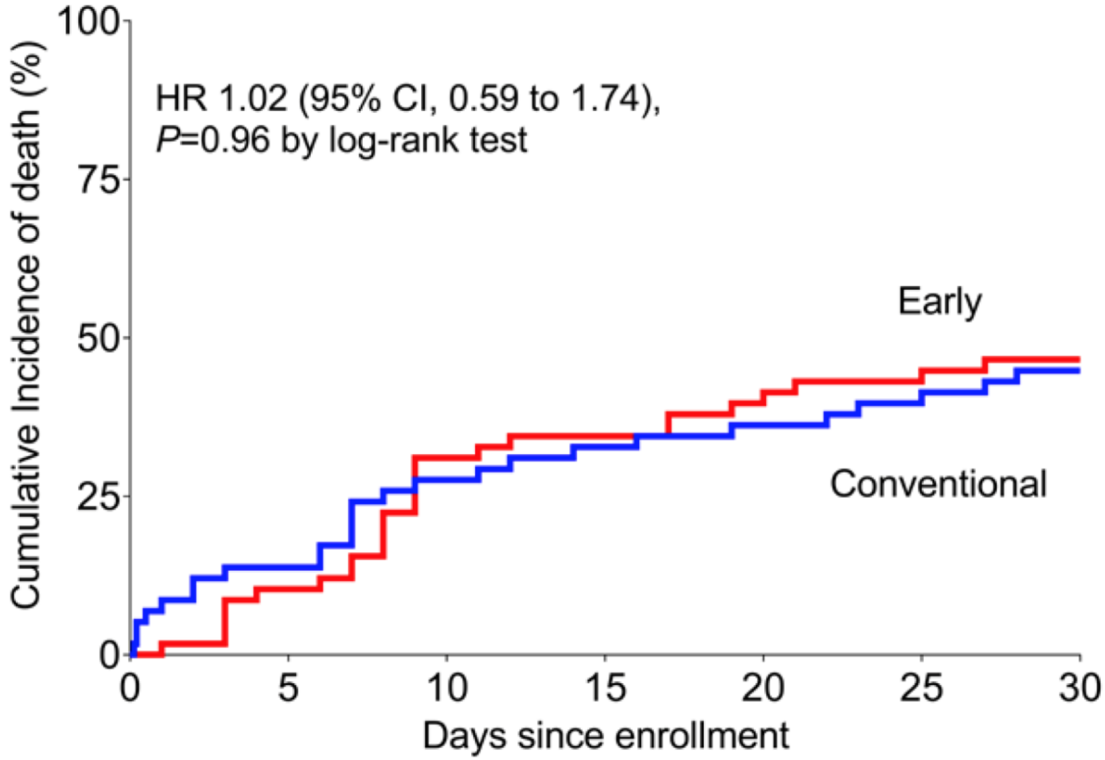
***Prophylactic** trial - randomized transseptal LA venting*



Kim MC et al. Circulation 2023

Early LV unloading versus Conventional VA ECMO

Randomized transseptal LA venting



No. at risk

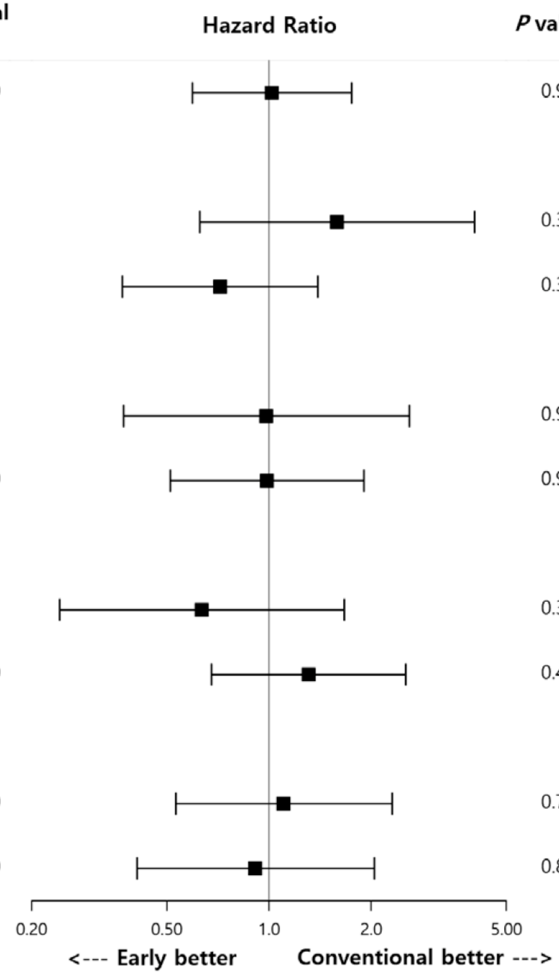
Early	58	53	45	39	35	33	31
Conventional	58	51	43	40	38	35	32

Kim MC et al. Circulation 2023

Early LV unloading versus Conventional VA ECMO

Randomized transseptal LA venting

Subgroup	Early N(%)	Conventional N(%)	*P* value	*P* for interaction
Overall	27/58 (46.6%)	26/58 (44.8%)	0.942	
Age, years				0.164
<70	10/24 (41.7%)	8/28 (28.6%)	0.334	
≥70	17/34 (50%)	18/30 (60%)	0.325	
Sex				0.924
Female	10/19 (52.6%)	7/15 (46.7%)	0.971	
Male	17/39 (43.6%)	19/43 (44.2%)	0.965	
Origin of cardiogenic shock				0.215
Non-ischemic	7/19 (36.8%)	10/20 (50%)	0.355	
Ischemic	20/39 (51.3%)	16/38 (42.1%)	0.426	
Extracorporeal CPR				0.746
No	16/33 (48.5%)	13/30 (43.3%)	0.789	
Yes	11/25 (44%)	13/28 (46.4%)	0.823	



Kim MC et al. Circulation 2023

Early LV unloading versus Conventional VA ECMO

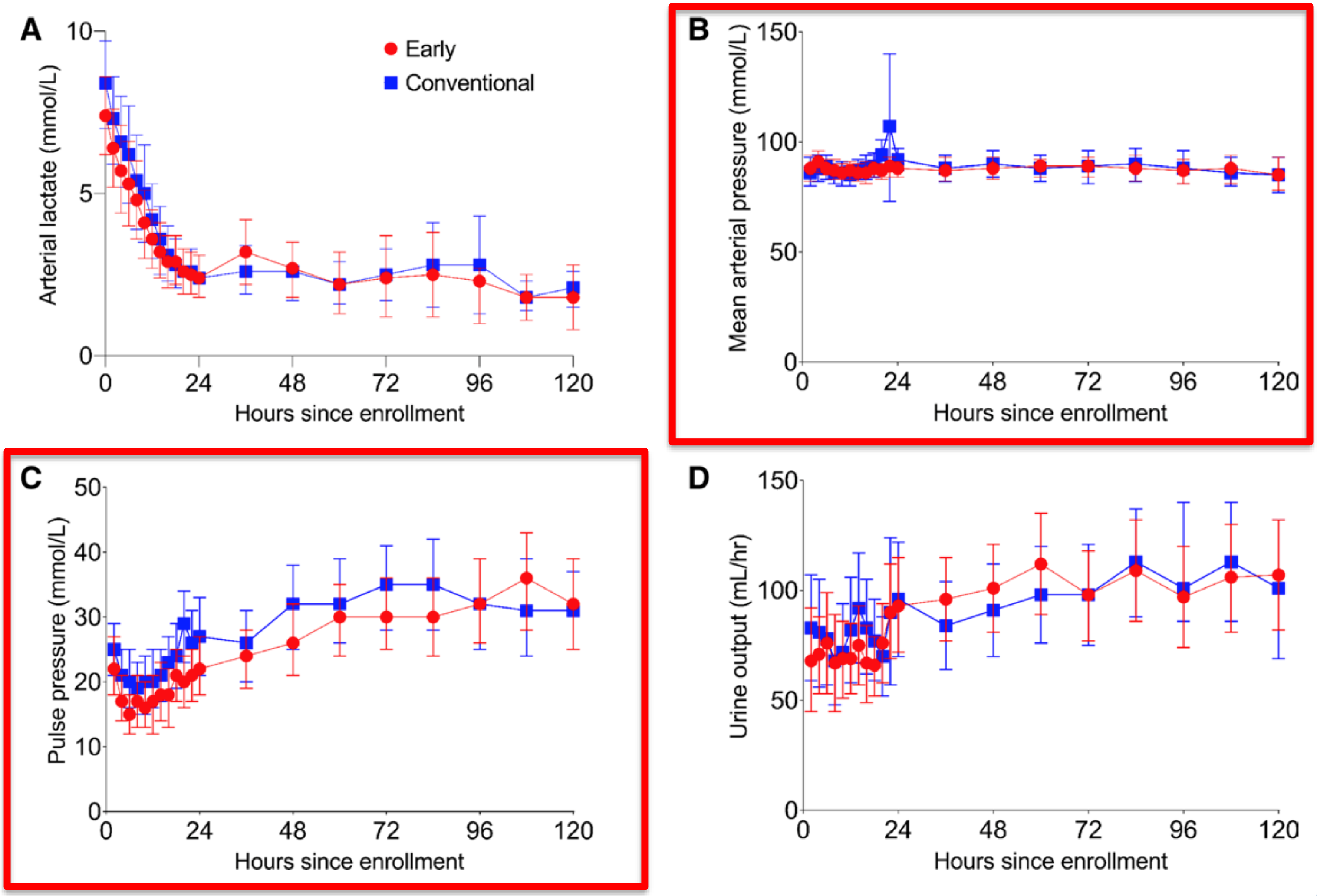
Prophylactic *trial - randomized transseptal LA venting*

- ‘1st’ RCT ‘early routine LV unloading’ *vs* conventional VA ECMO
  - **Early = <12 h after VA ECMO**
- No reduction of all-cause mortality at short term (30 days)
- ***50% crossed over for ‘rescue LV unloading - clear indication’***
  - Increased afterload
  - LV distension with blood stagnation
  - No or minimal opening of AoV with no or minimal arterial pulse wave
  - Medically refractory pulmonary congestion

Kim MC et al. Circulation 2023

Early LV unloading versus Conventional VA ECMO

Randomized transseptal LA venting



Kim MC et al. Circulation 2023

More evidence for LV unloading … ?

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Left Ventricular Unloading During Extracorporeal Membrane Oxygenation in Patients With Cardiogenic Shock

Juan J. Russo, MD,[a] Natasha Aleksova, MD,[b] Ian Pitcher, MD,[a] Etienne Couture, MD, MPH,[a] Pietro Di Santo, MD,[a] Sarah Visintini, BA, MLIS,[a] Trevor Simard, MD,[a] A. Reshad Garan, MD,[c] Koji Takeda, MD, PhD,[c] Ajay J. Kirtane, MD, SM,[c] Derek Y. So, MD, MSc,[a] Takayama, MD, PhD,[c] Benja…

ORIGINAL ARTICLE

Optimal Strategy and Ti… Venting During Veno… Support for Adult… …cular …real Life …ock

A Systematic Review a…

Abdulrahman A. Al-Fares, MD… A. Dave Nagpal, MD, MHS… …akis, MLIS; Michael A. McDonald, MD; …H; Eddy Fan, MD, PhD

ORIGINAL RESEARCH ARTICLE

Left Ventricular Unloading Is Associated With Lower Mortality in Patients With Cardiogenic Shock Treated With Venoarterial Extracorporeal Membrane Oxygenation …lts From an International, Multicenter Cohort Study

ASAIO Journal 2019

Adult Circulatory Support

Simultaneous Venoarterial Extracorporeal Membrane Oxygenation and Percutaneous Left Ventricular Decompression Therapy with Impella Is Associated with Improved Outcomes in Refractory Cardiogenic Shock

Sandeep M. Patel,* Jerry Lipinski,† Sadeer G. Al-Kindi,‡ Toral Patel,§ Petar Saric,§ Jun Li,‡ Fahd Nadeem,‡ …Ladas,§ Amer Alaiti,‡ Ann Phillips,‡ Benjamin Medalion,‡ Salil Deo,‡ Yakov Elgudin,‡ Marco A. Costa,‡ …Guilherme F. Attizzani,‡ Guilherme H. Oliveira,‡ Basar Sareyyupoglu,‡ and Hiram G. Bezerra‡

Early Impella Support in Postcardiac Arrest Cardiogenic Shock Complicating Acute Myocardial Infarction Improves Short- and Long-Term Survival*

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

VOL. 79, NO. 13, 20…

Mechanical Left Ventricular Unloading in Patients Undergoing Venoarterial Extracorporeal Membrane Oxygenation

E. Wilson Grandin, MD, MPH, MEd,[a,b] Jose I. Nunez, MD,[c] Brooks Willar, MD,[d] Kevin Kennedy, MS,[b] Peter Rycus, MPH,[e] Joseph E. Tonna, MD, MS,[e,f] Navin K. Kapur, MD,[g] Shahzad Shaefi, MD, MPH,[h] A. Reshad Garan, MD, MS[a]

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Clinical paper

Left-ventricular unloading in extracorporeal cardiopulmonary resuscitation due to acute myocardial infarction – A multicenter study

Tharusan Thevathasan[a,b,c,d,1], Megan A. Kenny[a,b,1], Finn J. Krause[a,b], … Thomas Wurster[a,c,d], Sebastian D. Boie[b], Julian Friebel[a,c,d], Wulf Knie… Arash Haghikia[a,c,d], Markus Reinthaler[a,d], Ursula Rauch-Kröhnert[a,d], … David M. Leistner[e], David Sinning[a,d], Georg Fröhlich[a], Bettina He… …k Spillmann[e], Damaris Praeger[f], Burkert Pieske[c,d,e], Karl Stan… …sser[a,c,d], Felix Balzer[b,c,1], Carsten Skurk[a,d,1,*]

JACC: HEART FAILURE

CLINICAL RESEARCH

Timing of Active Left Ventricular Unloading in Patients on Venoart… Extracorporeal Membrane Oxygenation Therapy

Benedikt Schrage, MD, PhD,[a,b,*] Jonas Sundermeyer, MD,[a,b,*] Stefan Blankenberg, M… Dennis Eckner, MD,[d] Matthias Eden, MD,[e] Ingo Eitel, MD,[b,f] Derk Frank, MD,[b,g] Norbert… Paulus Kirchhof, MD,[a,b,h] Danny Kupka, MD,[i] Ulf Landmesser, MD,[j] Axel Linke, MD,[k] Norman Mangner, MD,[k] Octavian Maniuc, MD,[m] Johannes Mierke, MD,[k] Sven Möbius… David A. Morrow, MD, MPH,[o] Marc Mourad, MD,[c] Peter Nordbeck, MD,[m] Martin Orban… Federico Pappalardo, MD,[q,r] Sandeep M. Patel, MD,[s] Matthias Pauschinger, MD,[t] Vitto… Darko Radakovic, MD,[u] P. Christian Schulze, MD, PhD,[n] … Carsten Skurk, MD,[j] Holger Thiele, MD…

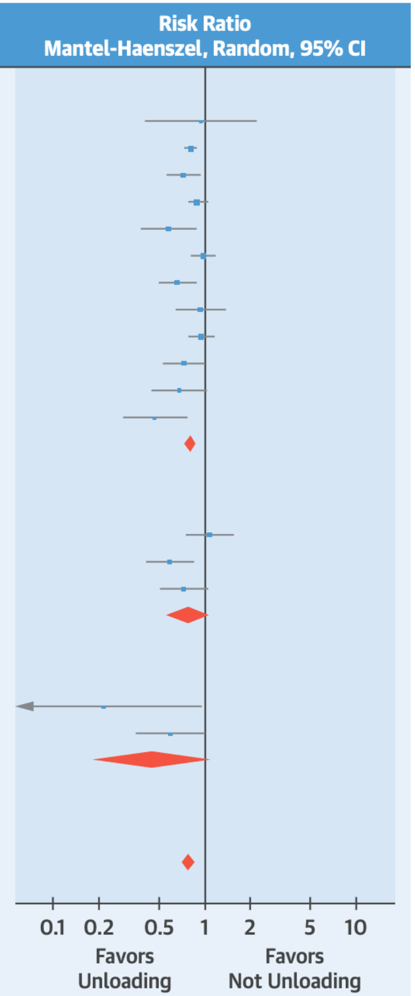
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 73, NO. 6, 2019

Left Ventricular Unloading During Extracorporeal Membrane Oxygenation in Patients With Cardiogenic Shock

Juan J. Russo, MD,[a] Natasha Aleksova, MD,[b] Ian Pitcher, MD,[a] Etienne Couture, MD, MPH,[a] Simon Parlow, MD,[a] Mohammad Faraz, MD,[a] Sarah Visintini, BA, MLIS,[a] Trevor Simard, MD,[a] Pietro Di Santo, MD,[a] Rebecca Mathew, MD,[a] Derek Y. So, MD, MSc,[a] Koji Takeda, MD, PhD,[c] A. Reshad Garan, MD,[c] Dimitrios Karmpaliotis, MD, PhD,[c] Hiroo Takayama, MD, PhD,[c] Ajay J. Kirtane, MD, SM,[c] Benjamin Hibbert, MD, PhD[a]

CENTRAL ILLUSTRATION Left Ventricular Unloading During Venoarterial Extracorporeal Membrane Oxygenation

Study or Subgroup	Unloading Events	Unloading Total	No Unloading Events	No Unloading Total	Weight
1.1.1 Intra-Aortic Balloon Pump					
Aoyama, 2014	22	35	2	3	1.2%
Aso, 2016	330	604	708	1,046	14.3%
Brechot, 2018	45	104	92	155	7.5%
Doll, 2004	105	143	62	76	11.7%
Kai Chen, 2018	17	38	17	22	3.9%
Lin, 2016	144	302	110	227	10.3%
Overtchouk, 2018	33	63	34	43	6.7%
Park, 2014	21	41	30	55	4.5%
Ro, 2014	41	60	139	193	9.7%
Sakamoto, 2012	62	94	4	4	5.6%
Tepper, 2018	15	30	22	30	3.9%
Wang, 2013	13	41	31	46	3.0%
Subtotal (95% CI)		**1,555**		**1,900**	**82.3%**
Total events	848		1,251		
1.1.2 Percutaneous Left-Ventricular Support					
Akanni, 2018	16	29	100	196	5.0%
Pappalardo, 2017	16	34	98	123	4.7%
Patel, 2018	17	30	28	36	4.9%
Subtotal (95% CI)		**93**		**355**	**14.6%**
Total events	49		226		
1.1.3 Right Upper Pulmonary Vein or Transseptal Left Atrial Cannula					
Poptsov, 2014	2	28	6	18	0.4%
Shmack, 2017	9	20	21	28	2.7%
Subtotal (95% CI)		**48**		**46**	**3.1%**
Total events	11		27		
Total (95% CI)		**1,696**		**2,301**	**100.0%**
Total events	908		1,504		

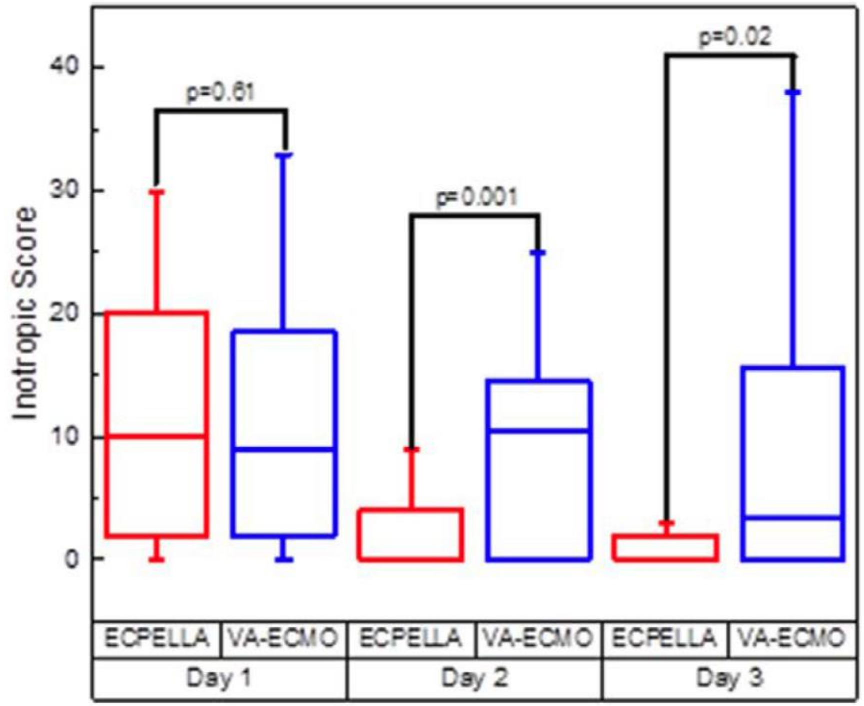


Russo, J.J. et al. J Am Coll Cardiol. 2019;73(6):654-62.

The association between left ventricular unloading during VA-ECMO for cardiogenic shock and all-cause mortality was assessed before and after stratification by left ventricular unloading strategy (IABP, pVAD, or RUPV or trans-septal left atrial cannula). The Mantel-Haenszel method was used to examine the overall risk ratio associated with left ventricular unloading during VA-ECMO using a random effects model. Left ventricular unloading during VA-ECMO for cardiogenic shock was associated with reduced mortality (RR: 0.79; 95% CI: 0.72 to 0.87; $p < 0.00001$). There was no heterogeneity in this association in relation to the specific left ventricular unloading strategy used ($p = 0.47$). CI = confidence interval; IABP = intra-aortic balloon pump; LA = left atrial; pVAD = percutaneous ventricular assist device; RR = relative risk; RUPV = right upper pulmonary vein; VA-ECMO = venoarterial extracorporeal membrane oxygenation.

Simultaneous Venoarterial Extracorporeal Membrane Oxygenation and Percutaneous Left Ventricular Decompression Therapy with Impella Is Associated with Improved Outcomes in Refractory Cardiogenic Shock

Sandeep M. Patel,* Jerry Lipinski,† Sadeer G. Al-Kindi,‡ Toral Patel,§ Petar Saric,§ Jun I
Alaiti,‡ Ann Phillips,‡ Benjamin Medalion,‡ Salil Deo,‡ Yakov Elgud
: Guilherme F. Attizzani,‡ Guilherme H. Oliveira,‡ Basar Sareyyupogi



Simultaneous Venoarterial Extracorporeal Membrane Oxygenation and Percutaneous Left Ventricular Decompression Therapy with Impella Is Associated with Improved Outcomes in Refractory Cardiogenic Shock

SANDEEP M. PATEL,*

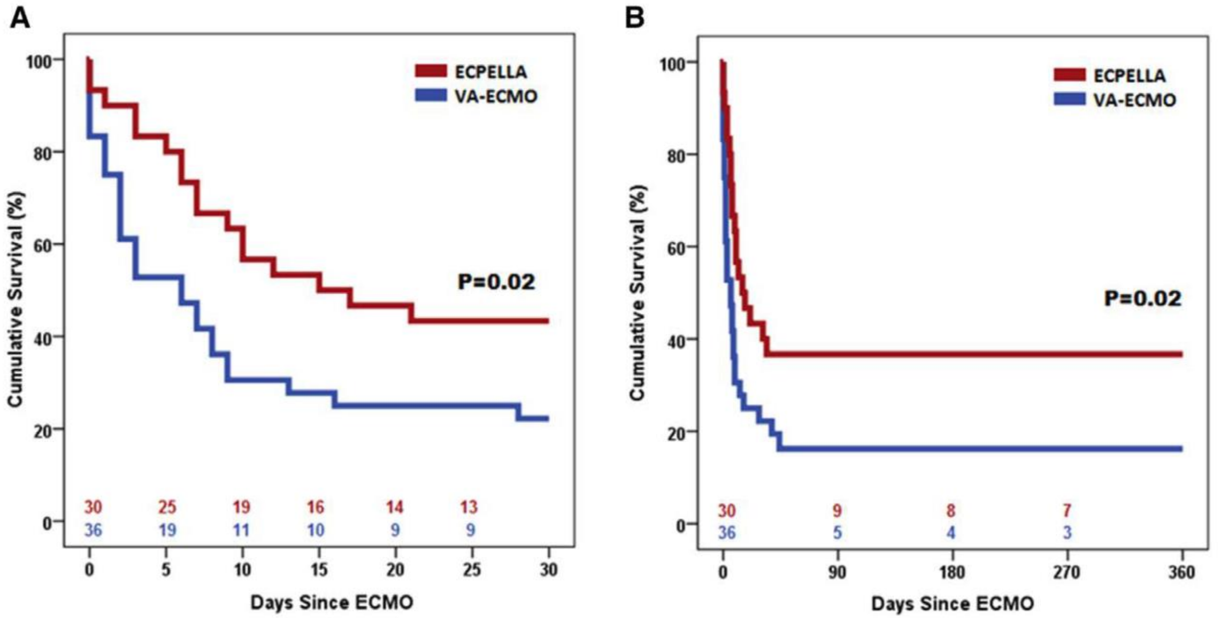
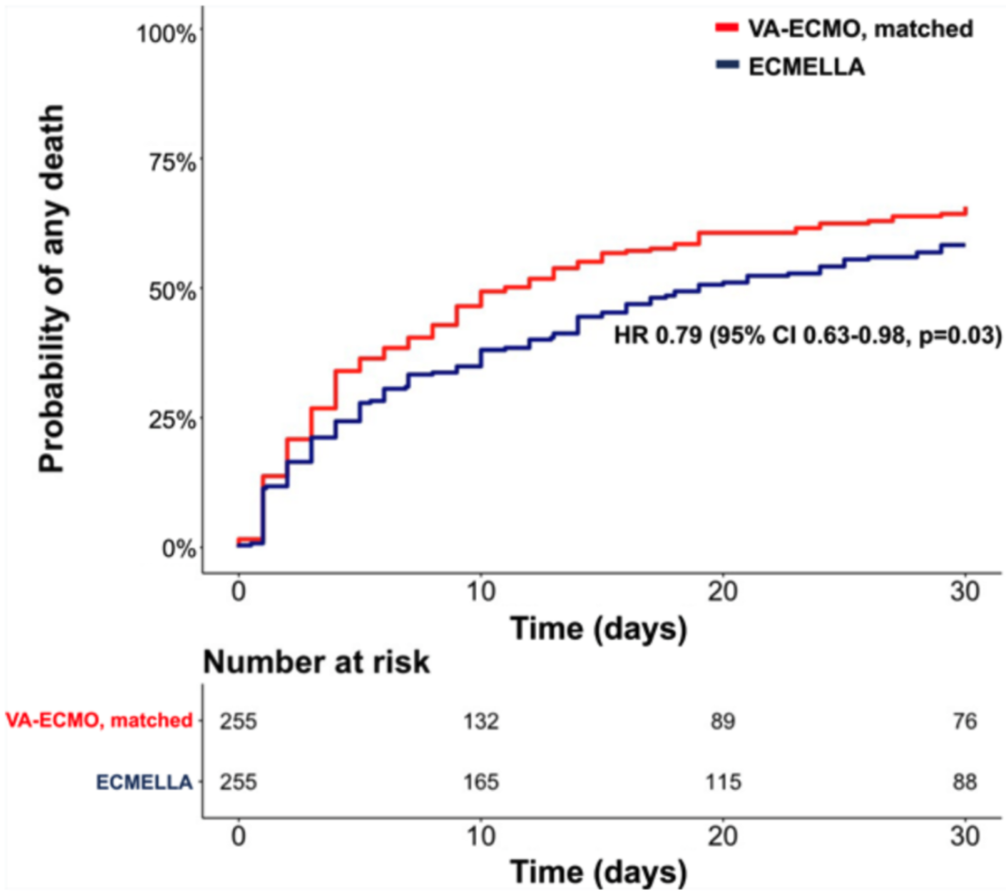


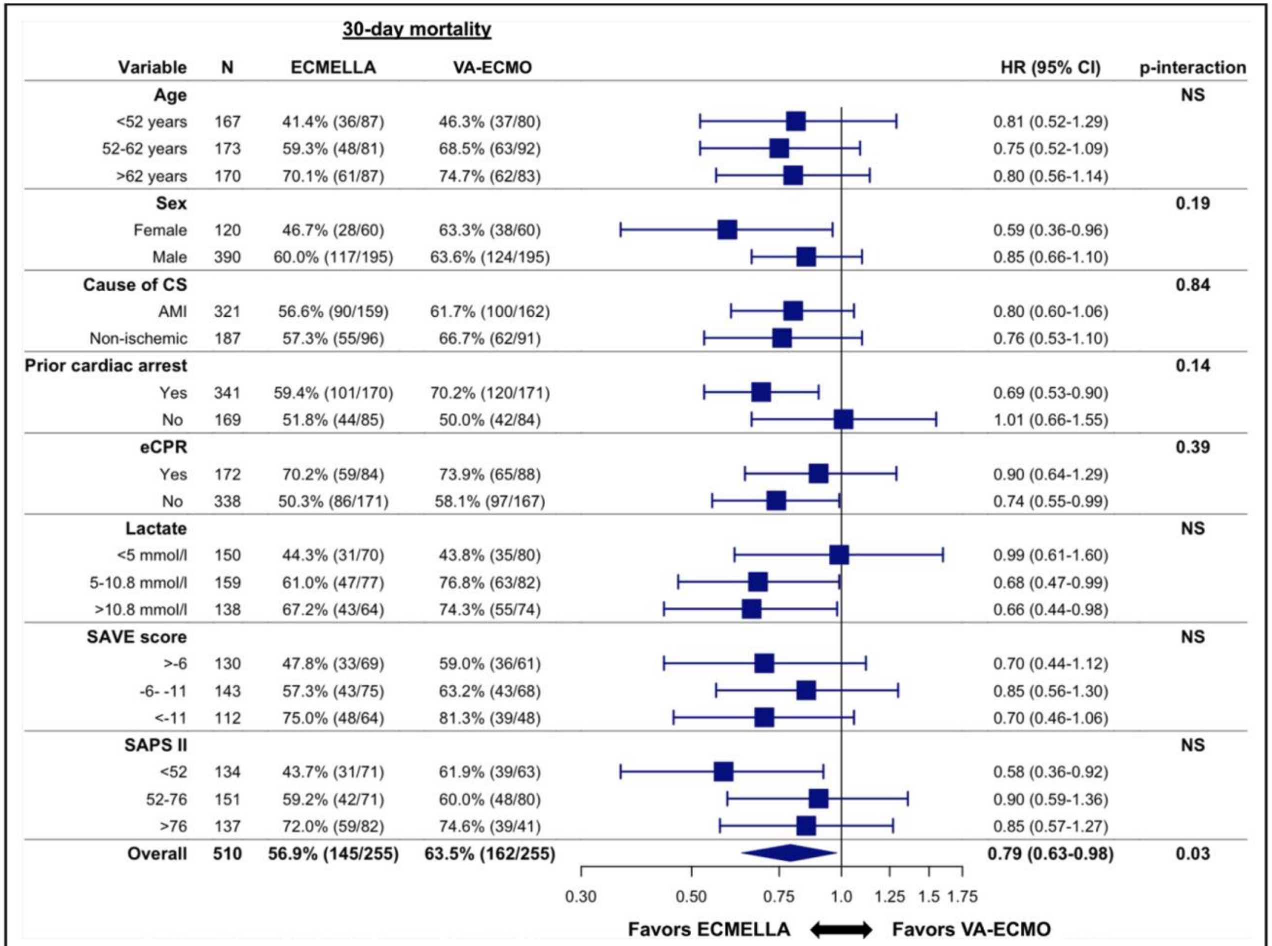
Figure 1. A: 30 day and (**B**) 1 year Kaplan–Meier survival estimates demonstrating statistically significant and maintained improved cumulative survival for the ECPELLA strategy as compared with VA-ECMO strategy. VA-ECMO, venoarterial extracorporeal membrane oxygenation. full color online

LV Unloading & Reduced Mortality in VA ECMO



Schrage B et al. Circulation 2020

LV Unloading &
Reduced Mortality in VA ECMO



Variable	N	30-day mortality ECMELLA	30-day mortality VA-ECMO	HR (95% CI)	p-interaction
Age					**NS**
<52 years	167	41.4% (36/87)	46.3% (37/80)	0.81 (0.52-1.29)	
52-62 years	173	59.3% (48/81)	68.5% (63/92)	0.75 (0.52-1.09)	
>62 years	170	70.1% (61/87)	74.7% (62/83)	0.80 (0.56-1.14)	
Sex					**0.19**
Female	120	46.7% (28/60)	63.3% (38/60)	0.59 (0.36-0.96)	
Male	390	60.0% (117/195)	63.6% (124/195)	0.85 (0.66-1.10)	
Cause of CS					**0.84**
AMI	321	56.6% (90/159)	61.7% (100/162)	0.80 (0.60-1.06)	
Non-ischemic	187	57.3% (55/96)	66.7% (62/91)	0.76 (0.53-1.10)	
Prior cardiac arrest					**0.14**
Yes	341	59.4% (101/170)	70.2% (120/171)	0.69 (0.53-0.90)	
No	169	51.8% (44/85)	50.0% (42/84)	1.01 (0.66-1.55)	
eCPR					**0.39**
Yes	172	70.2% (59/84)	73.9% (65/88)	0.90 (0.64-1.29)	
No	338	50.3% (86/171)	58.1% (97/167)	0.74 (0.55-0.99)	
Lactate					**NS**
<5 mmol/l	150	44.3% (31/70)	43.8% (35/80)	0.99 (0.61-1.60)	
5-10.8 mmol/l	159	61.0% (47/77)	76.8% (63/82)	0.68 (0.47-0.99)	
>10.8 mmol/l	138	67.2% (43/64)	74.3% (55/74)	0.66 (0.44-0.98)	
SAVE score					**NS**
>-6	130	47.8% (33/69)	59.0% (36/61)	0.70 (0.44-1.12)	
-6- -11	143	57.3% (43/75)	63.2% (43/68)	0.85 (0.56-1.30)	
<-11	112	75.0% (48/64)	81.3% (39/48)	0.70 (0.46-1.06)	
SAPS II					**NS**
<52	134	43.7% (31/71)	61.9% (39/63)	0.58 (0.36-0.92)	
52-76	151	59.2% (42/71)	60.0% (48/80)	0.90 (0.59-1.36)	
>76	137	72.0% (59/82)	74.6% (39/41)	0.85 (0.57-1.27)	
Overall	**510**	**56.9% (145/255)**	**63.5% (162/255)**	**0.79 (0.63-0.98)**	**0.03**

Figure 3. Association between ECMELLA use and 30-day all-cause mortality in prespecified subgroups.

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LV Unloading &
Reduced Mortality in VA ECMO *comes at a price!?*

Severe bleeding

Variable	N	ECMELLA	VA-ECMO	OR (95% CI)	p-interaction
Age					**NS**
<52 years	165	37.9% (33/87)	32.2% (19/78)	1.90 (0.97-3.77)	
52-62 years	172	42.0% (34/81)	18.7% (17/91)	3.15 (1.60-6.38)	
>62 years	170	35.6% (31/87)	10.8% (9/83)	4.55 (2.08-10.86)	
Sex					**0.05**
Female	120	51.7% (31/60)	15.0% (9/60)	6.06 (2.62-15.17)	
Male	387	40.0% (67/195)	18.8% (36/192)	2.27 (1.43-3.65)	
Cause of CS					**0.08**
AMI	320	40.3% (64/159)	17.5% (24/161)	3.85 (2.27-6.68)	
Non-ischemic	187	35.4% (34/96)	23.1% (21/91)	1.83 (0.97-3.51)	
Prior cardiac arrest					**0.43**
Yes	339	42.9% (73/170)	18.9% (32/169)	3.22 (1.99-5.31)	
No	168	29.4% (25/85)	15.7% (13/83)	2.24 (1.07-4.88)	
eCPR					**0.47**
Yes	171	45.2% (38/84)	25.3% (22/87)	2.44 (1.29-4.71)	
No	336	35.1% (60/171)	13.9% (23/165)	3.34 (1.97-5.82)	
Lactate					**NS**
<5 mmol/l	149	27.1% (19/70)	13.9% (11/79)	2.30 (1.02-5.41)	
5-10.8 mmol/l	159	46.8% (36/77)	15.9% (13/82)	4.66 (2.26-10.08)	
>10.8 mmol/l	136	43.8% (28/64)	22.2% (16/72)	2.72 (1.31-5.82)	
SAVE score					**NS**
>-6	130	31.9% (22/69)	14.8% (9/61)	2.70 (1.16-6.74)	
-6- -11	143	38.7% (29/75)	22.1% (15/68)	2.23 (1.08-4.75)	
<-11	112	54.7% (35/64)	35.6% (16/45)	2.19 (1.01-4.87)	
SAPS II					**NS**
<52	134	33.1% (24/71)	20.6% (13/63)	1.96 (0.91-4.40)	
52-76	151	26.8% (19/71)	18.8% (15/80)	1.58 (0.74-3.46)	
>76	137	52.4% (43/82)	30.8% (16/52)	2.48 (1.21-5.25)	
Overall	**507**	**38.4% (98/255)**	**17.9% (45/252)**	**2.87 (1.92-4.35)**	**<0.01**

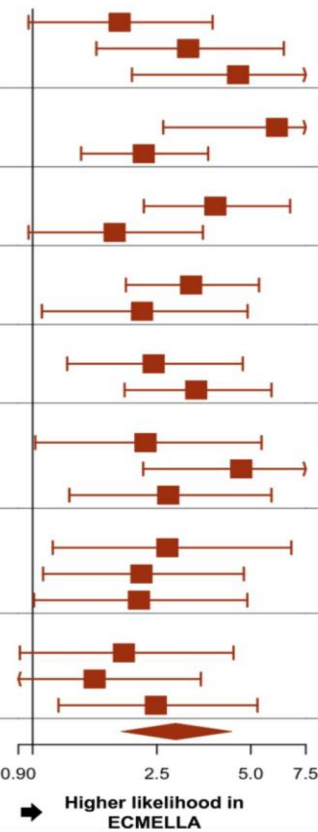

Figure 4. Association between ECMELLA use and severe bleeding in prespecified subgroups.

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LV Unloading & Reduced Mortality in VA ECMO *comes at a price!?*

Variable	N	ECMELLA	VA-ECMO	OR (95% CI)	p-interaction
		Intervention due to access-site related ischemia			
Age					NS
<52 years	165	24.1% (21/87)	12.8% (10/78)	2.16 (0.97-5.12)	
52-62 years	172	24.7% (20/81)	15.4% (14/91)	1.80 (0.85-3.93)	
>62 years	170	16.1% (14/87)	8.4% (7/83)	2.08 (0.82-5.77)	
Sex					0.38
Female	120	21.7% (13/60)	16.7% (10/60)	1.38 (0.56-3.53)	
Male	387	21.5% (42/195)	10.9% (21/192)	2.24 (1.28-4.01)	
Cause of CS					0.66
AMI	320	21.4% (34/159)	13.0% (21/161)	1.81 (1.01-3.33)	
Non-ischemic	187	21.9% (21/96)	11.0% (10/91)	2.27 (1.02-5.32)	
Prior cardiac arrest					0.21
Yes	339	25.3% (43/170)	12.4% (21/169)	2.39 (1.36-4.30)	
No	168	14.1% (12/85)	12.1% (10/83)	1.20 (0.49-3.01)	
eCPR					0.21
Yes	171	29.8% (25/84)	12.8% (11/87)	2.93 (1.36-6.65)	
No	336	17.5% (30/171)	12.1% (20/165)	1.54 (0.84-2.88)	
Lactate					NS
<5 mmol/l	149	18.6% (13/70)	8.9% (7/79)	2.35 (0.90-6.60)	
5-10.8 mmol/l	159	20.8% (16/77)	13.4% (11/82)	1.69 (0.74-4.02)	
>10.8 mmol/l	136	31.3% (20/64)	11.1% (8/72)	3.64 (1.52-9.46)	
SAVE score					NS
>-6	130	20.3% (14/69)	8.2% (5/61)	2.85 (1.02-9.31)	
-6- -11	143	22.7% (17/75)	13.2% (9/68)	1.92 (0.81-4.84)	
<-11	112	26.6% (17/64)	6.7% (3/45)	5.06 (1.57-22.79)	
SAPS II					NS
<52	134	15.5% (11/71)	9.5% (6/63)	1.74 (0.62-5.34)	
52-76	151	18.3% (13/71)	15.0% (12/80)	1.27 (0.54-3.03)	
>76	137	30.5% (25/82)	15.4% (8/52)	2.41 (1.03-6.19)	
Overall	**507**	**21.6% (55/255)**	**12.3% (31/252)**	**1.96 (1.22-3.20)**	**<0.01**

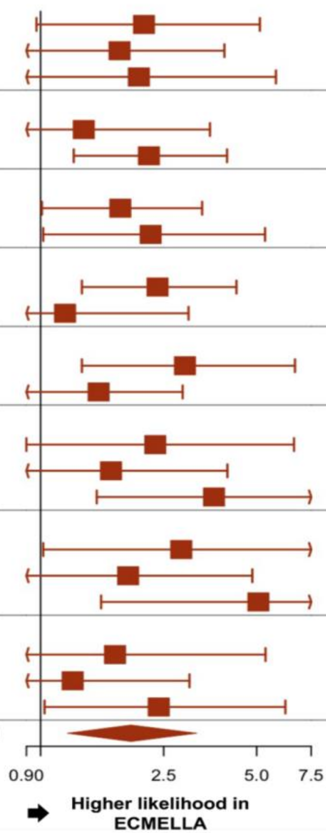

Figure 5. Association between ECMELLA use and intervention because of access site–related ischemia in prespecified subgroups.

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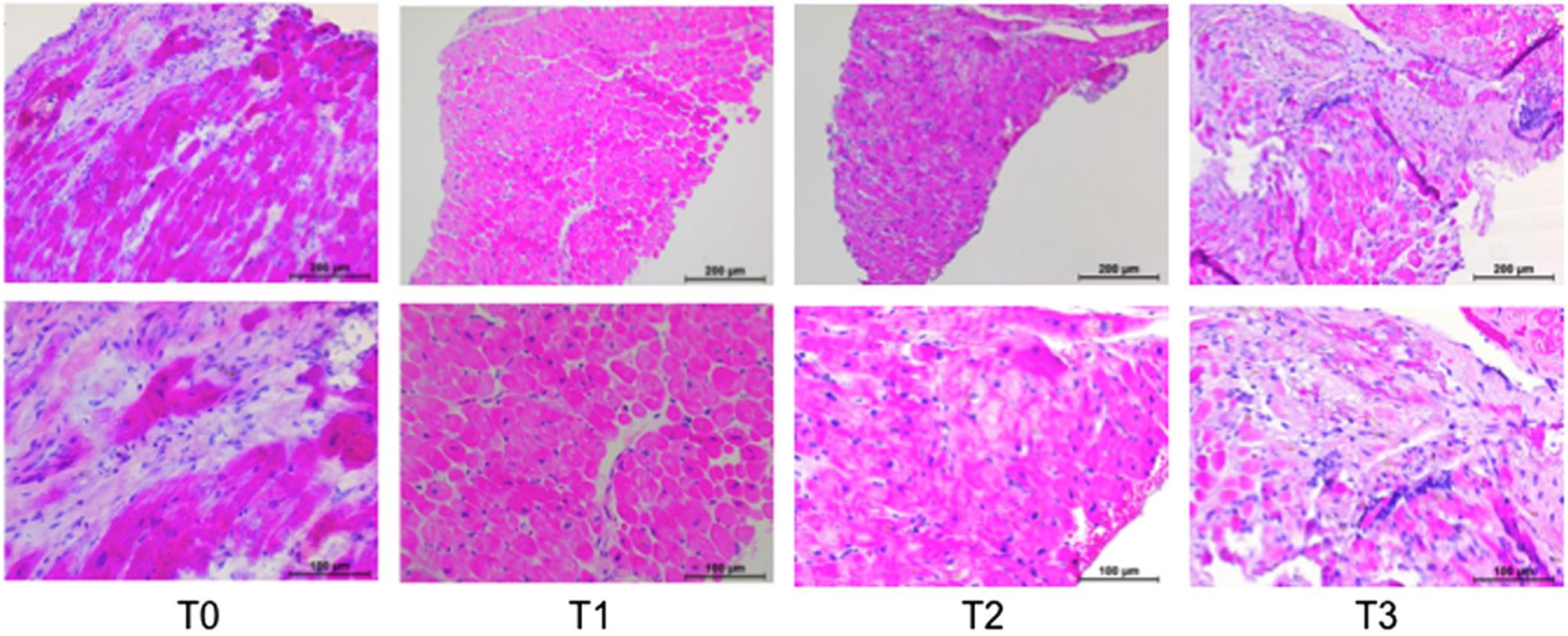
Mechanical Unloading in Fulminant Myocarditis

LV-IMPELLA, ECMELLA, BI-PELLA, and PROPELLA Concepts



Tschöpe C. et al. JCTR. 2019

Mechanical Unloading in Fulminant Myocarditis

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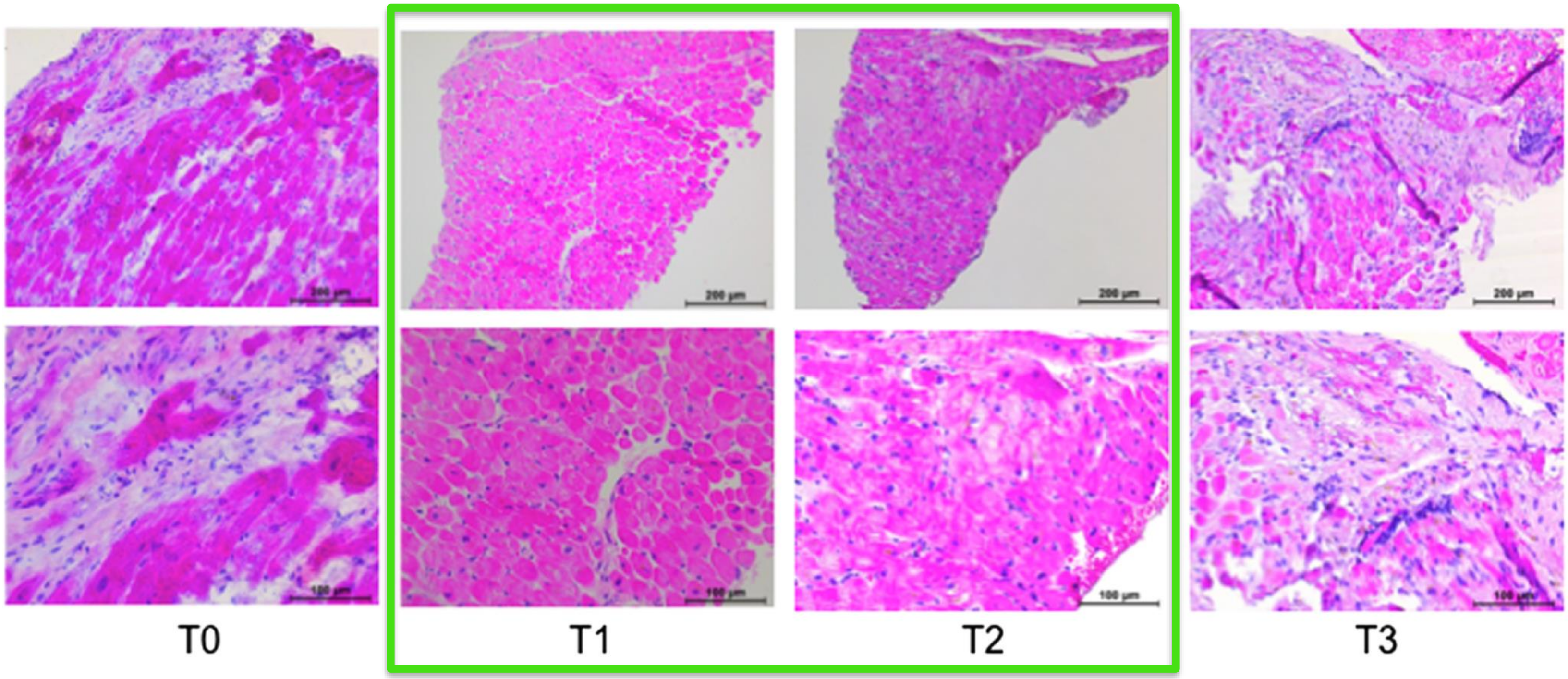
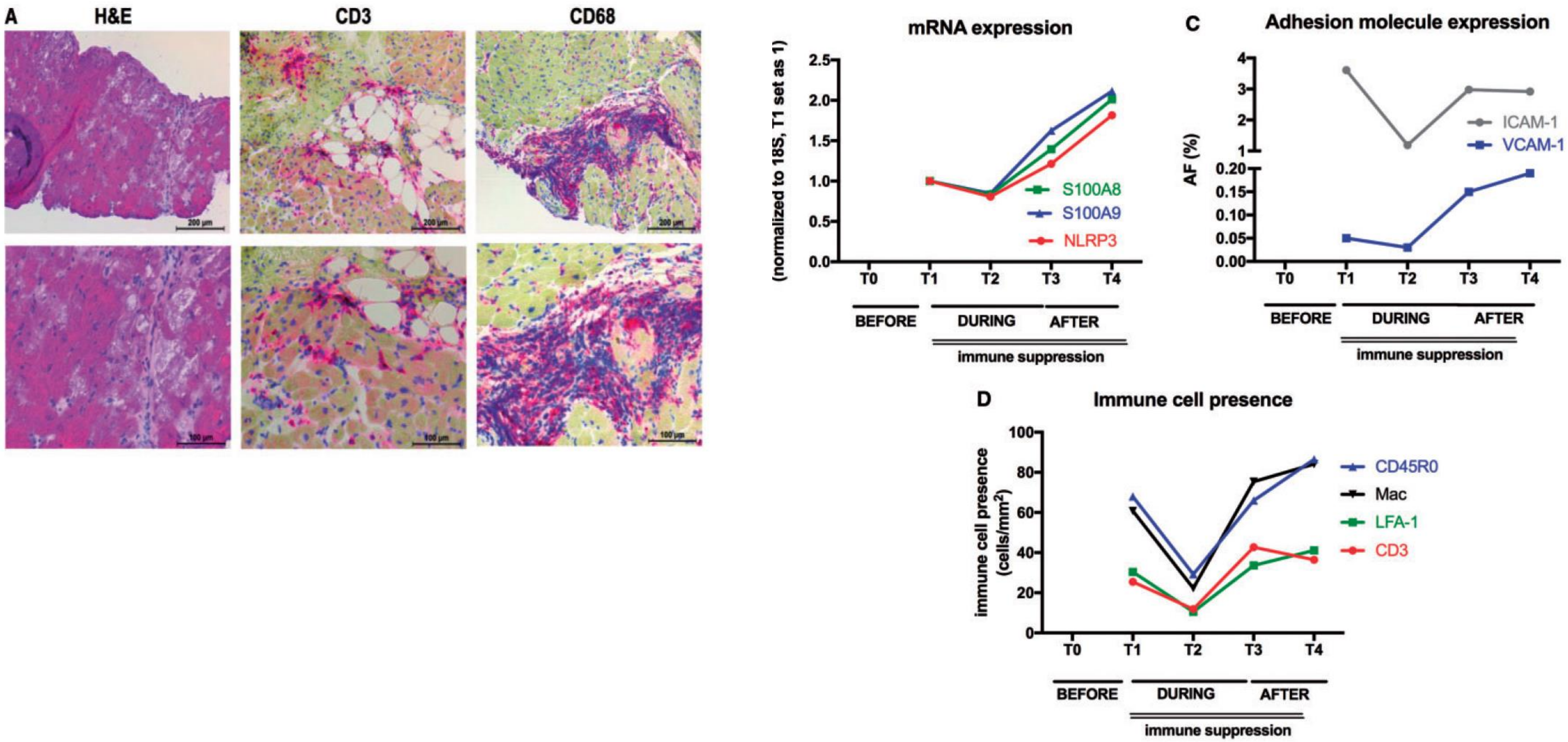


cardiac unloading effect !?

Tschöpe C. et al. JCTR. 2019

Mechanical Unloading in Fulminant Myocarditis
PROPELLA Concept



Spillmann F. et al. EHJ. 2019

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Resuscitation

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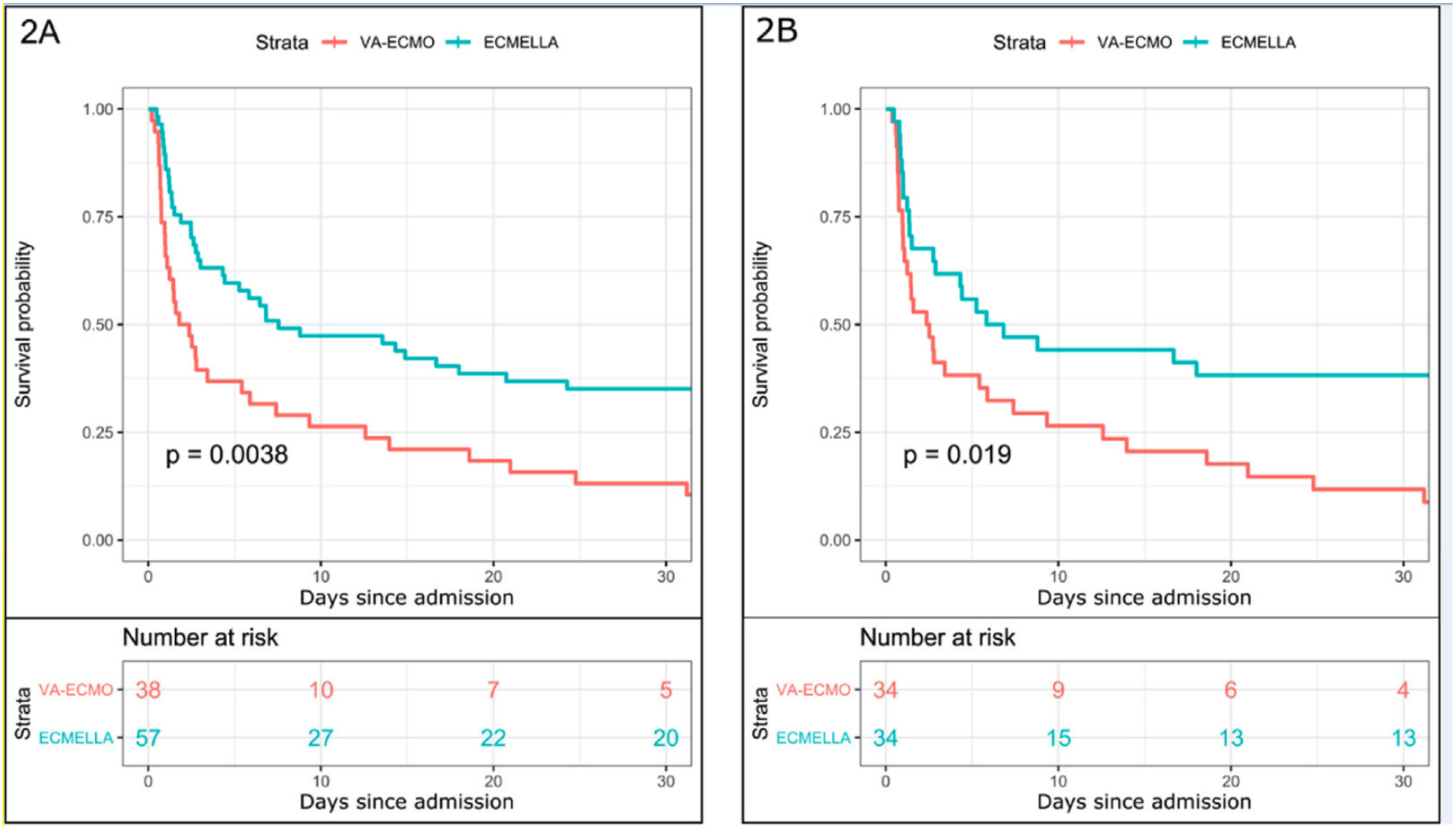
Clinical paper

Left-ventricular unloading in extracorporeal cardiopulmonary resuscitation due to acute myocardial infarction – A multicenter study

Tharusan Thevathasan[a,b,c,d,1], *Megan A. Kenny*[a,b,1], *Finn J. Krause*[a,b], *Julia Paul*[a,b], *Thomas Wurster*[a,c,d], *Sebastian D. Boie*[b], *Julian Friebel*[a,c,d], *Wulf Knie*[a], *Georg Girke*[a], *Arash Haghikia*[a,c,d], *Markus Reinthaler*[a,d], *Ursula Rauch-Kröhnert*[a,d], *David M. Leistner*[a,c,d], *David Sinning*[a,d], *Georg Fröhlich*[a], *Bettina Heidecker*[a,d], *Frank Spillmann*[e], *Damaris Praeger*[f], *Burkert Pieske*[c,d,e], *Karl Stangl*[d,f], *Ulf Landmesser*[a,c,d], *Felix Balzer*[b,c,1], *Carsten Skurk*[a,d,1,*]

ECPR – AMI *ECMELLA* vs *VA ECMO* survival

unmatched vs. propensity score-matched



Thevathasan T al. Resuscitation 2023

Early Impella Support in Postcardiac Arrest Cardiogenic Shock Complicating Acute Myocardial Infarction Improves Short- and Long-Term Survival*

Georgios Chatzis, MD, PhD[1,2]
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Ulrich Luesebrink, MD[1]
Holger Ahrens, MD[1]
Dimitar Divchev, MD[1]
Styliani Syntila, MD[1]
Nora Scheele, MD[1]
Hanna Al Eryani, MD[1]
Dimitris Tousoulis, MD, PhD, FESC, FACC[2]
Bernhard Schieffer, MD, PhD[1]
Konstantinos Karatolios, MD[1]

OBJECTIVES: Early mechanical circulatory support with Impella may improve survival outcomes in the setting of postcardiac arrest cardiogenic shock after out-of-hospital cardiac arrest complicating acute myocardial infarction. However, the optimal timing to initiate mechanical circulatory support in this particular setting remains unclear. Therefore, we aimed to compare survival outcomes of patients supported with Impella 2.5 before percutaneous coronary intervention (pre-PCI) with those supported after percutaneous coronary intervention (post-PCI).

DESIGN: Retrospective single-center study between September 2014 and December 2019 admitted to the Cardiac Arrest Center in Marburg, Germany.

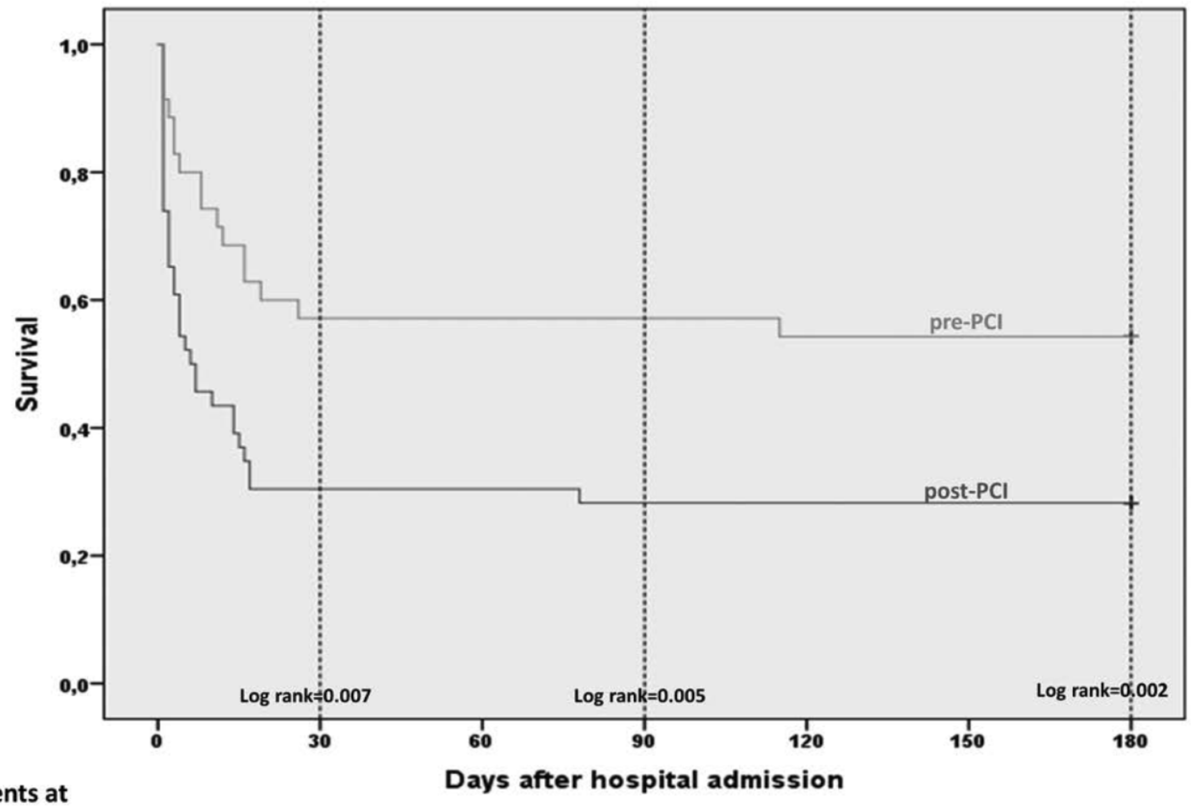
PATIENTS: Out of 2,105 patients resuscitated from out-of-hospital cardiac arrest due to acute myocardial infarction with postcardiac arrest cardiogenic shock between September 2014 and December 2019 and admitted to our regional cardiac arrest center, 81 consecutive patients receiving Impella 2.5 during admission coronary angiogram were identified.

OUTCOMES/MEASUREMENTS: Survival outcomes were compared between those with Impella support pre-PCI to those with support post-PCI.

Crit Care Med 2021

Impella 2.5 – AMI shock post cardiac arrest

pre PCI vs. post PCI



Patients at risk							
pre-PCI	35	19	19	19	18	18	18
post-PCI	46	14	14	13	13	13	13

Chatzis G et al. Crit Care Med 2021

Preclinical LV unloading

Impella® prior to reperfusion

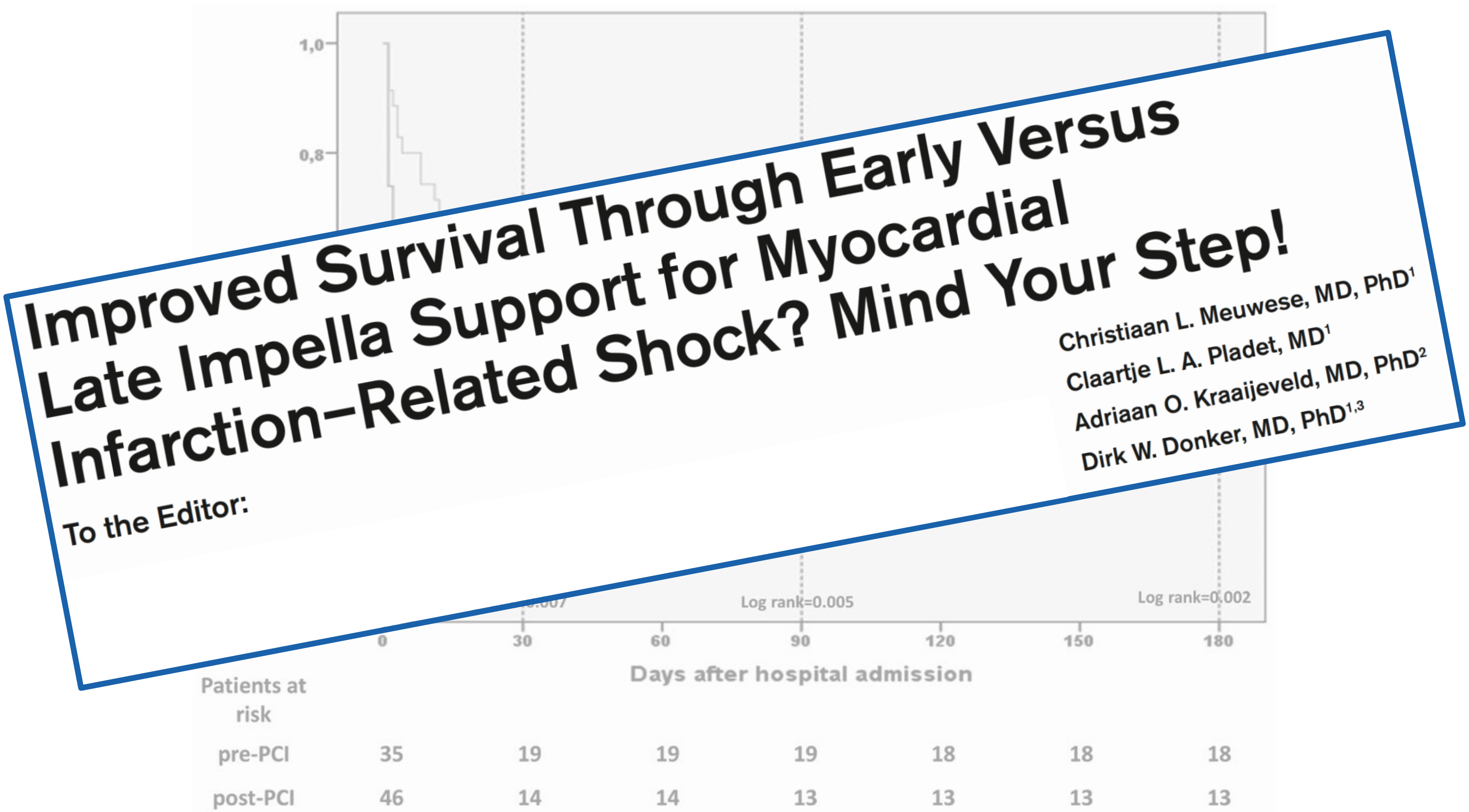
Animal/device	Occluded vessel	Duration of ischemia (min)	Duration of reperfusion (min)	Study design	Infarct size end point	Infarct size (%)	Study (year)
Sheep (Impella 5.0)	LAD	60	120	Group 1: reperfusion only (control) Group 2: full support from onset of ischemia (60 min) and during reperfusion Group 3: full support during reperfusion Group 4: partial support during reperfusion	Infarct percent size (TTC and Evan's blue)	Group 1: 67.2 ± 4.6% Group 2: 18.1 ± 10% Group 3: 41.6 ± 5.8% Group 4: 54.0 ± 8%	Meyns *et al.* (2003)
Swine (Impella CP®)	LAD	90	120	Group 1: reperfusion only (control) Group 2: 60 min support before reperfusion	Infarct percent size (TTC)	Group 1: 74 ± 11% Group 2: 42 ± 8%	Kapur *et al.* (2015)
Swine (Impella)	LAD	90	120	Group 1: reperfusion only (control) Group 2: 15 min support before reperfusion Group 3: 30 min support before reperfusion Group 4: 60 min support before reperfusion Group 5: 30 min reperfusion followed by LV unloading and an additional 120 min reperfusion	Reduction in infarct size† (TTC)	Group 1: no Group 2: no Group 3: yes Group 4: yes Group 5: no	Kapur *et al.* (2015)†
Swine (Impella LD)	LCx	120	120	Group 1: reperfusion only (control) Group 2: support (90 min after onset of ischemia and during reperfusion)	Infarct percent size	Group 1: 35.3 ± 6.2% Group 2: 18.1 ± 4.8%	Sun *et al.* (2015)
Swine (Impella CP)	LAD	90	120	Group 1: reperfusion only (control) Group 2: 15 min support before reperfusion Group 3: 30 min support before reperfusion Group 4: 30 min reperfusion followed by 90 min reperfusion with support	Infarct percent size (TTC and Evan's blue)	Group 1: 62.2 ± 1.7% Group 2: NS‡ Group 3: 33.3 ± 5% Group 4: NS‡	Esposito *et al.* (2018)
Canine (Impella CP)	LAD (+LCx)	180	60	Group 1: sham (thoracotomy only) Group 2: reperfusion only (control) Group 3: partial support (60 min after onset of ischemia to 60 min after reperfusion) Group 4: full support (60 min after onset of ischemia to 60 min after reperfusion)	Infarct percent size (TTC)	Group 1: NA Group 2: 16.3 ± 2.6% Group 3: 8.5 ± 4.3% Group 4: 2.1 ± 1.6%	Saku *et al.* (2018)
Swine (Impella CP)	LAD	120	180	Group 1: 30 min continued occlusion (control) Group 2: 30 min Impella support before reperfusion Group 3: 30 min extracorporeal membrane oxygenation support before reperfusion	Infarct percent size (TTC and Evan's blue)	Group 1: 52 ± 15% Group 2: 34 ± 6% Group 3: NS	Briceno *et al.* (2019)
Swine (Impella CP)	LAD	60	120	Group 1: reperfusion only (control) Group 2: support only before reperfusion Group 3: support with immediate reperfusion	Infarct percent size (TTC and Evan's blue)	Group 1: 54.7 ± 20.3% Group 2: 43.3 ± 24.6% Group 3: 22.1 ± 13.4%	Ko *et al.* (2020)

†This preclinical study was reported in a TCT presentation. An additional metric of infarct size reduction, infarct size as percentage of area at risk, was presented as a figure accompanying the presentation; however, exact measurements were not provided. Per the figure bar charts, infarct size as a percentage of area-at-risk was ~67% in group 1, ~60% in group 2, ~30% in group 3, ~40% in group 4 and ~55% in group 5, indicating that best infarct size outcome was achieved with 30 min of unloading prior to reperfusion.
‡Infarct percent sizes in group 2 and 4 were not provided; however, the authors state that unloading followed by perfusion in these two groups failed to reduce infarct size compared with reperfusion alone.
LAD: Left anterior descending; LCx: Left circumflex; LV: Left ventricle; NA: Not available; NS: No significant reduction; TTC: Triphenyltetrazolium chloride.

Parikh MJ et al. Future Cardiol. 2021

Impella 2.5 – AMI shock post cardiac arrest

pre PCI vs. post PCI



Chatzis G et al. Crit Care Med 2021

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Contents lists available at ScienceDirect
Cardiovascular Revascularization Medicine
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Delaying reperfusion plus left ventricular unloading reduces infarct size: Sub-analysis of DTU-STEMI pilot study

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[b] University of Oklahoma Medical Science, Oklahoma city, OK, United States of America
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[d] Columbia University Medical Center, New York, United States of America
[e] Hackensack Medical Center, Hoboken, NJ, United States of America
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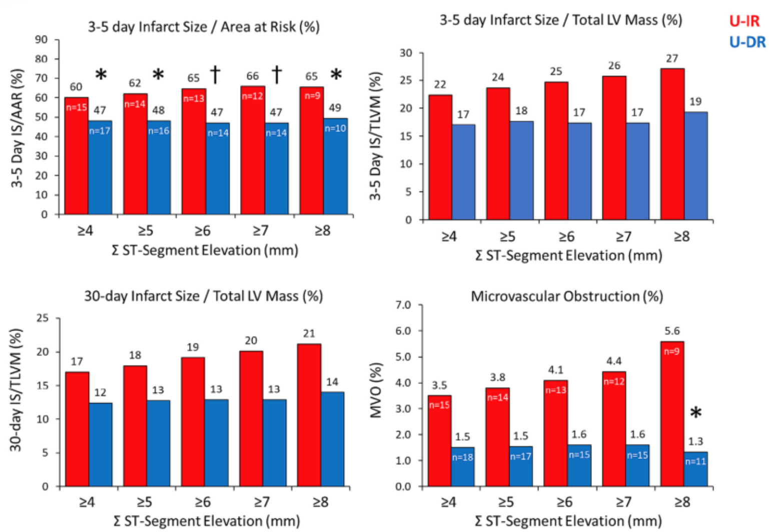
[g] St. Anthony's Hospital, Denver, Colorado, USA



*, p<0.05; †, p<0.01

Circulation

ORIGINAL RESEARCH ARTICLE

Unloading the Left Ventricle Before Reperfusion in Patients With Anterior ST-Segment–Elevation Myocardial Infarction

A Pilot Study Using the Impella CP

Editorial, see p 347

Navin K. Kapur, MD
et al

…KGROUND: In ST-segment–elevation myocardial infarction …), infarct size correlates directly with heart failure and mortality. …al testing has shown that, in comparison with reperfusion alone, …ally unloading the left ventricle (LV) before reperfusion reduces … and that 30 minutes of unloading activates a cardioprotective … limits reperfusion injury. The DTU-STEMI pilot trial (Door-To-…MI Pilot Trial) represents the first exploratory study testing …ading and delayed reperfusion in patients with STEMI …nic shock is safe and feasible.

…lticenter, prospective, randomized exploratory safety …e assigned 50 patients with anterior STEMI to LV …the Impella CP followed by immediate reperfusion (U-…ed reperfusion after 30 minutes of unloading (U-DR). The …fety outcome was a composite of major adverse cardiovascular …erebrovascular events at 30 days. Efficacy parameters included the assessment of infarct size by using cardiac magnetic resonance imaging.

RESULTS: All patients completed the U-IR (n=25) or U-DR (n=25) protocols with respective mean door-to-balloon times of 72 versus 97 minutes. Major adverse cardiovascular and cerebrovascular event rates were not statistically different between the U-IR versus U-DR groups (8% versus 12%, respectively, P=0.99). In comparison with the U-IR group, delaying reperfusion in the U-DR group did not affect 30-day mean infarct size measured as a percentage of LV mass (15±12% versus 13±11%, U-IR versus U-DR, P=0.53).

CONCLUSIONS: We report that LV unloading using the Impella CP device with a 30-minute delay before reperfusion is feasible within a relatively short time period in anterior STEMI. The DTU-STEMI pilot trial did not identify prohibitive safety signals that would preclude proceeding to a larger pivotal study of LV unloading before reperfusion. An appropriately powered pivotal trial comparing LV unloading before reperfusion to the current standard of care is required.

CLINICAL TRIAL REGISTRATION: URL: https://www.clinicaltrials.gov. Unique identifier: NCT03000270.

The full author list is available on page 345.

Key Words: heart-assist devices ■ heart failure ■ heart ventricles ■ myocardial infarction ■ reperfusion injury

Sources of Funding, see page 345

https://www.ahajournals.org/journal/circ

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January 15, 2019 337

JACC: HEART FAILURE
VOL. 11, NO. 3, 2023

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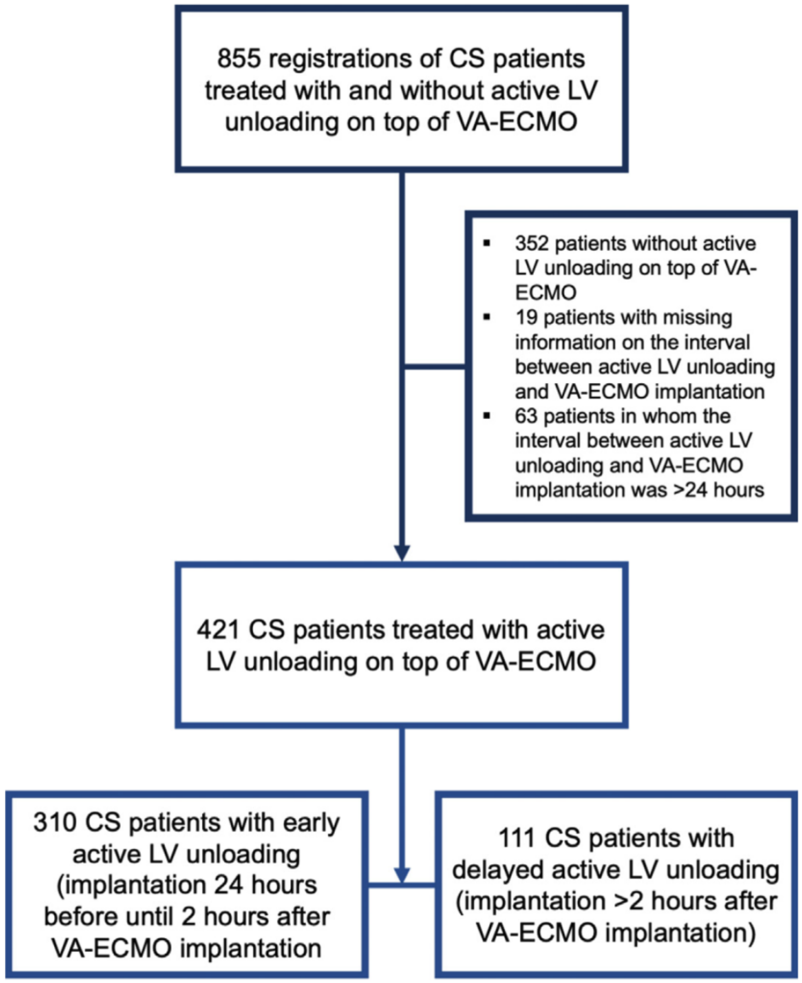
CLINICAL RESEARCH

Timing of Active Left Ventricular Unloading in Patients on Venoarterial Extracorporeal Membrane Oxygenation Therapy

Benedikt Schrage, MD, PhD,[a,b,*] Jonas Sundermeyer, MD,[a,b,*] Stefan Blankenberg, MD,[a,b] Pascal Colson, MD,[c] Dennis Eckner, MD,[d] Matthias Eden, MD,[e] Ingo Eitel, MD,[b,f] Derk Frank, MD,[b,g] Norbert Frey, MD,[e] Tobias Graf, MD,[b,f] Paulus Kirchhof, MD,[a,b,h] Danny Kupka, MD,[i] Ulf Landmesser, MD,[j] Axel Linke, MD,[k] Nicolas Majunke, MD,[l] Norman Mangner, MD,[k] Octavian Maniuc, MD,[m] Johannes Mierke, MD,[k] Sven Möbius-Winkler, MD,[n] David A. Morrow, MD, MPH,[o] Marc Mourad, MD,[c] Peter Nordbeck, MD,[m] Martin Orban, MD,[p] Federico Pappalardo, MD,[q,r] Sandeep M. Patel, MD,[s] Matthias Pauschinger, MD,[d] Vittorio Pazzanese, MD,[q,t] Darko Radakovic, MD,[u] P. Christian Schulze, MD, PhD,[n] Clemens Scherer, MD,[p] Robert H.G. Schwinger, MD,[v] Carsten Skurk, MD,[j] Holger Thiele, MD,[l] Anubodh Varshney, MD,[o] Lukas Wechsler, MD,[v] Dirk Westermann, MD[w]

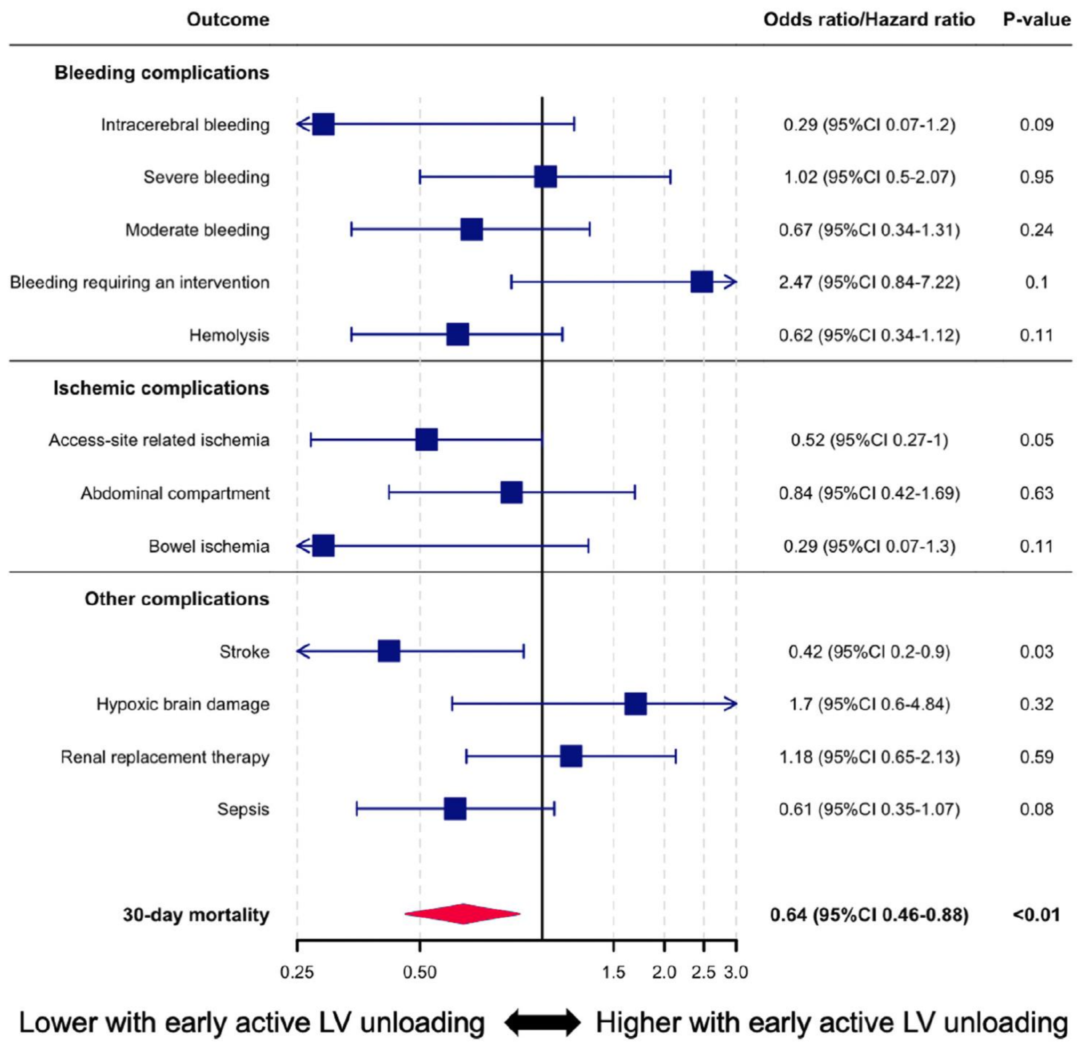
FIGURE 1 Study Flowchart



CS = cardiogenic shock; LV = left ventricular; VA-ECMO = venoarterial extracorporeal membrane oxygenation therapy.

Schrage B et al. J Am Coll Cardiol HF 2023

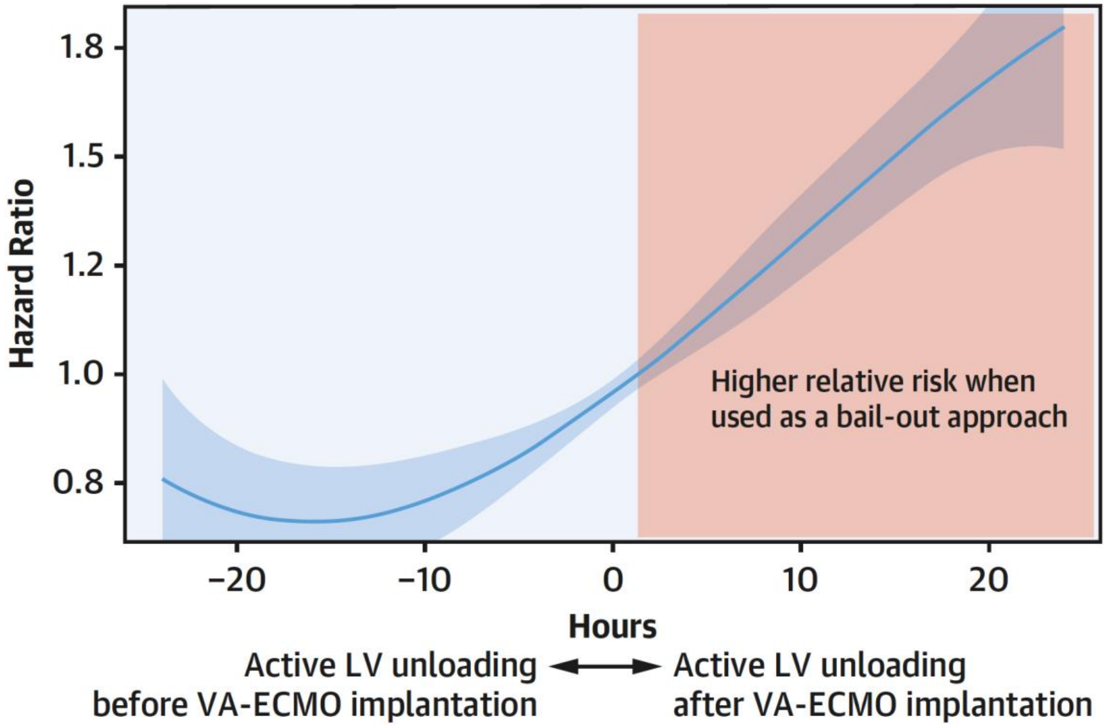
FIGURE 2 Association Between Timing of Active LV Unloading and 30-Day All-Cause Mortality as Well as Safety Endpoints



Abbreviation as in Figure 1.

Schrage B et al. J Am Coll Cardiol HF 2023

CENTRAL ILLUSTRATION Association Between Timing of Active LV Unloading and 30-Day Mortality



Schrage B, et al. J Am Coll Cardiol HF. 2023;11(3):321-330.

The y-axis displays the interval between initiation of active left ventricular (LV) unloading and venoarterial extracorporeal membrane oxygenation (VA-ECMO) implantation in hours, with negative values indicating initiation of active LV unloading before VA-ECMO implantation. The x-axis displays the HR for the outcome of 30-day mortality based on an adjusted Cox regression model.

Schrage B et al. J Am Coll Cardiol HF 2023

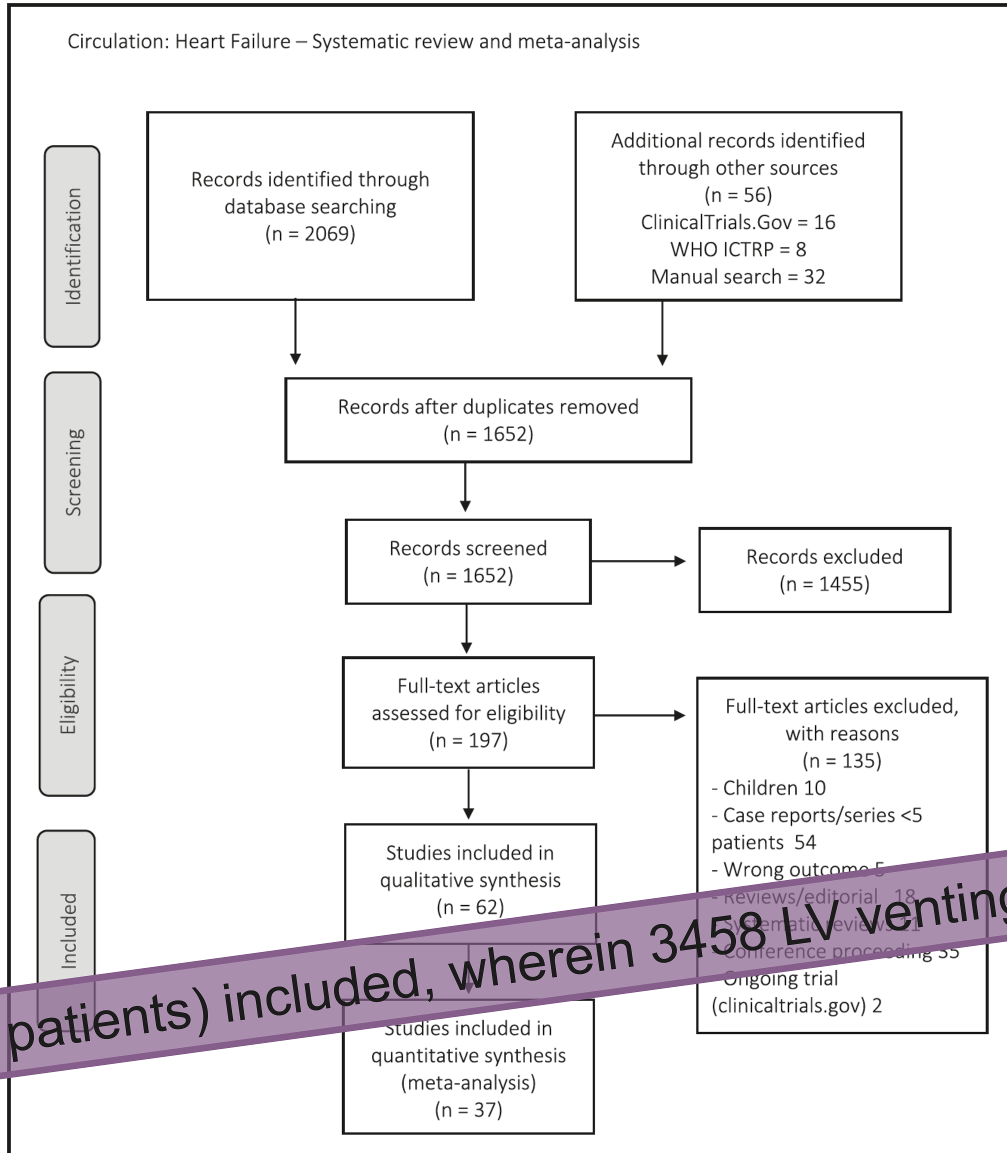
ORIGINAL ARTICLE

Optimal Strategy and Timing of Left Ventricular Venting During Veno-Arterial Extracorporeal Life Support for Adults in Cardiogenic Shock

A Systematic Review and Meta-Analysis

Abdulrahman A. Al-Fares, MD*; Varinder K. Randhawa, MD, PhD*; Marina Englesakis, MLIS; Michael A. McDonald, MD; A. Dave Nagpal, MD, MHSc; Jerry D. Estep, MD; Edward G. Soltesz, MD, MPH; Eddy Fan, MD, PhD

Circulation: Heart Failure 2019



62 studies (7995 patients) included, wherein 3458 LV venting during VA ECMO

Circulation: Heart Failure 2019

ORIGINAL ARTICLE

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Study	Events	Total	Events	Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.2 Impella						
Akanni 2019	16	29	87	196	5.6%	1.24 [0.86, 1.79]
Mourad 2018	4	11	4	16	0.8%	1.45 [0.46, 4.61]
Subtotal (95% CI)		**40**		**212**	**6.5%**	**1.26 [0.89, 1.78]**
Total events	20		91			
1.1.4 Mixed						
Doll 2004 (3)	92	144	37	75	8.1%	1.30 [1.00, 1.68]
Patel 2019 (4)	17	30	28	36	5.7%	0.73 [0.51, 1.04]
Ro 2014 (5)	42	60	139	193	10.5%	0.97 [0.81, 1.17]
Schmack 2017 (6)	9	20	21	28	3.3%	0.60 [0.35, 1.02]
Subtotal (95% CI)		**254**		**332**	**27.7%**	**0.91 [0.69, 1.21]**
Total events	160		225			
Total (95% CI)		**1453**		**1637**	**100.0%**	**0.86 [0.77, 0.96]**
Total events	755		971			

Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P

Test for overall effect: Z = 1.31 (P

[0.36, 1.19]

Z = 1.40 (P = 0.16)

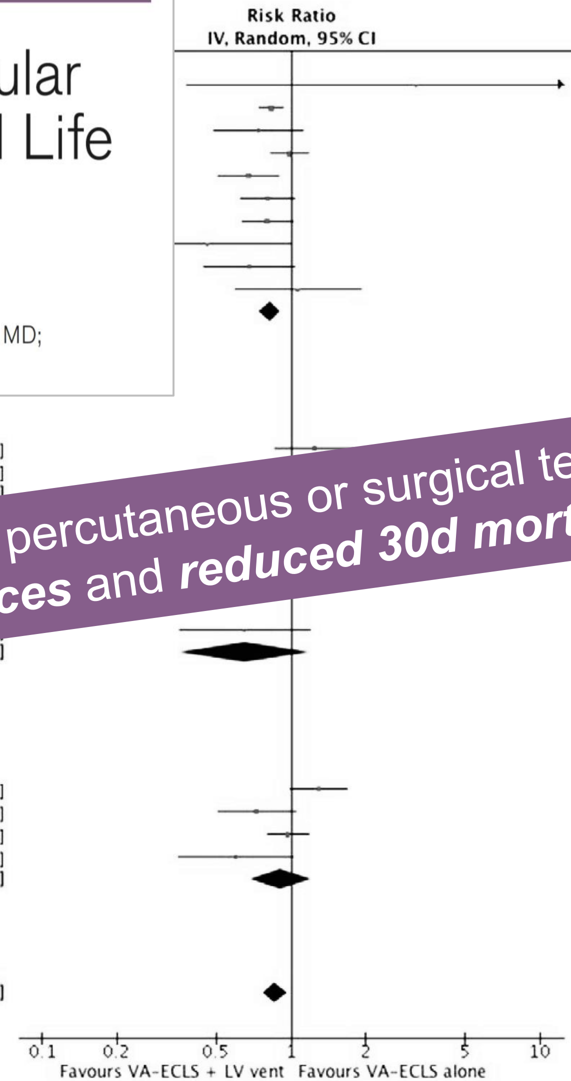
(1.1.4 Mixed) Heterogeneity: Tau² = 0.06; Chi² = 10.34, df = 3 (P = 0.02); I² = 71%

Test for overall effect: Z = 0.64 (P = 0.52)

(Total) Heterogeneity: Tau² = 0.02; Chi² = 31.22, df = 16 (P = 0.01); I² = 49%

Test for overall effect: Z = 2.67 (P = 0.008)

Test for subgroup differences: Chi² = 6.42, df = 3 (P = 0.09), I² = 53.2%



Footnotes

(1) Propensity matched

(2) Propensity matched

(3) Predominantly IABP + LA vents in 3 patients

(4) Predominantly Impella + surgical vent in 17 patients (LV, PA, LA)and IABP in 15 patients

(5) Predominantly IABP + LV vent in 6 patients (at RUPV or atrial septostomy)

(6) Predominantly LV surgical vent + IABP in 17 patients

Early (<12h) LV venting (IABP, Impella or other percutaneous or surgical technique) is associated with ***increased weaning succes*** and ***reduced 30d mortality.***

Circulation: Heart Failure 2019

ORIGINAL ARTICLE

Optimal Strategy and Timing of Left Ventricular Venting During Veno-Arterial Extracorporeal Life Support for Adults in Cardiogenic Shock

A Systematic Review and Meta-Analysis

Abdulrahman A. Al-Fares, MD*; Varinder K. Randhawa, MD, PhD*; Marina Englesakis, MLIS; Michael A. McDonald, MD; A. Dave Nagpal, MD, MHSc; Jerry D. Estep, MD; Edward G. Soltesz, MD, MPH; Eddy Fan, MD, PhD

Early (<12h) LV venting (IABP, Impella or other percutaneous or surgical technique) is associated with ***increased weaning succes*** and ***reduced 30d mortality.***

… was associated with ***longer duration of ECLS and mechanical ventilation,*** *without impacting overall ICU length of stay*

1.1.2 Impella

Akanni 2019	16	29	87	196	5.6%	1.24 [0.86, 1.79]
Mourad 2018	4	11	4	16	0.8%	1.45 [0.46, 4.61]
Subtotal (95% CI)		**40**		**212**	**6.5%**	**1.26 [0.89, 1.78]**
Total events	20		91			

Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.8…

Test for overall effect: Z = 1.31 (P = 0.1…

… [0.36, 1.19]

… Z = 1.40 (P = 0.16)

1.1.4 Mixed

Doll 2004 (3) 9…

Patel 2019 (4)…

… [0.69, 1.21]

… df = 3 (P = 0.02); I² = 71%

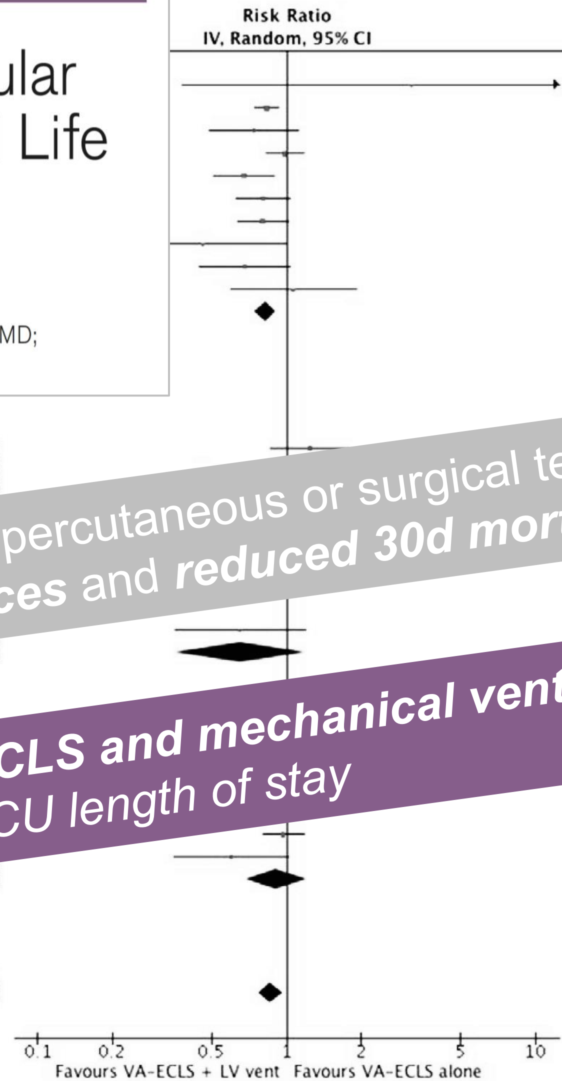
… Z = 0.64 (P = 0.52)

Total (95% CI)		**1453**		**1637**	**100.0%**	**0.86 [0.77, 0.96]**
Total events	755		971			

Heterogeneity: Tau² = 0.02; Chi² = 31.22, df = 16 (P = 0.01); I² = 49%

Test for overall effect: Z = 2.67 (P = 0.008)

Test for subgroup differences: Chi² = 6.42, df = 3 (P = 0.09), I² = 53.2%



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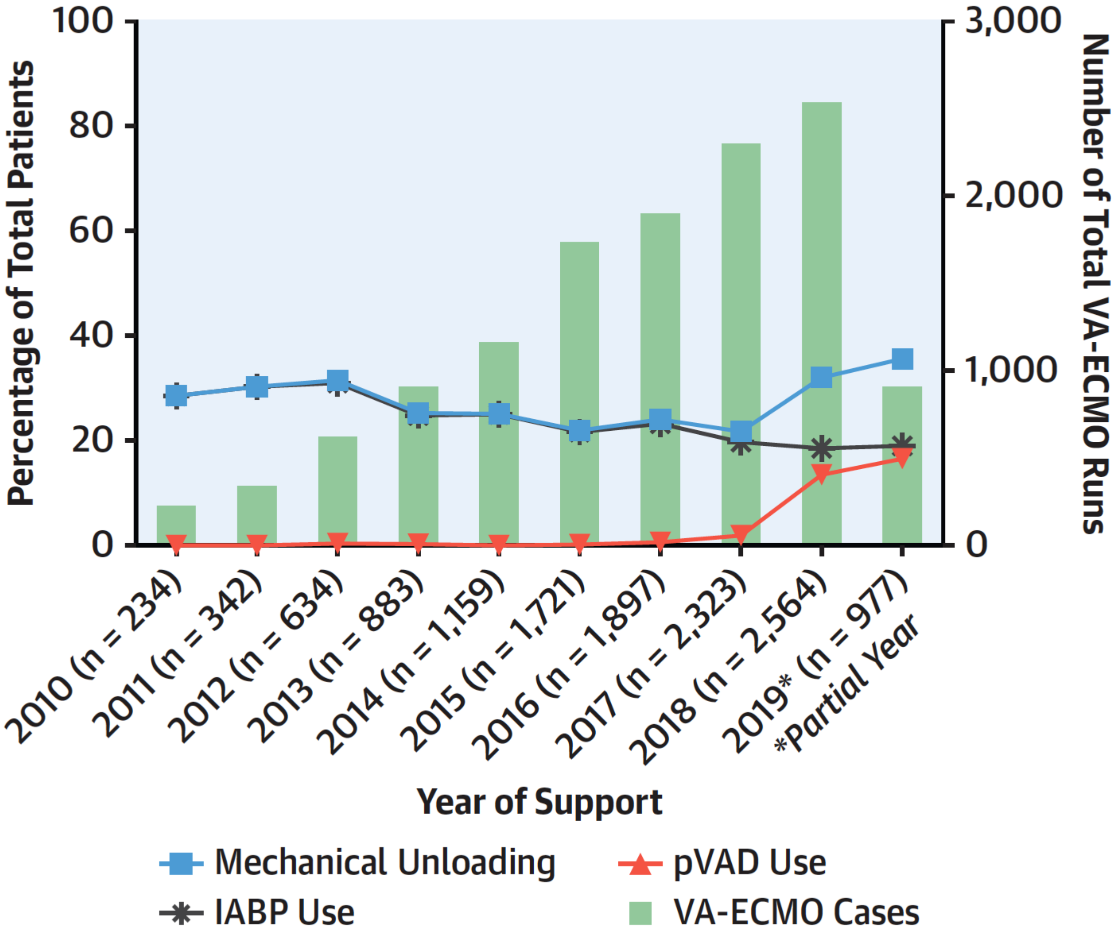
(6) Predominantly LV surgical vent + IABP in 17 patients

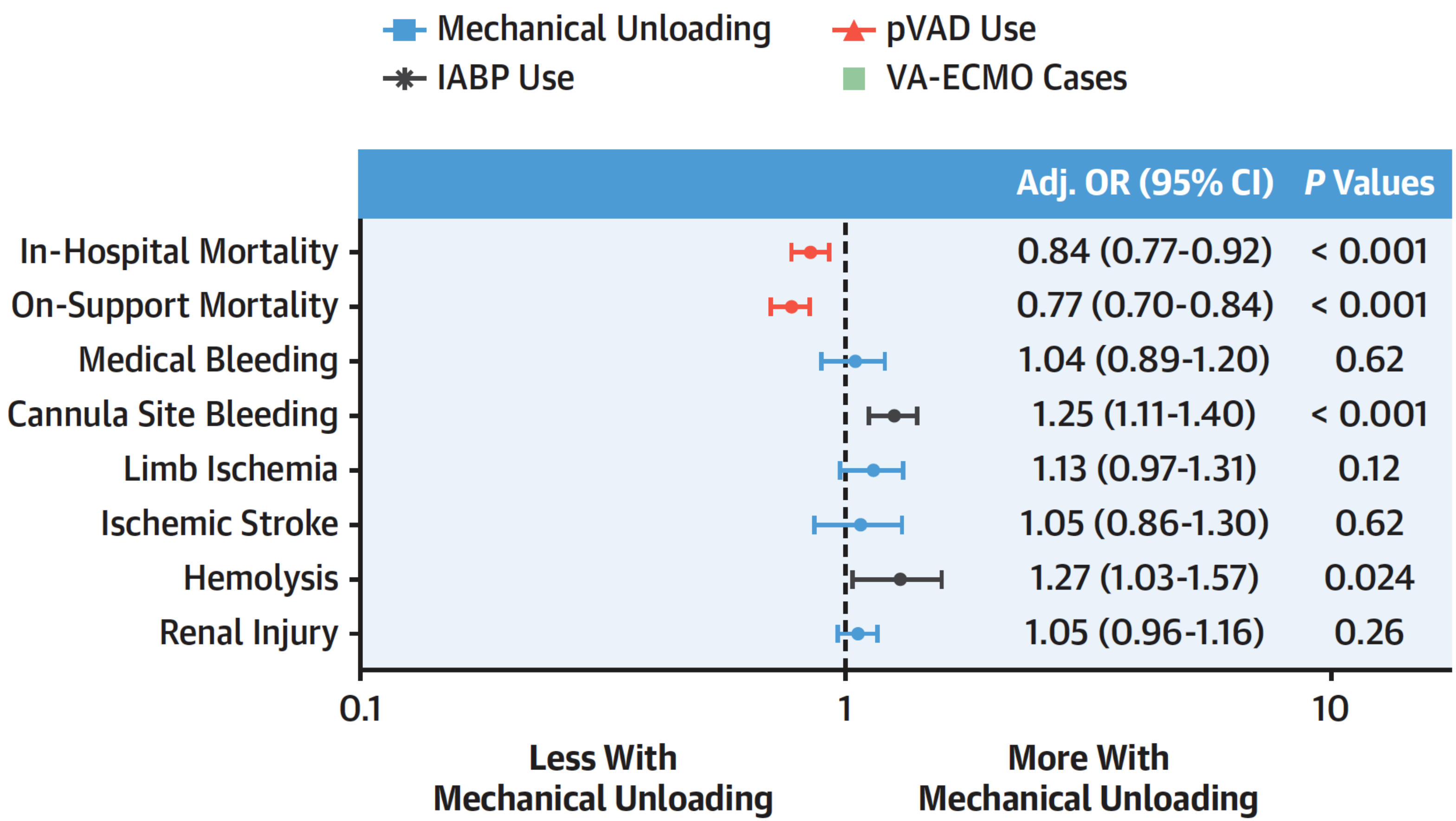
Circulation: Heart Failure 2019

LV Mechanical Unloading & Outcomes During VA ECMO



Grandin EW et al. JACC 2022

LV Mechanical Unloading & Outcomes During VA ECMO



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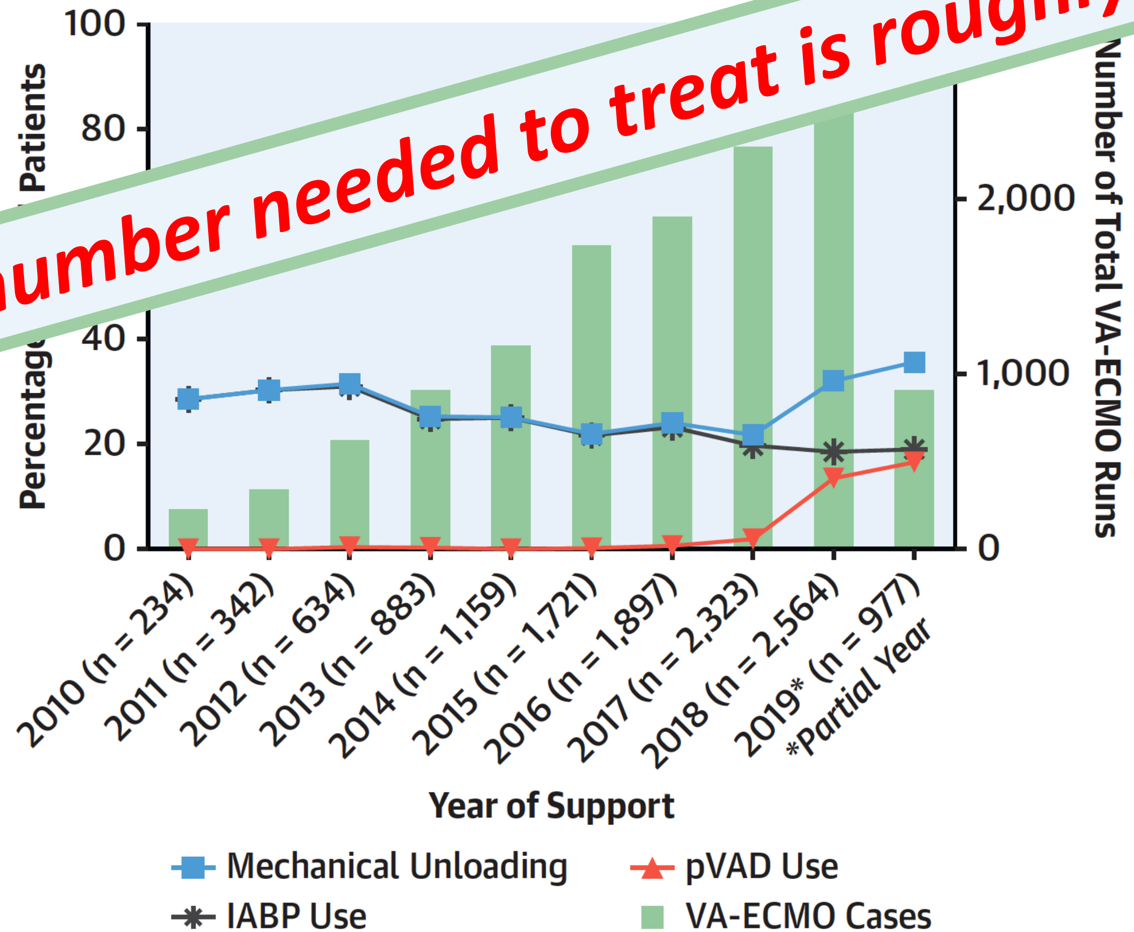
LV Mechanical Unloading & Outcomes During VA ECMO

The number needed to treat is roughly 30



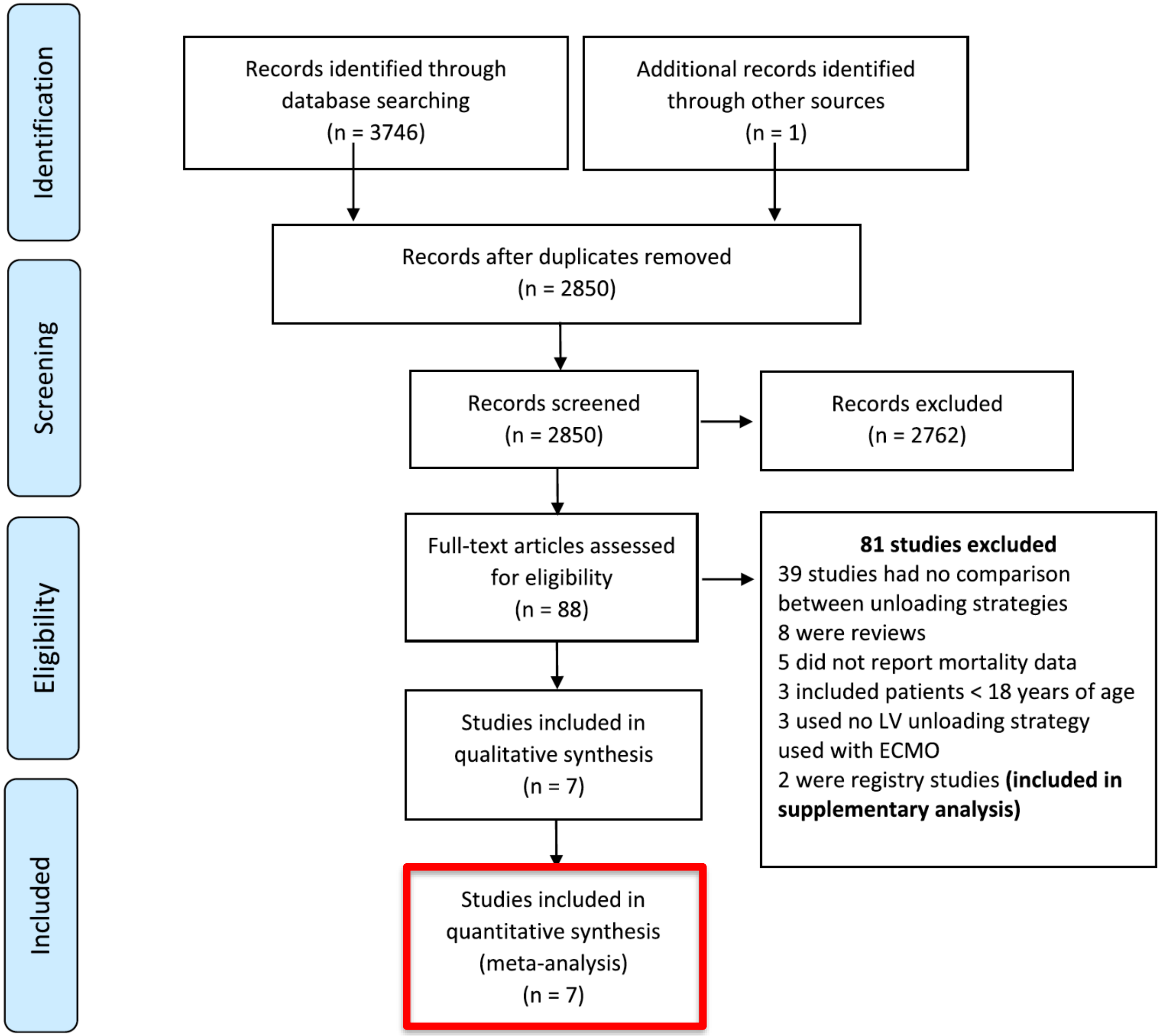
Grandin EW et al. JACC 2022

Donker DW et al. JACC 2022

Left Ventricular Unloading With Impella Versus IABP in Patients With VA-ECMO: A Systematic Review and Meta-Analysis

Kruti D. Gandhi, MD[a,1], Errol C. Moras, MD[a,1], Shailesh Niroula, MBBS[b], Persio D. Lopez, MD MSHS[c], Devika Aggarwal, MBBS[c], Kirtipal Bhatia, MD[c], Yoni Balboul, MD[a], Joseph Daibes, DO[c], Ashish Correa, MD[d], Abel Casso Dominguez, MD[c], Edo Y. Birati, MD[e], David A. Baran, MD[f], Gregory Serrao, MD[d], Kiran Mahmood, MD[d], Saraschandra Vallabhajosyula, MD, MSc[g], and Arieh Fox, MD[d,*]

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) use for circulatory support in cardiogenic shock results in increased left ventricular (LV) afterload. The use of concomitant Impella or intra-aortic balloon pump (IABP) have been proposed as adjunct devices for LV unloading. The authors sought to compare head-to-head efficacy and safety outcomes between the 2 LV unloading strategies. We conducted a search of Medline, EMBASE, and Cochrane databases to identify studies comparing the use of Impella to IABP in patients on VA-ECMO. The primary outcome of interest was in-hospital mortality. The secondary outcomes included transition to durable LV assist devices/cardiac transplantation, stroke, limb ischemia, need for continuous renal replacement therapy, major bleeding, and hemolysis. Pooled risk ratios (RRs) with 95% confidence interval and heterogeneity statistic I^2 were calculated using a random-effects model. A total of 7 observational studies with 698 patients were included. Patients on VA-ECMO unloaded with Impella vs IABP had similar risk of short-term all-cause mortality, defined as either 30-day or in-hospital mortality- 60.8% vs 64.9% (RR 0.93 [0.71 to 1.21], $I^2 = 71\%$). No significant difference was observed in transition to durable LV assist devices/cardiac transplantation, continuous renal replacement therapy initiation, stroke, or limb ischemia between the 2 strategies. However, the use of VA-ECMO with Impella was associated with increased risk of major bleeding (57.2% vs 39.7%) (RR 1.66 [1.12 to 2.44], $I^2 = 82\%$) and hemolysis (31% vs 7%) (RR 4.61 [1.24 to 17.17], I2 = 66%) compared with VA-ECMO, along with IABP. In conclusion, in patients requiring VA-ECMO for circulatory support, the concomitant use of Impella or IABP had comparable short-term mortality. However, Impella use was associated with increased risk of major bleeding and hemolysis. **(Am J Cardiol 2023;208:53−59)**



Ghandi KD et al. Am J Cardiol 2023

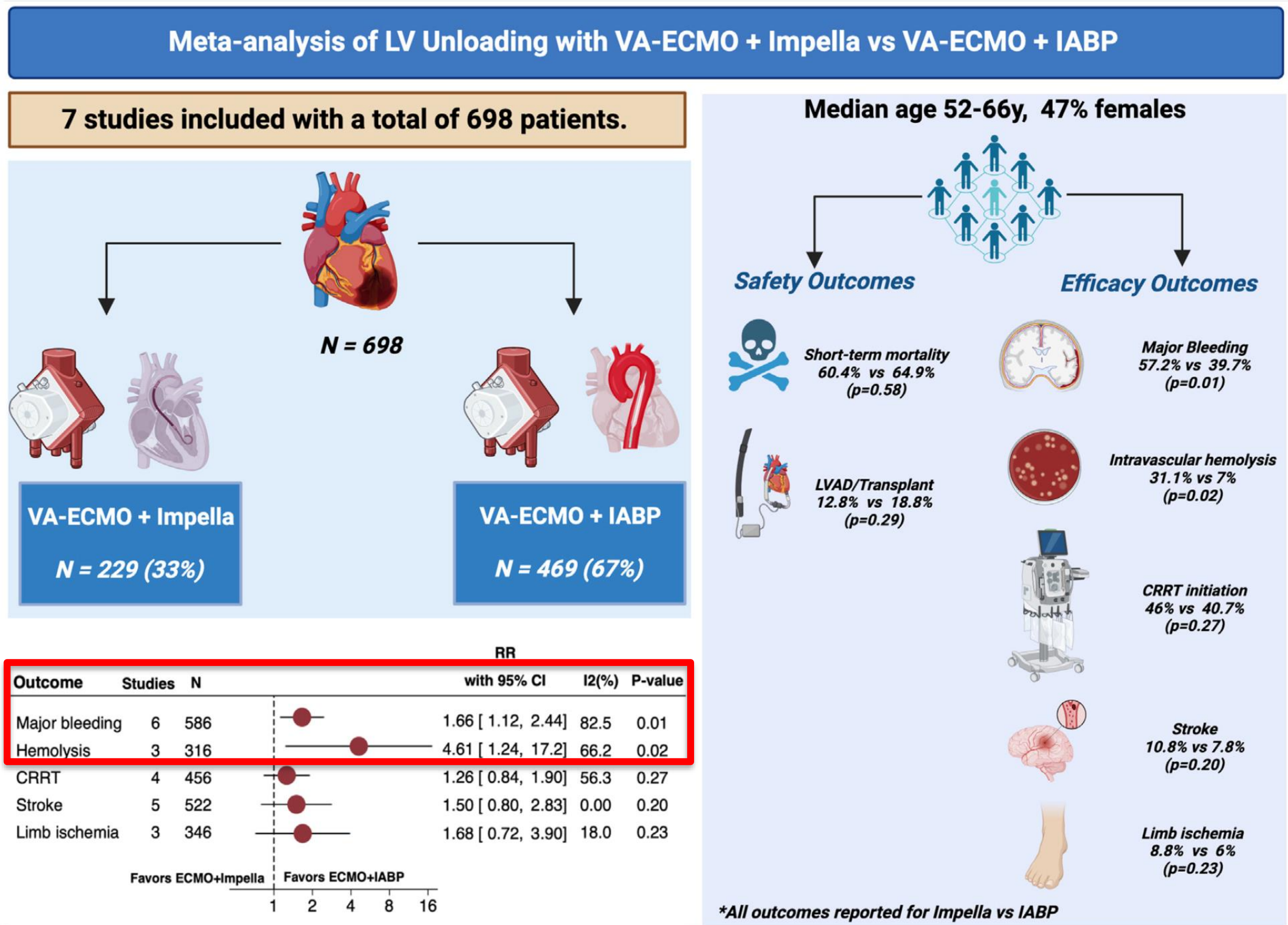
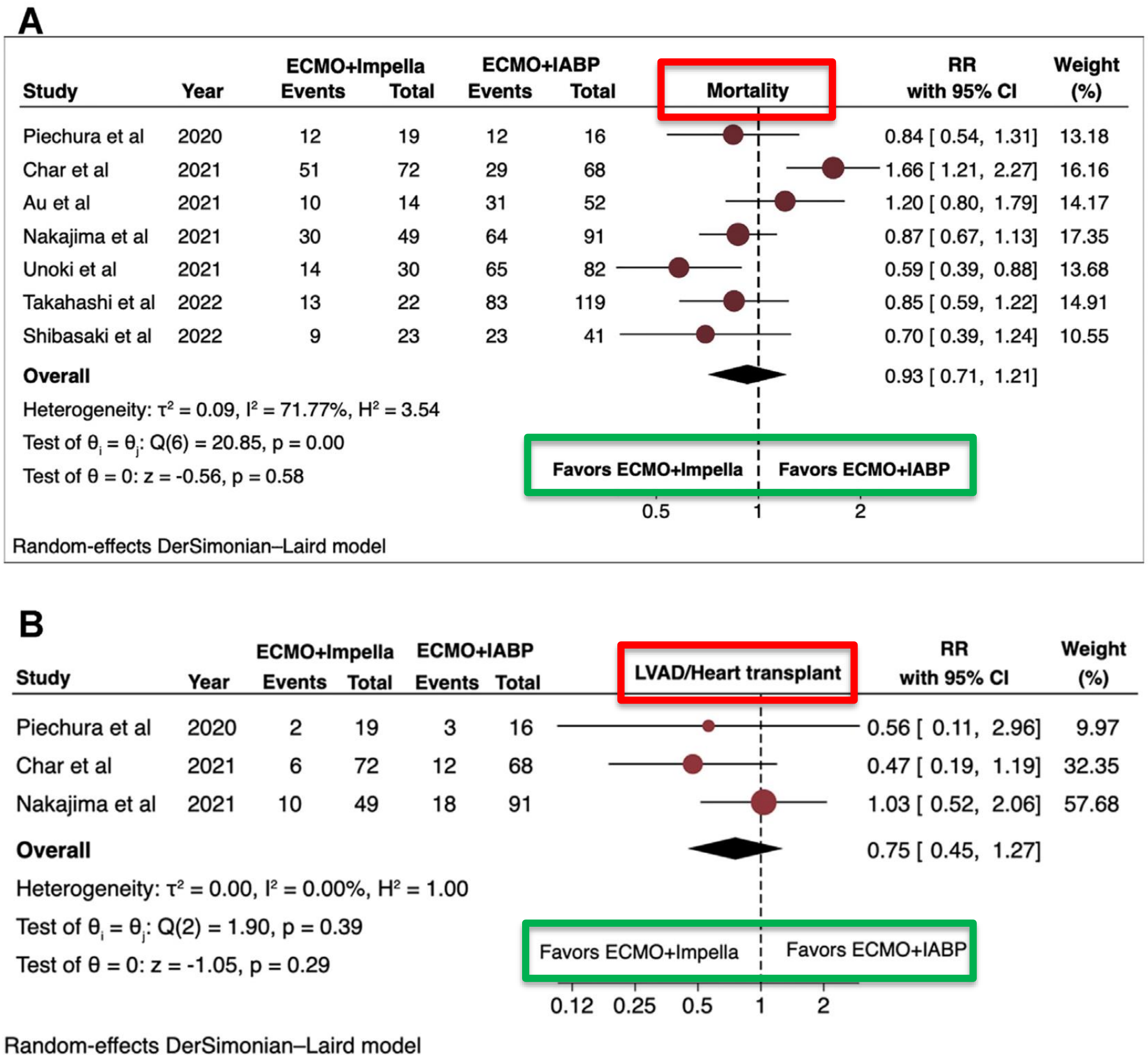


Figure 4. Meta-analysis of LV unloading with VA-ECMO+Impella versus VA-ECMO+IABP.

Ghandi KD et al. Am J Cardiol 2023



Ghandi KD et al. Am J Cardiol 2023

Intensive Care Med (2024) 50:209–221
https://doi.org/10.1007/s00134-023-07278-3

SYSTEMATIC REVIEW

Mechanical circulatory support for cardiogenic shock: a network meta-analysis of randomized controlled trials and propensity score-matched studies

Christopher Jer Wei Low[1], Ryan Ruiyang Ling[1], Michele Petrova Xin Ling Lau[1], Nigel Sheng Hui Liu[1], Melissa Tan[2], Chuen Seng Tan[1,3], Shir Lynn Lim[1,4,5], Bram Rochwerg[6,7], Alain Combes[8,9], Daniel Brodie[10], Kiran Shekar[11,12,13,14], Susanna Price[15,16], Graeme MacLaren[1,2] and Kollengode Ramanathan[1,2*]

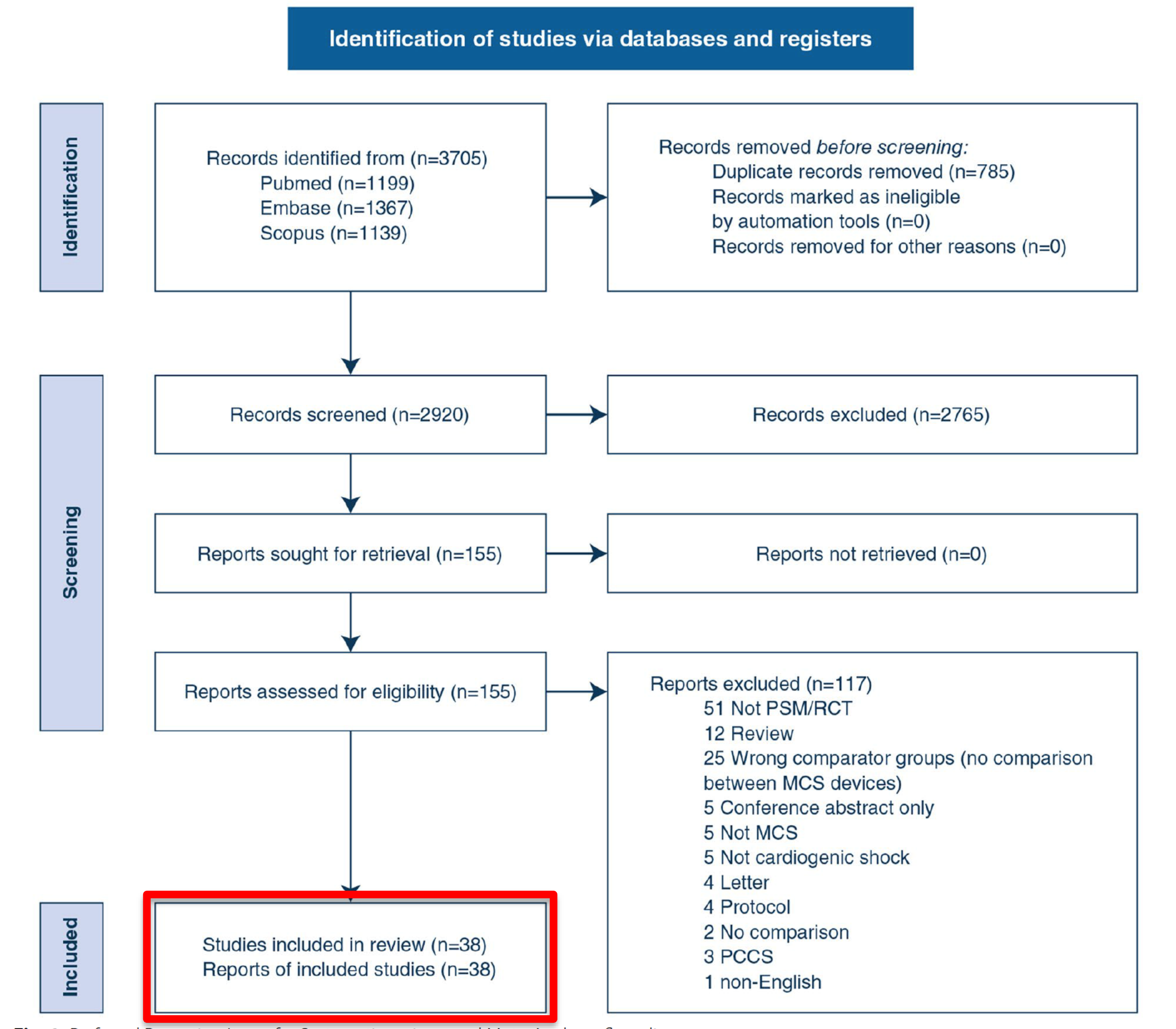


Fig. 1 Preferred Reporting Items for Systematic reviews and Meta-Analyses flow diagram

Low CJW et al. Am J Cardiol 2023

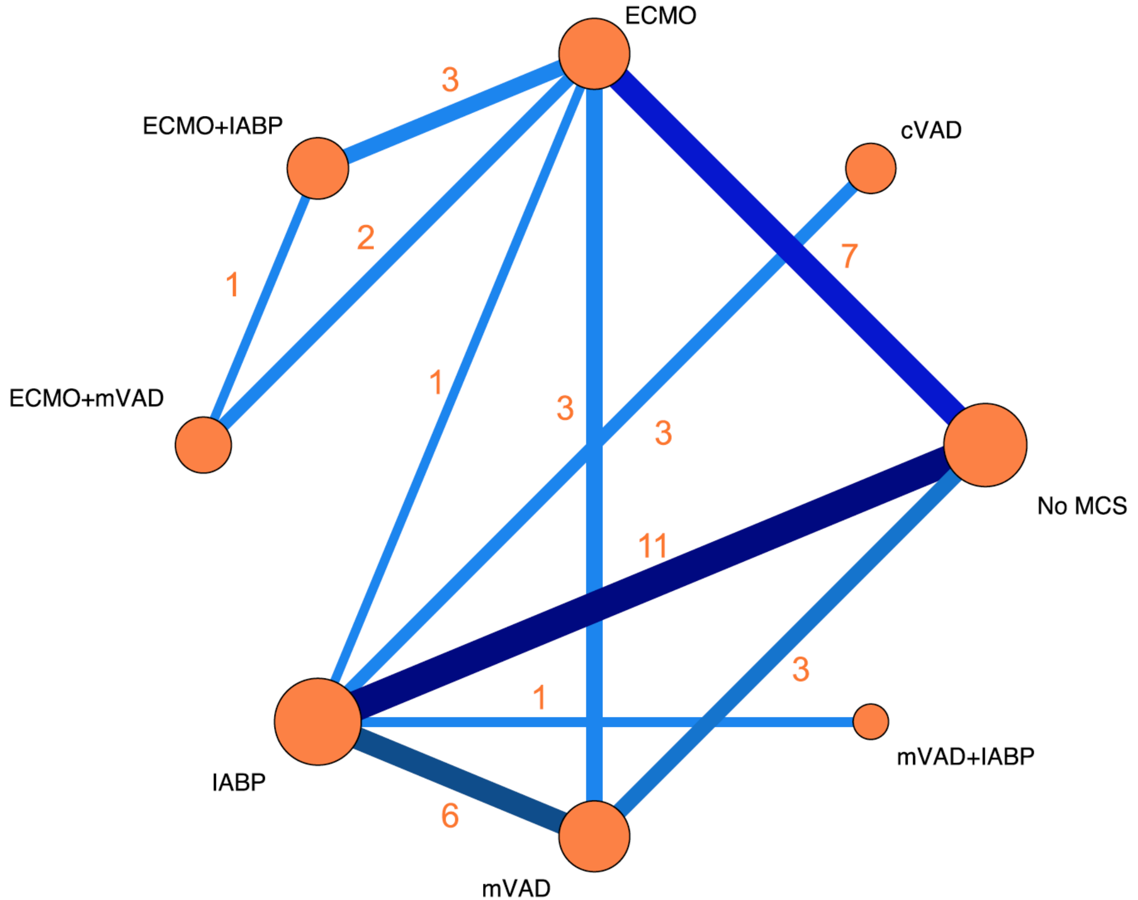


Fig. 2 Network geometry plot for the primary analysis. The size of each node (circle) represents the number of studies reporting on the intervention. The thickness and depth of color of each edge (line) represent the number of studies in each pairwise comparison

Low CJW et al. Am J Cardiol 2023

Another plea for temporary MCS …

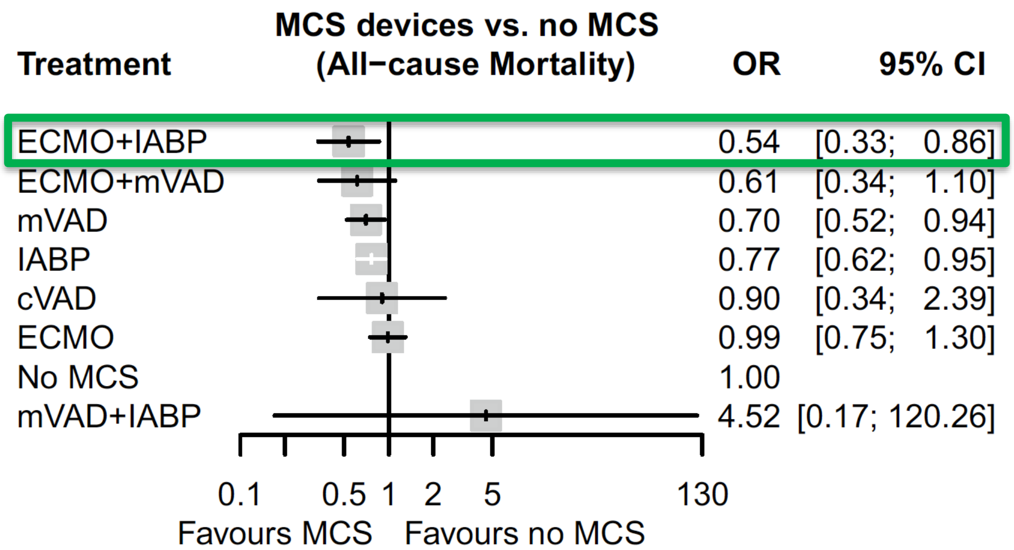


Fig. 3 Network forest plot demonstrating network estimates for all outcomes. While the IABP and mVAD estimates demonstrate significance here, we derived the final estimates from direct and indirect estimates, respectively, for those outcomes, based on our supplemental Methods

Low CJW et al. Am J Cardiol 2023

De Backer *et al. Critical Care* (2024) 28:203
https://doi.org/10.1186/s13054-024-04988-y

Critical Care

COMMENT **Open Access**

Mechanical circulatory support in cardiogenic shock: microaxial flow pumps for all and VA-ECMO consigned to the museum?

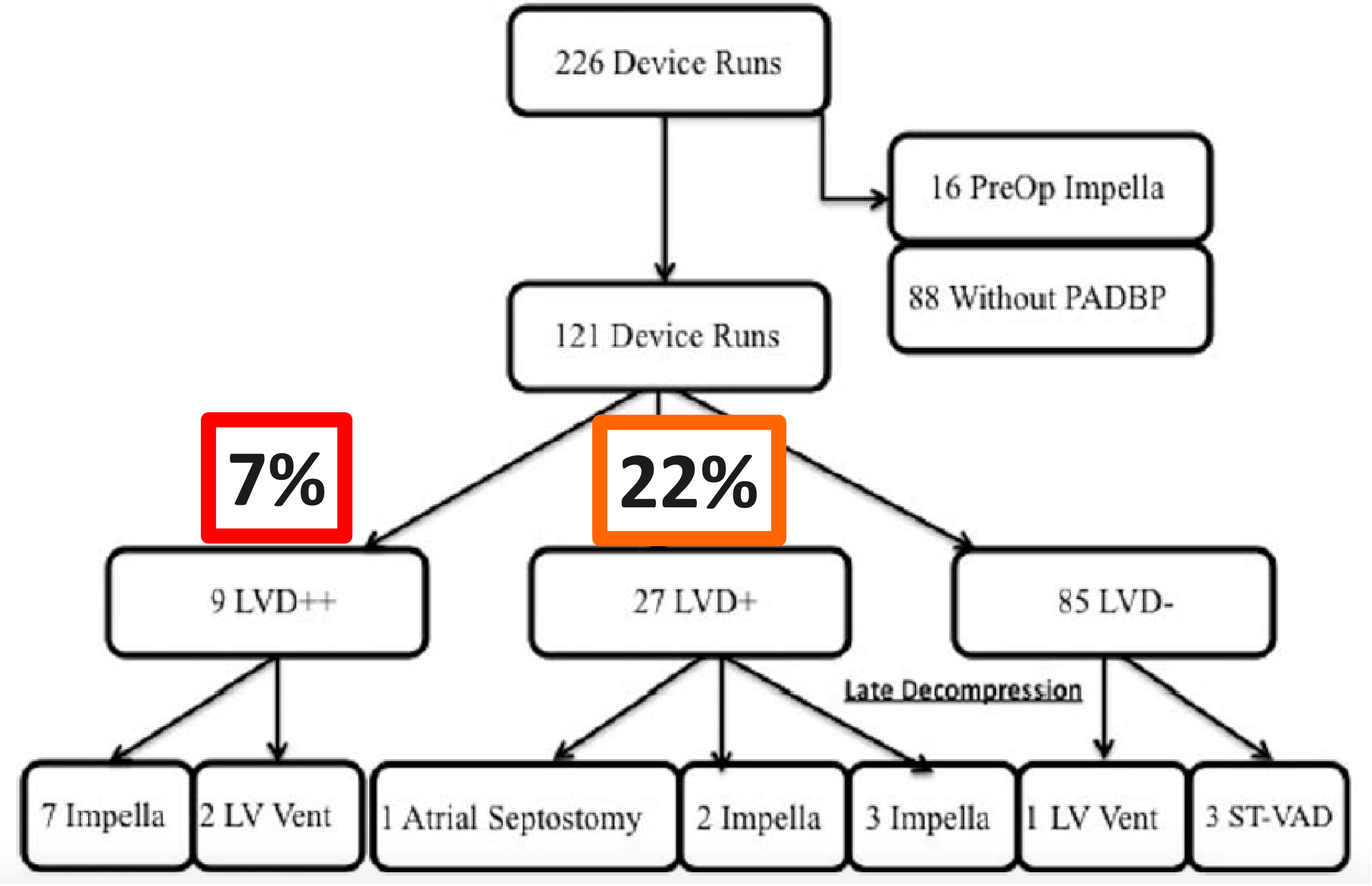
Daniel De Backer[1*], Dirk W. Donker[2,3], Alain Combes[4], Alexandre Mebazaa[5], Jacob E. Moller[6,7] and Jean-Louis Vincent[8]

Table 1 Main differences in the three largest randomized controlled trials (RCTs) on mechanical circulatory support (MCS) in cardiogenic shock

	Ostadal et al. [4]	**Thiele et al. [5]**	**Moller et al. [9]**
MCS type	VA-ECMO	VA-ECMO	MFP
Patients	SCAI D-E	SCAI C-E (SCAI C 53%)	SCAI C-E (SCAI C 55%)
Cardiac arrest exclusions (proportion of included patients who were post-CA)	Comatose after cardiac arrest excluded (post-CA 11%)	CPR > 45 min excluded (post-CA 78%)	Comatose after cardiac arrest excluded (post-CA 20%)
Mechanical ventilation at inclusion	70%	88%	18%
Unloading strategy	22%	6%	Not relevant
Rescue MCS in control group	Rescue VA-ECMO 39%	Rescue VA-ECMO 13% Rescue MFP 13%	Rescue VA-ECMO 13%
Additional MCS in intervention group	0%	0%	Rescue VA-ECMO 12% Other MFP 16%

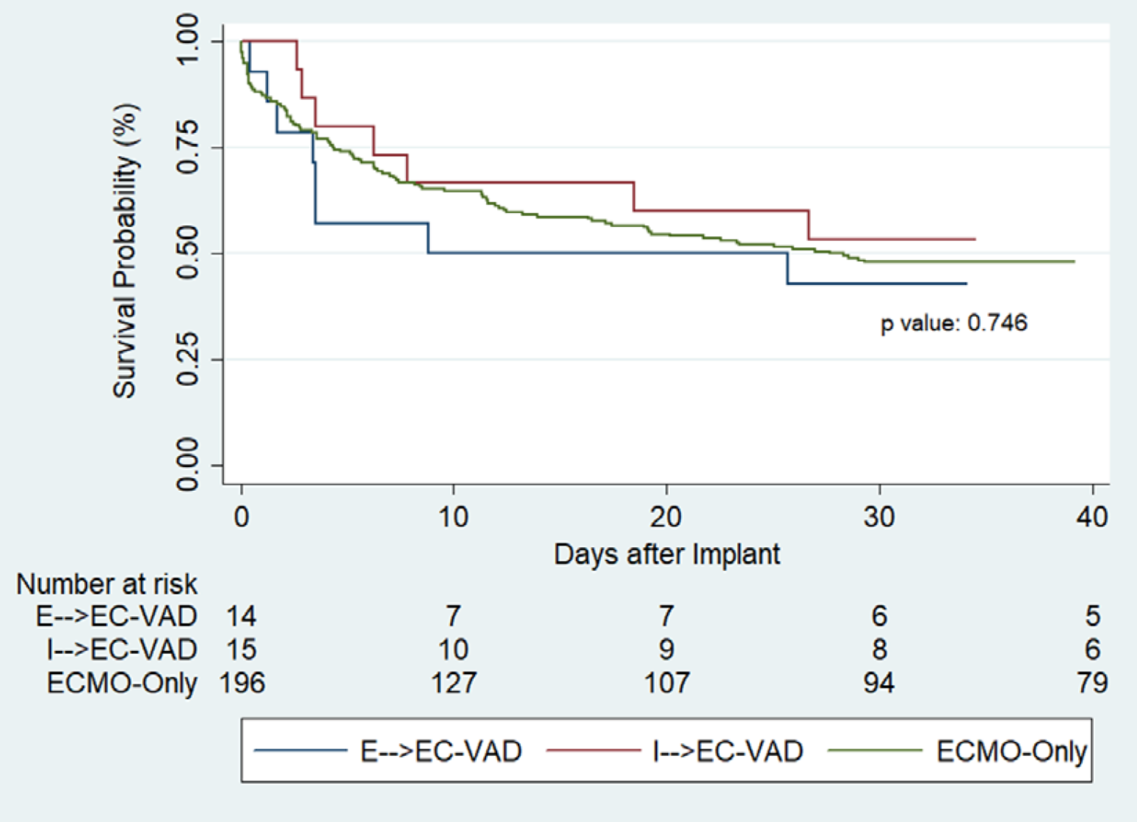
Incidence and Implications of Left Ventricular Distention During Venoarterial Extracorporeal Membrane Oxygenation Support

Lauren K. Truby,* Koji Takeda,† Christine Mauro,‡ Melana Yuzefpolskaya,* Arthur R. Garan,* Ajay J. Kirtane,* Veli K. Topkara,* Darryl Abrams,* Daniel Brodie,* Paolo C. Colombo,* Yoshifumi Naka,† and Hiroo Takayama†

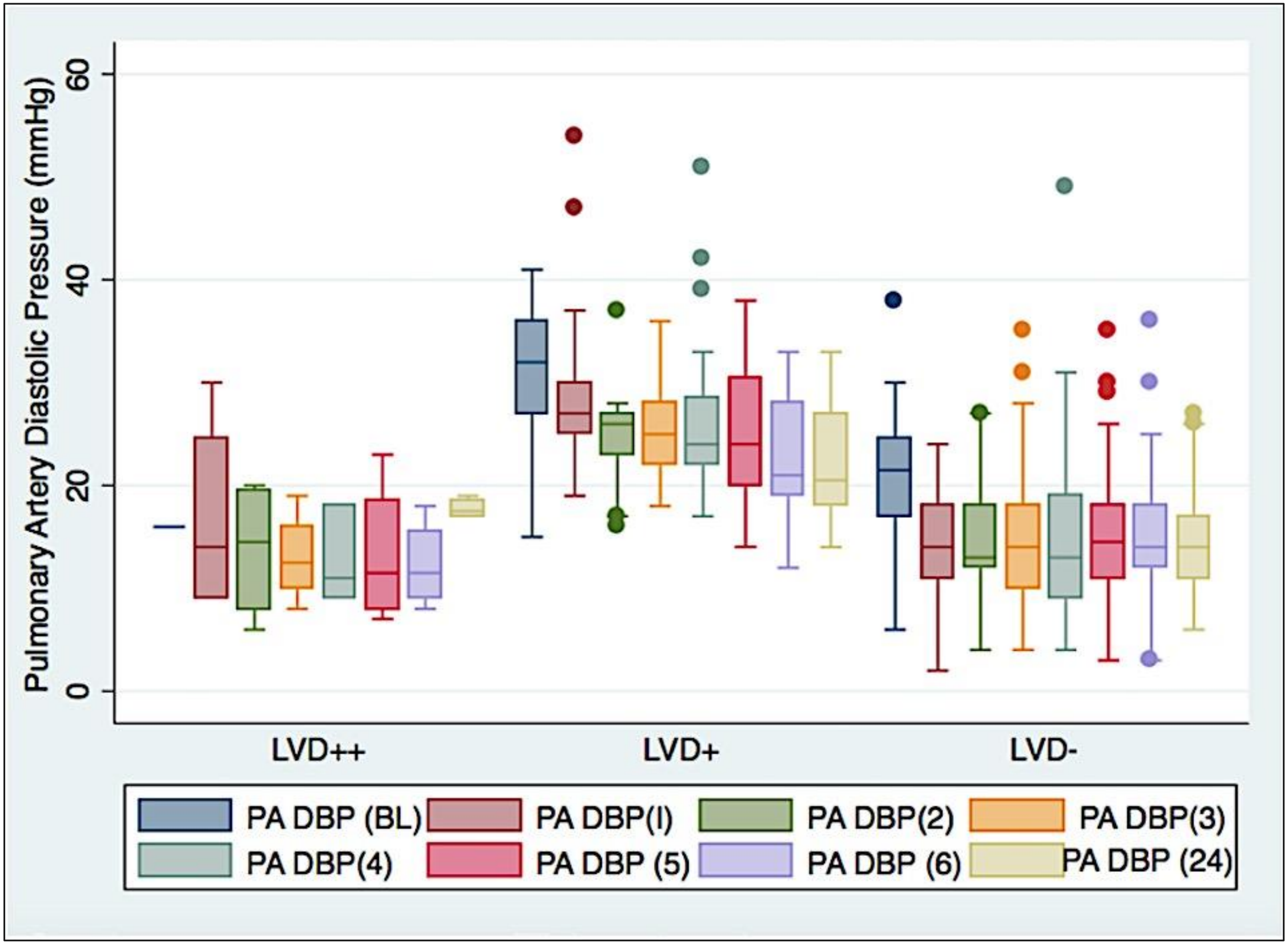


EC-VAD: Combined Use of Extracorporeal Membrane Oxygenation and Percutaneous Microaxial Pump Left Ventricular Assist Device

Olutosin J. Akanni,* Koji Takeda,* Lauren K. Truby,† Paul A. Kurlansky,* Codruta Chiuzan,‡ Jiho Han,* Veli K. Topkara,† Melana Yuzefpolskaya,† Paolo C. Colombo,† Dimitrios Karmpaliotis,† Jeffery W. Moses,† Yoshifumi Naka,* A. Reshad Garan,† Ajay J. Kirtane,† and Hiroo Takayama*



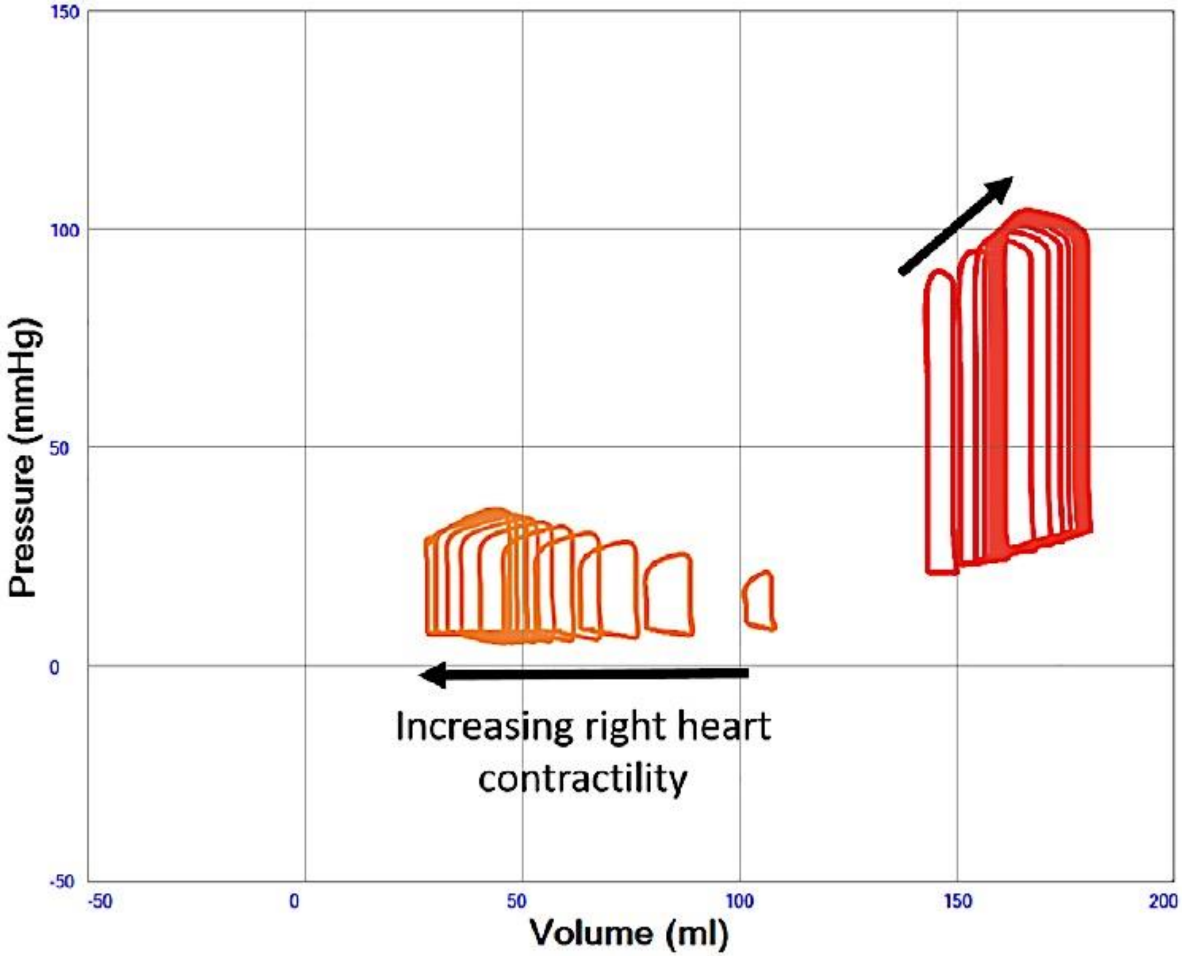
Pulmonary artery diastolic P (= LVEDP)



Truby LK et al. ASAIO J 2017

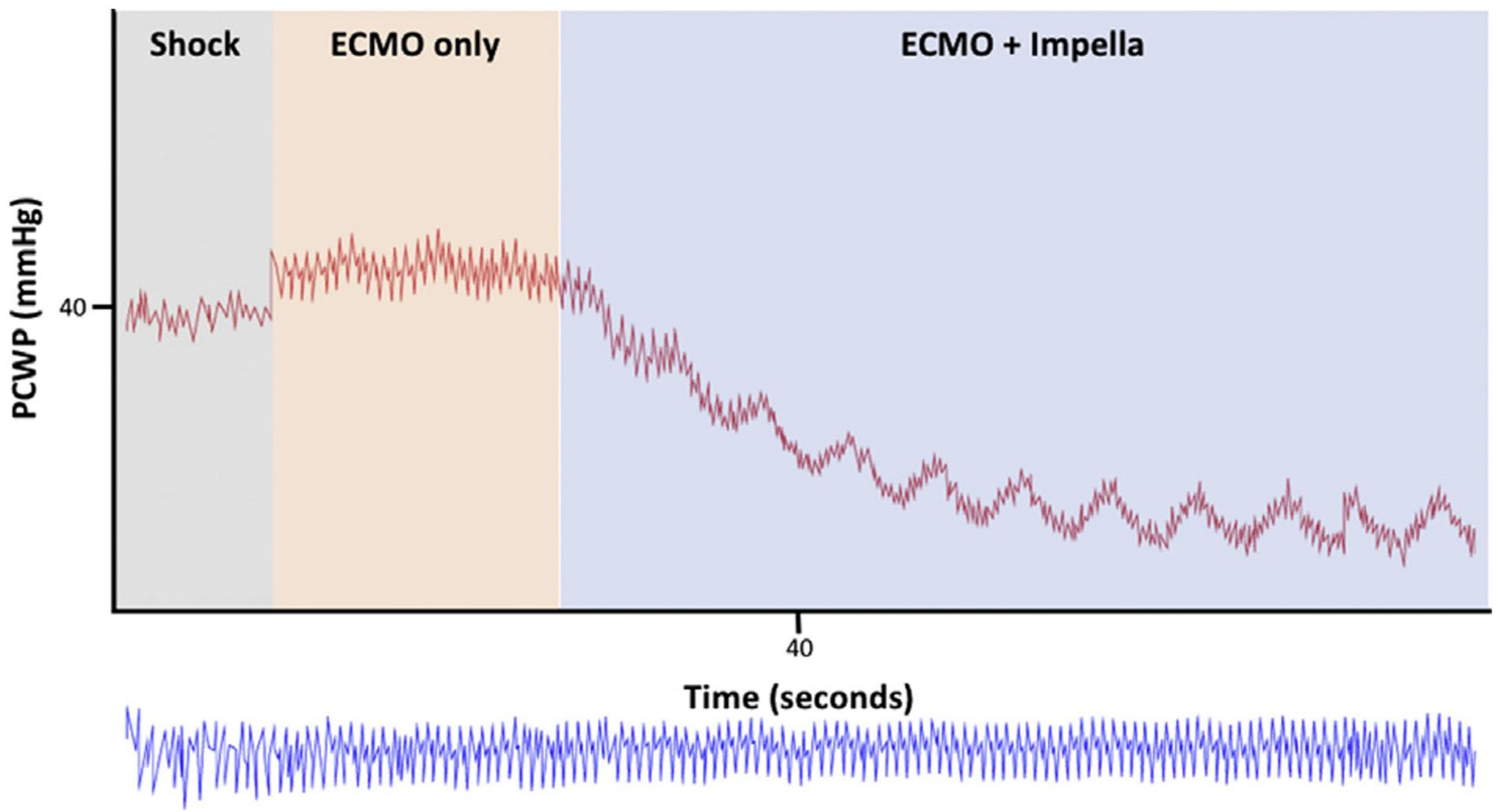
Mechanistic insights – physiological reasoning

RV - LV interdependence in ECMO



Donker DW et al. ASAIO J 2021

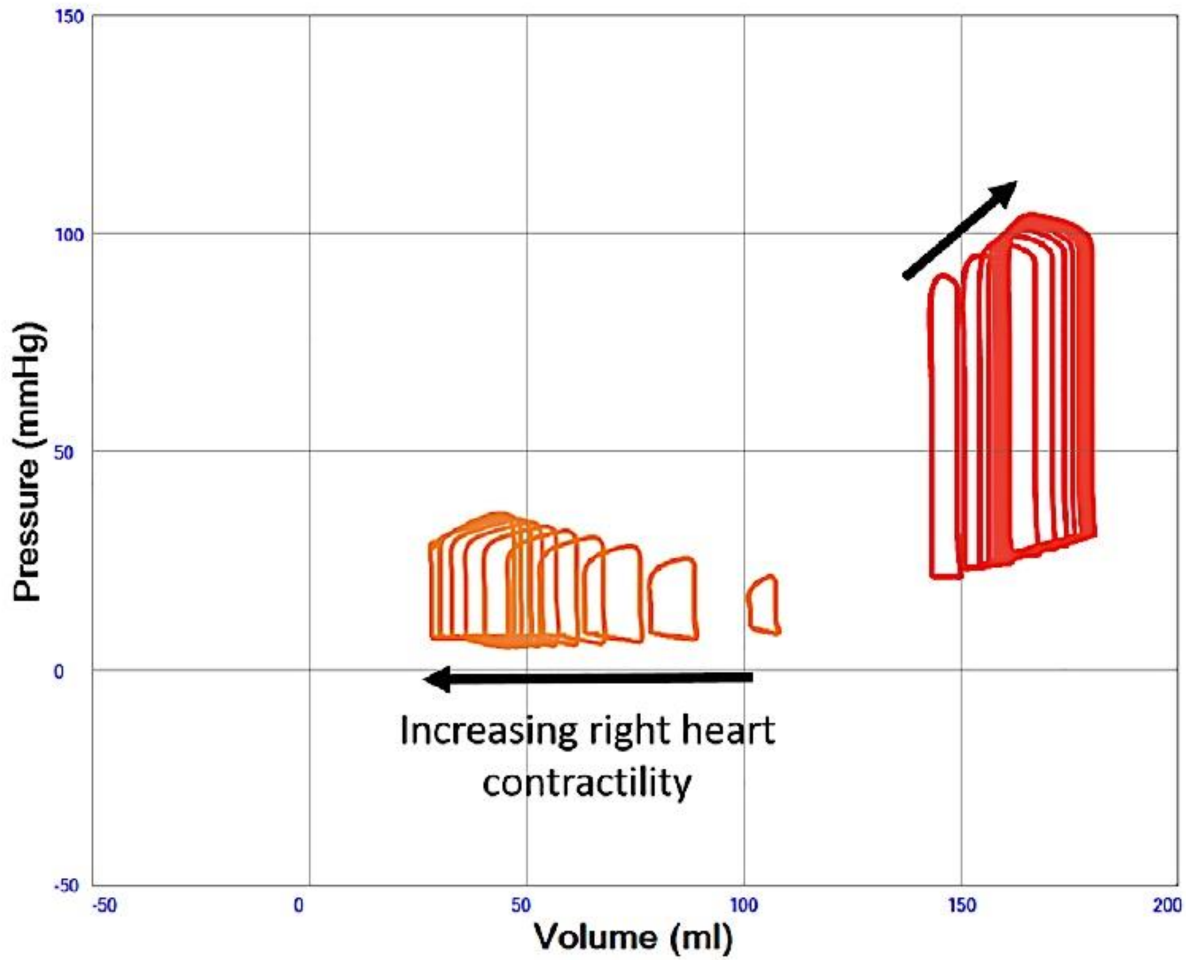
IMPOSSIBLE without … RV-LV interdependency under ECMO



Schrage B et al. JACC HF 2018

Mechanistic insights – physiological reasoning

RV - LV interdependence in ECMO



Donker DW et al. ASAIO J 2021

VA ECMO *versus* native heart

competition in peripheral VA ECMO

Courtesy of Alois Philipp, Regensburg

RESUSCITATION 195 (2024) 110122

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Resuscitation

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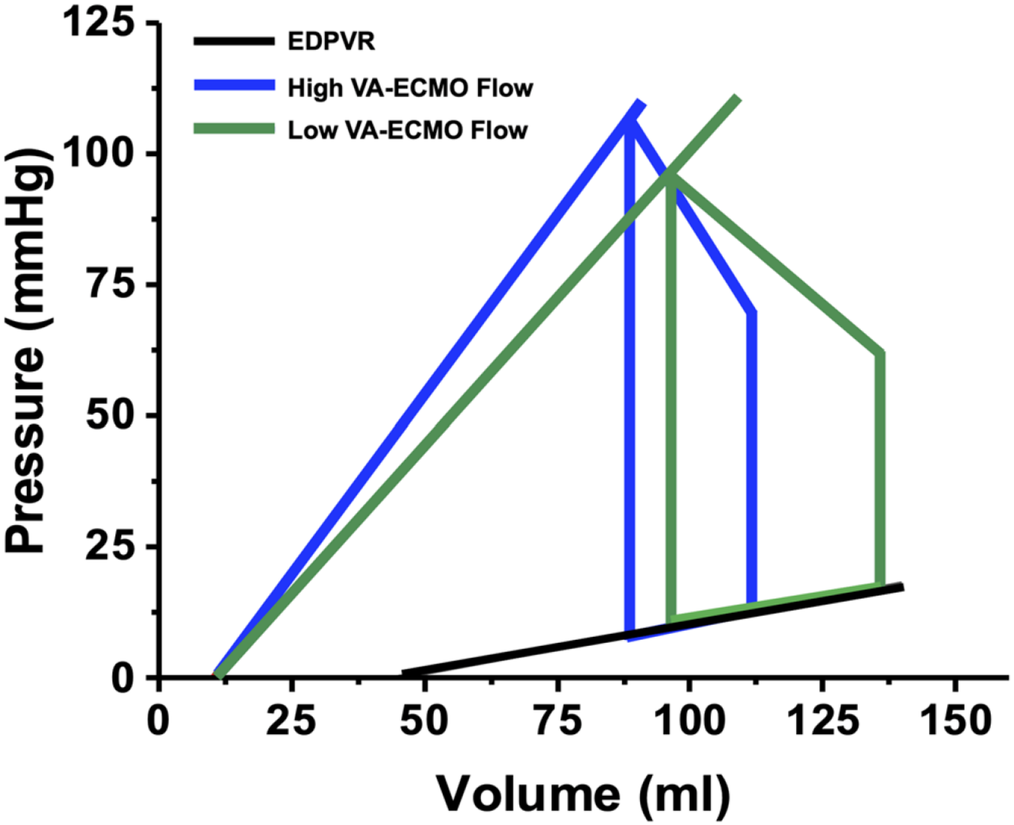
Editorial

Left ventricular unloading during VA-ECMO: A Gordian knot of physiology

We suggest that the best way to break the Gordian knot of unloading is to refine our understanding of VA-ECMO physiology. **Left ventricular unloading has been theoretically proposed to have two main physiologic benefits in patients on VA-ECMO: (1) reduction in left ventricular afterload and (2) a reduction of LV preload** and, consequently, pulmonary vascular pressures – particularly pulmonary capillary wedge pressure. **However, these theoretical benefits are not supported by strong physiologic data.**

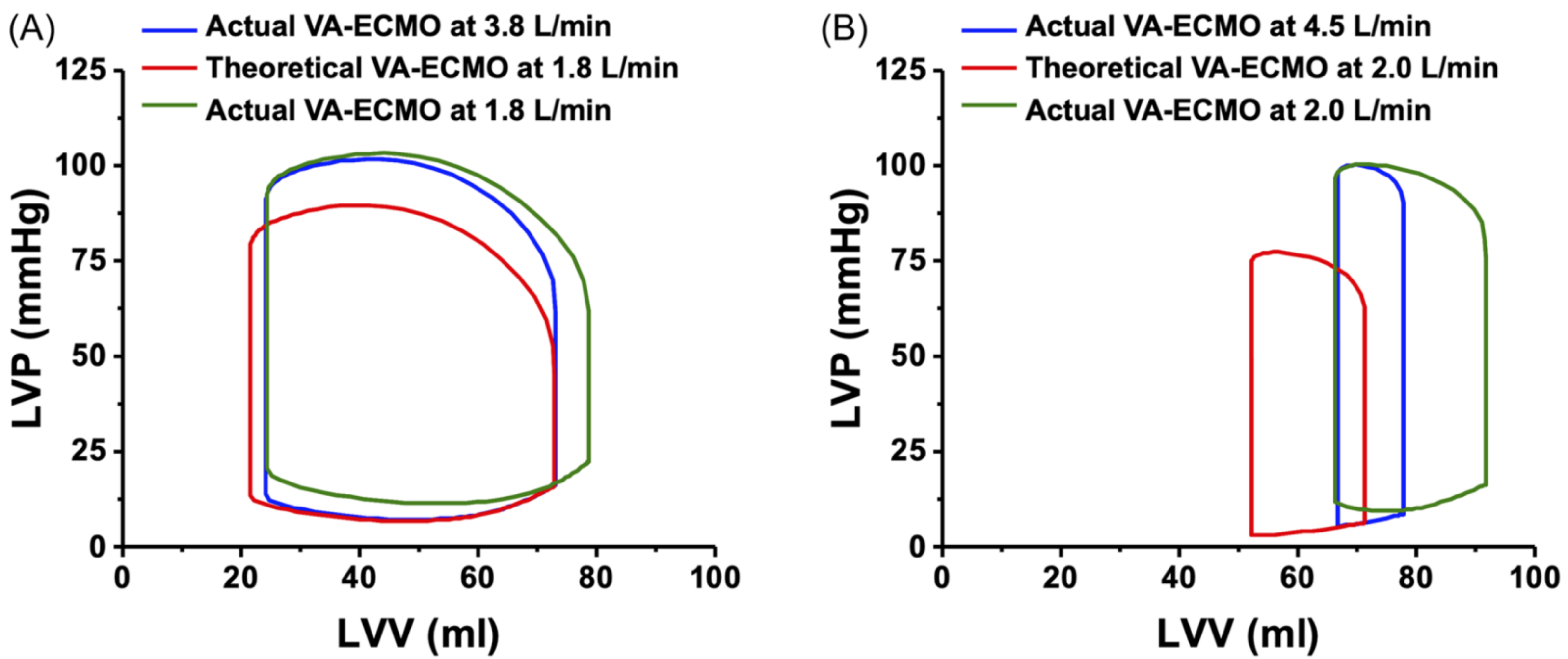
Rajat Kalra et al. Resuscitation 2024

Gordian knot ?



Rajat Kalra et al. Catheter Cardiovasc Interv. 2024

Discrepancy between *theory* and *practice* ?



CENTRAL ILLUSTRATION 1 Invasive and theoretical left ventricular pressure volume loops at high and low VA-ECMO support.

Rajat Kalra et al. Catheter Cardiovasc Interv. 2024

Special Issue: EuroELSO 2024

Perfusion

Perfusion
2024, Vol. 39(1S) 5S–12S

DOI: 10.1177/02676591241237639
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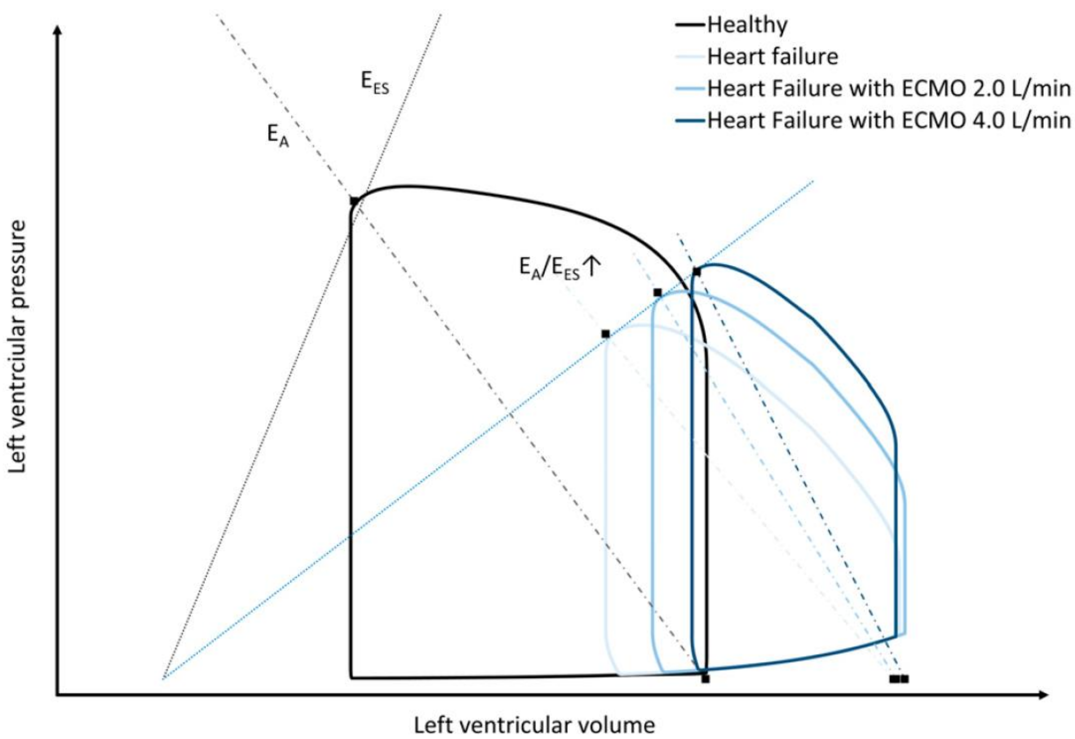
The physiology of venoarterial extracorporeal membrane oxygenation - A comprehensive clinical perspective

Libera Fresiello,[1] Jeannine A.J. Hermens,[2] Lara Pladet,[2] Christiaan L. Meuwese[3,4] and Dirk W. Donker[1,2]



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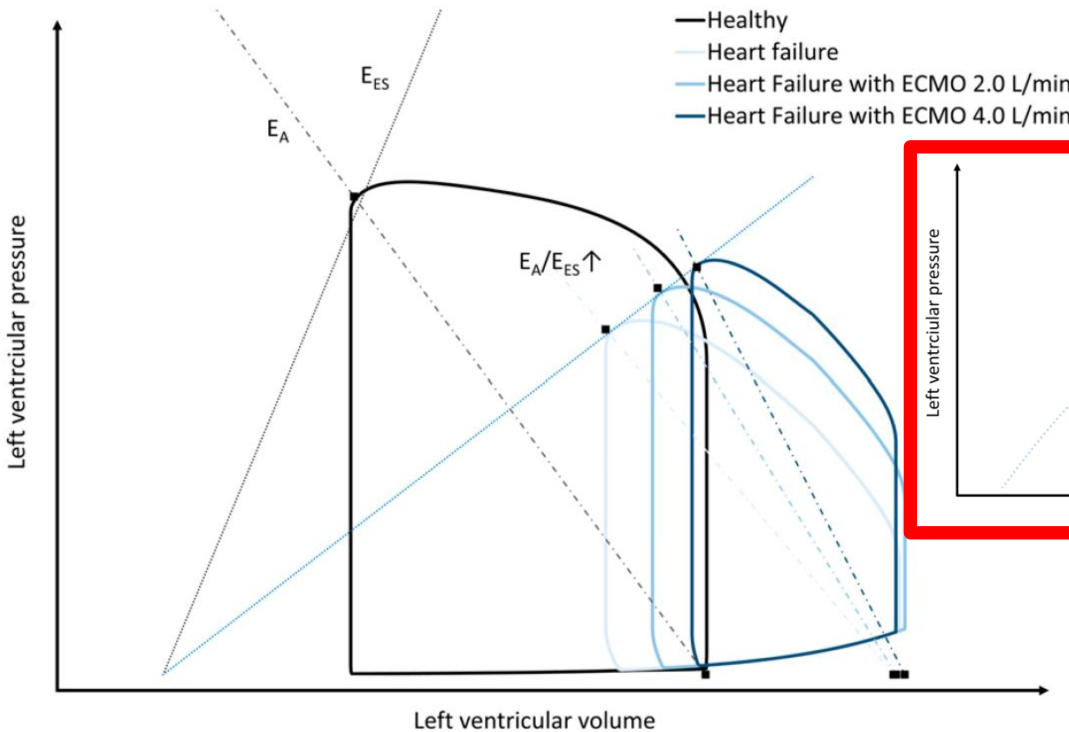
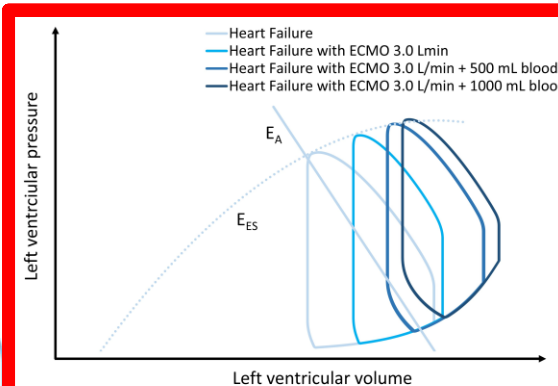
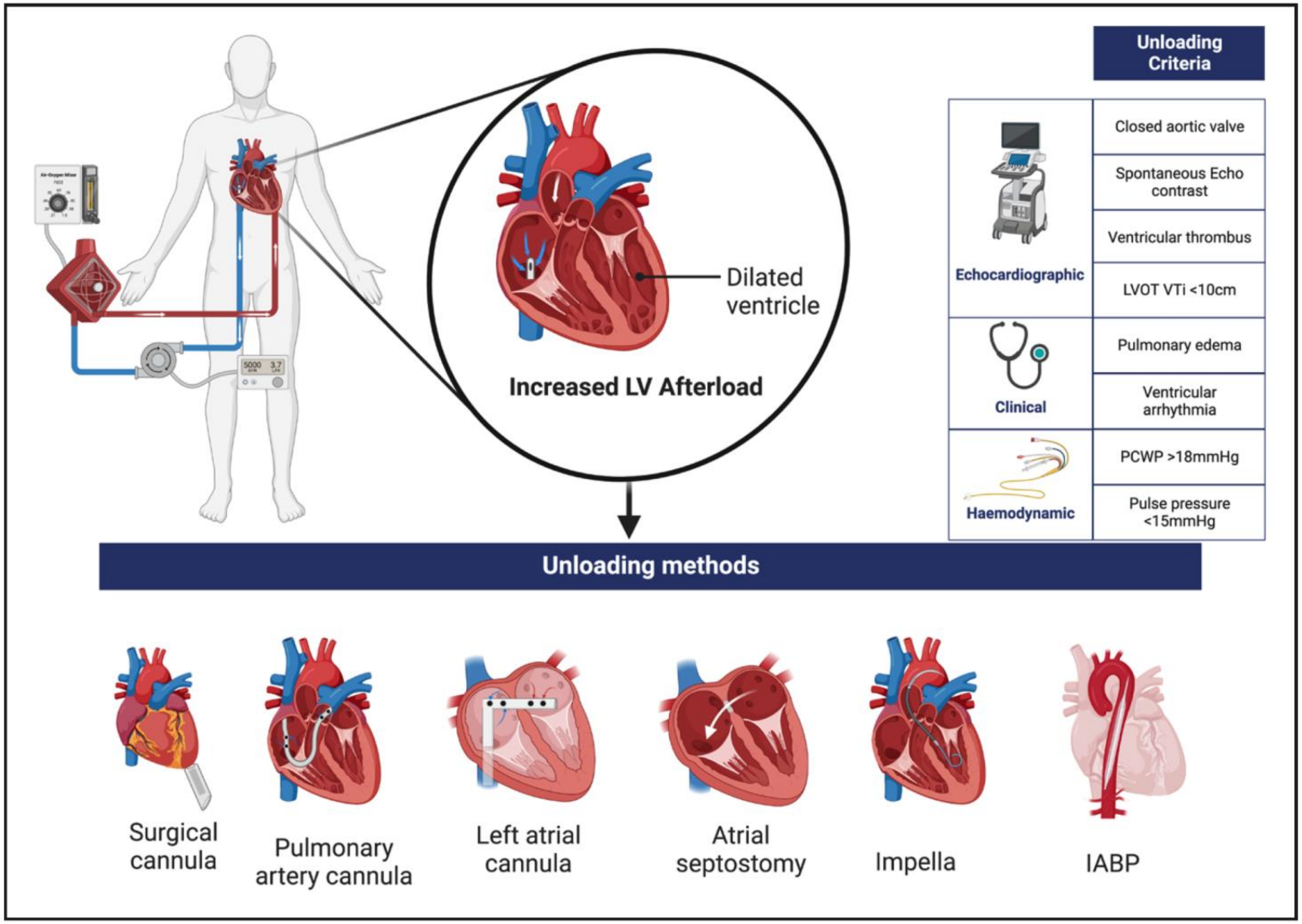




Cardiac (un-)loading conditions under VA ECMO

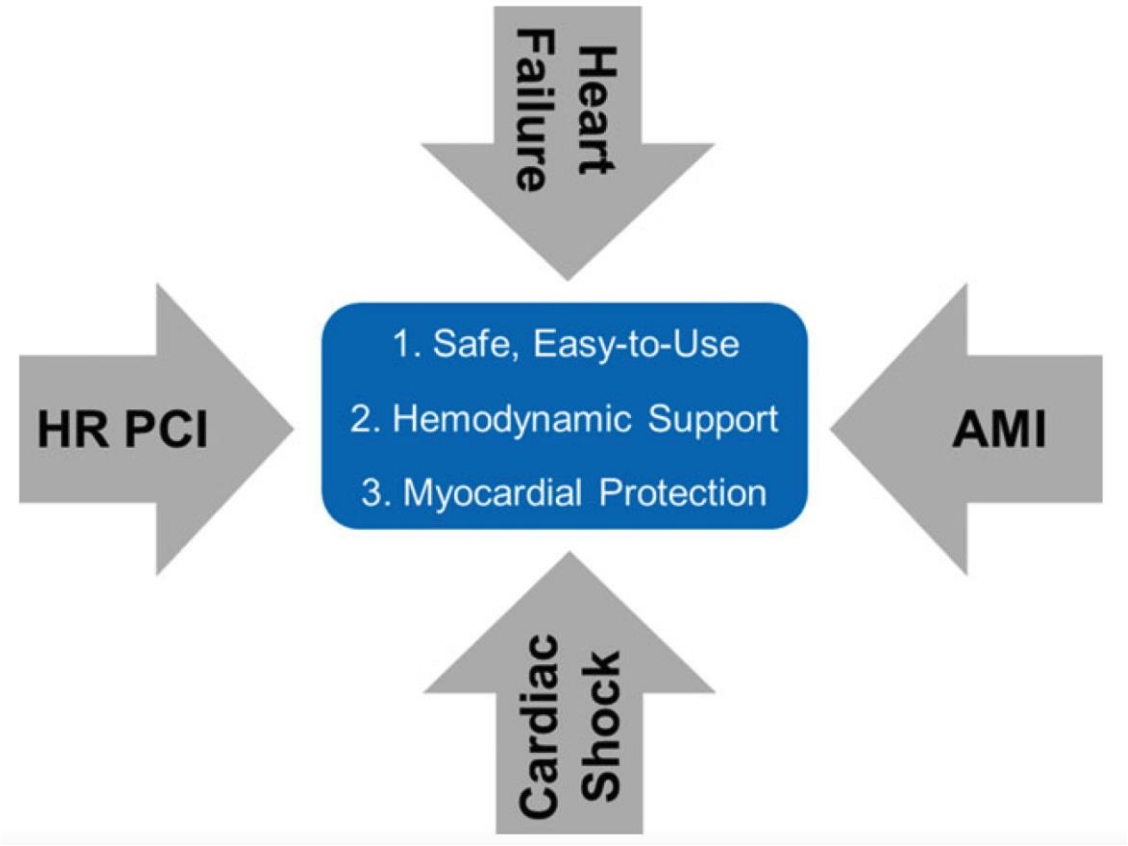
an intricate patient - device interaction



Ezad SM et al. Circulation 2023

Cardiac mechanical support

The *ideal* device !?



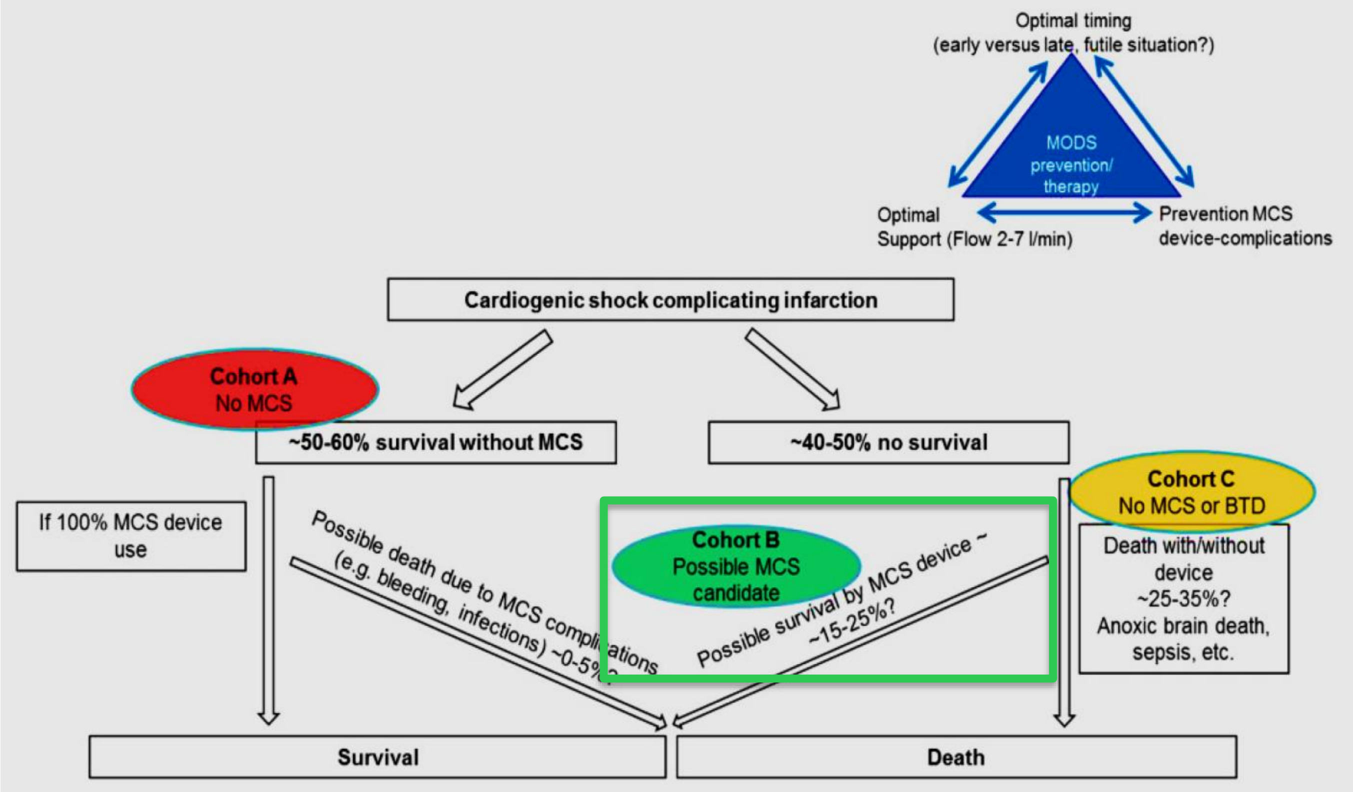
Burkhoff D. et al. Catheterization and Cardiovascular Interventions ***2012***

ESC
European Society of Cardiology
European Heart Journal (2019) **40**, 2671–2683
doi:10.1093/eurheartj/ehz363

CLINICAL REVIEW
Clinical update

Management of cardiogenic shock complicating myocardial infarction: an update 2019

Holger Thiele[1,2]*, E. Magnus Ohman[3], Suzanne de Waha-Thiele[4], Uwe Zeymer[5], and Steffen Desch[1,2]



Multicenter RCT – ECMELLA - VA ECMO

… recruiting

UNLOAD-ECMO

funded by the dutch heart foundation
Hartstichting

REMAP ECMO

clinicaltrials.gov NCT 05913622

Dutch ECLS Study group

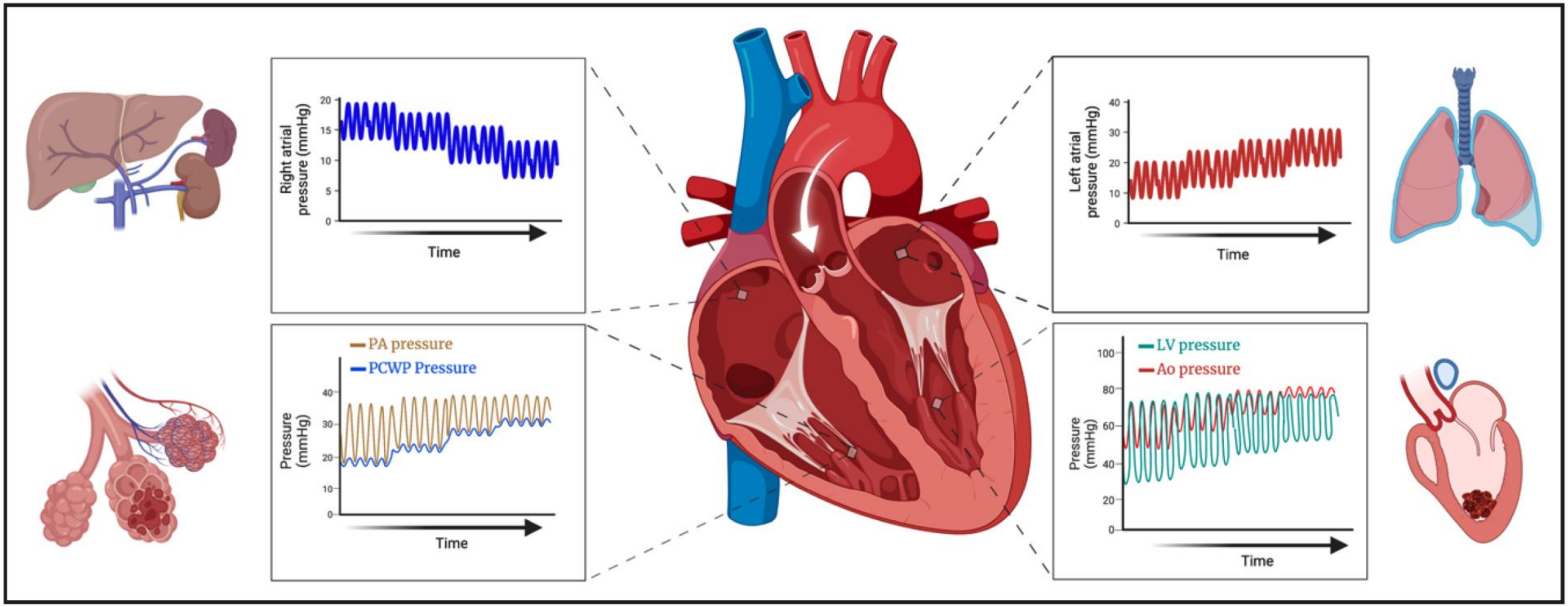
LUMC · HagaZiekenhuis · UMC Utrecht · Amsterdam UMC Universitair Medische Centra · umcg · isala · Radboudumc university medical center

Erasmus MC · catharina ziekenhuis · St Antonius een santeon ziekenhuis · Amphia · Maastricht UMC+ · olvg

c.meuwese@erasmusmc.nl

The hemodynamics of VA ECMO

an intricate patient - device interaction



Ezad SM et al. Circulation 2023

Take home messages

LV unloading trials - VA ECMO & MCS

- Experimental data provide …
  - ✔ **mechanistic rationale**

- Epidemiological evidence …
  - ✔ **hypothesis generating**
  - ✔ **backbone** for daily clinical decision making

  - ✔ LV unloading/ adjunct LV unloading
    - **- early & tailored**
    - - **careful weighing** considerable risks & benefits
    - - **limited group** of **well-selected** patients

- Bedside reasoning remains crucial …
  - ✔ points to **complexity** of individual cases
  - ✔ underscores: **NOT one size fits all !!!**

Thank you !

University of Twente – TechMed Center

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