LV unloading after VA-ECMO : Routine vs. Optional?

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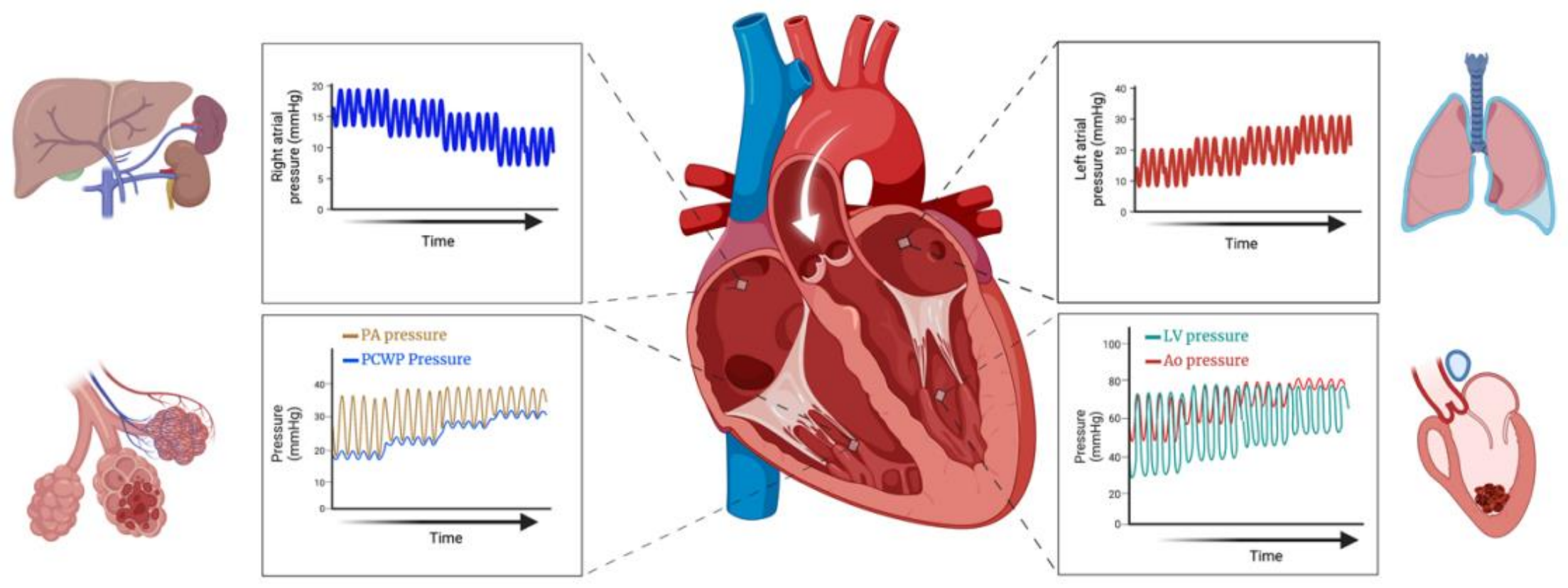
Disclosure

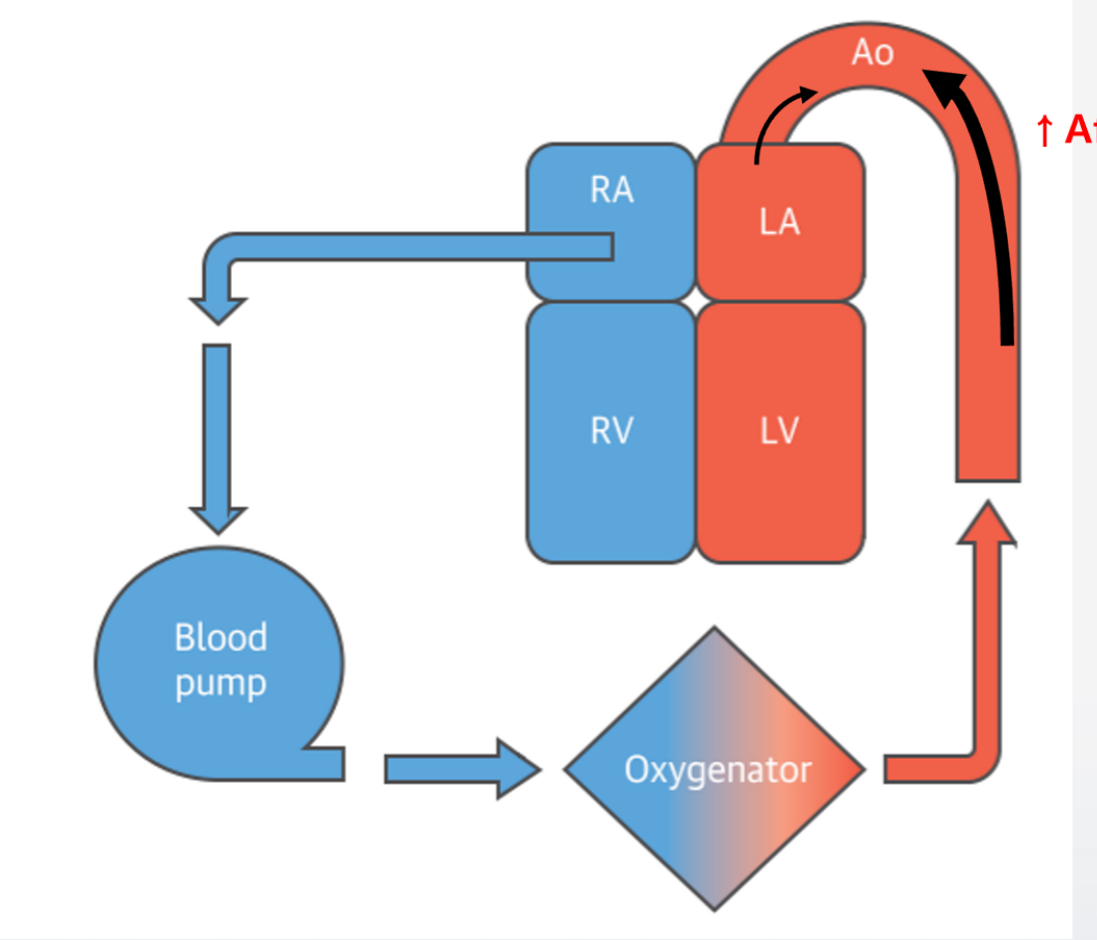
- I have nothing to disclose

Hemodynamic effects of VA-ECMO



Circulation 2023;147:1237.

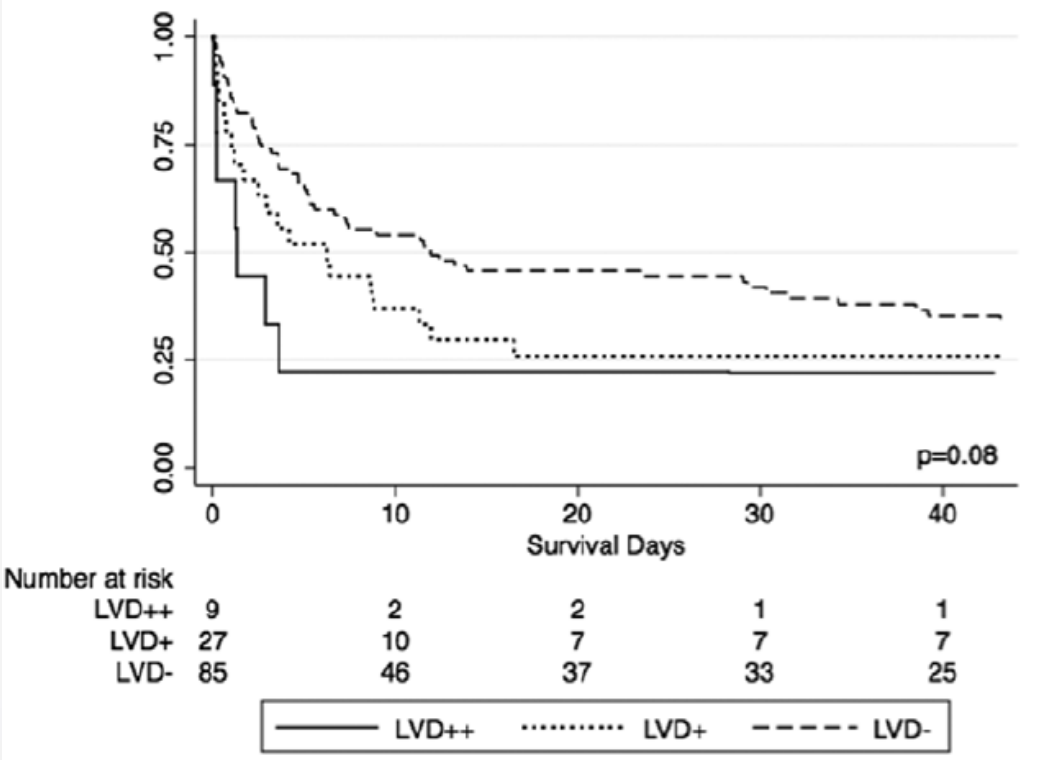
Consequences of LV distension

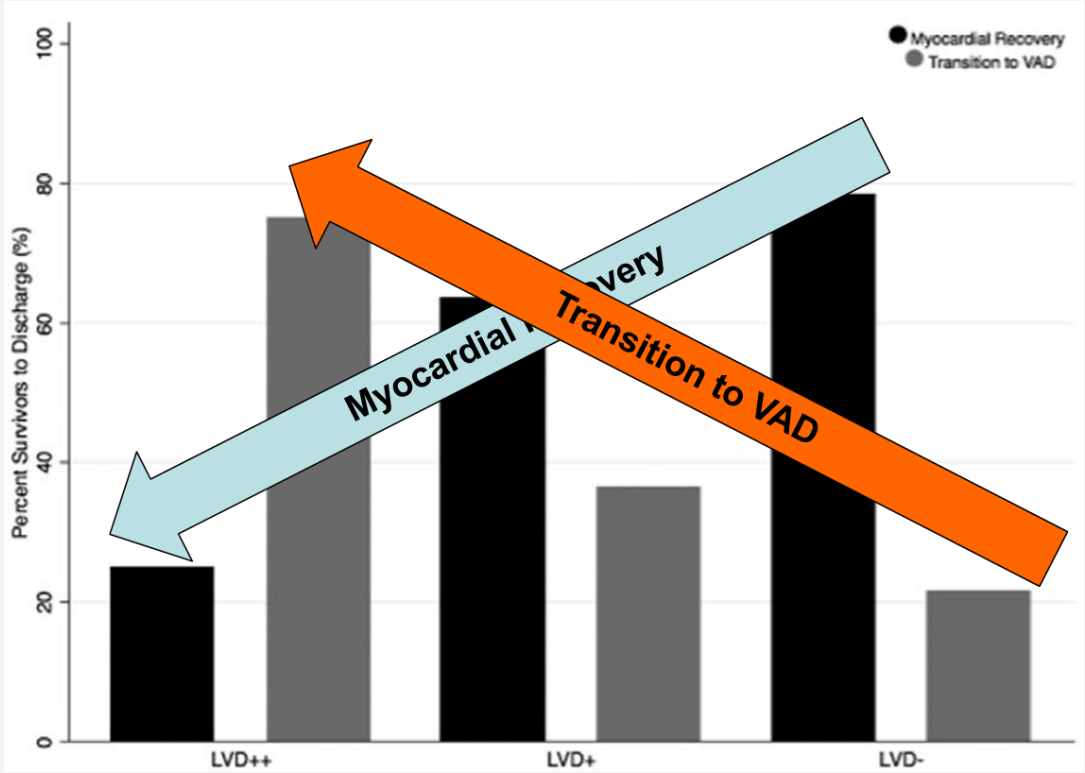


Intracardiac SEC/thrombi
Refractory pulmonary edema
Refractory ventricular arrhythmia

Clinical impact of LV distension

Incidence of LV distension: 30%





- LVD+ (23%): evidence of pulmonary edema and PADBP > 25 mmHg within the first 2 hours
- LVD++ (7%): need for LV unloading immediately because of pulmonary edema, VT or significant blood stagnation within LV

ASAIO J. 2017;63.257.

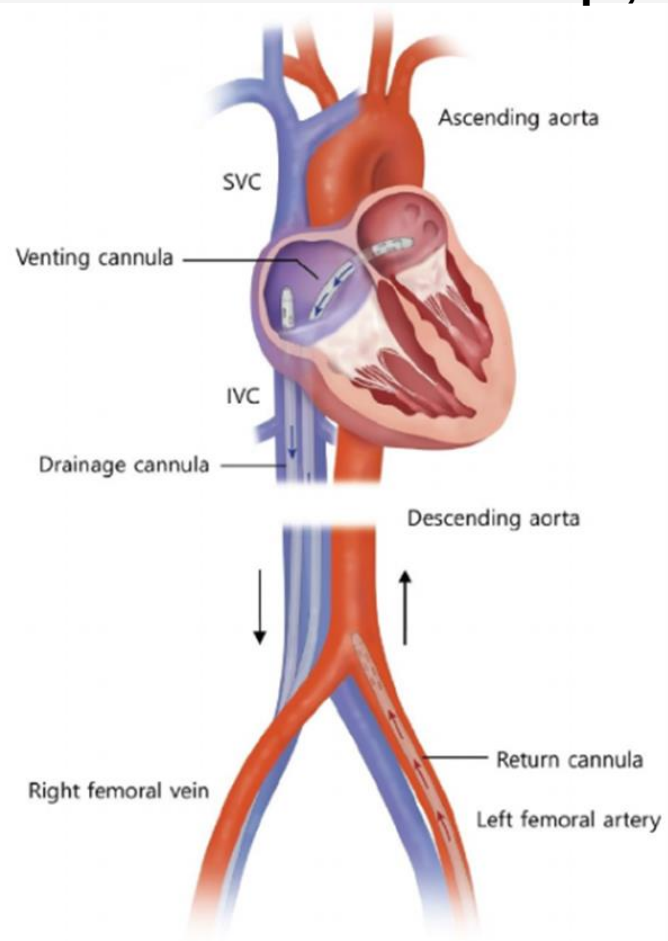
Percutaneous LV unloading modalities

Decompression Technique	Degree of Unloading	Technical Demand	Limitations
Transaortic pigtail	Partial	+	Limited unloading
IABP	Partial	+	Limited unloading, need for stable rhythm, possible decrease in cerebral circulation
Pulmonary artery cannula	Partial	++	Suboptimal flow
Atrial septostomy (Inoue balloon)	Partial	++++	Large residual iASD
Transaortic LV cannula via femoral or subclavian artery approach	Complete	++	Large arterial cannula needed
Impella + ECMO	Complete	++	Inability to use in patients with PAD and mechanical valves, hemolysis, device migration
Transseptal LV cannula	Complete	+++	iASD
TandemHeart + ECMO	Complete	++++	Expensive, limited availability, iASD

J Card Surg 2016;31:177-82.

Transseptal LA cannulation increased the rate of ECMO weaning, but not in-hospital mortality

124 pt, cardiogenic shock, Asan medical center



Variables (unit)	Total (N = 124)	Venting (N = 62)	Control (N = 62)	*P* value
Weaning from ECMO	62 (50.0%)	38 (61.3%)	24 (38.7%)	.012
Cardiac transplantation	25 (20.2%)	18 (29.0%)	7 (11.3%)	.014
Recovery	37 (29.8%)	20 (32.3%)	17 (27.4%)	.137
Weaning failure	62 (50.0%)	24 (38.7%)	38 (61.3%)	.012
Total ECMO running time (hours)[a]	156 (67-156)	237 (124-334)	71 (19-200)	<.001
ICU day (days)[a]	13.5 (5-29)	19 (10-43)	9.5 (3-18)	<.001
Hospital day (days)[a]	25.5 (8-84)	48.5 (16-98)	14 (4-57)	.001
Inhospital mortality	79 (63.7%)	35 (56.5%)	43 (69.4%)	.191
Complications		8 (12.9%)	7 (11.3%)	.783
Bleeding		3 (4.8%)	4 (6.5%)	
Limb ischemia		0 (0.0%)	3 (4.8%)	
Cardiac tamponade		2 (3.2%)	0 (0.0%)	
Thrombosis		3 (4.8%)	0 (0.0%)	

Aritif Organs. 2021;45:390-398.

Elective decompression of the LV in pediatric patients may reduce the duration of VA-ECMO

84 pt, cardiogenic shock, Single center, Australia

TABLE 6. *Outcomes on ECMO*

	Elective left heart decompression ($n = 29$)	Emergency left heart decompression ($n = 22$)	P
ECMO duration (h)			
All patients	128 (97.59, 158.66)	236 (133.78, 338.51)	0.013
Survivors	120 (63, 177)	141 (77, 205)	0.55
Died	133 (94, 173)	354 (143, 566)	0.002
Cardiac patients	122 (80.58, 163.93)	111 (63.71, 158.12)	0.73
Noncardiac patients	138 (85.95, 189.51)	295 (150.89, 438.29)	0.02
Noncardiac patients who died	98 (55.06, 142.60)	413 (158.89, 666.70)	0.0002
Duration of left heart venting (h)	111 (83.33, 138.12)	154 (93.66, 214.99)	0.13
Duration of mechanical ventilation (h)	320 (111.01, 529.51)	289 (49.53, 528.60)	0.84
Oxygen duration (h)	33 (−3.54, 68.84)	194 (−100.61, 489.41)	0.12
Weaned to LVAD, n (%)	7 (24)	3 (13)	0.34
Hours in ICU, n (%)	448 (297.38, 599.69)	817 (313.05, 1321.19)	0.08
Survival, ECMO, n (%)	18 (62)	14 (63)	0.57
Survival, ICU, n (%)	11 (38)	10 (45)	0.40

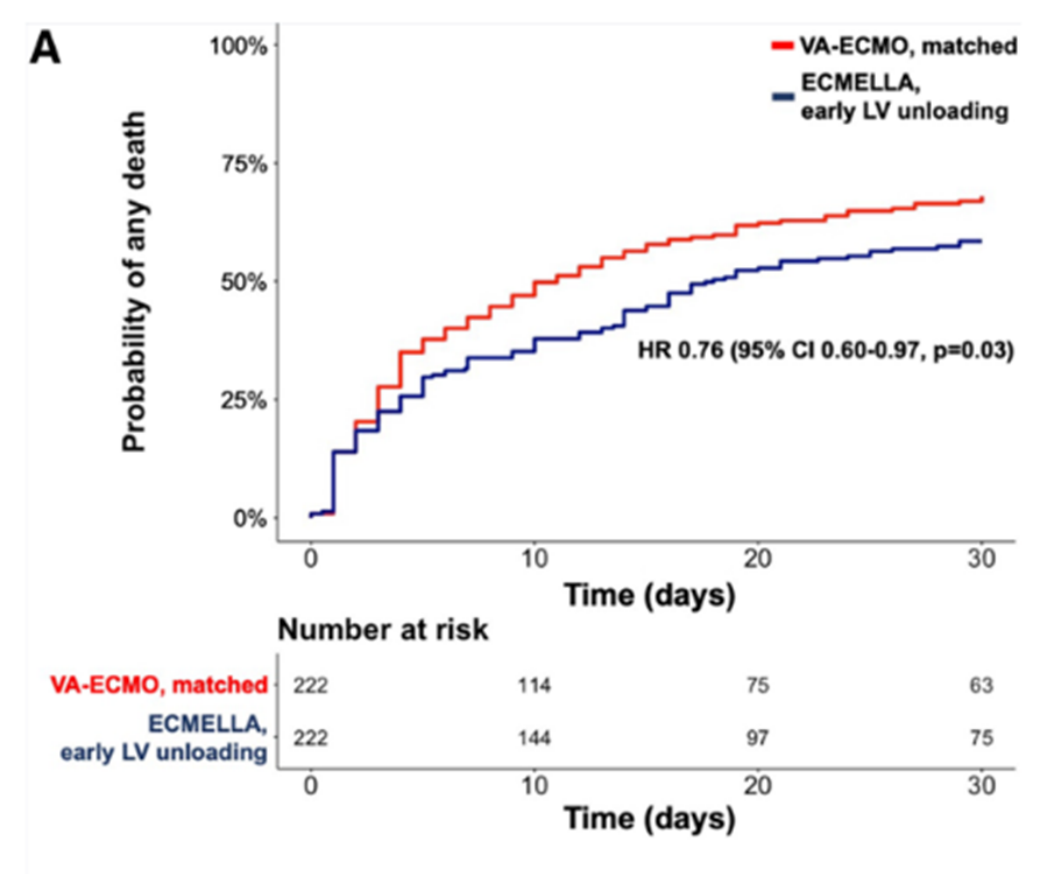
All data given as mean (95% CI) unless otherwise indicated.

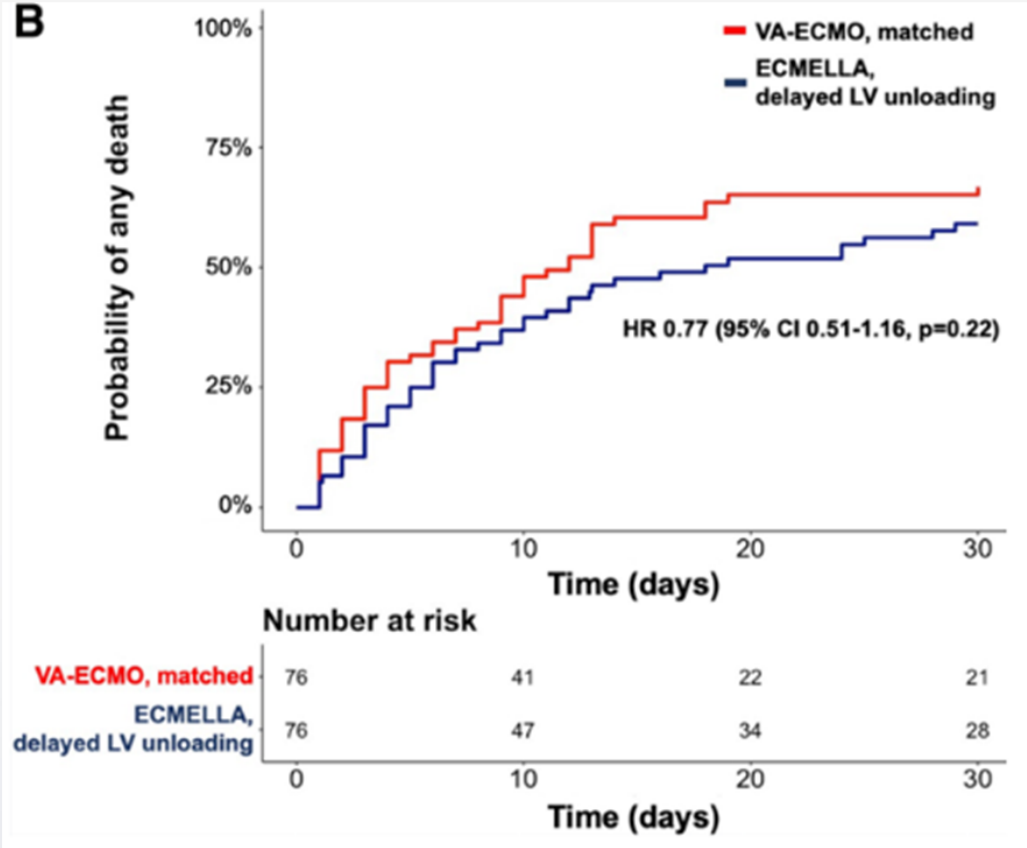
Artif Organs 2015;39(4):319-26.

LV unloading is associated with lower mortality in cardiogenic shock treated with VA-ECMO

686 pt, cardiogenic shock, 16 centers, Europe

Early unloading: < 2 hours after VA-ECMO





Circulation. 2020;142(22):2095-2106.

Prophylactic LHD was associated with a lower early mortality rate compared with therapeutic LHD

50 pt, cardiogenic shock, Korea

Table 3 Treatment characteristics in intensive care unit

Variables	Therapeutic LHD (n=32)	Prophylactic LHD (n=18)	P value
ECMO management			
Left heart decompression			
Time interval after ECMO initiation, hours	38.8 (12.8–101.4)	0 (0–0)	<0.001
Percutaneous technique	14 (43.8)	18 (100.0)	<0.001

Table 4 Clinical outcomes

Variables	Therapeutic LHD (n=32)	Prophylactic LHD (n=18)	P value
30-day mortality	11 (34.4)	1 (5.6)	0.036
90-day mortality	14 (43.8)	4 (22.2)	0.128
Duration on ECMO, days	10.5 (5.1–20.4)	15.4 (7.0–28.3)	0.332
Weaning success	20 (62.5)	15 (83.3)	0.123
ECMO support after initial successful weaning	1 (3.1)	1 (5.6)	>0.999
ECMO-related complications			
Limb ischemia	4 (12.5)	1 (5.6)	0.642
Cannula insertion site bleeding	6 (18.8)	6 (33.3)	0.309
Cannula insertion site infection	3 (9.4)	3 (16.7)	0.654
Ischemic or hemorrhagic stroke	3 (9.4)	2 (11.1)	>0.999
Gastrointestinal bleeding	3 (9.4)	2 (11.1)	>0.999
Septostomy-associated complications	3 (9.4)*	1 (5.6)†	>0.999

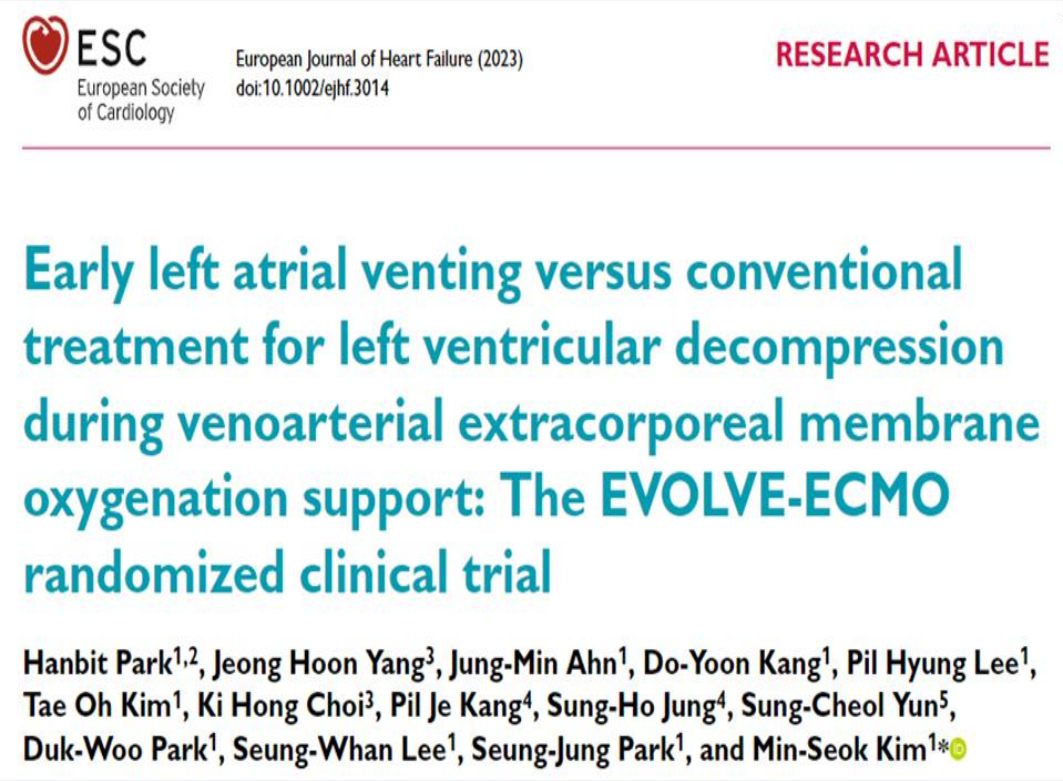
J Thorac Dis. 2019;11(9):3746-56.

Timing of LV unloading

- In current evidence, early LV unloading strategy was associated with favor clinical outcomes (such as mortality and weaning of VA-ECMO)
- However, the previous studies were observational studies. The level of evidence was low.
- Nonrandomized observational studies may have significantly affected the results owing to potential selection bias.

Timing of LV unloading

2 RCTs from Korea, 2023



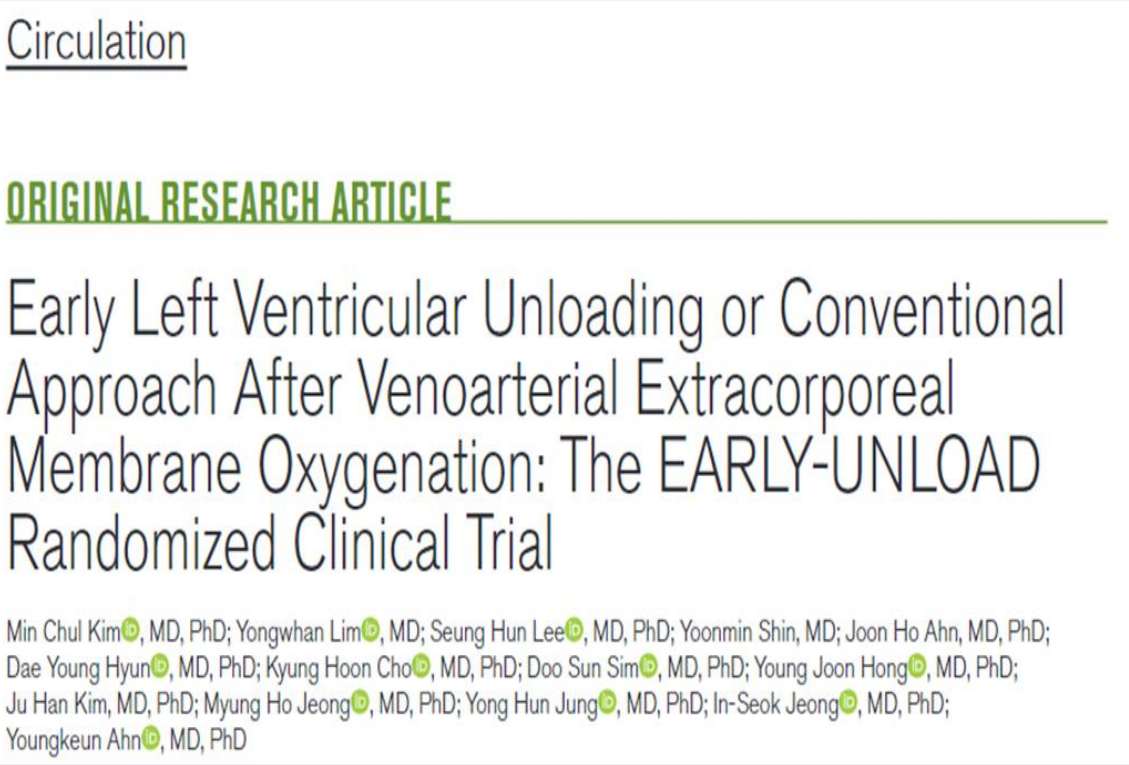
ESC European Society of Cardiology

European Journal of Heart Failure (2023)
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]*



Circulation

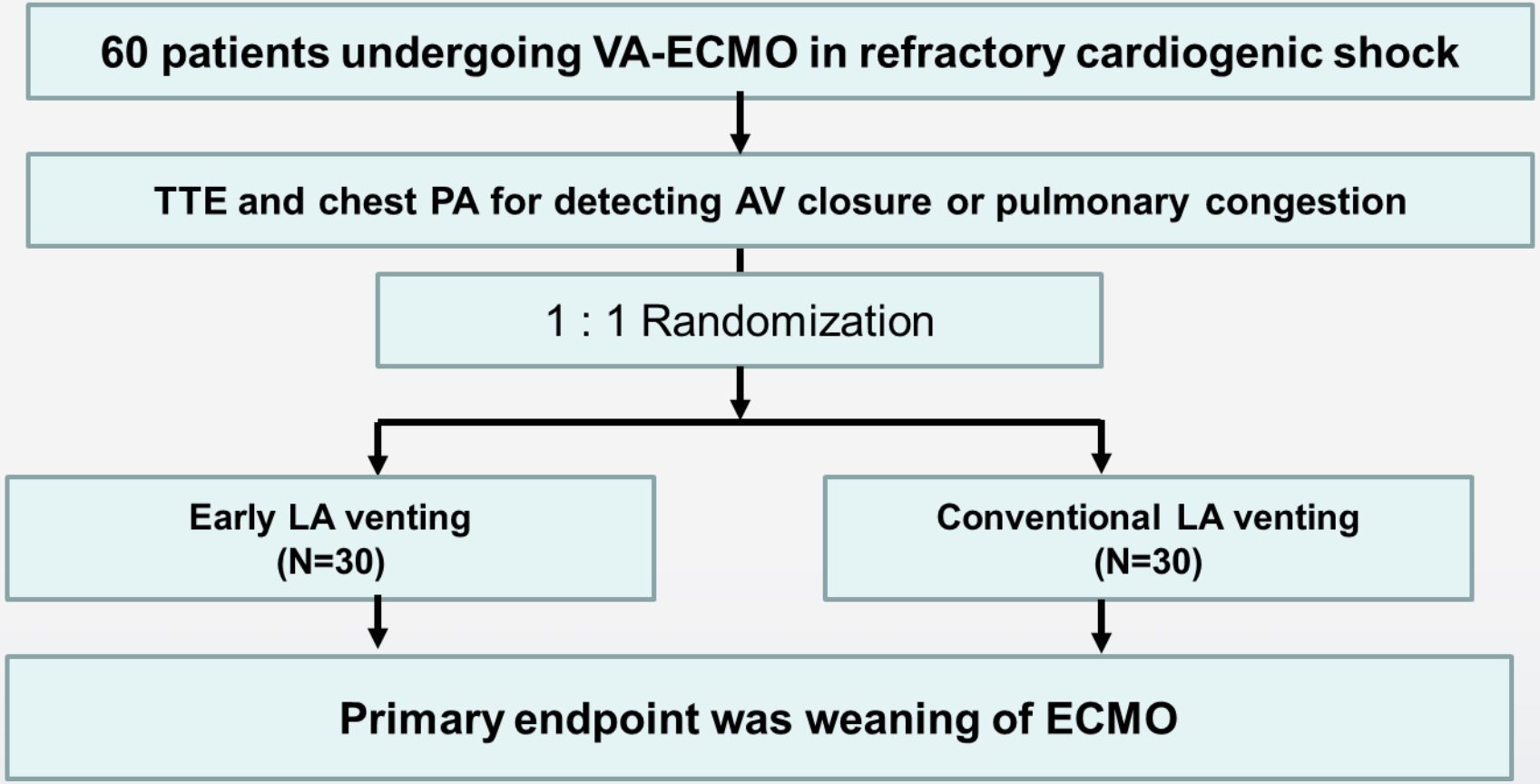
ORIGINAL RESEARCH ARTICLE

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

Early Left Atrial Venting Versus Conventional Treatment For Left VEntricular Distention During Venoarterial ExtraCorporeal Membrane Oxygenation Support

EVOLVE-ECMO trial



Eur J Heart Fail. 2023;25(11):2037-46.

Study Endpoints

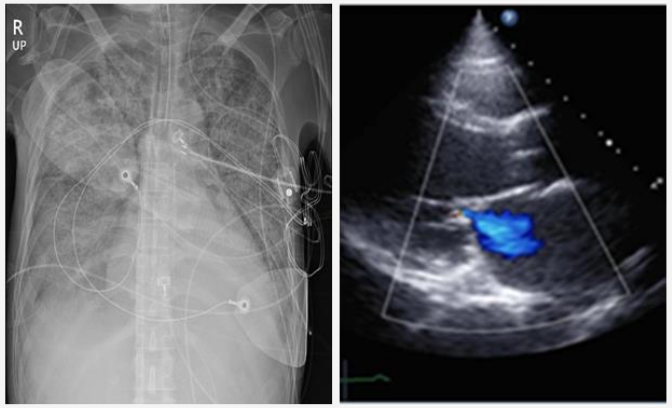
- The primary endpoint: the rate of a weaning from VA-ECMO during index admission

- The secondary endpoints
  - the rate of survival to discharge
  - successful HT or LV assist device (LVAD) implantation
  - the duration of mechanical ventilation (MV)
  - improvement of pulmonary edema
  - any adverse events related to the VA-ECMO

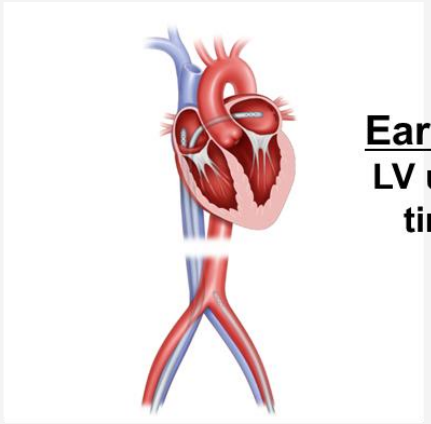
Eur J Heart Fail. 2023;25(11):2037-46.

Trial procedure

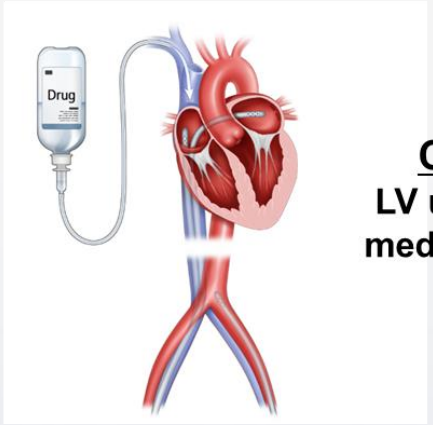
Profound cardiogenic shock during VA-ECMO



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 edema identified

Time to LV unloading:
Early (29/30, 97%): 2.4 hour
Conventional (23/30, 77%): 48.4 hour

Eur J Heart Fail. 2023;25(11):2037-46.

Baseline characteristics

	Early group (n=30)	Conventional group (n=30)	P
Age, years	63.9 ± 12.8	60.5 ± 12.2	0.302
Male, n (%)	19 (63.3)	20 (66.7)	0.787
BMI, kg/m^2	23.9 ± 4.4	23.4 ± 4.6	0.676
SAVE score	-5.7 ± 5.7	-4.7 ± 4,6	0.470
Congestive heart failure, n (%)	3 (10.0)	0 (0.0)	0.237
Previous myocardial infarction, n (%)	10 (33.3)	13 (43.3)	0.426
Extracorporeal CPR, n (%)	9 (30.0)	9 (30.0)	0.999
Etiology of cardiogenic shock			0.367
Acute myocardial infarction, n (%)	9 (30.0)	13 (43.3)	0.284
Dilated cardiomyopathy, n (%)	8 (26.7)	5 (16.7)	0.347
Ischemic cardiomyopathy, n (%)	2 (6.7)	3 (10.0)	0.999
Valvular heart disease, n (%)	2 (6.7)	1 (3.3)	0.999
Myocarditis, n (%)	2 (6.7)	6 (20.0)	0.254
Arrhythmia, n (%)	5 (16.7)	1 (3.3)	0.195
Others, n (%)	2 (6.7)	1 (3.30)	0.999

Eur J Heart Fail. 2023;25(11):2037-46.

Clinical outcomes

	Early group (n=30)	Conventional group (n=30)	Relative risk (95% CI)	P
Primary outcome: weaning of VA-ECMO	21 (70.0)	23 (76.7)	0.91 (0.67-1.24)	0.386
Secondary outcomes				
Survival to discharge	16 (53.3)	15 (50.0)	1.14 (0.42-3.15)	0.796
In-hospital cardiovascular mortality	5 (16.7)	5 (16.7)	1.00 (0.26-3.89)	0.999
Bridge to heart transplantation or LVAD	12 (40.0)	11 (36.7)	1.15 (0.41-3.26)	0.791
Bridge to heart transplantation	7 (23.3)	9 (30.0)	0.71 (0.23-2.25)	0.559
Bridge to LVAD	5 (16.7)	2 (6.7)	2.80 (0.50-15.73)	0.424
Duration of ECMO, days	17.3 ± 21.2	22.6 ± 30.2		0.438
Mechanical ventilation	26 (86.7)	29 (96.7)	0.22 (0.02-2.14)	0.353
Duration of mechanical ventilation, days	12.9 ± 14,2	36.4 ± 71.2		0.092
Free days of Inotropic agent, days	13.0 ± 16.0	29.4 ± 41.9		0.053
Length of hospitalization, days	47.8 ± 40.2	62.1 ± 50.6		0.229
Length of ICU admission, days	23.2 ± 22.9	31.3 ± 27.5		0.221
CRRT, n (%)	19 (63.3)	18 (60.0)	1.15 (0.41-3.26)	0.791

Eur J Heart Fail. 2023;25(11):2037-46.

Clinical outcomes

	Early group (n=30)	Conventional group (n=30)	Relative risk (95% CI)	P
Adverse events, n (%)	16 (53.3)	23 (76.7)	0.35 (0.12-1.06)	0.058
Ischemic stroke, n (%)	5 (16.7)	2 (6.7)	2.80 (0.50-15.73)	0.228
Hemorrhagic stroke, n (%)	3 (10.0)	2 (6.7)	1.56 (0.24-10.05)	0.640
Cardiac tamponade, n (%)	1 (3.3)	1 (3.3)	1.00 (0.06-16.76)	0.999
Puncture site bleeding, n (%)	6 (20.0)	5 (16.7)	1.25 (0.34-4.64)	0.739
Gastrointestinal bleeding, n (%)	2 (3.3)	5 (16.7)	0.29 (0.05-1.55)	0.129
Limb ischemia, n (%)	4 (13.3)	4 (13.3)	1.00 (0.23-4.43)	0.999

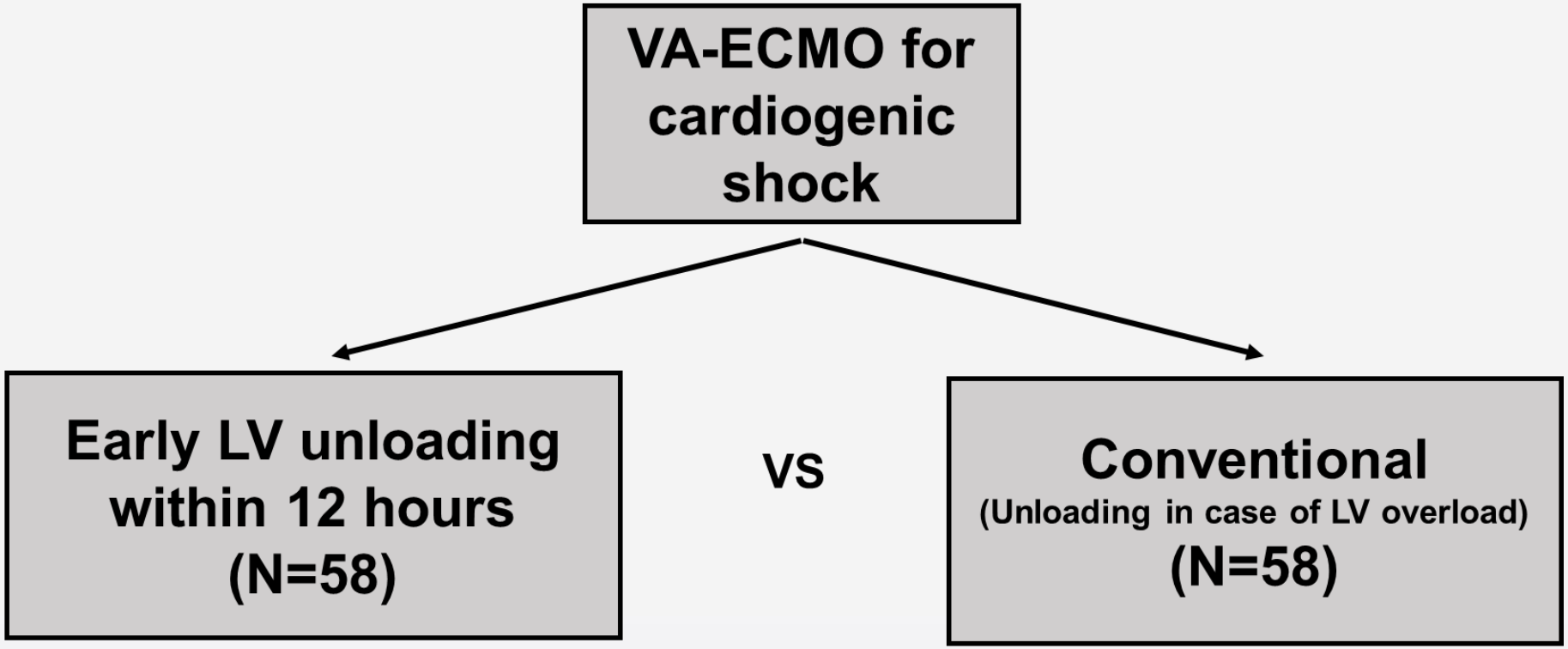
Eur J Heart Fail. 2023;25(11):2037-46.

Conclusion

- Early LV unloading strategy did not increase the weaning rate from VA-ECMO compared with a conventional approach.
- These findings therefore do not support the systematic use of early LV unloading following VA-ECMO insertion.
- However, this trial was underpowered and inconclusive because of small sample size and study design.
- Further larger-scale studies will thus be essential to establish the optimal timing of LV unloading during VA-ECMO.

Eur J Heart Fail. 2023;25(11):2037-46.

EARLY-UNLOAD trial



Unloading modality: Transseptal left atrial cannulation

Time to LV unloading:
Early (58/58, 100%): 1.1 hour, Conventional (29/58, 50%): 21.8 hour

Circulation. 2023;148:1570-81.

Study endpoints

- Primary endpoint: all-cause mortality at 30 days

- Secondary endpoints
  - a composite of all-cause mortality or transseptal LA cannulation at 30 days
  - cardiac or non-cardiac death at 30 days
  - in-hospital mortality
  - the rate of VA-ECMO weaning
  - the duration of VA-ECMO
  - the rate of disappearance of pulmonary congestion
  - the rate of mechanical ventilation weaning

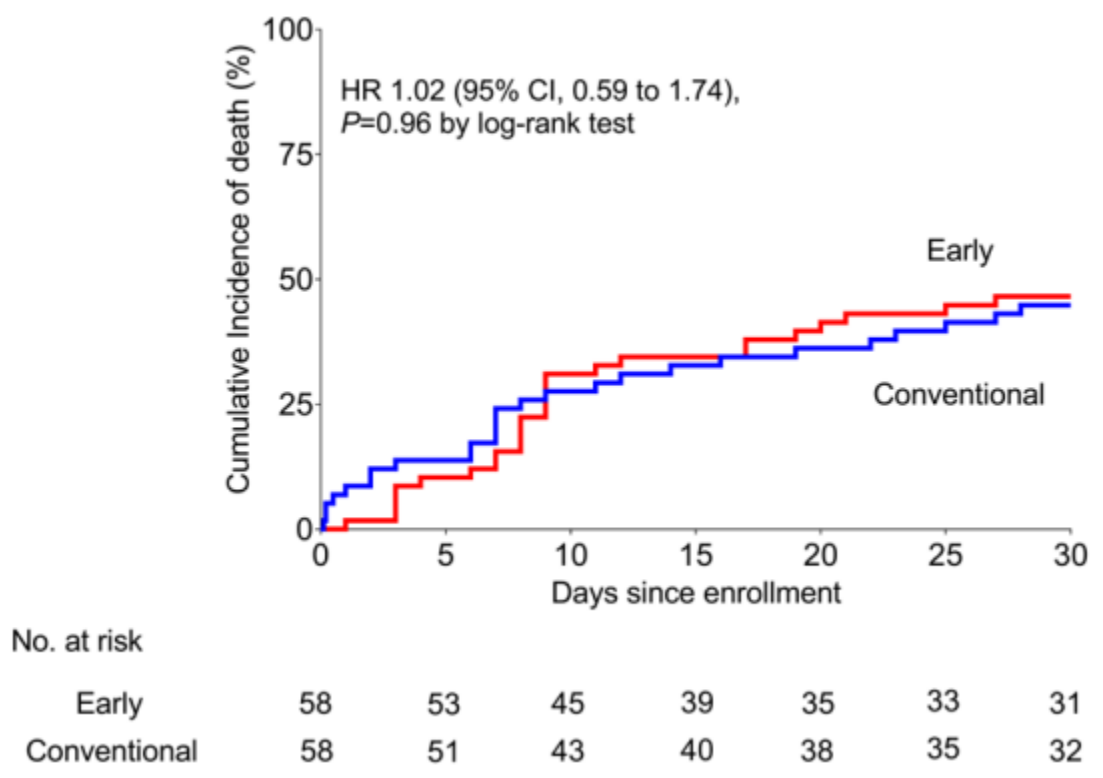
Circulation. 2023;148:1570-81.

Baseline characteristics

Characteristic	Total (N=116)	Early (N=58)	Conventional (N=58)	*P* value
Age, y	67.6±13.5	67.8±14.4	67.3±12.8	0.849
Men, n (%)	82 (70.7)	39 (67.2)	43 (74.1)	0.415
Body mass index, kg/m^2 (IQR)	23.6 (21.7 to 25.9)	23.5 (21.6 to 26.1)	23.6 (22.0 to 25.2)	0.753
Medical history, n (%)				
Hypertension	65 (56.0)	33 (56.9)	32 (55.2)	0.852
Diabetes	50 (43.1)	24 (41.4)	26 (44.8)	0.708
Current smoking	40 (34.5)	18 (31.0)	22 (37.9)	0.435
Cerebrovascular accident	11 (9.5)	5 (8.6)	6 (10.3)	0.751
Chronic kidney disease	21 (18.1)	13 (22.4)	8 (13.8)	0.228
Atrial fibrillation	15 (12.9)	7 (12.1)	8 (13.8)	0.782
Ischemic heart disease	25 (21.6)	8 (13.8)	17 (29.3)	0.042
Myocardial infarction	18 (15.5)	5 (8.6)	13 (22.4)	0.040
Percutaneous coronary intervention	22 (19.0)	7 (12.1)	15 (25.9)	0.058
Coronary artery bypass grafting	2 (1.7)	1 (1.7)	1 (1.7)	1.000
Causes of cardiogenic shock, n (%)				
Acute myocardial infarction	77 (66.4)	39 (67.2)	38 (65.5)	0.685
Decompensation of heart failure	16 (13.8)	6 (10.3)	10 (17.2)	
Fulminant myocarditis	10 (8.6)	6 (10.3)	4 (6.9)	
Others‡	13 (11.2)	7 (12.1)	6 (10.3)	

Circulation. 2023;148:1570-81.

All-cause mortality at 30 days



Circulation. 2023;148:1570-81.

Clinical outcomes

Outcome	Early (N=58)	Conventional (N=58)	Hazard ratio (95% CI)	*P* value
Primary outcome				
All-cause death†	27 (46.6)	26 (44.8)	1.02 (0.59–1.74)	0.942
Secondary outcomes				
Key secondary outcome				
All-cause death or rescue transseptal cannulation†	27 (46.6)	38 (65.5)	0.44 (0.27–0.72)	0.001
Other secondary outcomes				
Rescue transseptal cannulation†		29 (50.0)		
Cardiac death†	24 (41.4)	24 (41.4)	0.98 (0.56–1.73)	0.943
Noncardiac death†	3 (5.2)	2 (3.4)	1.48 (0.25–8.89)	0.665
In-hospital death	30 (51.7)	29 (50.0)	1.19 (0.70–2.02)	0.518
Weaning from VA-ECMO	32 (55.2)	31 (53.4)	1.06 (0.65–1.74)	0.809
Duration of VA-ECMO, d (IQR)	7 (4–10)	7 (4–12)		0.283
Disappearance of pulmonary congestion on chest x-ray imaging	41 (70.7)	43 (74.1)	0.72 (0.47–1.11)	0.137
Time to disappearance of pulmonary congestion, d (IQR)	3 (2–6)	5 (3–7)		0.027
Weaning from mechanical ventilator	23/41 (56.1)	24/41 (58.5)	0.85 (0.48–1.52)	0.584
Duration of mechanical ventilator, d (IQR)	5 (3–9)	4 (2–8)		0.225
Duration of in-hospital stay, d (IQR)				
Intensive care unit	10 (7–16)	8 (7–21)		0.771
In-hospital	17 (10–26)	16 (10–28)		0.802

Circulation. 2023;148:1570-81.

Clinical outcomes

Safety outcomes				
Critical limb ischemia	3 (5.2)	4 (6.9)	0.73 (0.16–3.26)	0.679
Infection	21 (36.2)	19 (32.8)	1.09 (0.58–2.04)	0.788
Stroke	6 (10.3)	5 (8.8)	1.23 (0.37–4.02)	0.734
BARC bleeding type 3 or 5	6 (10.3)	8 (13.8)	0.86 (0.29–2.57)	0.794
Transseptal cannulation-related complications				
Cardiac tamponade during transseptal cannulation	2 (3.4)	0		
Aorta injury	0	0		
Iatrogenic atrial septal defect#	3/36 (8.3)	0/16 (0)		

Circulation. 2023;148:1570-81.

Conclusion

- Among patients with cardiogenic shock undergoing VA-ECMO, early routine left ventricular unloading with transseptal left atrial cannulation did not reduce 30-day mortality compared with the conventional strategy.

- Further multicenter trials using other unloading modalities are warranted to investigate the efficacy of early routine left ventricular unloading.

Summary

- Peripheral VA-ECMO has an inherent limitation of increasing LV afterload, and subsequent pulmonary congestion.
- Several mechanical circulatory strategies can be used to achieve LV unloading if conservative measures prove to be insufficient.
- Many data indicate the benefit of LV unloading when overt complications of increased afterload are developed.
- Recent two RCTs did not support the systematic use of early LV unloading following VA-ECMO insertion.
- Further large-scale trials using other unloading modalities are warranted.