Early vs. Conventional LV unloading in VA-ECMO: The EVOLVE-ECMO trial

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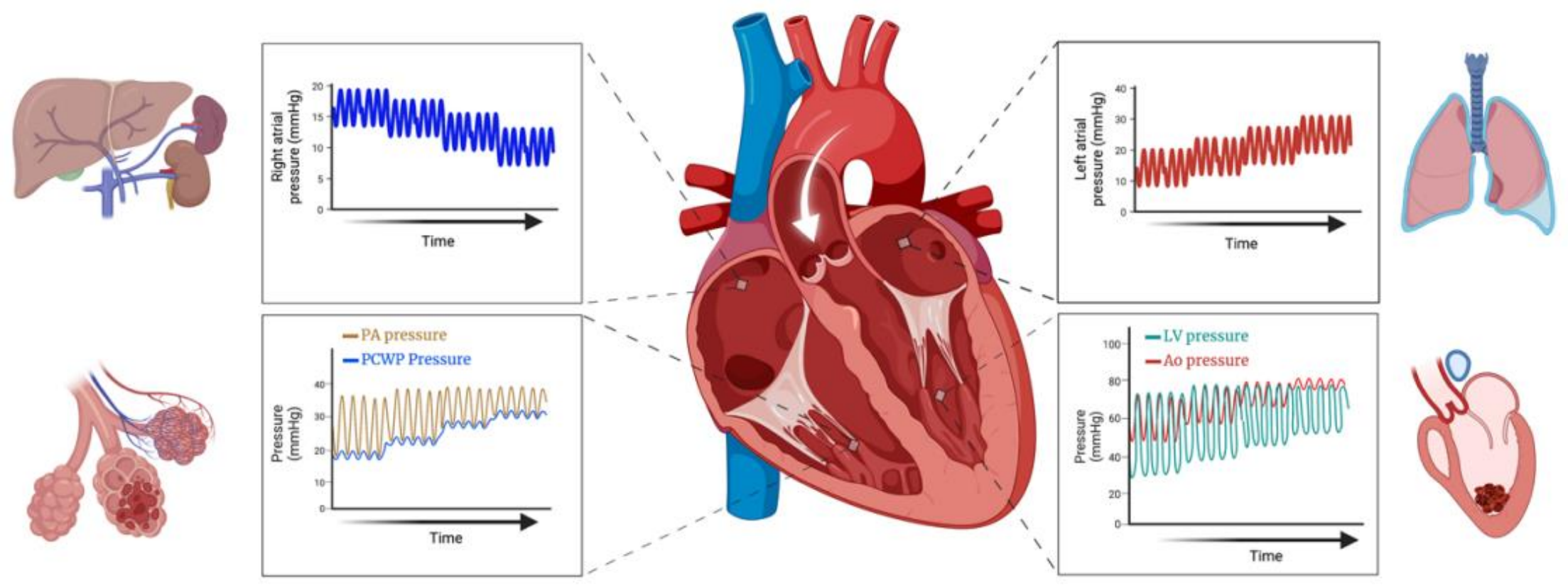
Disclosure

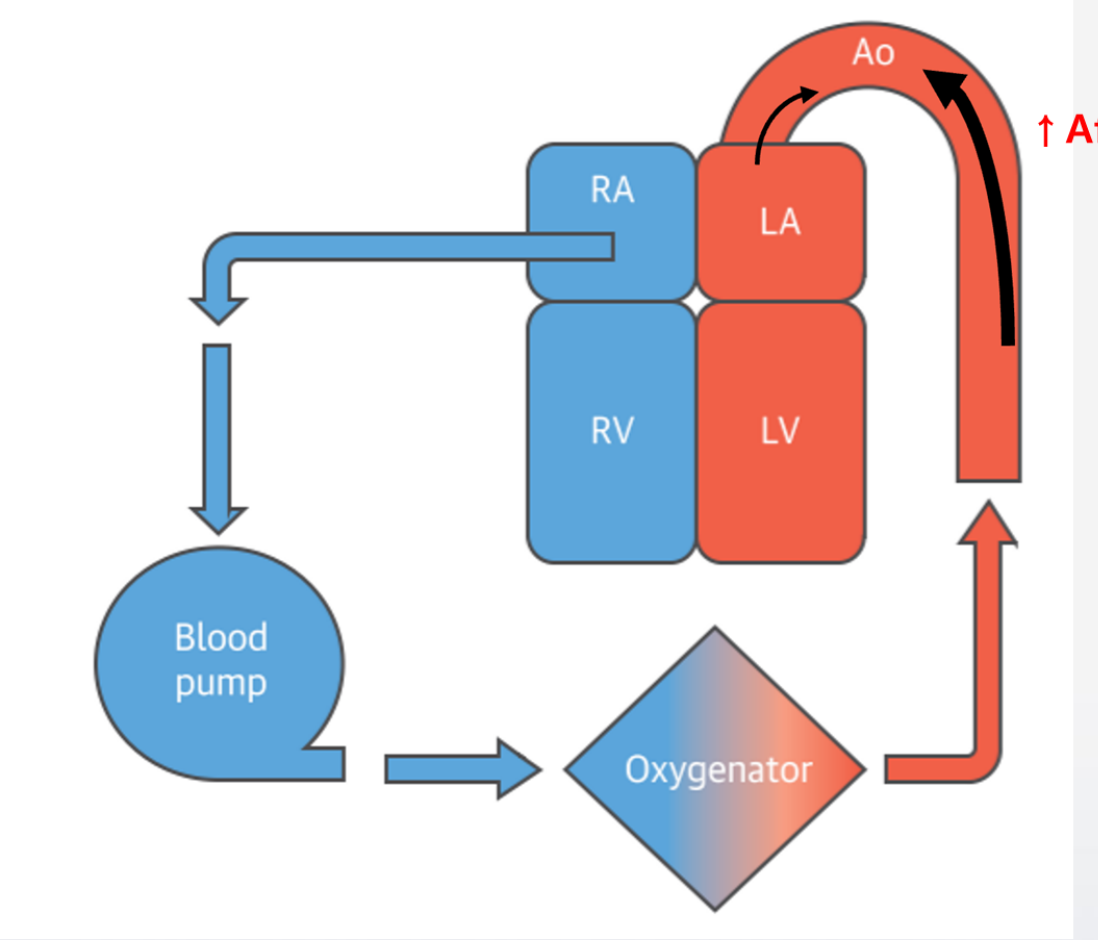
- I have nothing to disclose.

Hemodynamic effects of VA-ECMO



Circulation 2023;147:1237.

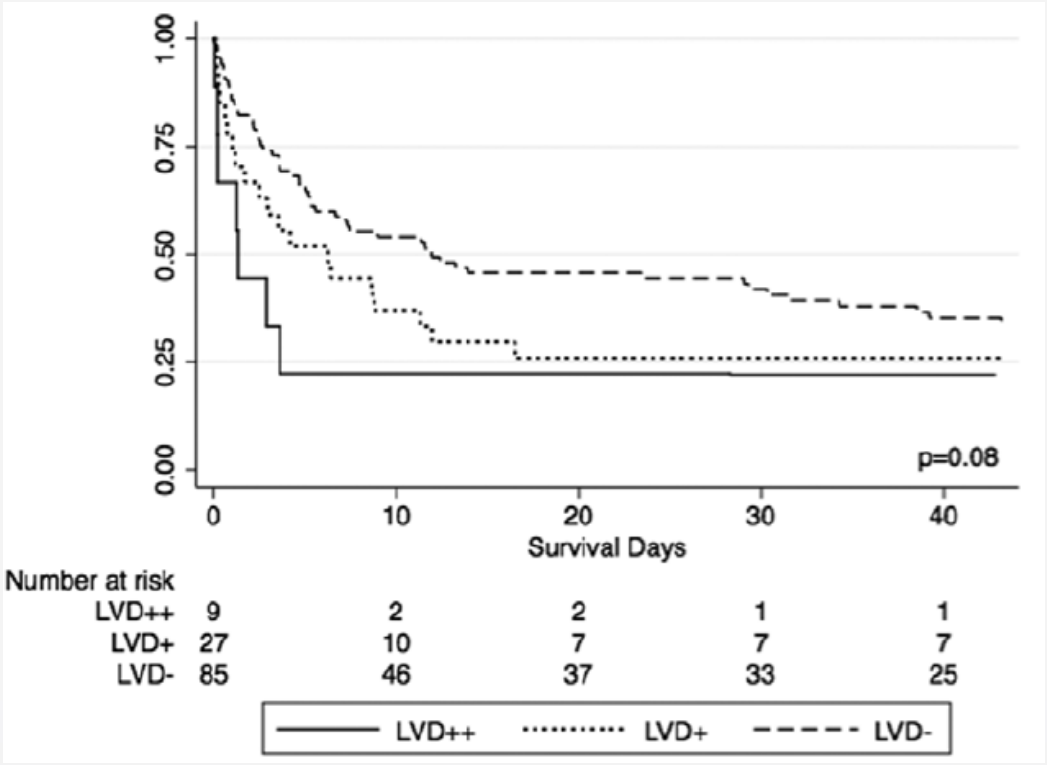
Consequences of LV distension

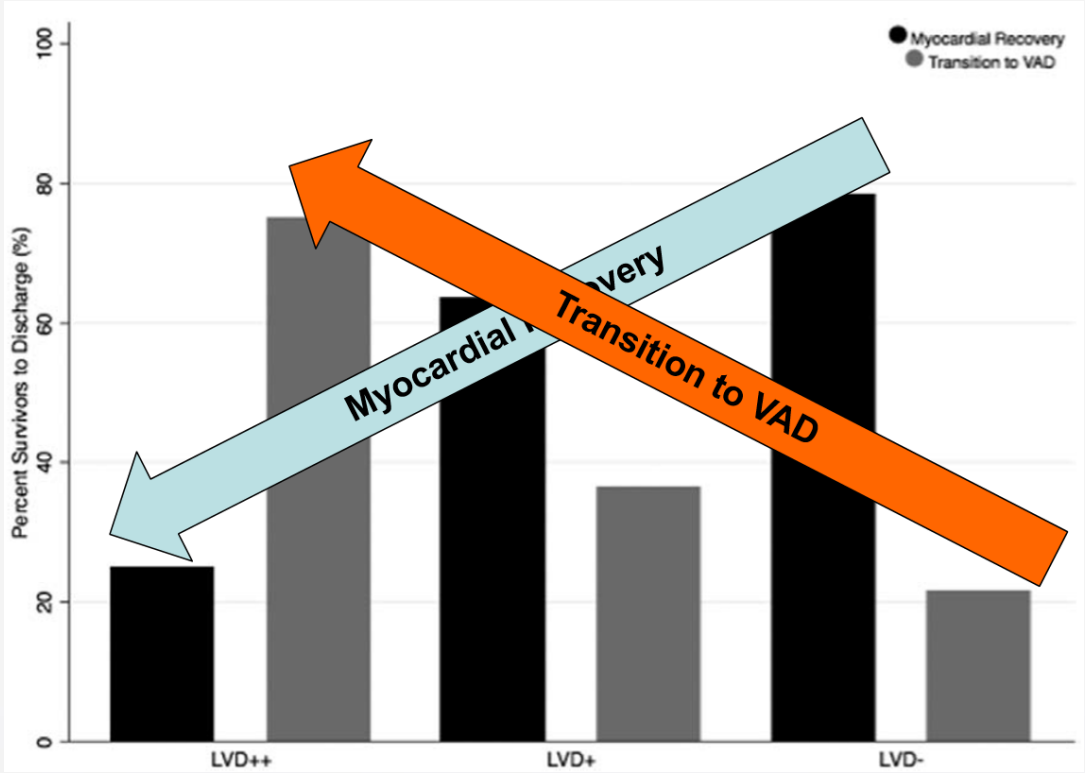


Intracardiac SEC/thrombi
Refractory pulmonary edema
Refractory ventricular arrhythmia

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.

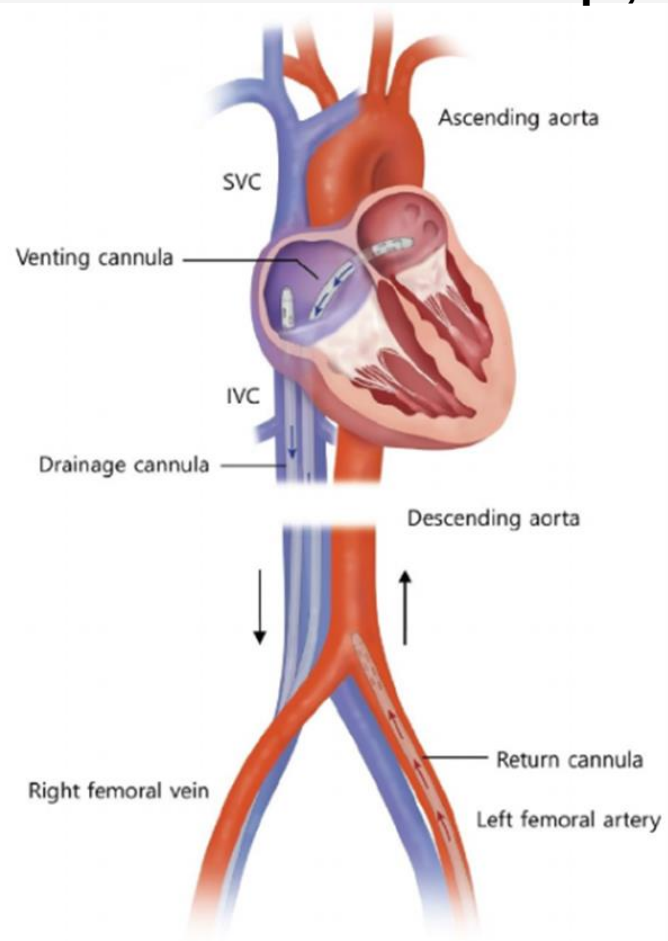
Percutaneous LV unloading modalities

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

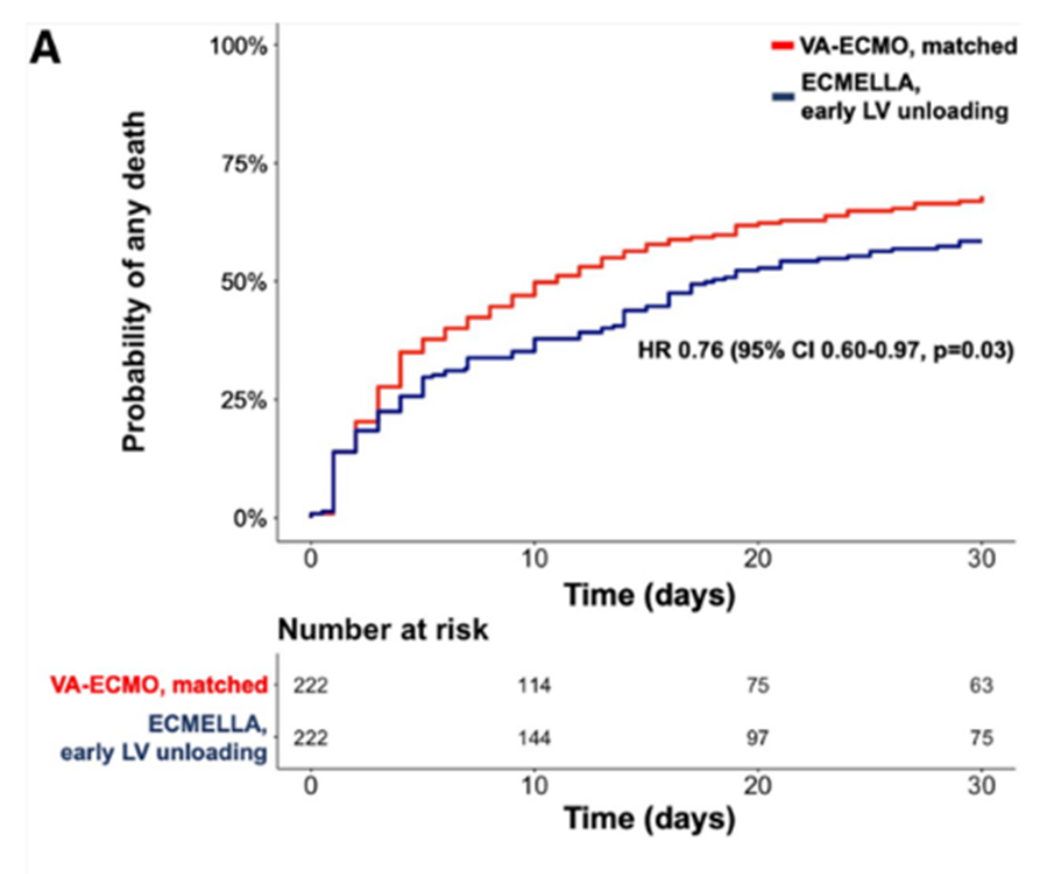
All data given as mean (95% CI) unless otherwise indicated.

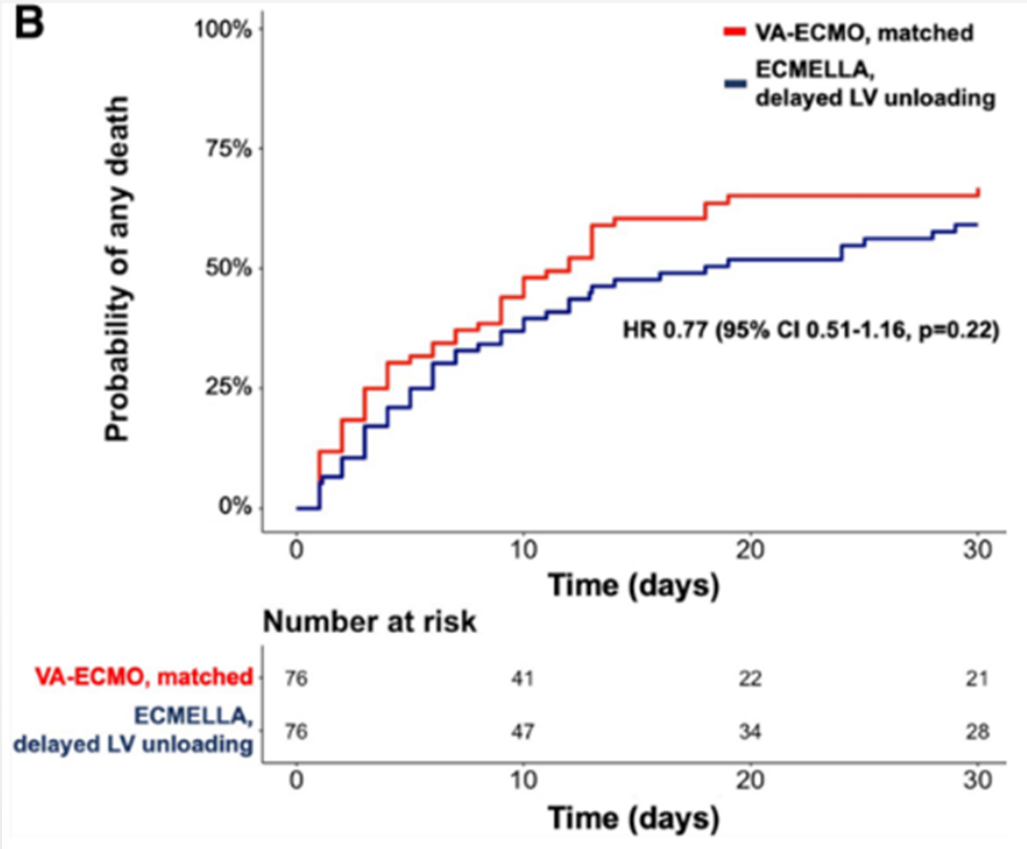
Artif Organs 2015;39(4):319-26.

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.

Early Left Atrial Venting Versus Conventional Treatment For LV Decompression During VA-ECMO :EVOLVE-ECMO trial

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

Study objectives

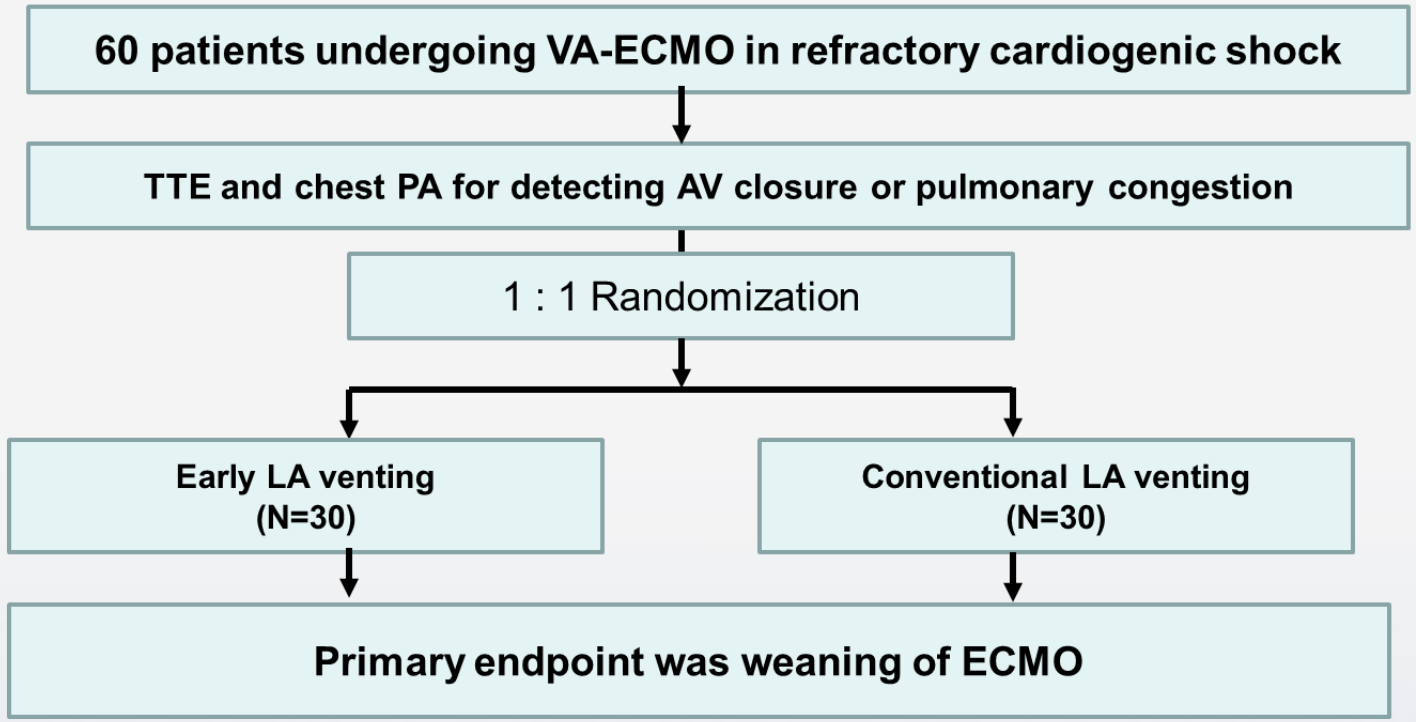
- To assess the feasibility of an early LV unloading strategy compared with a conventional strategy during VA-ECMO in patients with profound cardiogenic shock

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

Study design

Early Left Atrial **V**enting Versus C**o**nventional Treatment For **L**eft **VE**ntricular Distention During Venoarterial **E**xtra**C**orporeal **M**embrane **O**xygenation 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

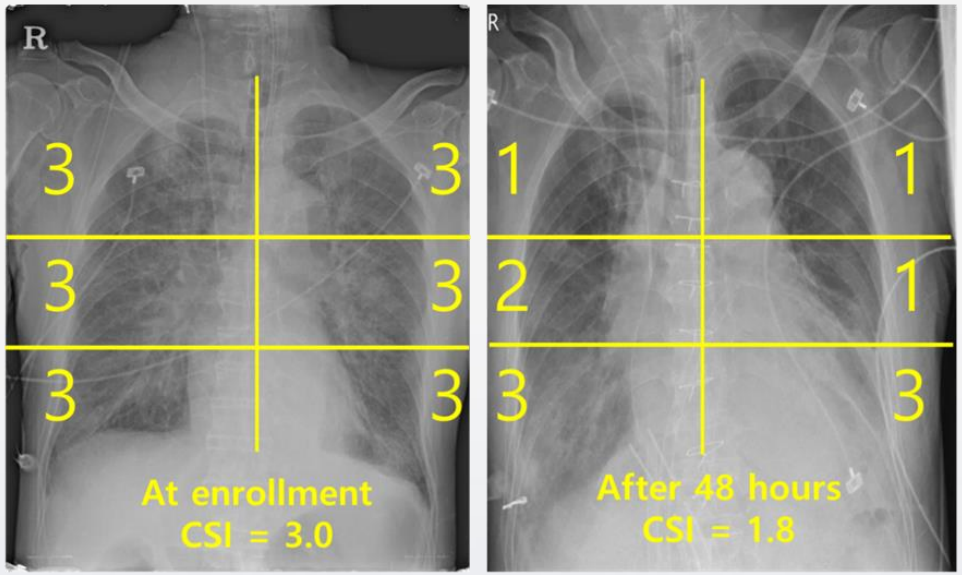
- The secondary endpoints
  - the rate of survival to discharge
  - successful HT or LV assist device (LVAD) implantation
  - the duration of mechanical ventilation (MV)
  - improvement of pulmonary edema
  - any adverse events related to the VA-ECMO

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

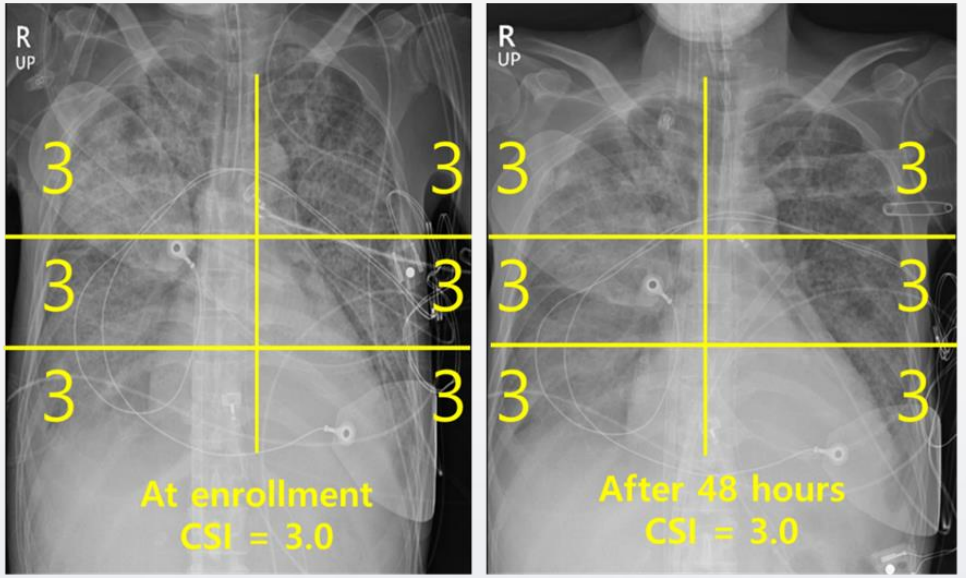
Evaluation of pulmonary edema: Congestion score index (CSI)

- Score 1: cephalization (superior area), perihilar haze or perivascular/peribronchial cuffing, or Kerley A lines (middle area), Kerley B, or C lines (inferior area)
- Score 2: interstitial alveolar localized/ mild alveolar pulmonary edema
- Score 3: intense alveolar pulmonary edema

Early group



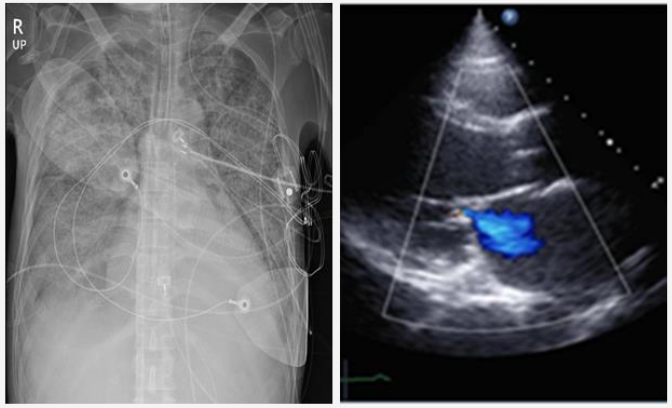
Conventional group



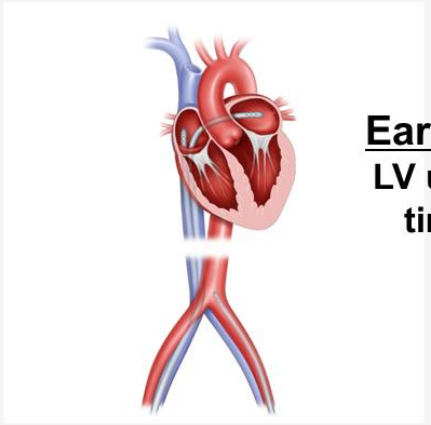
Eur J Heart Fail. 2023;25(11):2037-46.

Trial procedure

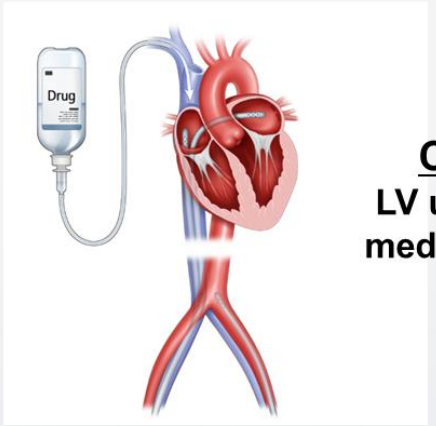
Profound cardiogenic shock during VA-ECMO



Randomization 1:1



Early LV unloading strategy
LV unloading performed at the time of VA-ECMO insertion



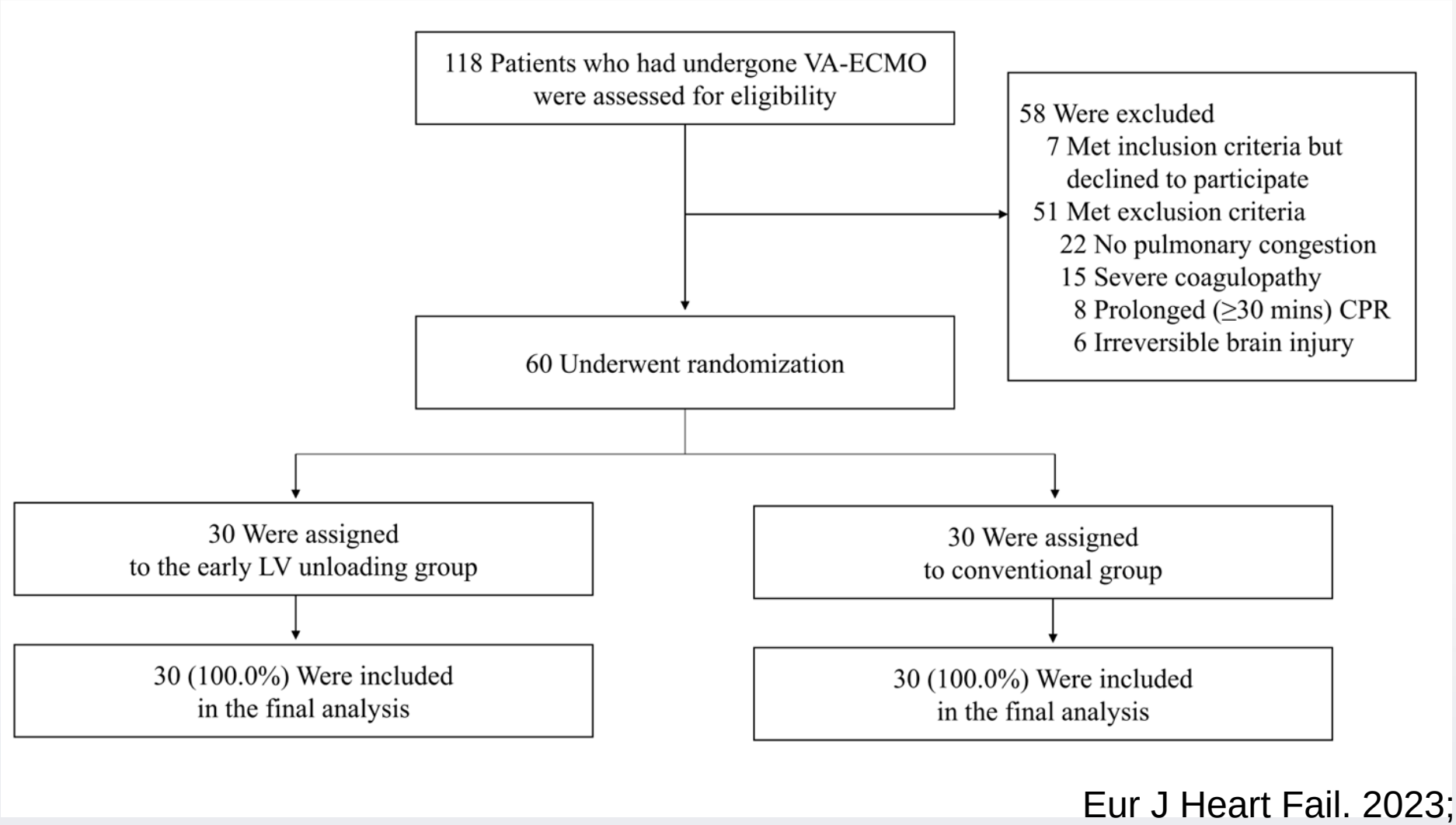
Conventional strategy
LV unloading performed when medically refractory pulmonary edema identified

Time to LV unloading:
Early: 2.4 hour, Conventional 48.4 hour

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

Study Flow

From December 2018 to August 2022, patients were enrolled in AMC and SMC



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.

Baseline characteristics

	Early group (n=30)	Conventional group (n=30)	P
Vital signs at randomization			
Systolic blood pressure, mmHg	95.8 ± 25.2	86.3 ± 17.2	0.099
Mean blood pressure, mmHg	77.9 ± 20.4	71.9 ± 15.1	0.206
Heart rate. /min	82.2 ± 28.0	93.8 ± 29.2	0.124
Laboratory data at randomization			
Leukocyte, x 1000/μL	11.4 ± 3.9	12.9 ± 5.6	0.230
Hemoglobin, g/dL	10.9 ± 2.8	10.9 ± 2.9	0.953
Platelet. x 1000/μL	192.3 ± 66.6	150.0 ± 98.2	0.055
PT, INR	2.2 ± 2.0	2.1 ± 2.8	0.852
C-reactive protein	6.5 ± 7.7	5.3 ± 5.6	0.536
Creatinine, mg/dL	1.8 ± 0.9	1.5 ± 0.9	0.282
BUN, g/dL	32.8 ± 22.4	30.9 ± 19.1	0.724
BNP, pg/mL	1034.0 [364.3-1737.8]	964.5 [501.5-4582.3]	0.768
Troponin I, ng/mL	1657.6 ± 7665.9	2209.5 ± 10214.8	0.830
Lactic acid, mmol/L	5.1 ± 4.2	5.3 ± 3.6	0.908
Echocardiographic data at randomization			
Left ventricular ejection fraction, %	24.2 ± 13.7	28.3 ± 13.2	0.316
Pulmonary edema 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

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

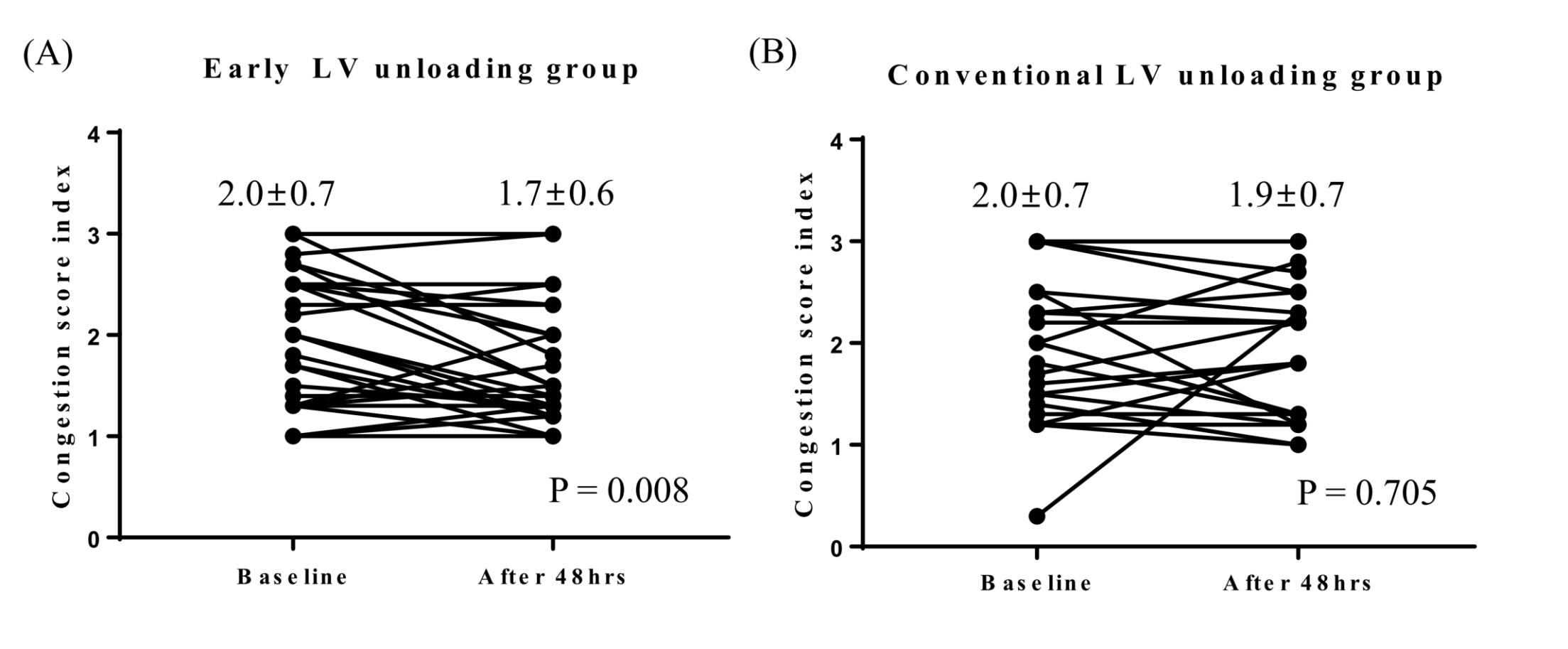
Eur J Heart Fail. 2023;25(11):2037-46.

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.

Change of pulmonary CSI from baseline to 48 hours after LV unloading



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

Limitation

- Small sample size and underpowered

  “Phase 2 trial”

- Impella® is not yet available in Korea

  “Previous studies indicated no interaction between the type of LV unloading and LV unloading, mortality”

Conclusion

- We found that our early LV unloading strategy did not increase the weaning rate from VA-ECMO compared with a conventional approach, , although it did rapidly improve pulmonary congestion.

- Our current findings therefore do not support the systematic use of early LV unloading following VA-ECMO insertion.

- However, these present analyses were 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.