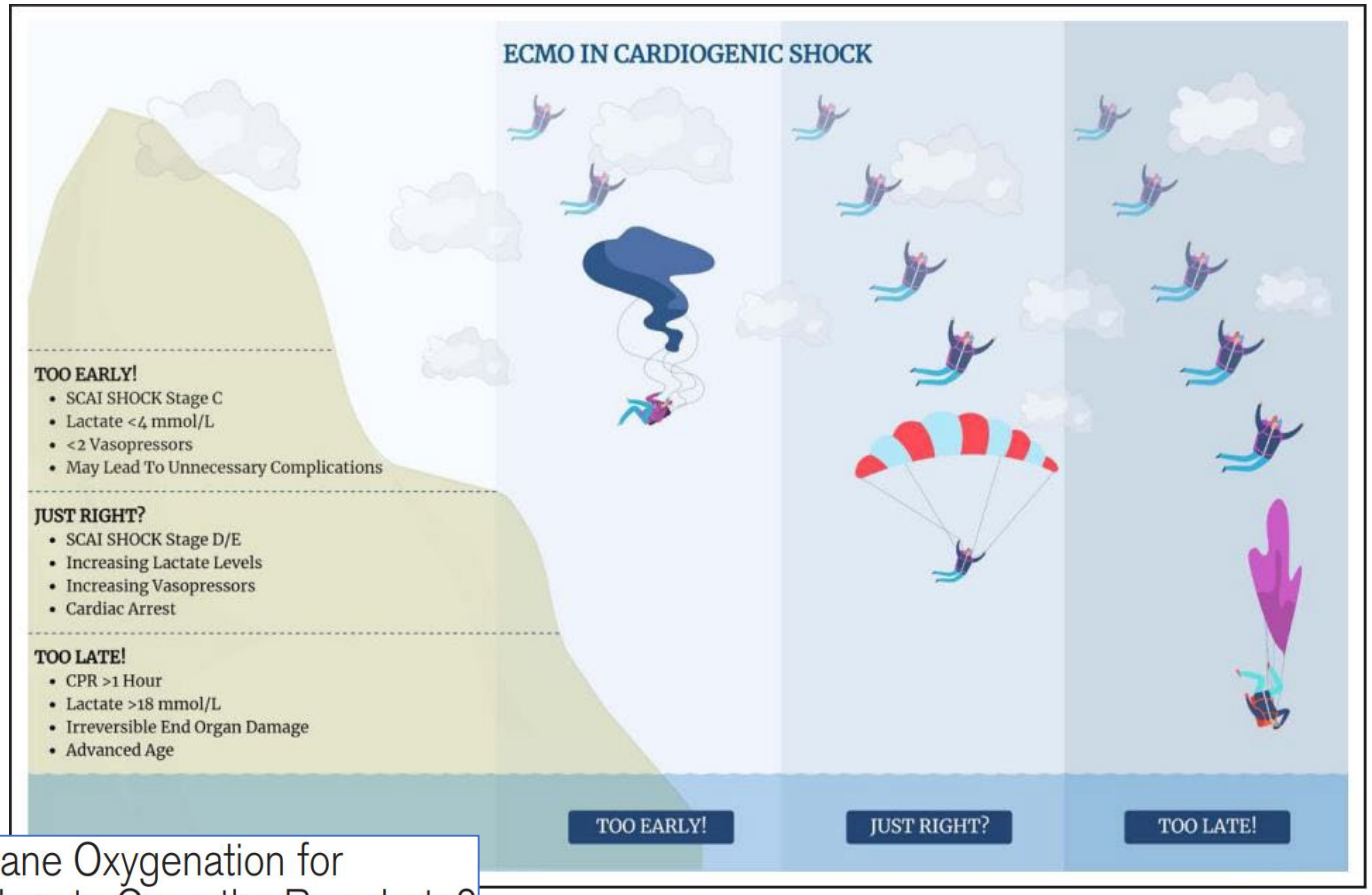
Clinical case

Physiopathological based approach for mechanical circulatory support titration



Extracorporeal Membrane Oxygenation for Cardiogenic Shock: When to Open the Parachute?

Timothy D. Henry, MD; Demetri Yannopoulos, MD; Sean van Diepen, MD, MSc

Circulation. 2023;147:465–468.

Index H

67-years-old man, Male

Past medical history:

Arterial hypertension (Olmesartan)

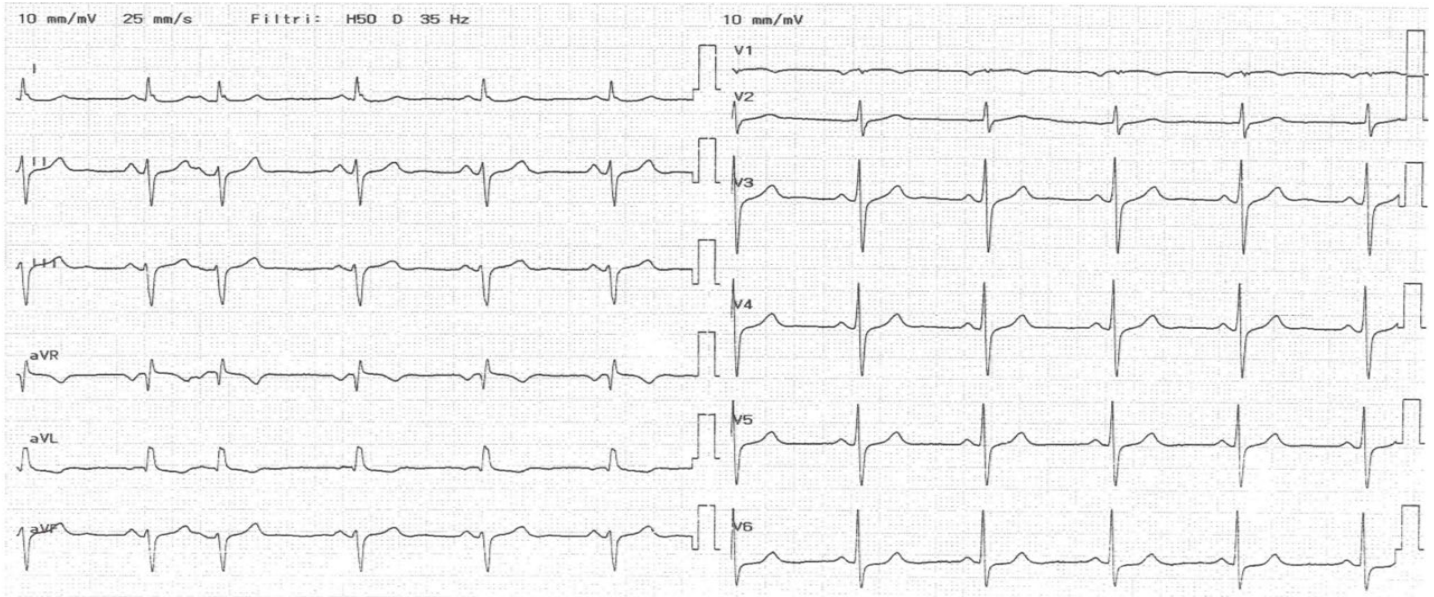
Reason for admission

One episode typical chest pain at rest and exertional angina since 24 h

(spontaneously regressed

ED- t0 09.10

- Typical chest pain VAS 8/10
- Blood pressure 150/100 mmHg
- Respiratory rate 18 BPM
- SatO2 in ambient air 96%
- Crackles at right base
- **HsTNI 82 ng/L (t0)**



Emergency department - t1

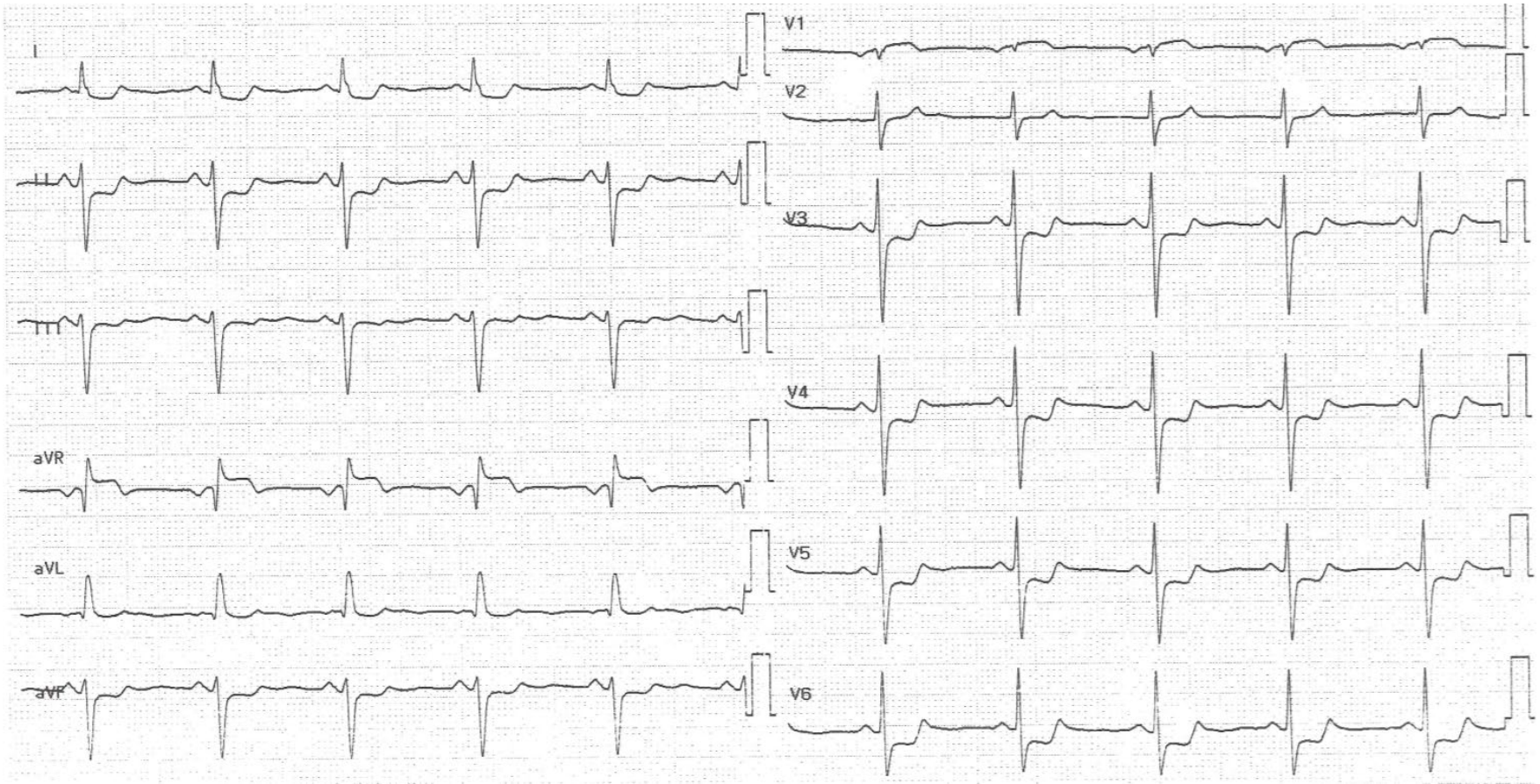
10:40 PM

Cardiology evaluation

New episode of angor

- Blood pressure 165/105 mmHg

Diagnosis of SCA-NSTE.



Start therapy

- Aspirin 300 mg
- Mophine sc 5 mg
- NTG ev infusion 1mg/h

Echocardiography:

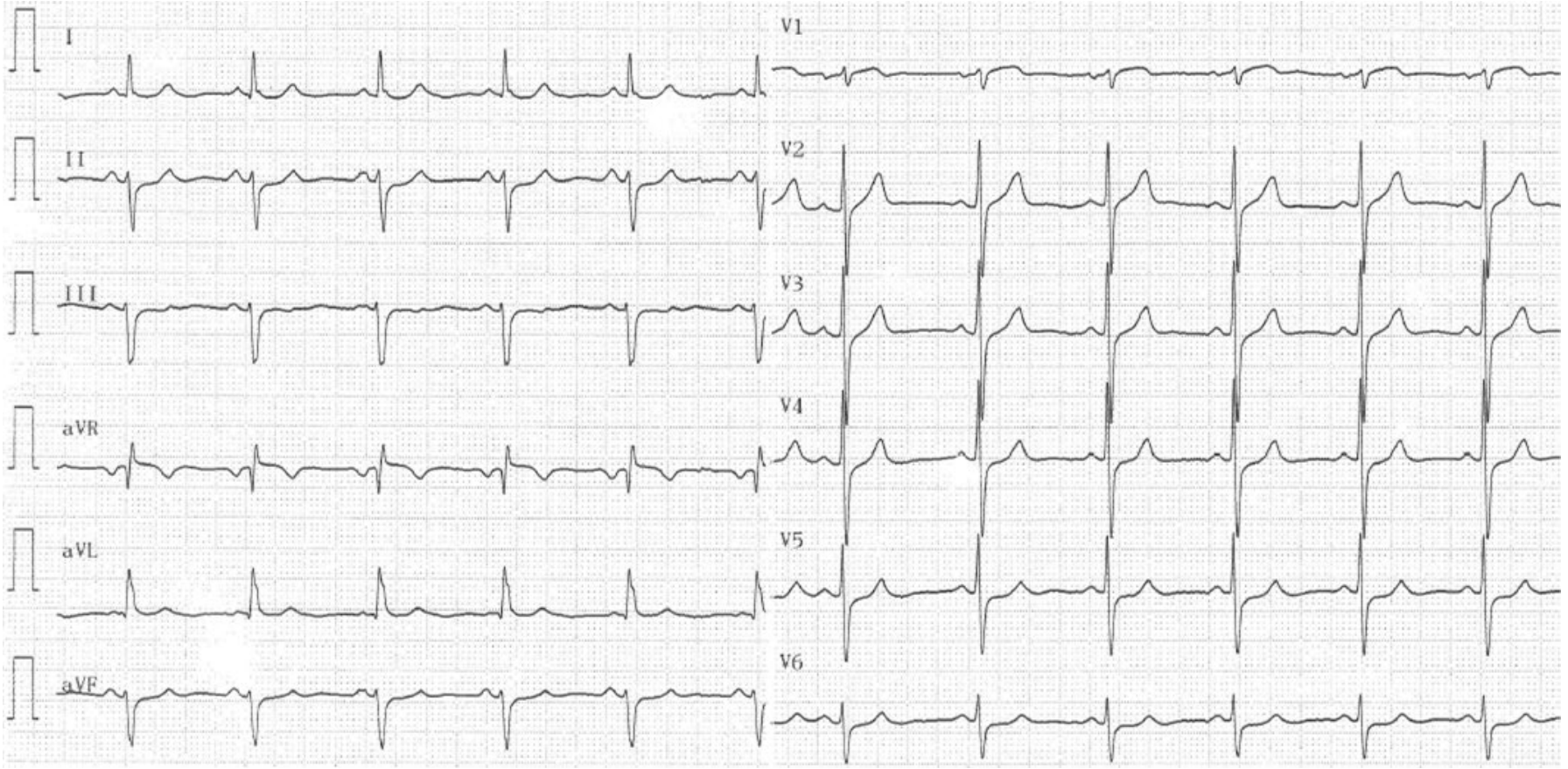
Normal global funciton with midl hypokinesia .

Cardiology ward - t0 01:29 AM

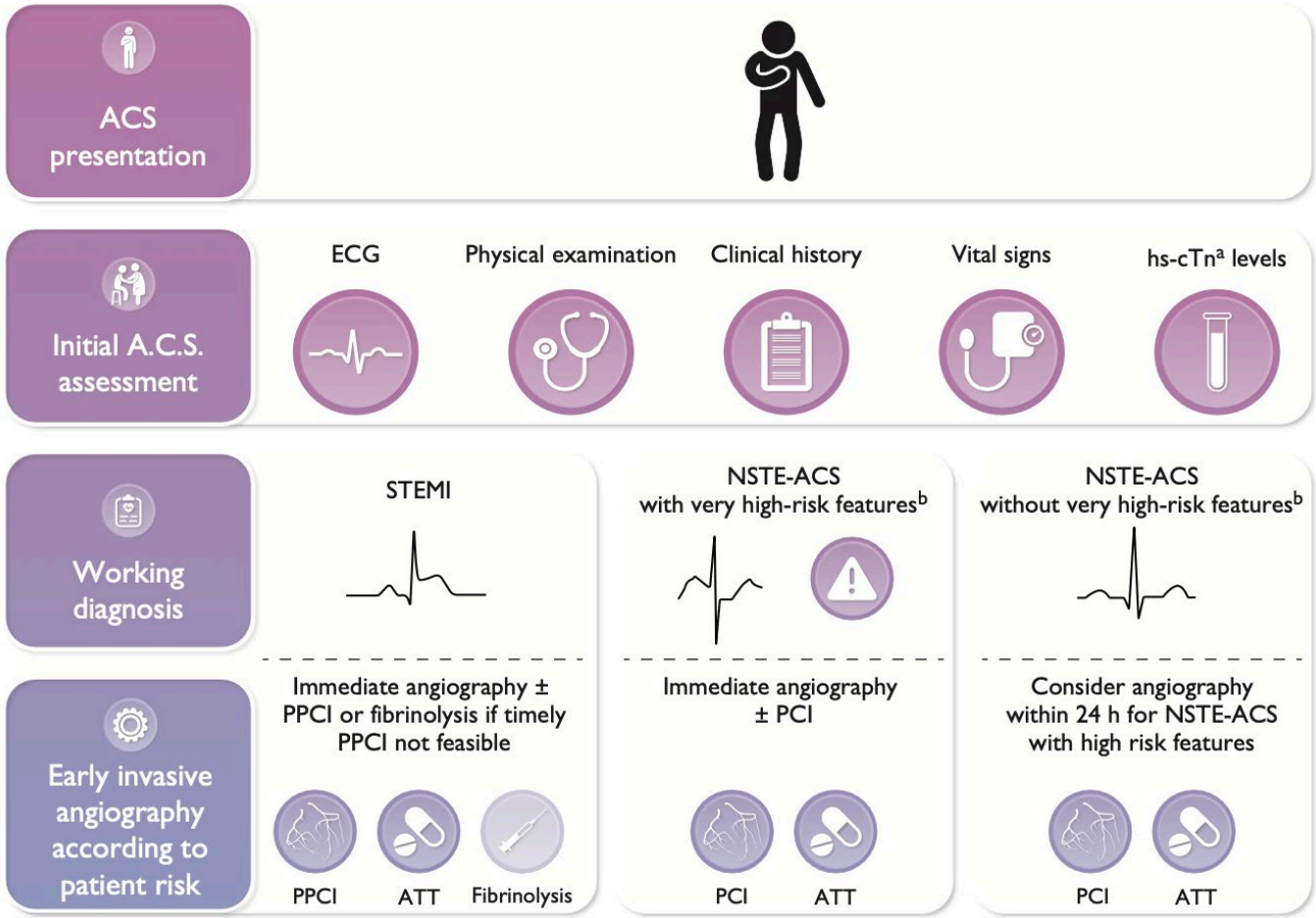
NTG ongoing

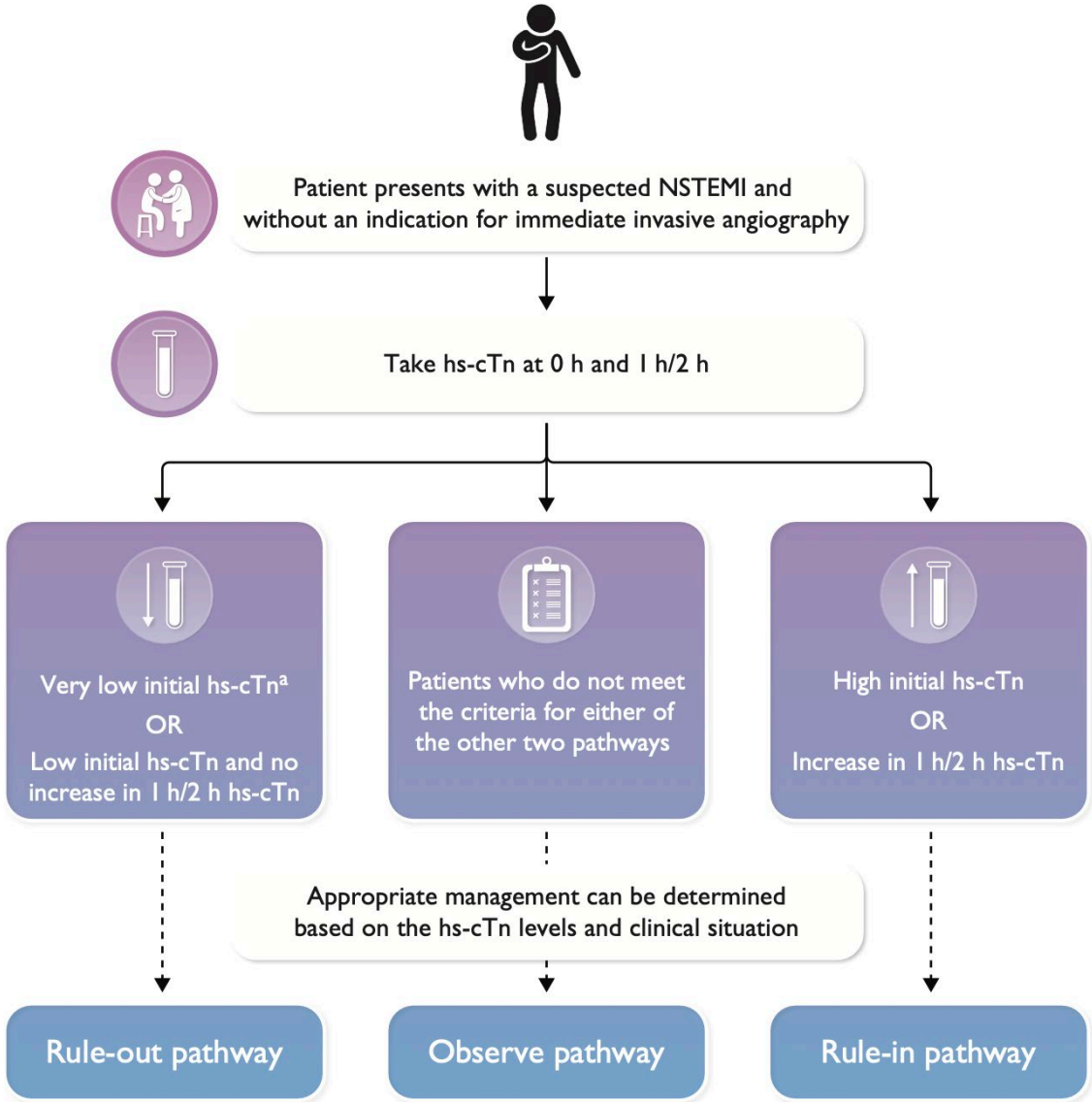
- Mild chest pain
  VAS 1/10
- Blood pressure
  120/85 mmHg
- Normal 12-lead ECG
  SR at 85 bpm

Echocardiography:
global systolic function preserved in the presence of mild dorsal hypokinesia



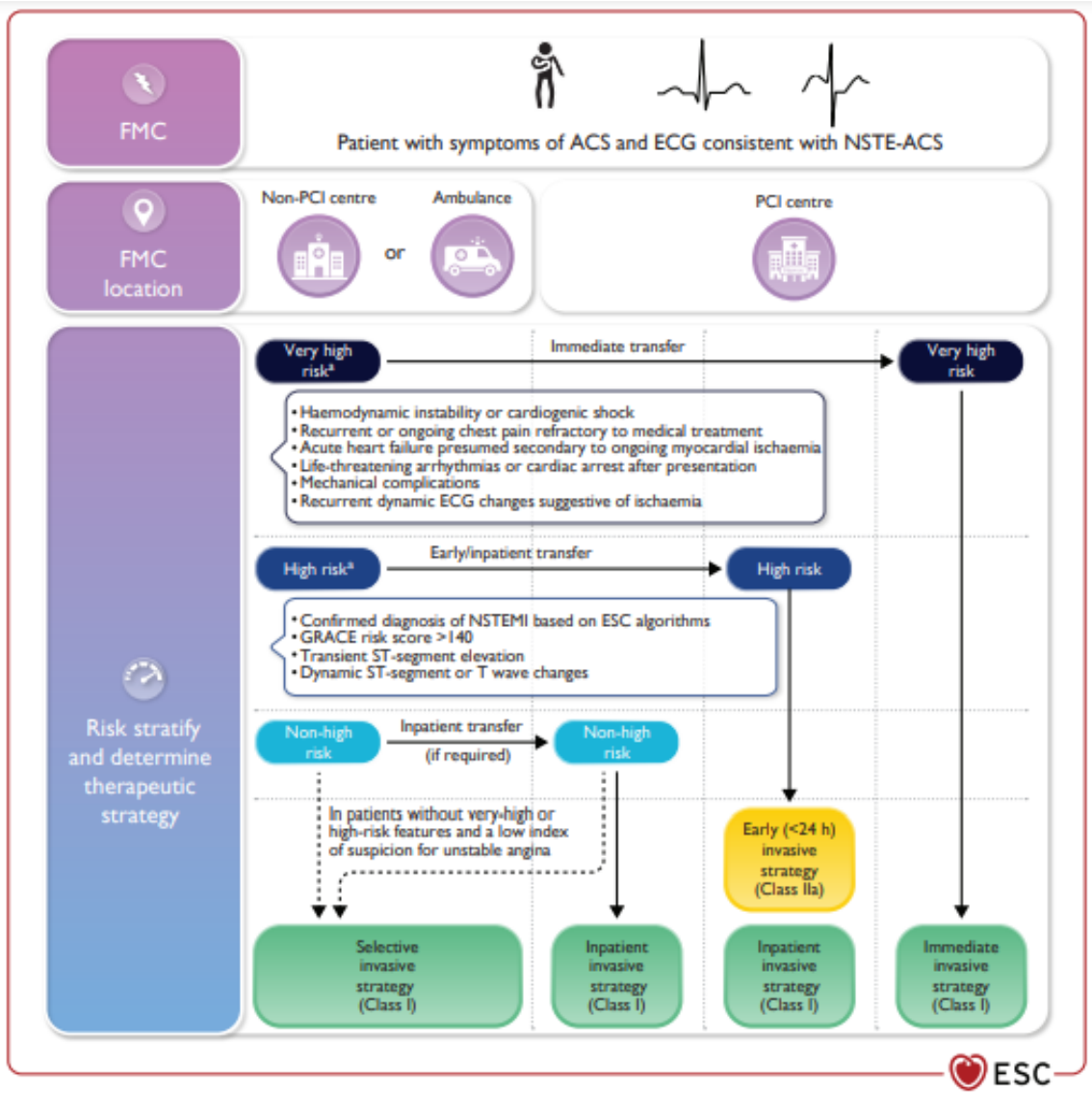
ACS treatment bundles





European Heart Journal (2023) **00**, 1–107

ACS treatment bundles



GRACE ACS Risk and Mortality Calculator

Estimates admission to 6 month mortality for patients with acute coronary syndrome.

When to Use | Pearls/Pitfalls | Why Use

Age	69	years
Heart rate/pulse	65	beats/min
Systolic BP	150	mm Hg

114 points
GRACE Score

6 %
Probability of death from admission to 6 months

Cardiology ward - 08:11 AM

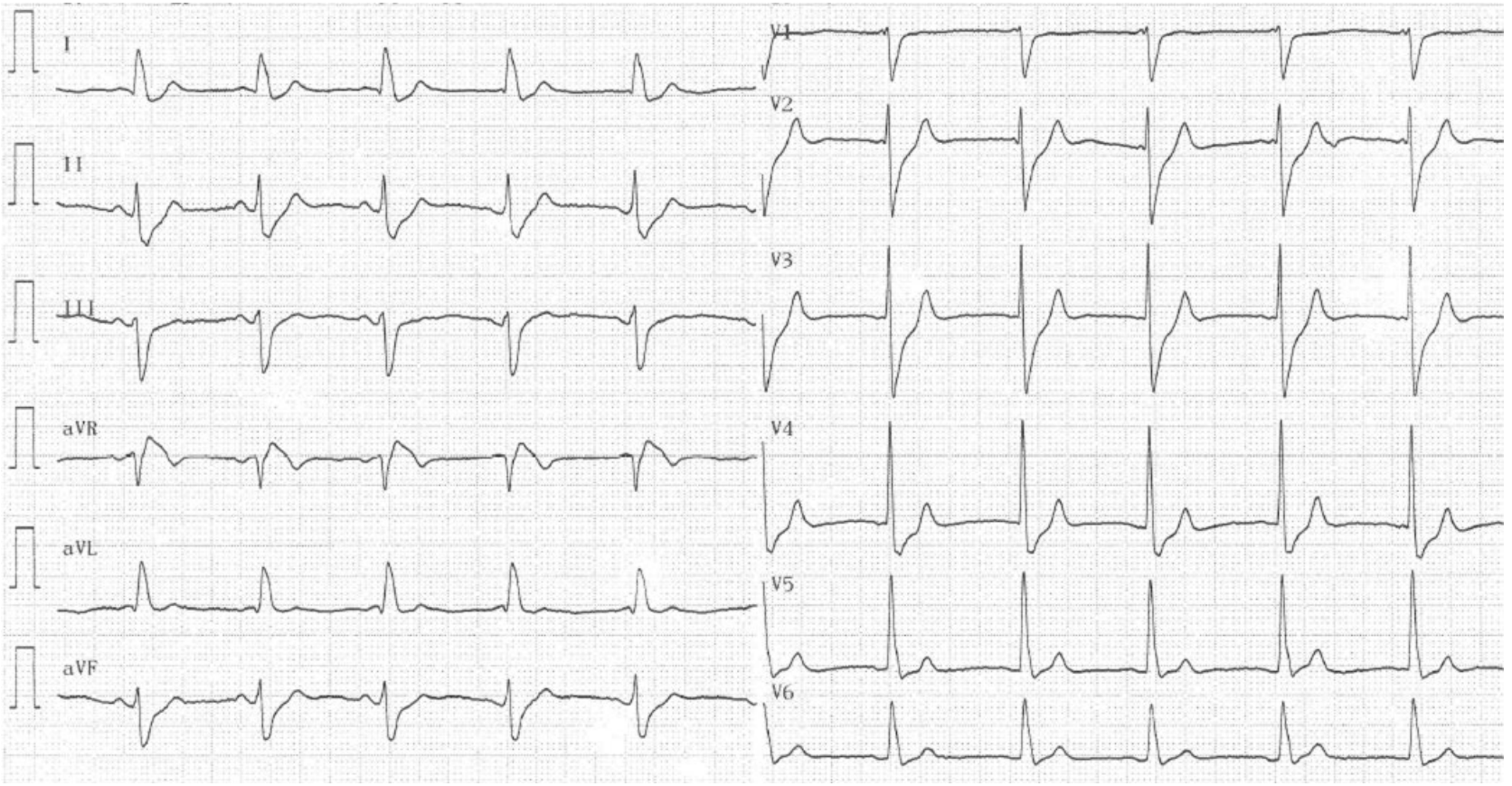
NTG ongoing - HsTNI 569 ng/L (12 h)

Chest pain

- Cold sweats
- Blood pressure 102/80mmHg

Stop NTG

Echocardiography:
severe LV systolic dysfunction.



Cath Lab

08:11
Chest pain

08:22
PEA
RCP+1mg
EPI

08:24
ROSC

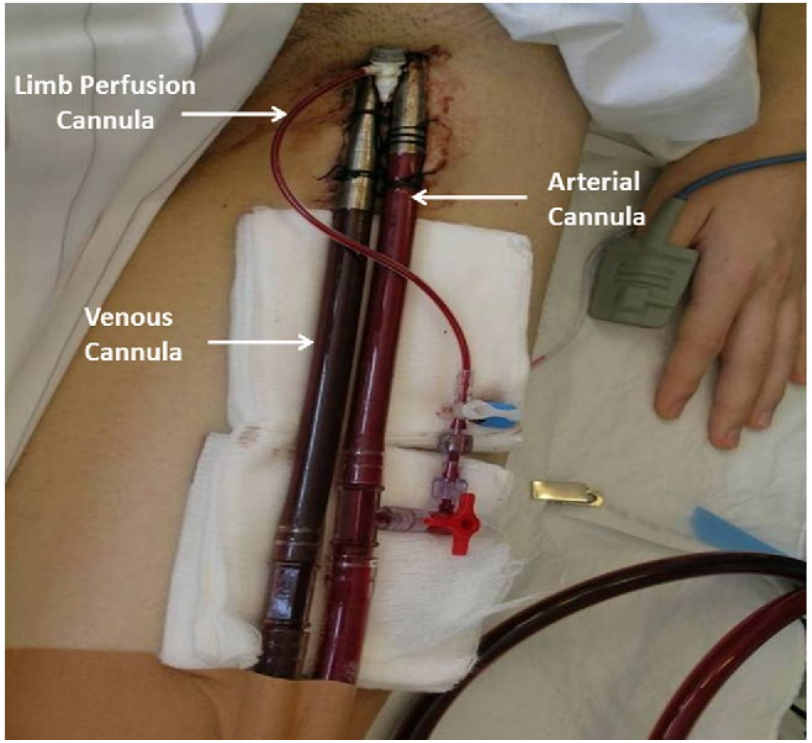
08:27
MET
arrival

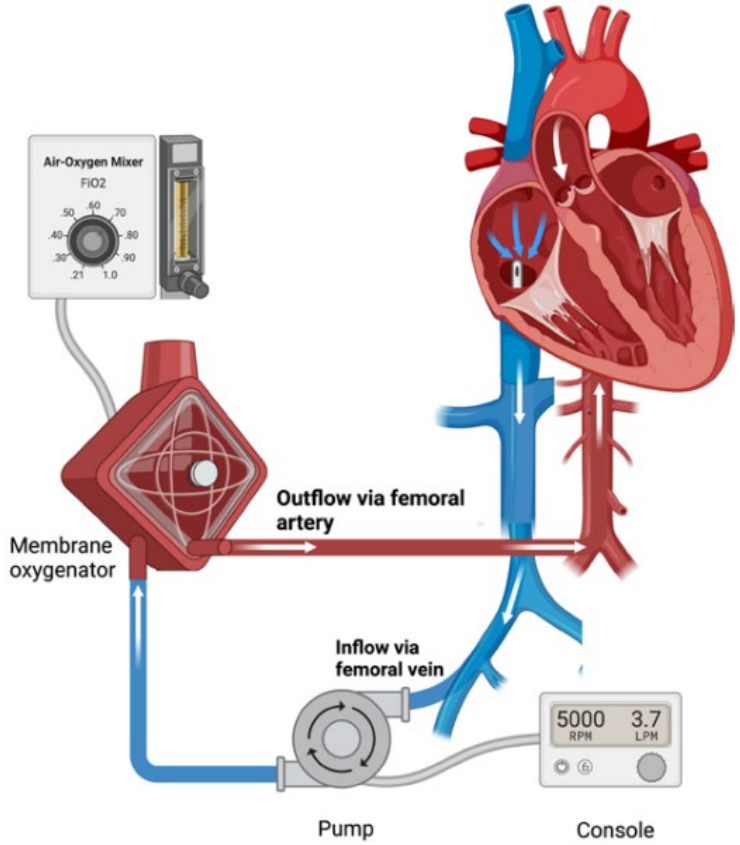
08:35
Transport to
Cath lab

08:44
FV 1 shock
ROSC

09:01
Asystole

09:16
Start VA-
ECMO





09.20
ROSC

Total low flow period = 32 min

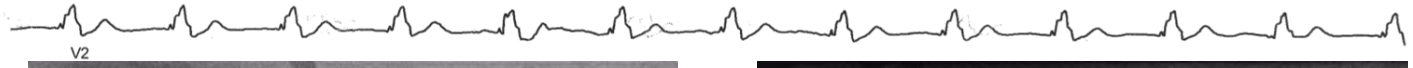
Cath Lab

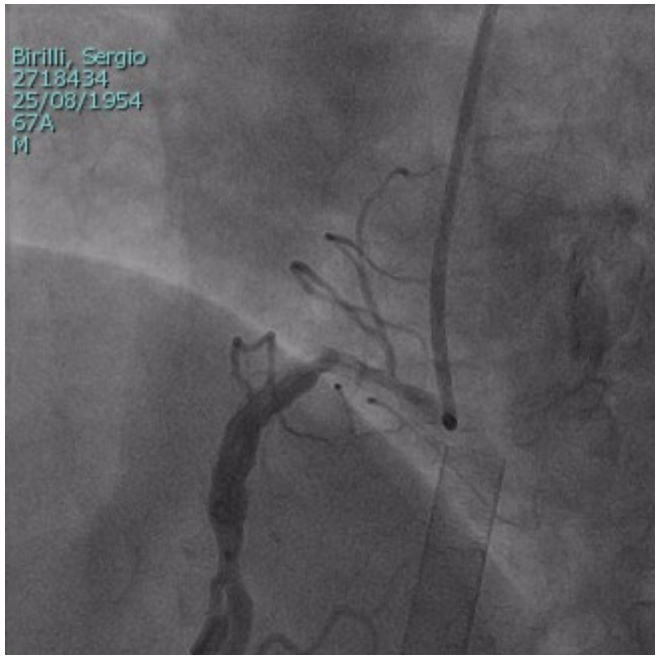
Coronary angiography

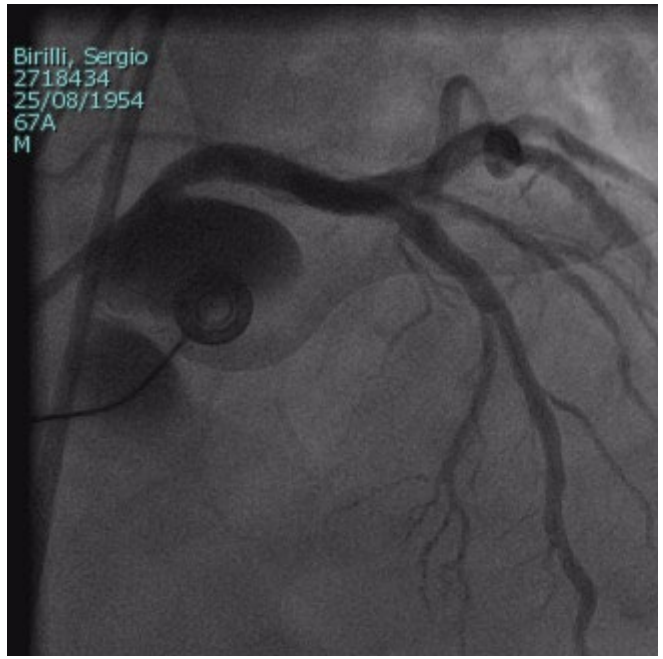
MCS ongoing

08:11	08:22	08:24	08:32	08:45	08:54	09:01	09:10	09:26	09:40
Chest pain	PEA RCP+1mg EPI	ROSC	MET arrival	Transport to Cath lab	FV 1 shock ROSC	Asystole	IOT CVC	Start VA-ECMO	ROSC

- Only Culprit-vessel PCI

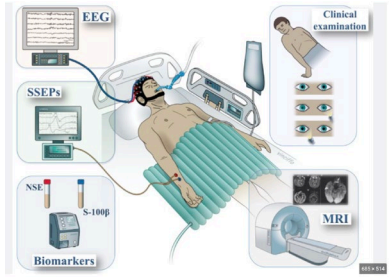




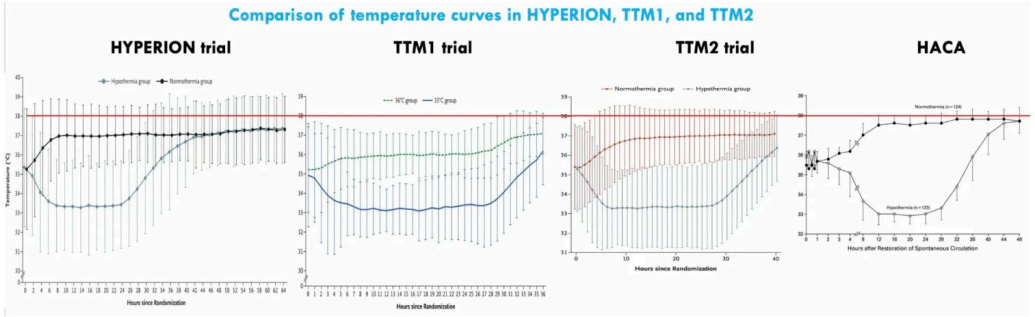


V-A side treatment bundles

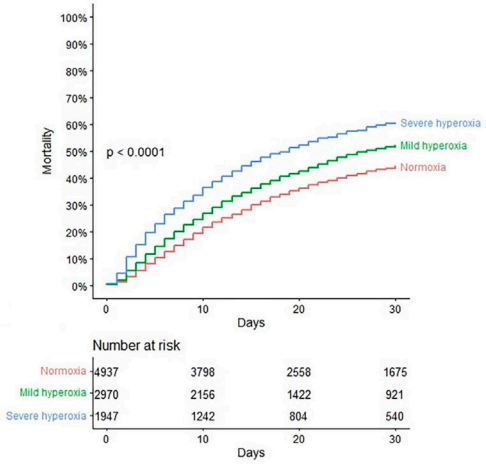
Sedation: Midazolam (no evidence but less hemodynamic impactful)



TTM: no evidence but avoid fever!

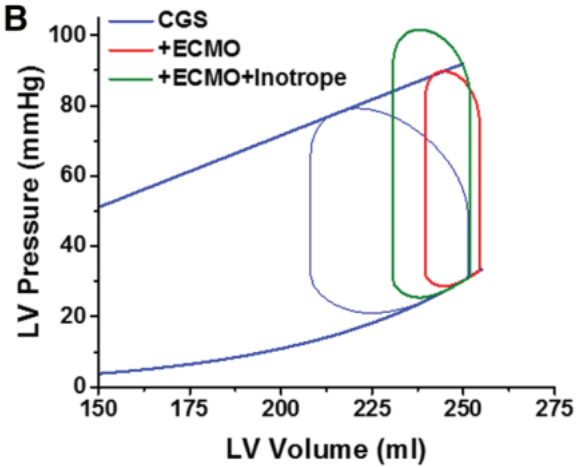


Protective VAM, P/F 200: Hyperoxemia is bad!



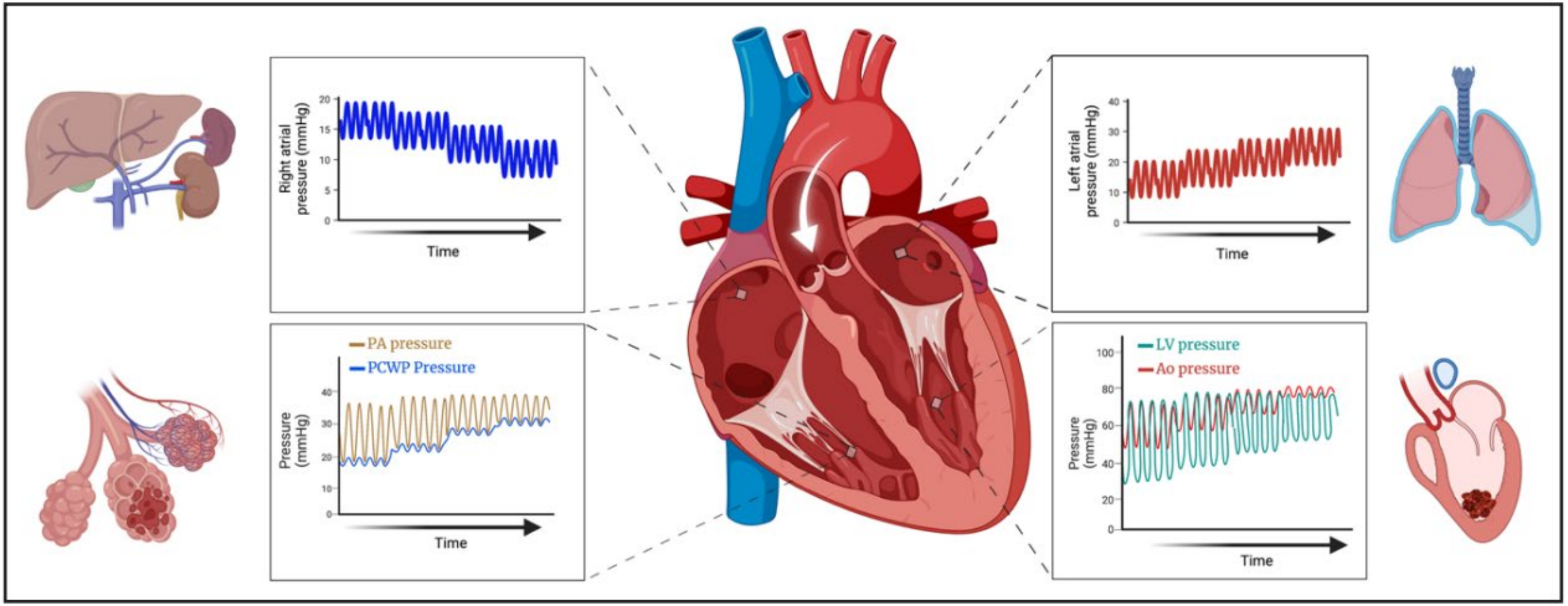
Epinephrine 0,02 mcg/kg/min

No evidence at all: may favor the residual inotropism to promote native ejection



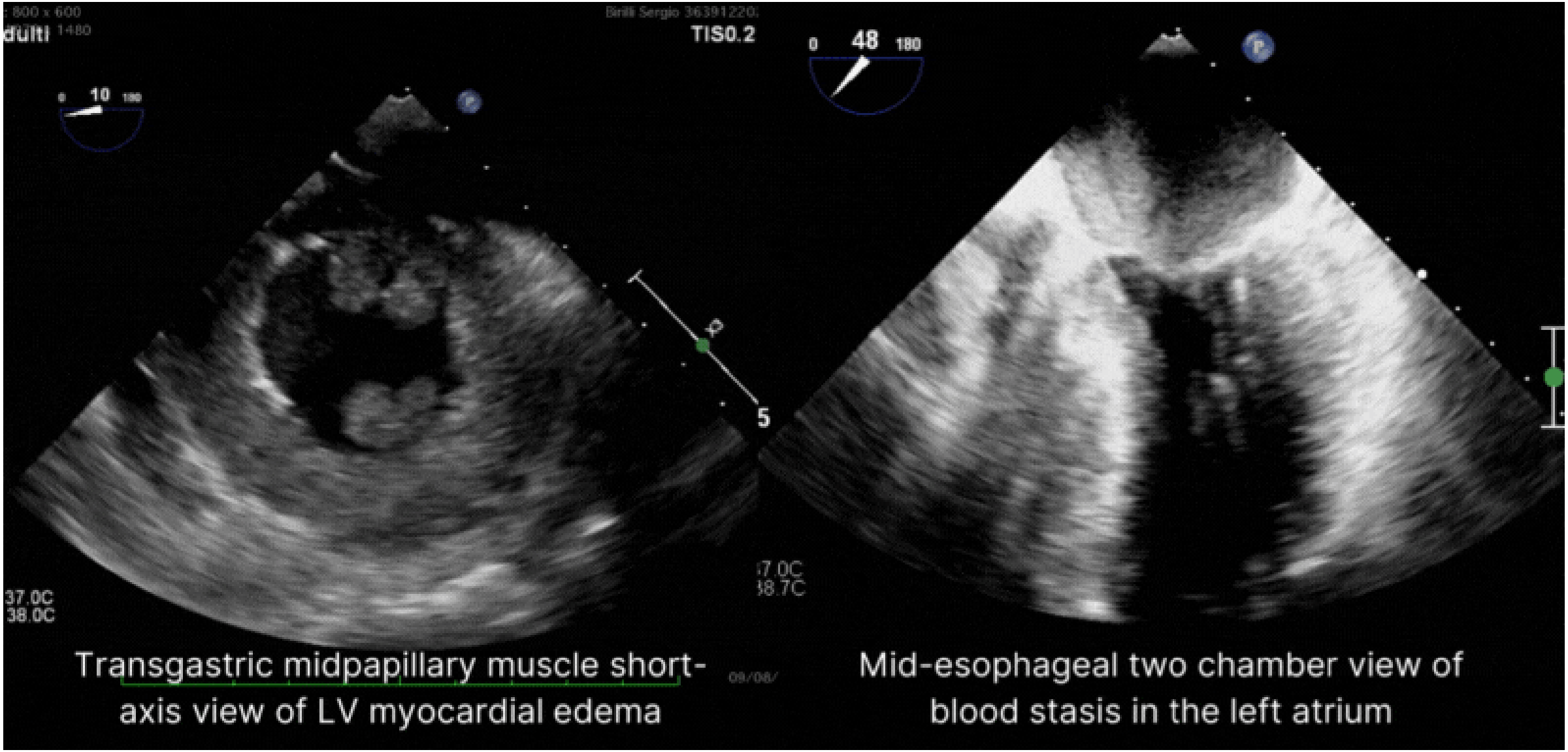
Hemodynamic effects of VA-ECMO:

- ECMO-VA BF 3L/min; GF 3L/min
- **PCWP 21 mmHg**

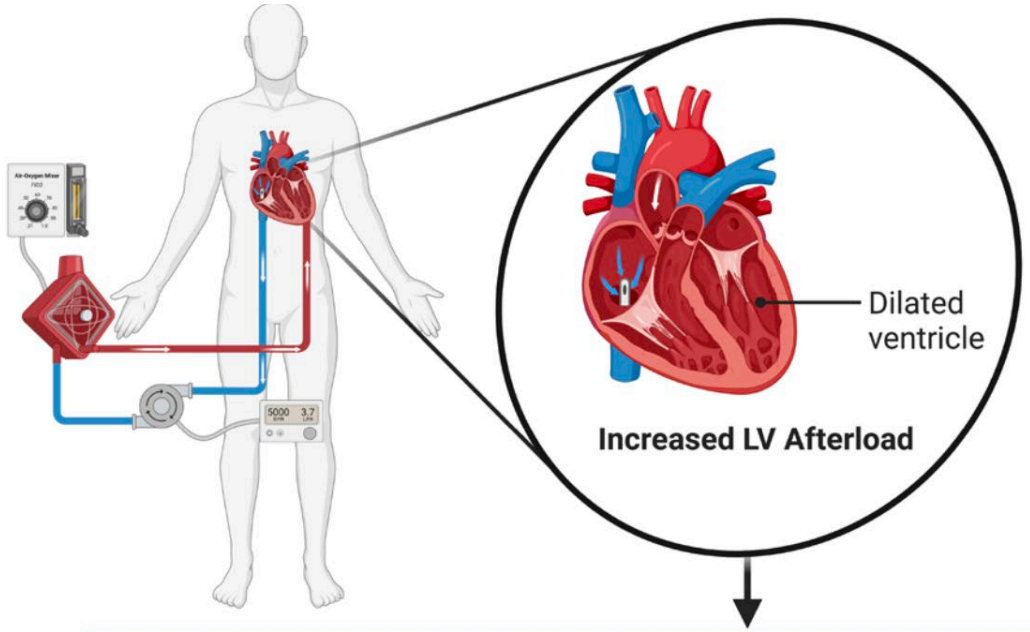


Circulation. 2023;147:1237–1250.

TTE in cath lab

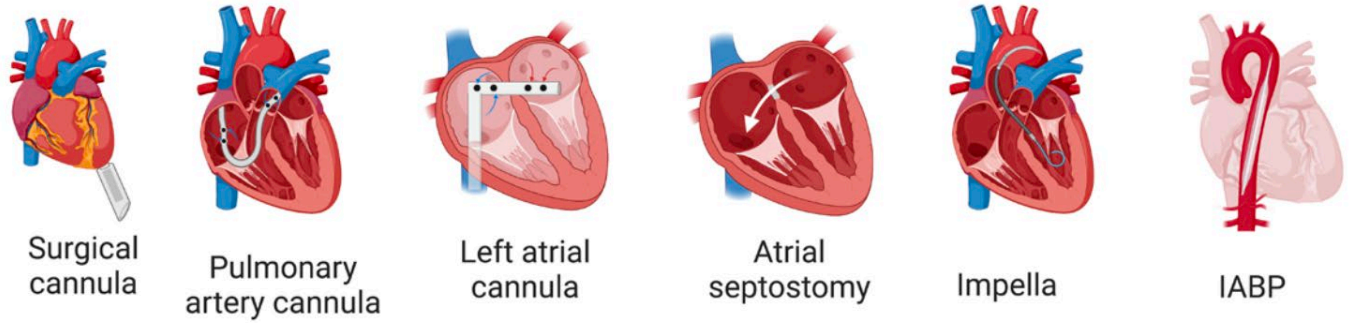


Unloading the Left Ventricle in Venoarterial ECMO: In Whom, When, and How?



Unloading Criteria	
Echocardiographic	Closed aortic valve
	Spontaneous Echo contrast
	Ventricular thrombus
	LVOT VTi <10cm
Clinical	Pulmonary edema
	Ventricular arrhythmia
Haemodynamic	PCWP >18mmHg
	Pulse pressure <15mmHg

Unloading methods



Drawbacks:

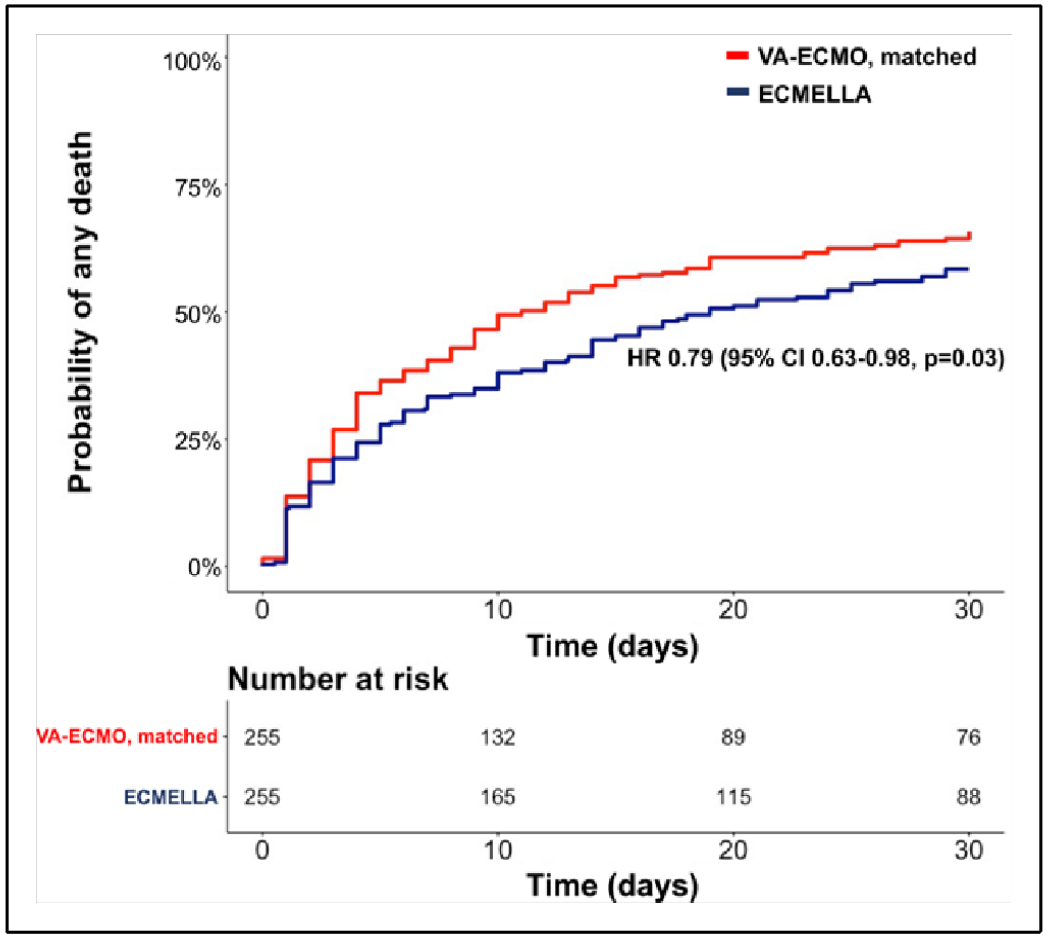
- Surgical cannula: High risk/ Time
- Pulmonary artery cannula: RV failure
- Left atrial cannula: Only PCWP reduction
- Atrial septostomy: Low/null support
- Impella: LV cavity
- IABP: Low support

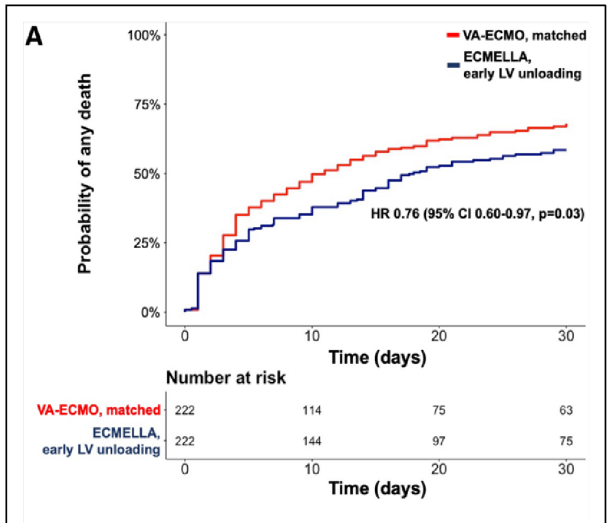
Circulation. 2023;147:1237–1250.

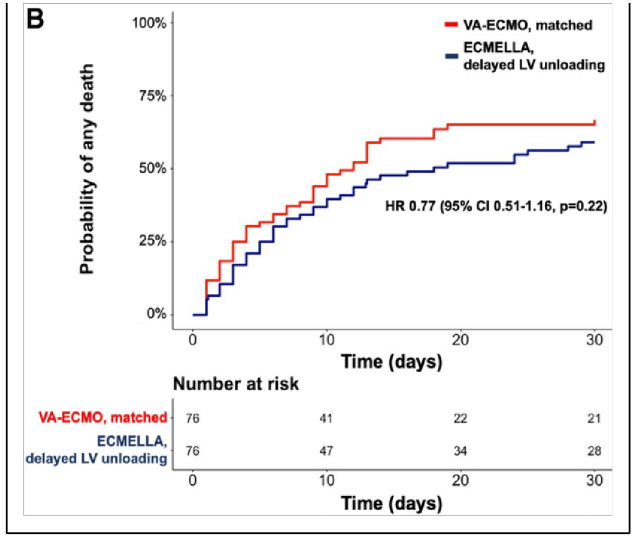
LV Unloading

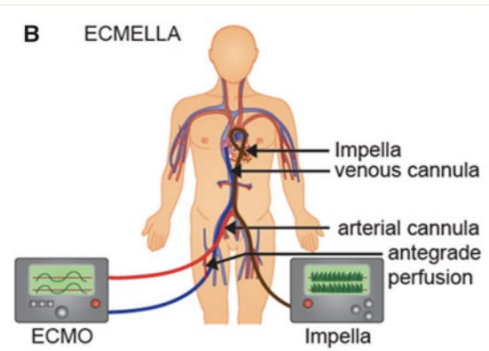
Left Ventricular Unloading Is Associated With Lower Mortality in Patients With Cardiogenic Shock Treated With Venoarterial Extracorporeal Membrane Oxygenation

Results From an International, Multicenter Cohort Study

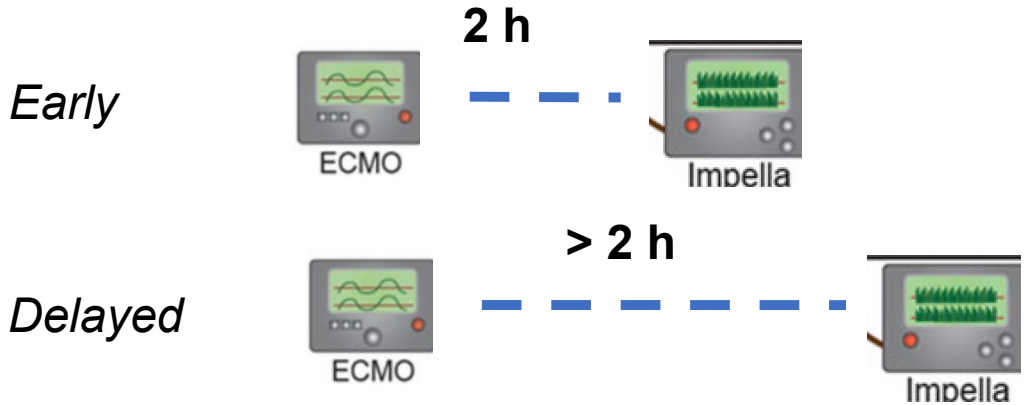






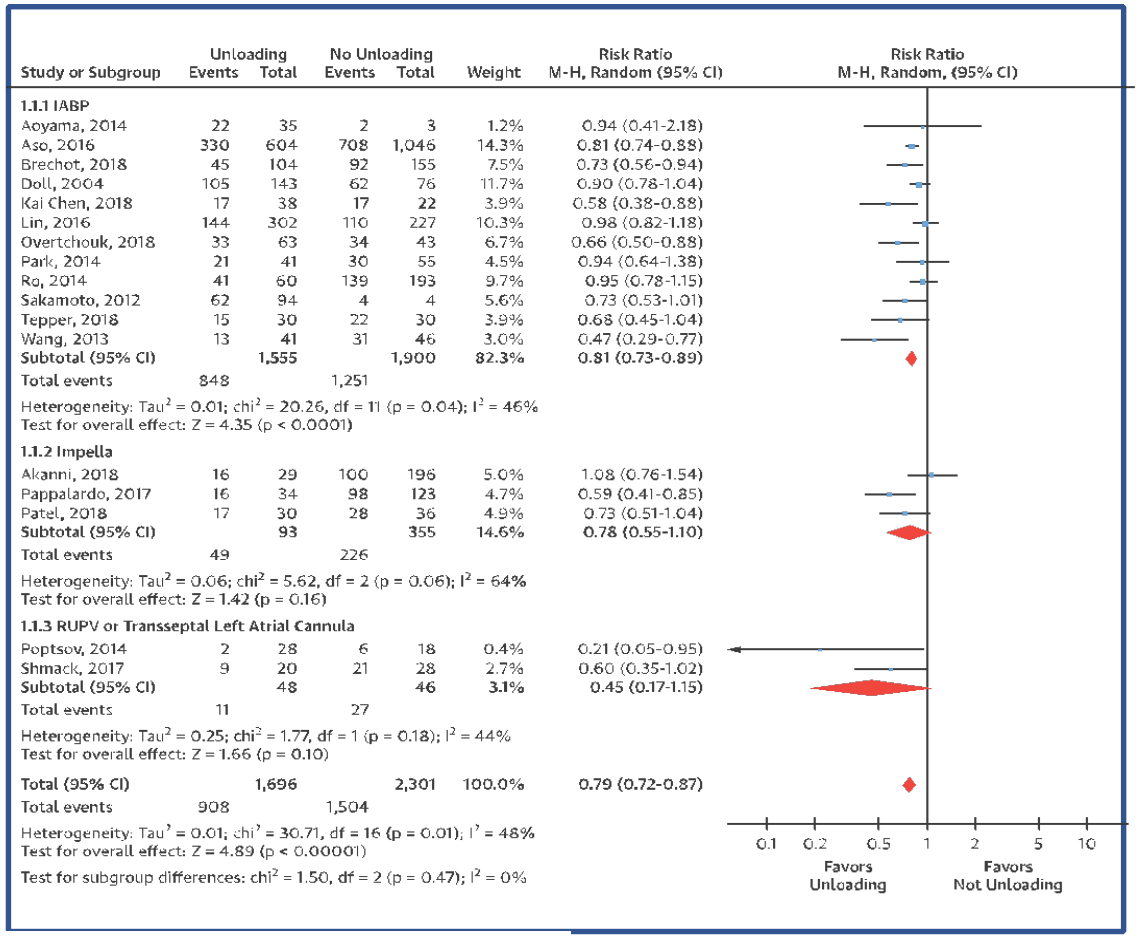


Circulation. 2020;142:2095–2106.



LV Unloading

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



Study or Subgroup	Unloading Events	Unloading Total	No Unloading Events	No Unloading Total	Weight	Risk Ratio M-H, Random (95% CI)
1.1.1 IABP						
Aoyama, 2014	22	35	2	3	1.2%	0.94 (0.41-2.18)
Aso, 2016	330	604	708	1,046	14.3%	0.81 (0.74-0.88)
Brechot, 2018	45	104	92	155	7.5%	0.73 (0.56-0.94)
Doll, 2004	105	143	62	76	11.7%	0.90 (0.78-1.04)
Kai Chen, 2018	17	38	17	22	3.9%	0.58 (0.38-0.88)
Lin, 2016	144	302	110	227	10.3%	0.98 (0.82-1.18)
Overtchouk, 2018	33	63	34	43	6.7%	0.66 (0.50-0.88)
Park, 2014	21	41	30	55	4.5%	0.94 (0.64-1.38)
Ro, 2014	41	60	139	193	9.7%	0.95 (0.78-1.15)
Sakamoto, 2012	62	94	4	4	5.6%	0.73 (0.53-1.01)
Tepper, 2018	15	30	22	30	3.9%	0.68 (0.45-1.04)
Wang, 2013	13	41	31	46	3.0%	0.47 (0.29-0.77)
Subtotal (95% CI)		**1,555**		**1,900**	**82.3%**	**0.81 (0.73-0.89)**
Total events	848		1,251			
Heterogeneity: $Tau^2 = 0.01$; $chi^2 = 20.26$, df = 11 (p = 0.04); $I^2 = 46\%$						
Test for overall effect: Z = 4.35 (p < 0.0001)						
1.1.2 Impella						
Akanni, 2018	16	29	100	196	5.0%	1.08 (0.76-1.54)
Pappalardo, 2017	16	34	98	123	4.7%	0.59 (0.41-0.85)
Patel, 2018	17	30	28	36	4.9%	0.73 (0.51-1.04)
Subtotal (95% CI)		**93**		**355**	**14.6%**	**0.78 (0.55-1.10)**
Total events	49		226			
Heterogeneity: $Tau^2 = 0.06$; $chi^2 = 5.62$, df = 2 (p = 0.06); $I^2 = 64\%$						
Test for overall effect: Z = 1.42 (p = 0.16)						
1.1.3 RUPV or Transseptal Left Atrial Cannula						
Poptsov, 2014	2	28	6	18	0.4%	0.21 (0.05-0.95)
Shmack, 2017	9	20	21	28	2.7%	0.60 (0.35-1.02)
Subtotal (95% CI)		**48**		**46**	**3.1%**	**0.45 (0.17-1.15)**
Total events	11		27			
Heterogeneity: $Tau^2 = 0.25$; $chi^2 = 1.77$, df = 1 (p = 0.18); $I^2 = 44\%$						
Test for overall effect: Z = 1.66 (p = 0.10)						
Total (95% CI)		**1,696**		**2,301**	**100.0%**	**0.79 (0.72-0.87)**
Total events	908		1,504			
Heterogeneity: $Tau^2 = 0.01$; $chi^2 = 30.71$, df = 16 (p = 0.01); $I^2 = 48\%$						
Test for overall effect: Z = 4.89 (p < 0.00001)						
Test for subgroup differences: $chi^2 = 1.50$, df = 2 (p = 0.47); $I^2 = 0\%$						

Risk Ratio M-H, Random, (95% CI)

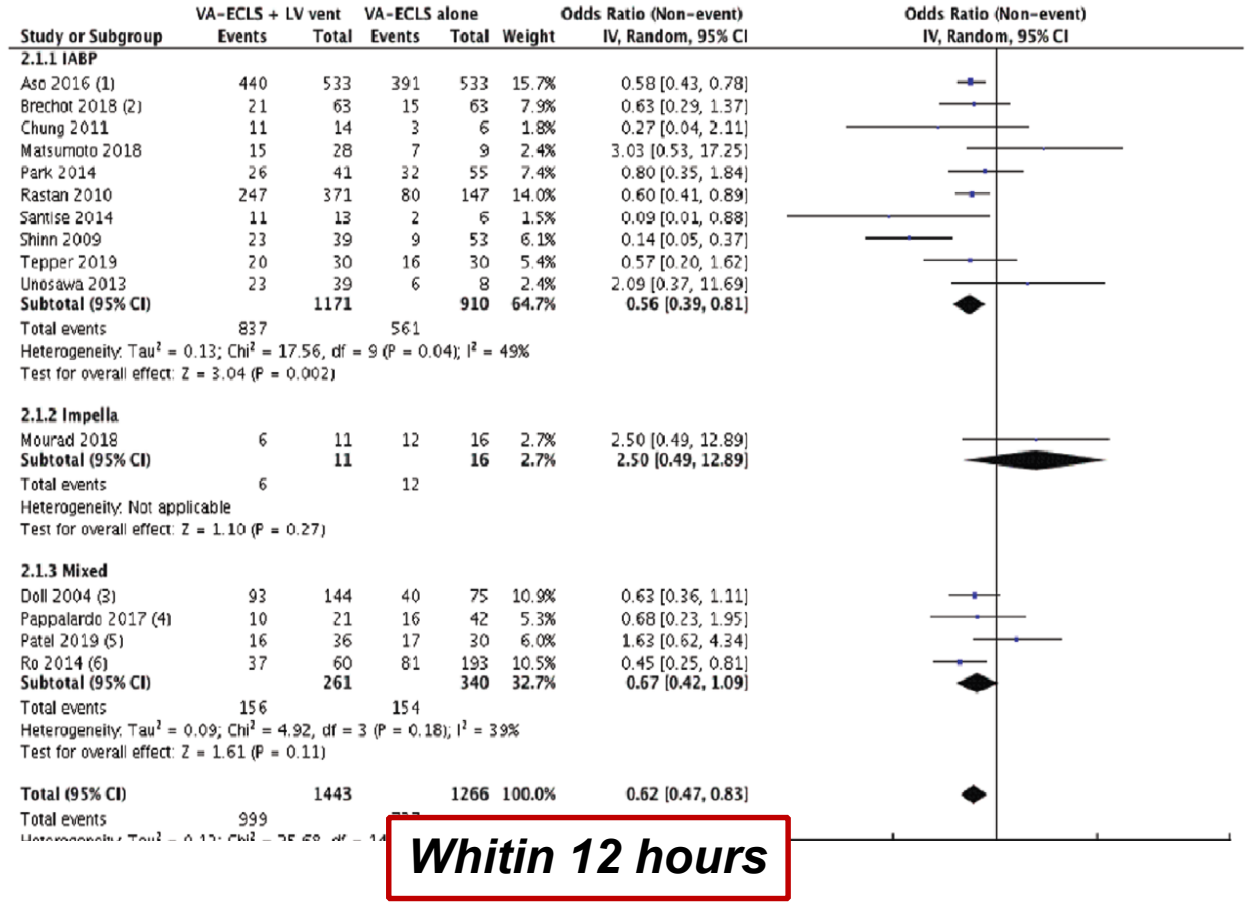
0.1 0.2 0.5 1 2 5 10

Favors Unloading | Favors Not Unloading

(J Am Coll Cardiol 2019;73:654-62)

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



Study or Subgroup	VA-ECLS + LV vent Events	VA-ECLS + LV vent Total	VA-ECLS alone Events	VA-ECLS alone Total	Weight	Odds Ratio (Non-event) IV, Random, 95% CI
2.1.1 IABP						
Aso 2016 (1)	440	533	391	533	15.7%	0.58 [0.43, 0.78]
Brechot 2018 (2)	21	63	15	63	7.9%	0.63 [0.29, 1.37]
Chung 2011	11	14	3	6	1.8%	0.27 [0.04, 2.11]
Matsumoto 2018	15	28	7	9	2.4%	3.03 [0.53, 17.25]
Park 2014	26	41	32	55	7.4%	0.80 [0.35, 1.84]
Rastan 2010	247	371	80	147	14.0%	0.60 [0.41, 0.89]
Santise 2014	11	13	2	6	1.5%	0.09 [0.01, 0.88]
Shinn 2009	23	39	9	53	6.1%	0.14 [0.05, 0.37]
Tepper 2019	20	30	16	30	5.4%	0.57 [0.20, 1.62]
Unosawa 2013	23	39	6	8	2.4%	2.09 [0.37, 11.69]
Subtotal (95% CI)		**1171**		**910**	**64.7%**	**0.56 [0.39, 0.81]**
Total events	837		561			
Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 17.56$, df = 9 (P = 0.04); $I^2 = 49\%$						
Test for overall effect: Z = 3.04 (P = 0.002)						
2.1.2 Impella						
Mourad 2018	6	11	12	16	2.7%	2.50 [0.49, 12.89]
Subtotal (95% CI)		**11**		**16**	**2.7%**	**2.50 [0.49, 12.89]**
Total events	6		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.10 (P = 0.27)						
2.1.3 Mixed						
Doll 2004 (3)	93	144	40	75	10.9%	0.63 [0.36, 1.11]
Pappalardo 2017 (4)	10	21	16	42	5.3%	0.68 [0.23, 1.95]
Patel 2019 (5)	16	36	17	30	6.0%	1.63 [0.62, 4.34]
Ro 2014 (6)	37	60	81	193	10.5%	0.45 [0.25, 0.81]
Subtotal (95% CI)		**261**		**340**	**32.7%**	**0.67 [0.42, 1.09]**
Total events	156		154			
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 4.92$, df = 3 (P = 0.18); $I^2 = 39\%$						
Test for overall effect: Z = 1.61 (P = 0.11)						
Total (95% CI)		**1443**		**1266**	**100.0%**	**0.62 [0.47, 0.83]**
Total events	999					

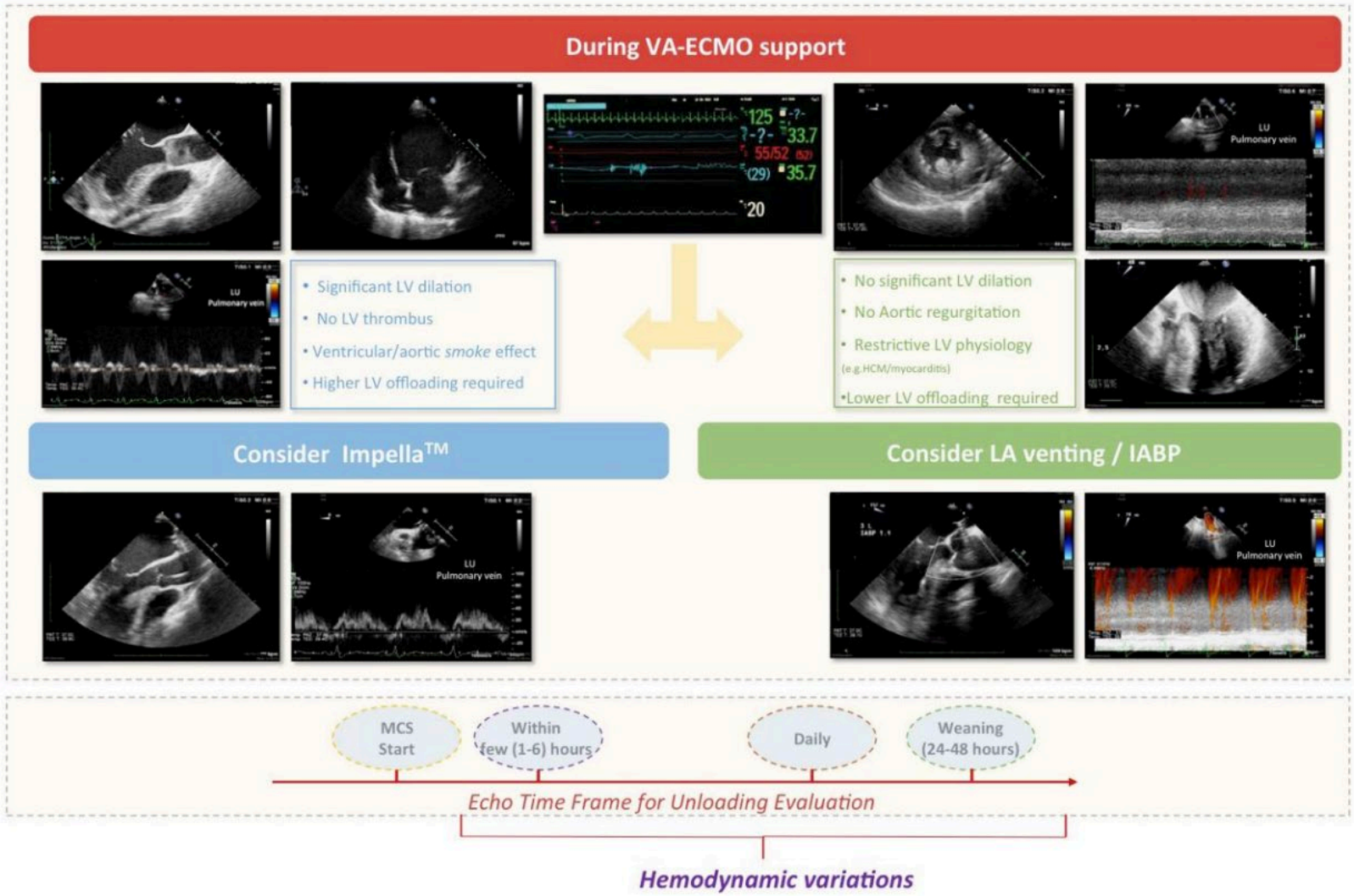
Odds Ratio (Non-event) IV, Random, 95% CI

Whitin 12 hours

Circ Heart Fail. 2019;12:e006486.

How to unload the left ventricle during veno-arterial extracorporeal membrane oxygenation

Guido Tavazzi [1,2], Carlos L. Alviar [3]*, Costanza Natalia Julia Colombo[4,2], Valentino Dammassa [4,5], Susanna Price [5,6], and Christophe Vandenbriele[7]



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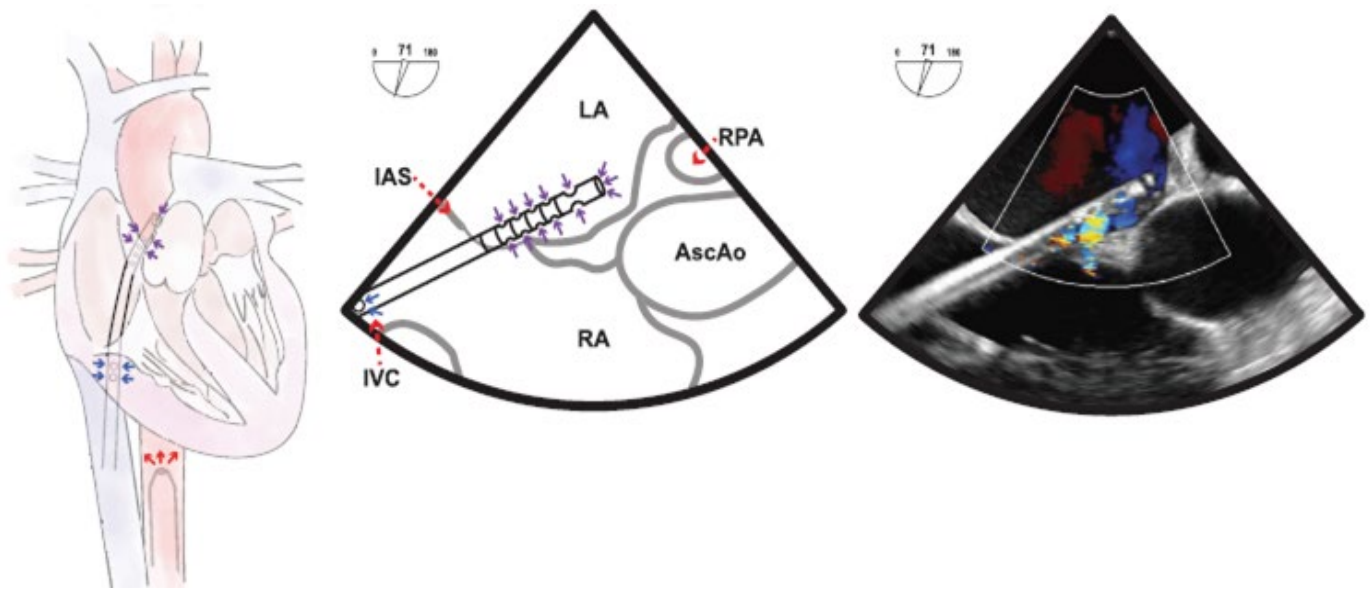
DOI: 10.1111/echo.15266

Echocardiography WILEY

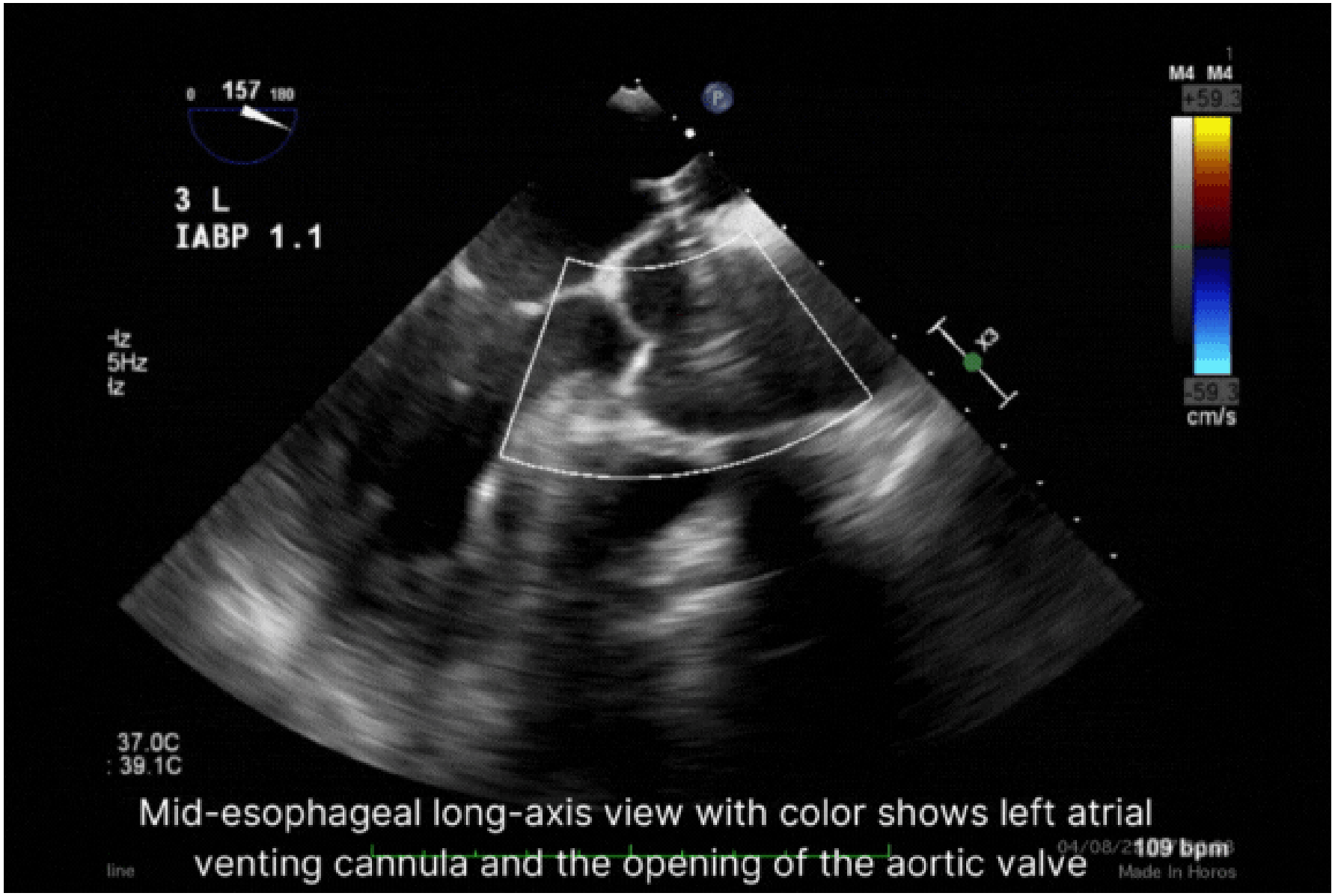
INVITED REVIEW

Echocardiography for extracorporeal membrane oxygenation

Patrick T. Hussey MD[1] | Gregory von Mering MD[2] | Navin C. Nanda MD[2] | Mustafa I. Ahmed MD[2] | Dylan R. Addis MD[3]



LV Unloading

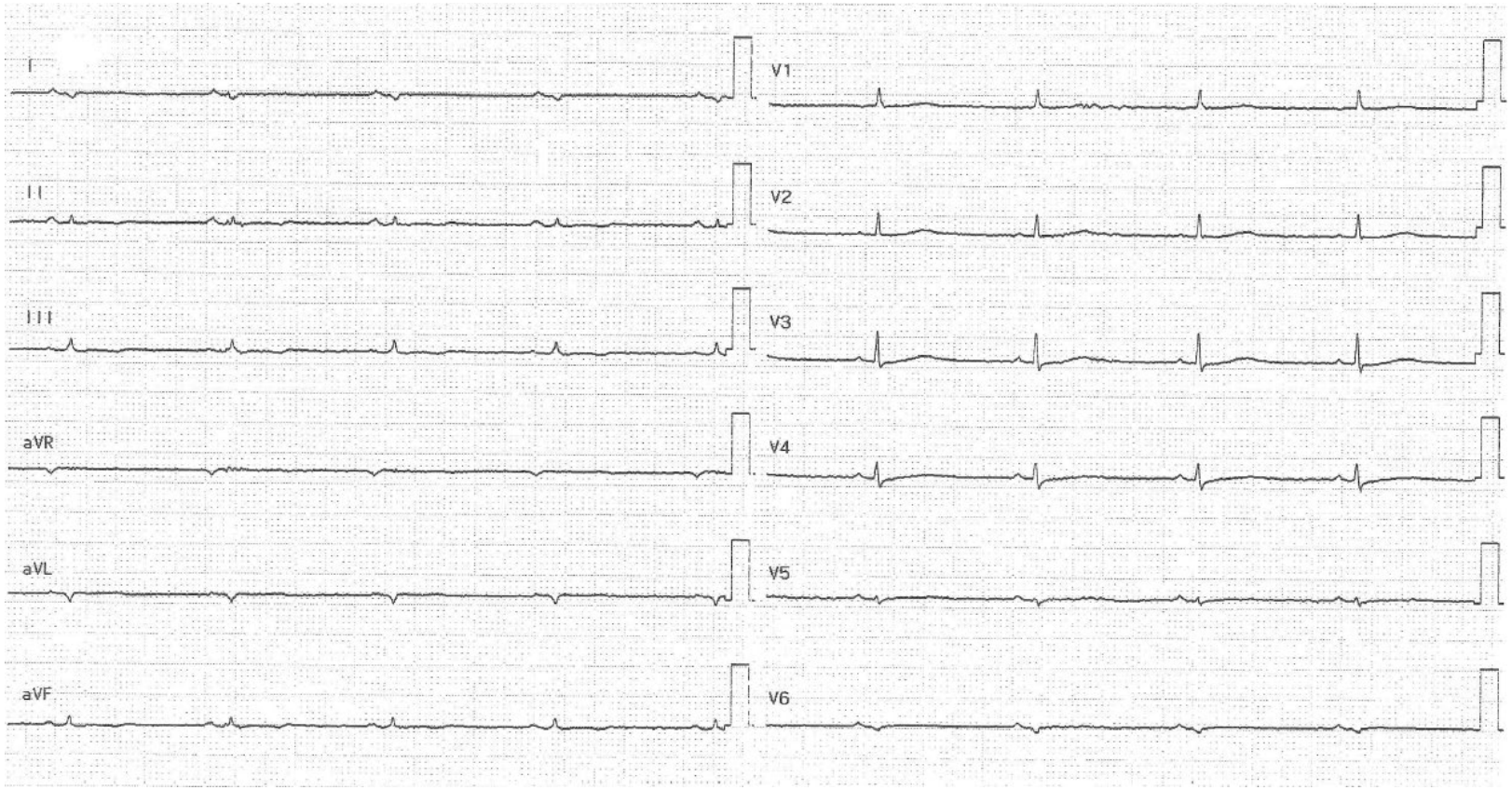


ICU ward

Day 1
TTM ongoing

NSE(48h-72h)	
Native lung VAM	12 BPM
Membrane lung GF	3 L/m
ECMO BF	3 L/m
Vasopressor	↔
HsTNI	↑690350 ng/L
BNP	40 pg/mL
PVC	7 mmHg
PCWP	15 mmHg
SVO2	65%
Transeptal cannula Q	1,5 L/m
CRRT	NO
Ecocardiography	IVS,AW,PW 20 mm

Severe post-ROSC LV myocardial edema.

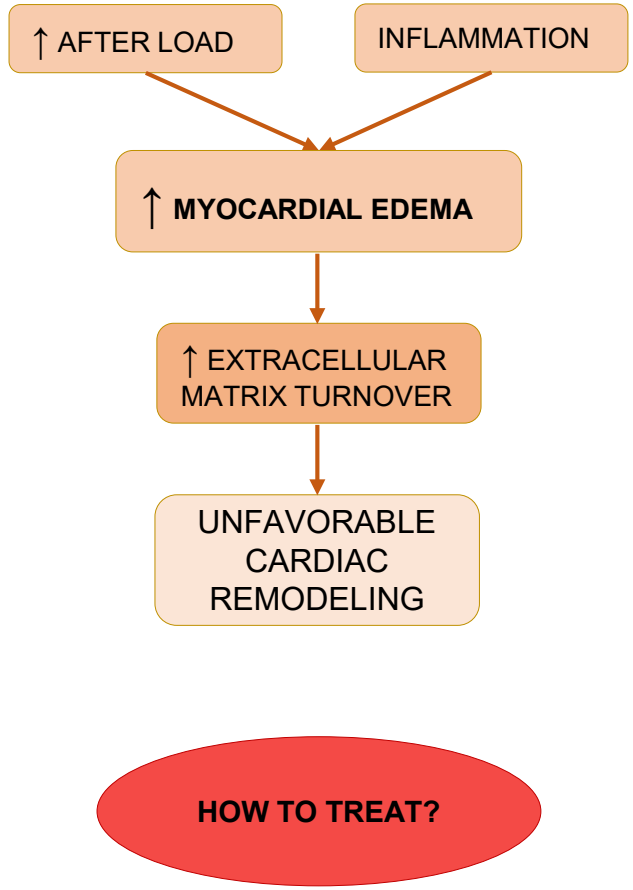


ICU ward

- Mild pupillary anisocoria
  - Head CT scan: acute cerebellar infarction

Day 1 TTM ongoing	Day 2 X Epinephrine V CRRT	Day 3 Neurological Evalutaion	Day 4 ECMO circuit changed	Day 5 Collegial discussion

NSE(48h-72h)			66,5 ng/mL	23,4 ng/mL	
Native lung VAM	12 BPM	5 BPM	10 BPM	10 BPM	10 BPM
Membrane lung GF	3 L/m	2 L/m	5 L/m	3,5 L/m	2 L/m
ECMO BF	3 L/m	3,5 L/m	4 L/m	4 L/m	4 L/m
Vasopressor	↔	↓	↔	↓	↓
HsTNI	↑690350 ng/L	↑813730 ng/L	↓309830 ng/L	↓187700 ng/L	↓137490 ng/L
BNP	40 pg/mL		95 pg/mL		239 pg/mL
PVC	7 mmHg	10 mmHg	14 mmHg	10 mmHg	8 mmHg
PCWP	15 mmHg	13 mmHg	16 mmHg	16 mmHg	13 mmHg
SVO2	65%	63%		69%	69%
Transeptal cannula Q	1,5 L/m	1,5 L/m	1,5 L/m	1,5 L/m	1,5 L/m
CRRT		√	√	√	
Ecocardiography	IVS,AW,PW 20 mm				IVS,AW,PW 18 mm



ICU ward

Day 1 TTM ongoing → Day 2 X Epinephrine V CRRT → Day 3 Neurological Evalutaion → Day 4 ECMO circuit changed → Day 5 Collegial discussion → Day 6-8 DESAMETASONE → Day 9 LEVOSIMENDAN 12,5 mg in 24 h

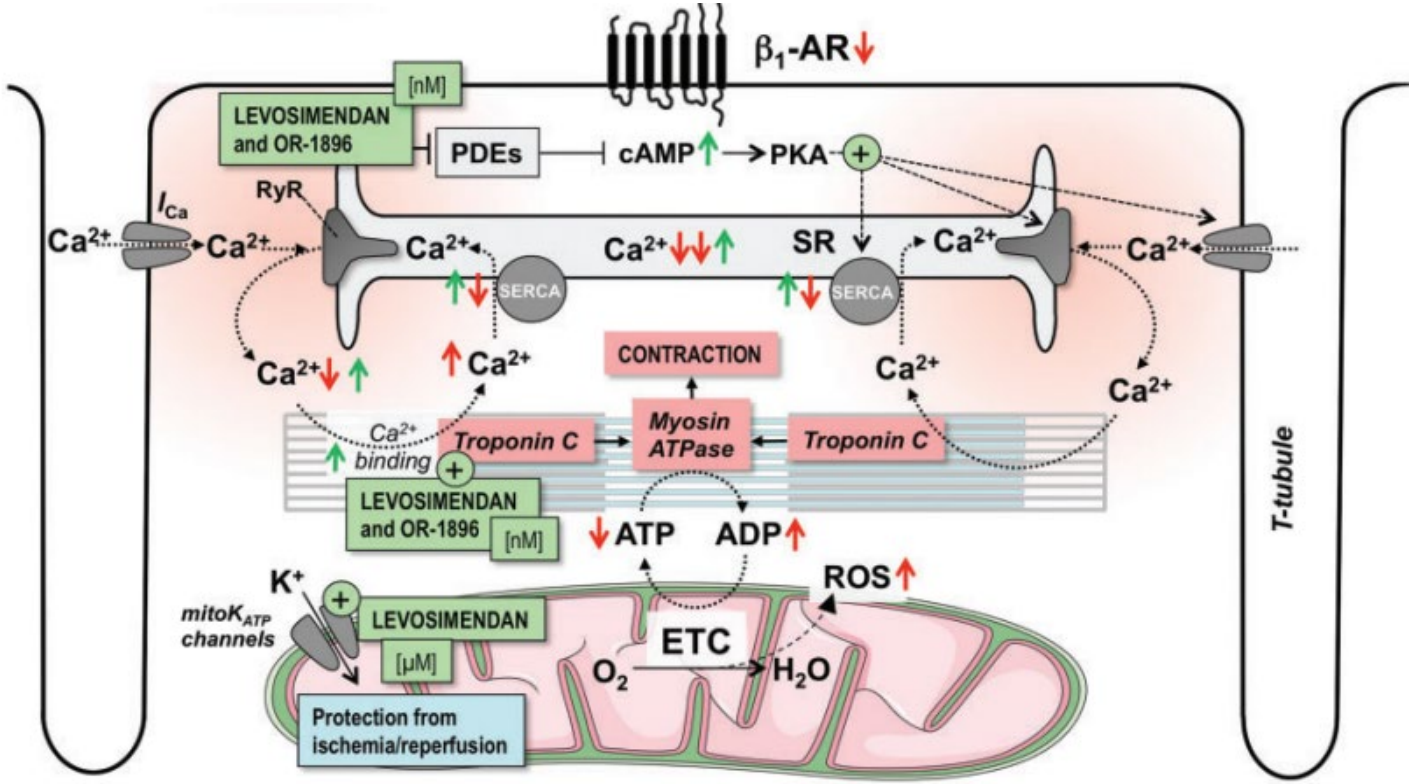
NSE(48h-72h)			66,5 ng/mL	23,4 ng/mL			
Native lung VAM	12 BPM	5 BPM	10 BPM	10 BPM	10 BPM	10 BPM	10 BPM
Membrane lung GF	3 L/m	2 L/m	5 L/m	3,5 L/m	2 L/m	2 L/m	2,5 L/m
ECMO BF	3 L/m	3,5 L/m	4 L/m	4 L/m	4 L/m	4 L/m	3,8 L/m
Vasopressor	↔	↓	↔	↓	↓	↓	↓
HsTNI	↑690350 ng/L	↑813730 ng/L	↓309830 ng/L	↓187700 ng/L	↓137490 ng/L	↑190910 ng/L	↓ 80404 ng/L
BNP	40 pg/mL		95 pg/mL		239 pg/mL	357 pg/mL	396 pg/mL
PVC	7 mmHg	10 mmHg	14 mmHg	10 mmHg	8 mmHg	10 mmHg	9 mmHg
PCWP	15 mmHg	13 mmHg	16 mmHg	16 mmHg	13 mmHg	15 mmHg	20 mmHg
SVO2	65%	63%		69%	45%	60%	
Transeptal cannula Q	1,5 L/m	1,5 L/m	1,5 L/m	1,5 L/m	1,5 L/m	1,4 L/m	1,4 L/m
CRRT		√	√	√		√	√
Ecocardiography	IVS,AW,PW 20 mm				IVS,AW,PW 17 mm		IVS,AW,PW 15 mm

Off label high-dose corticosteroids: **DESAMETASONE 20mg QD for 3 days**

Weaning - when and how?

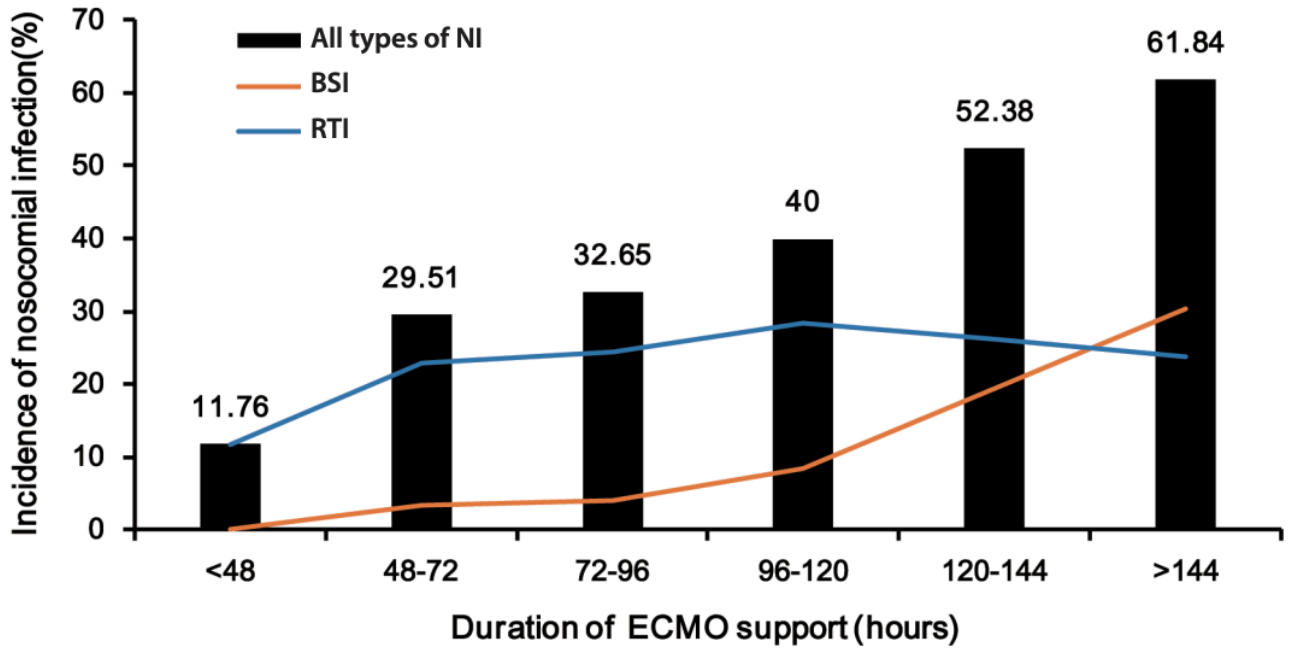
Levosimendan as a pleiotropic agent:

- Inotropic (troponin C e PDE3 inib)
- Vasodilator (K+ channel$_{ATP}$)
- Cardioprotective (mitochondrial K+ channelATP)
- Lusitropic (diastolic relaxation)



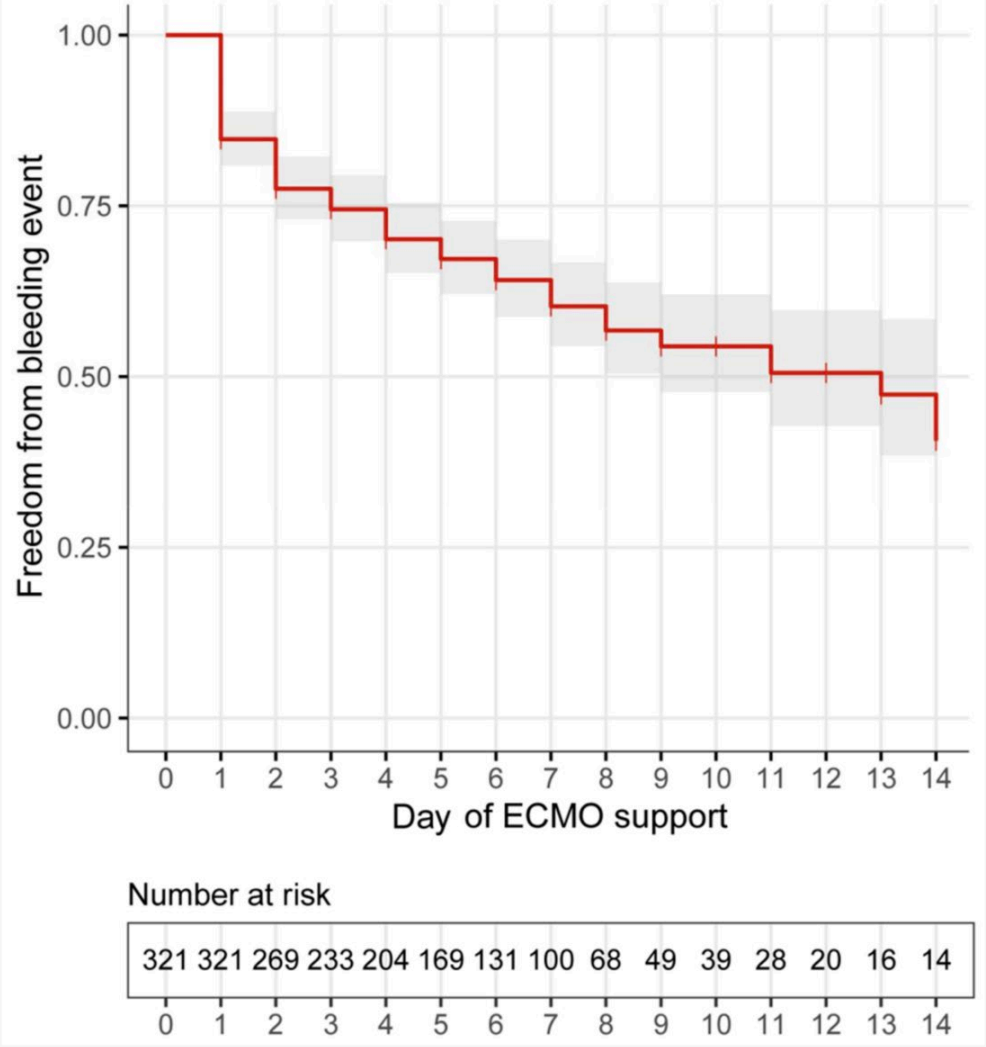
European Heart Journal (2018) **00**, 1–19

Infection and bleeding



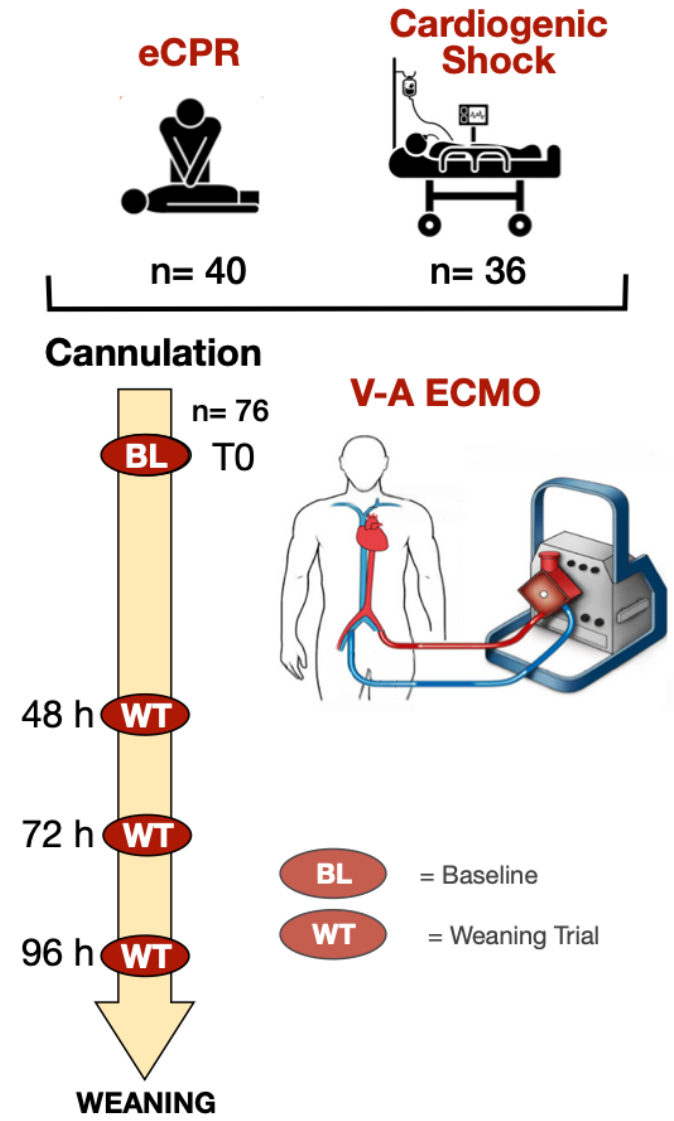
Infection patients	4	18	16	24	22	47
Patients at risk	34	61	49	60	42	76

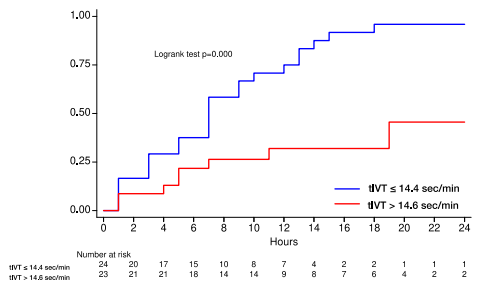
Figure 2. Kaplan-Meier curve: time from ECMO initiation to bleeding event (n = 321, median estimate 13 days, 95% CI 9.3–16.7). ECMO: extracorporeal membrane oxygenation.



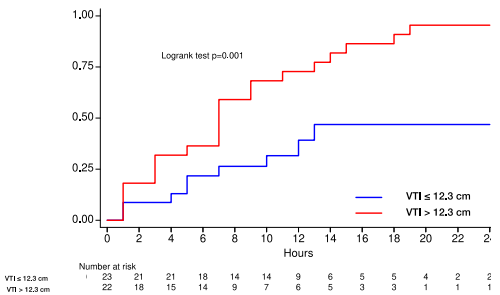
J. Clin. Med. **2022**, *11*(9), 2314;

Echocardiographic parameters for weaning from Extracorporeal Membrane Oxygenation – a physiological approach

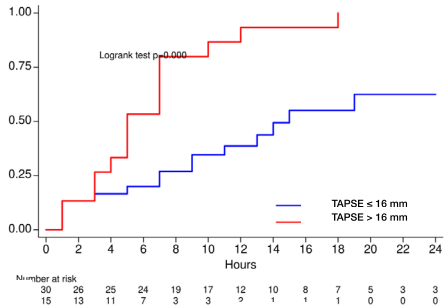




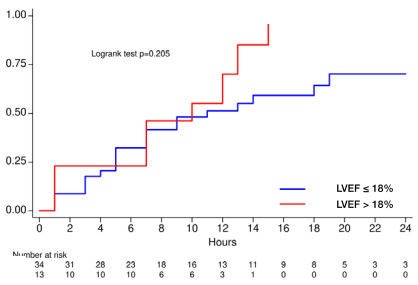
t-IVT



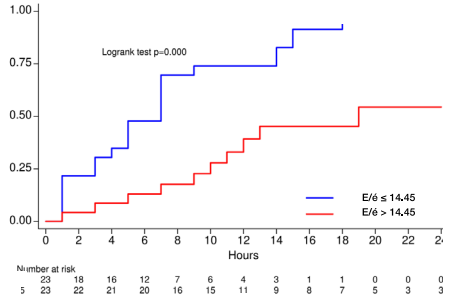
LV VTI



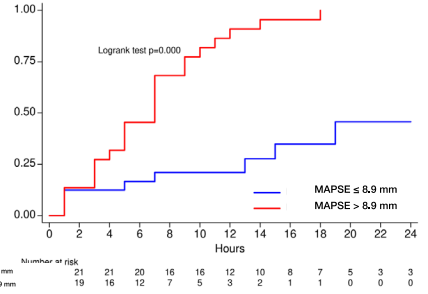
TAPSE



LVEF



E/é



MAPSE

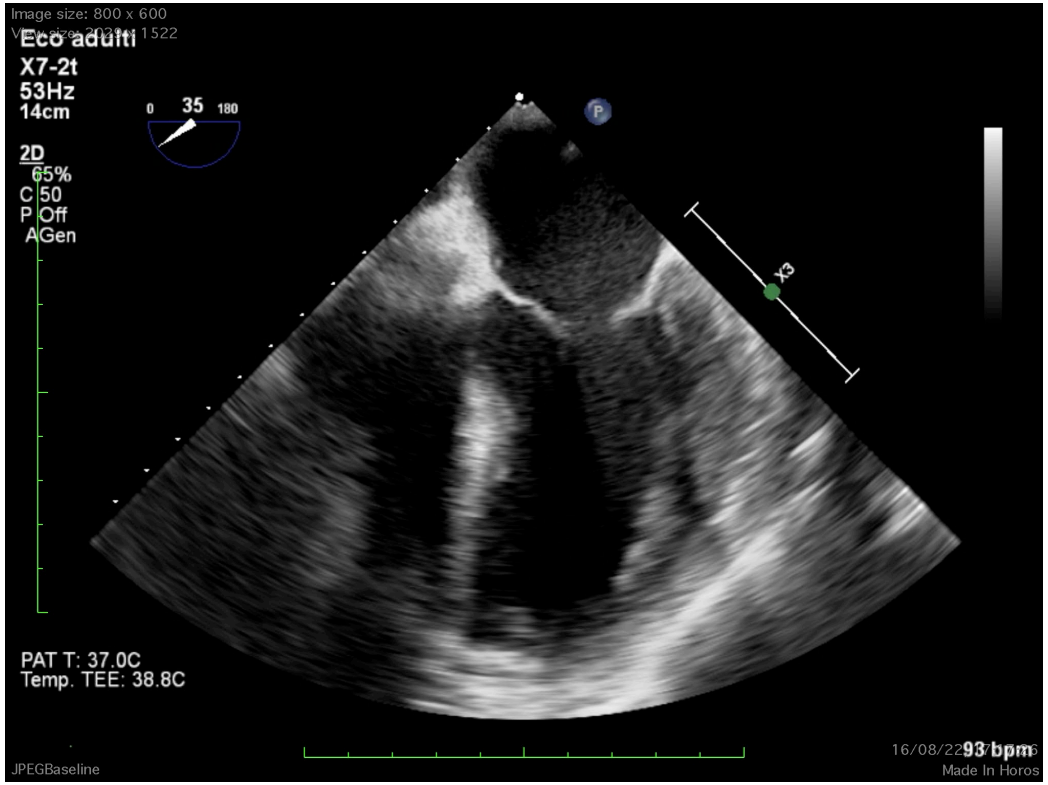
Tavazzi, Colombo, Camporotondo, Pellegrini…In Review JASE

- FBS: blood bronchial secretions

ICU ward

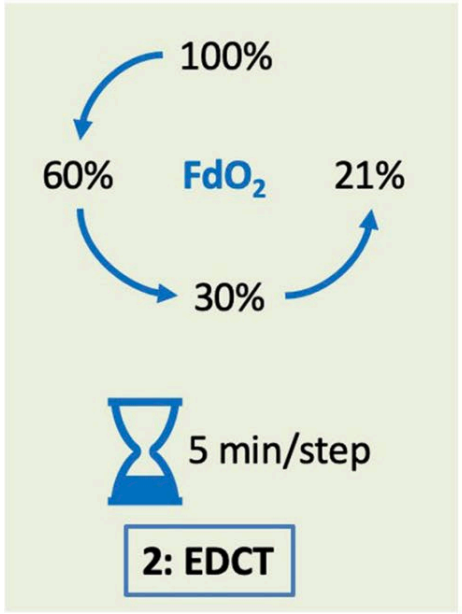
Target: reduce anticoagulation

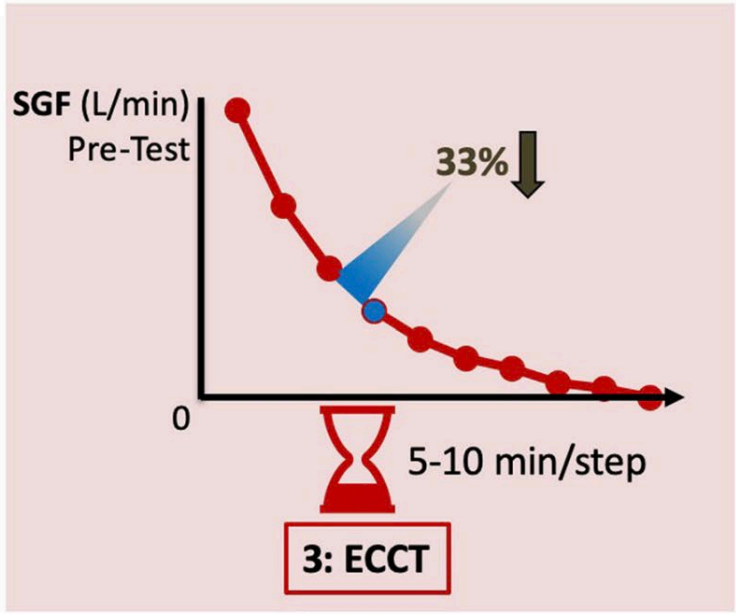
- Echocardiography:
  - **LV** performance still unable to remove ECMO
  - **RV** systolic function **TAPSE 19 mm** and **PAPi 1.2**



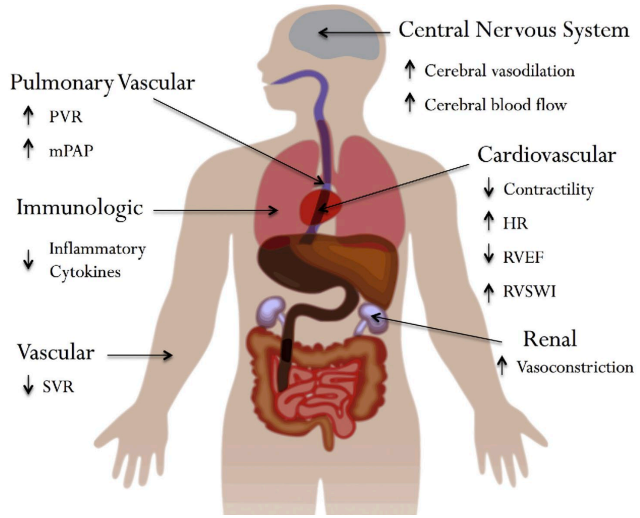
Weaning trial from Oxy ⇩ *Sweep flow and optimizing ventilation and respiratory mechanics (prote)*

Oxy weaning





- ✓ *Driving pressure*
- ✓ *Plateau pressure*
- ✓ *PEEP*
- ✓ *FiO2*
- ✓ *CP*

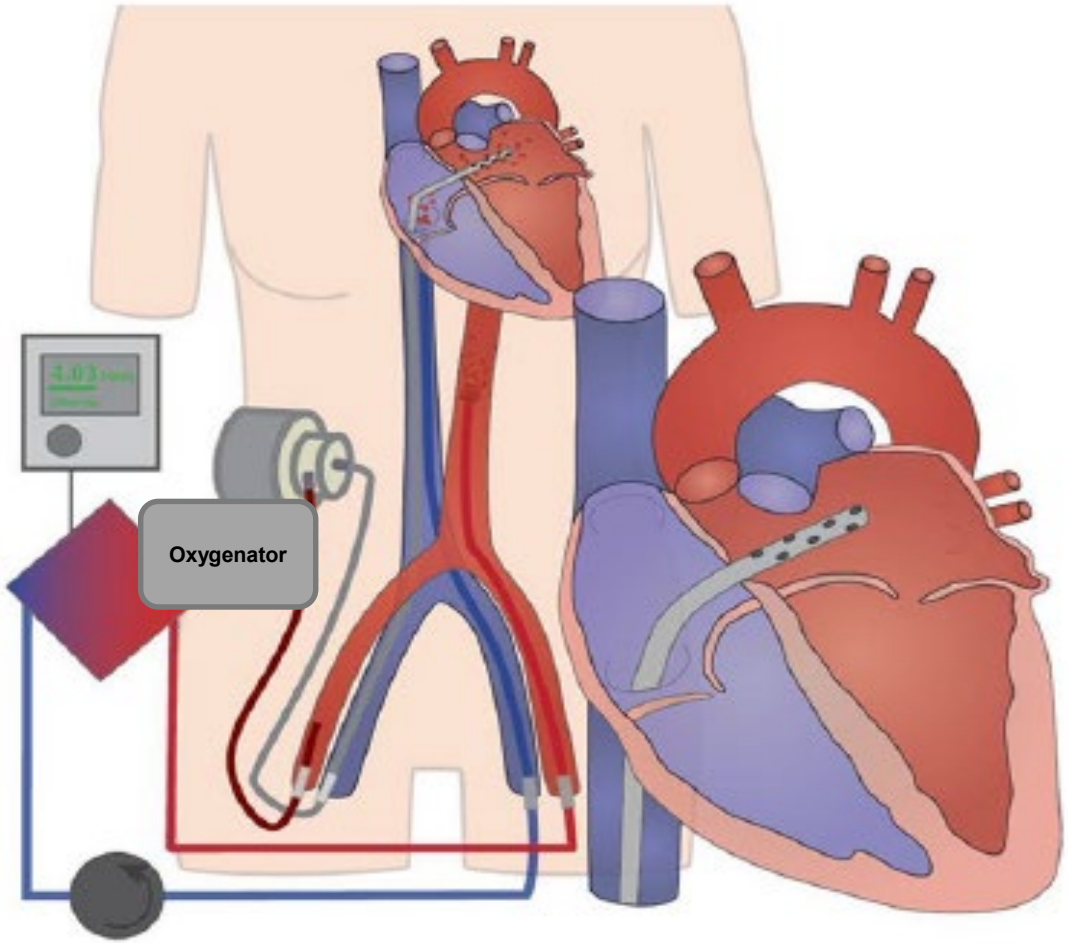


ICU ward

Further reduction of anticoagulation

Day 12
× Oxygenator

LVAD setting Q 2,5 L/m without inotropes



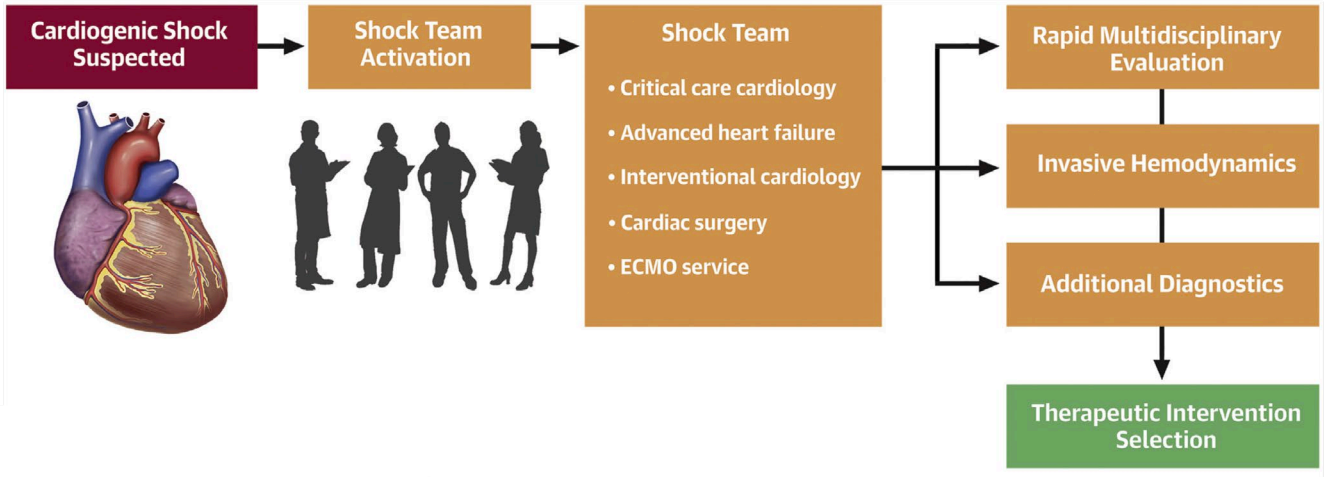
- airway hemorrhage with severe hypoxia occurred
- urgent FBS prevented a new episode of CA
- EmoC + for mdr bacterial (Enterobacter Ludwigii)

Cardiac transplantation or LVAD as destination therapy?

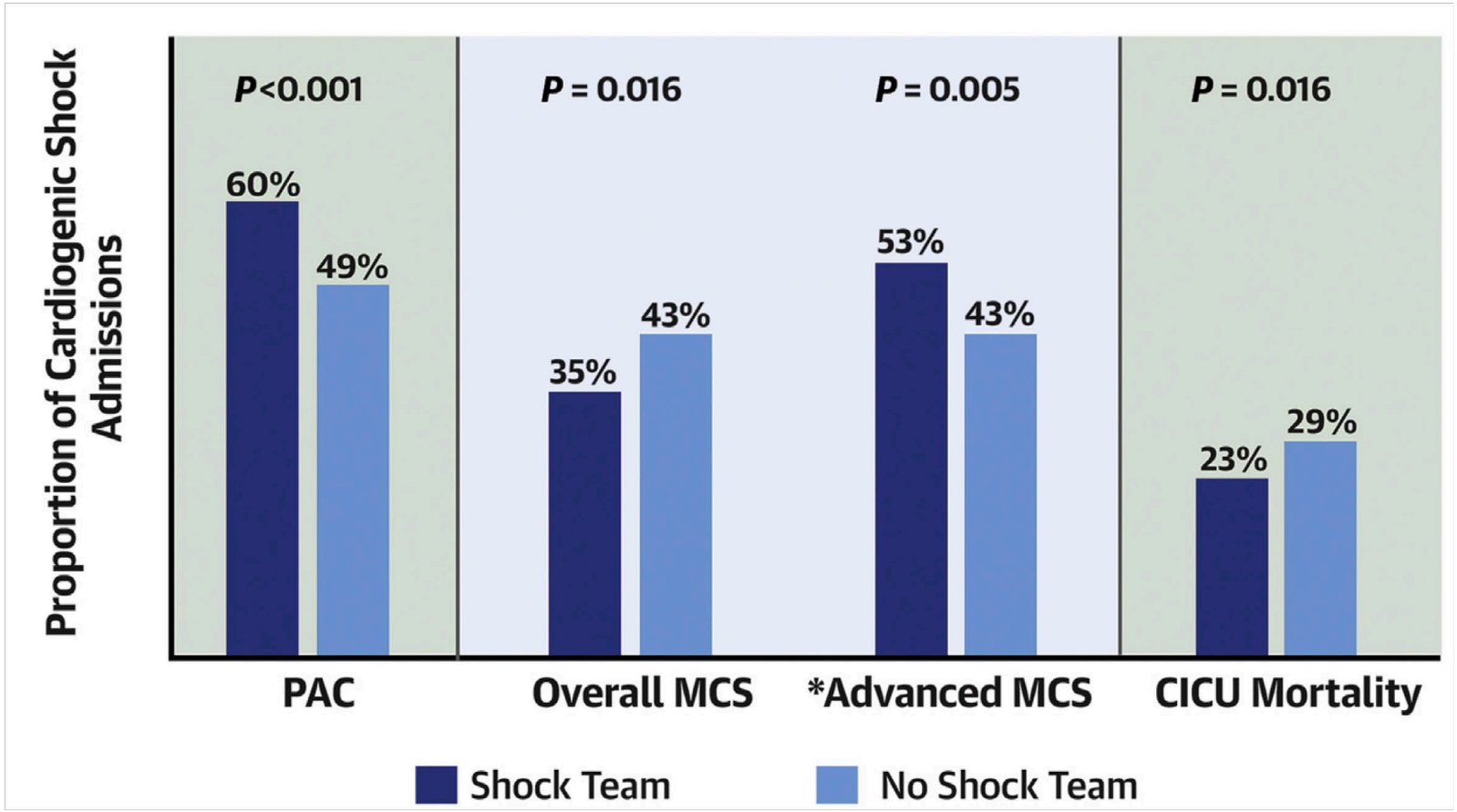
Contraindications

- Cerebellum acute ischemia
- Alveolar bleeding
- Severe hemodynamics impairment (Intermacs 1)
- Refractory AKI and the need of hemodialysis treatment
- Mdr bacterial colonization (E.Ludwigii)

Management and Outcomes of Cardiogenic Shock in Cardiac ICUs With Versus Without Shock Teams

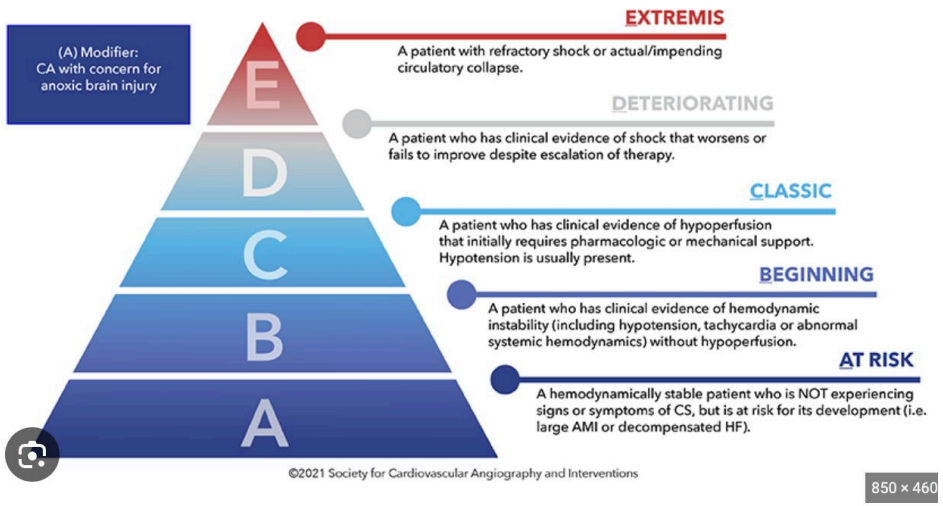


Shock Team vs No Shock Team Center Population Characteristics	
Cardiogenic shock admissions (n)	546 vs 696
AMI-CS (%)	27 vs 28
Admission lactate (mmol/L)	2.3 vs 2.3
PCWP (mm Hg)	25 vs 22
CI (L/min/m²)	1.9 vs 2.0
CPO (W)	0.62 vs 0.64

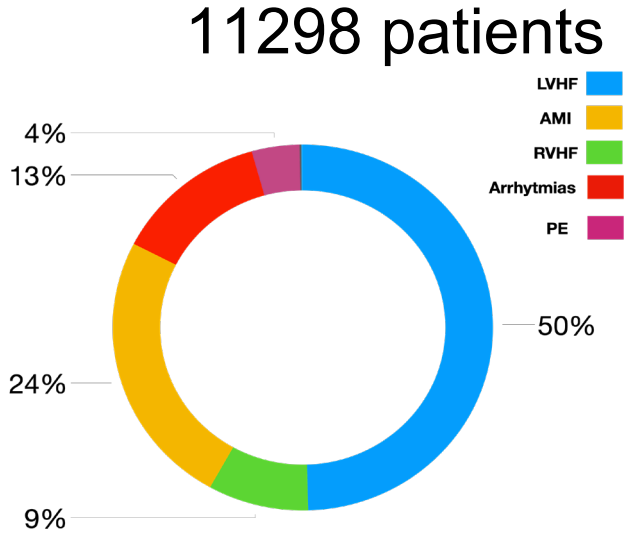


Gaps in evidence in CS

- Phenotypes - features and management



Italian Nationwide Registry of CS in ICU



Gaps in evidence in CS

- Phenotypes - features and management

- MCS – kind, timing

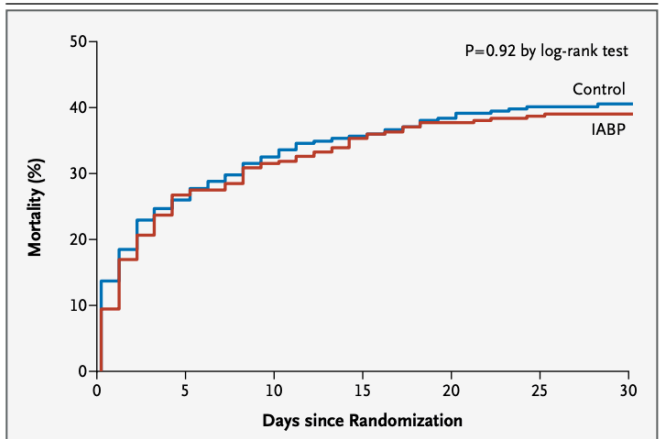


Figure 1. Time-to-Event Curves for the Primary End Point.
Time-to-event curves are shown through 30 days after randomization for the primary end point of all-cause mortality. Event rates represent Kaplan–Meier estimates.

N Engl J Med 2012;367:1287-96.

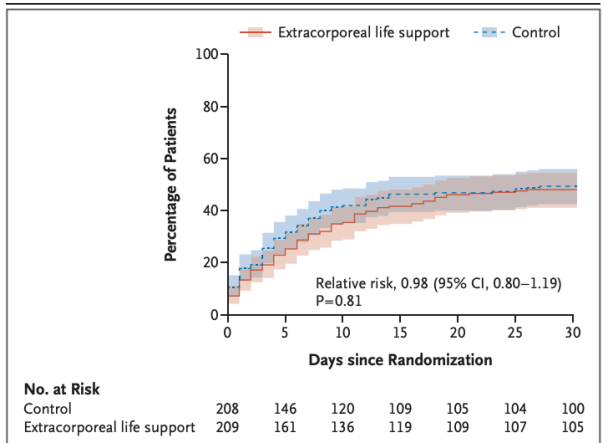
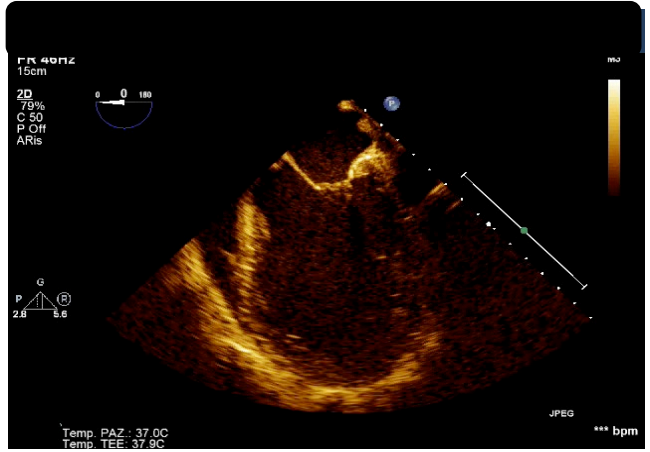
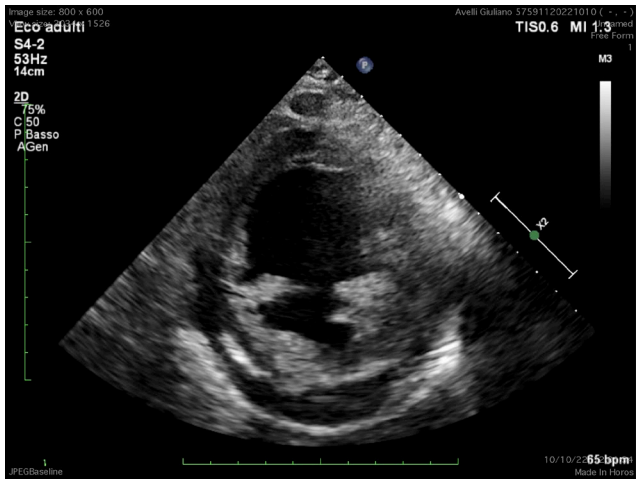
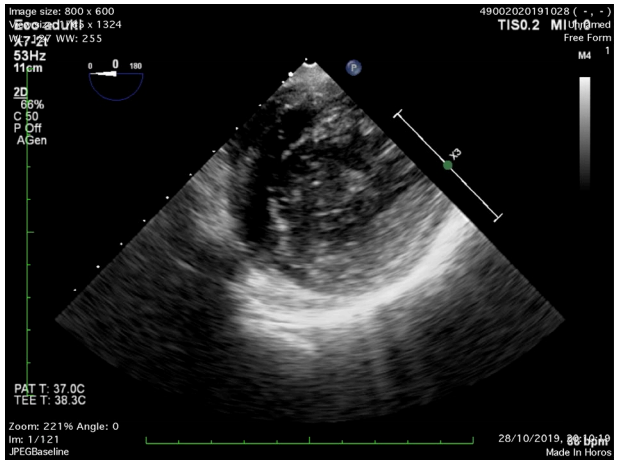


Figure 1. Death from Any Cause at 30 Days.
Shown are the time-to-event curves for death from any cause at 30 days (the primary outcome) among the patients who received extracorporeal life support plus medical therapy as compared with those who received only medical therapy (control). The shaded areas indicate the 95% confidence intervals.

N Engl J Med 2023;389:1286-97.

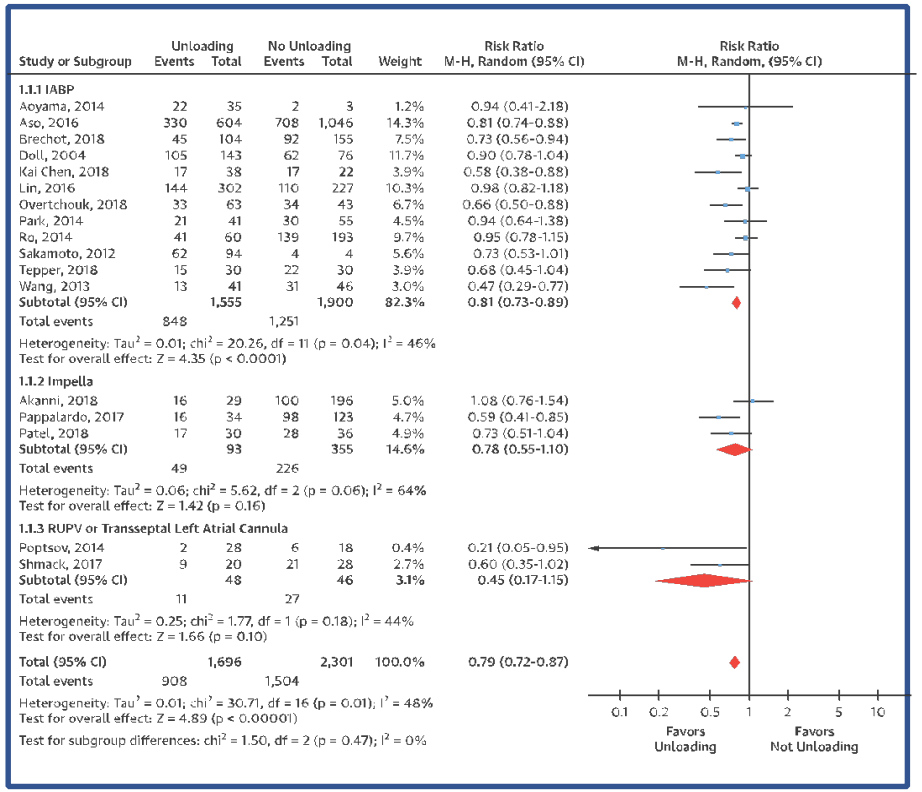






Gaps in evidence in CS

- Phenotypes - features and management
- MCS – kind, timing
- Unloading



Study or Subgroup	Unloading Events	Unloading Total	No Unloading Events	No Unloading Total	Weight	Risk Ratio M-H, Random (95% CI)
1.1.1 IABP						
Aoyama, 2014	22	35	2	3	1.2%	0.94 (0.41-2.18)
Aso, 2016	330	604	708	1,046	14.3%	0.81 (0.74-0.88)
Brechot, 2018	45	104	92	155	7.5%	0.73 (0.56-0.94)
Doll, 2004	105	143	62	76	11.7%	0.90 (0.78-1.04)
Kai Chen, 2018	17	38	17	22	3.9%	0.58 (0.38-0.88)
Lin, 2016	144	302	110	227	10.3%	0.98 (0.82-1.18)
Overtchouk, 2018	33	63	34	43	6.7%	0.66 (0.50-0.88)
Park, 2014	21	41	30	55	4.5%	0.94 (0.64-1.38)
Ro, 2014	41	60	139	193	9.7%	0.95 (0.78-1.15)
Sakamoto, 2012	62	94	4	4	5.6%	0.73 (0.53-1.01)
Tepper, 2018	15	30	22	30	3.9%	0.68 (0.45-1.04)
Wang, 2013	13	41	31	46	3.0%	0.47 (0.29-0.77)
Subtotal (95% CI)		**1,555**		**1,900**	**82.3%**	**0.81 (0.73-0.89)**
Total events	848		1,251			
Heterogeneity: $Tau^2 = 0.01$; $chi^2 = 20.26$, df = 11 (p = 0.04); $I^2 = 46\%$						
Test for overall effect: Z = 4.35 (p < 0.0001)						
1.1.2 Impella						
Akanni, 2018	16	29	100	196	5.0%	1.08 (0.76-1.54)
Pappalardo, 2017	16	34	98	123	4.7%	0.59 (0.41-0.85)
Patel, 2018	17	30	28	36	4.9%	0.73 (0.51-1.04)
Subtotal (95% CI)		**93**		**355**	**14.6%**	**0.78 (0.55-1.10)**
Total events	49		226			
Heterogeneity: $Tau^2 = 0.06$; $chi^2 = 5.62$, df = 2 (p = 0.06); $I^2 = 64\%$						
Test for overall effect: Z = 1.42 (p = 0.16)						
1.1.3 RUPV or Transseptal Left Atrial Cannula						
Poptsov, 2014	2	28	6	18	0.4%	0.21 (0.05-0.95)
Shmack, 2017	9	20	21	28	2.7%	0.60 (0.35-1.02)
Subtotal (95% CI)		**48**		**46**	**3.1%**	**0.45 (0.17-1.15)**
Total events	11		27			
Heterogeneity: $Tau^2 = 0.25$; $chi^2 = 1.77$, df = 1 (p = 0.18); $I^2 = 44\%$						
Test for overall effect: Z = 1.66 (p = 0.10)						
Total (95% CI)		**1,696**		**2,301**	**100.0%**	**0.79 (0.72-0.87)**
Total events	908		1,504			
Heterogeneity: $Tau^2 = 0.01$; $chi^2 = 30.71$, df = 16 (p = 0.01); $I^2 = 48\%$						
Test for overall effect: Z = 4.89 (p < 0.00001)						
Test for subgroup differences: $chi^2 = 1.50$, df = 2 (p = 0.47); $I^2 = 0\%$						

Risk Ratio M-H, Random, (95% CI)

0.1 0.2 0.5 1 2 5 10

Favors Unloading | Favors Not Unloading

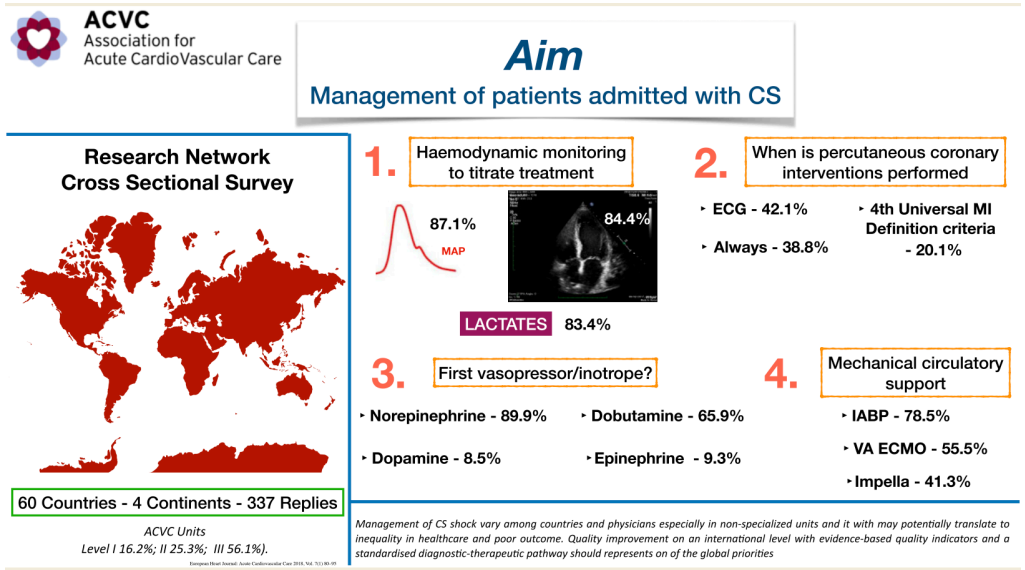
(J Am Coll Cardiol 2019;73:654-62)

Gaps in evidence in CS

- Phenotypes - features and management
- MCS – kind, timing
- Unloading
- Standardization

Epidemiology, monitoring, and treatment strategy in cardiogenic shock. A multinational cross-sectional survey of ESC-acute cardiovascular care association research section

Guido Tavazzi [1,2]*, Xavier Rossello [3,4,5], Johannes Grand [6], Marek Gierlotka[7], Alessandro Sionis [4,8], Ingo Ahrens[9], Christian Hassager[6,10], and Susanna Price [11,12]



European Heart Journal: Acute Cardiovascular Care (2022) **00**, 1–6

Gaps in evidence in CS

- Phenotypes - features and management
- MCS – kind, timing
- Unloading
- Standardization
- Follow-up