Data S1. Supplemental Methods

VA-ECMO management protocol

VA-ECMO indications and management were based on our local protocol and available guidelines through a multidisciplinary team including cardiologists, intensivists, and cardiac surgeons. Briefly, VA-ECMO was discussed for RCS defined by persisting mismatch between oxygen supplies and tissue needs due to a pump dysfunction despite inotrope and/or vasopressor perfusion. In case of RCA, VA-ECMO implantation was discussed only for selected patients (≤ 70 yo, witnessed cardiac arrest, BMI < 40 kg/m², end-tidal CO2 > 10 mmHg, pH level > 6.9 and lactatemia < 25 mmol/L at ICU arrival). Contra-indications to VA-ECMO were common: age > 80 years; anticoagulation contraindication; severe peripheral artery disease; significant aortic regurgitation; life expectancy less than 5 years due to associated chronic or acute illness and severe post anoxic coma. Anticipated directives were also taken into consideration.

VA-ECMO was initiated under general anesthesia by femoral approach thanks to a modified Seldinger technique. The circuit used includes a venous inflow cannula (23 to 29 Fr) inserted up to the inferior vena cava-right atrium junction, a SORIN® centrifuge pump with a D905® oxygenator (or a MAQUET® centrifuge pump with a QUADROX® oxygenator), and an arterial outflow cannula (19 to 21 Fr) inserted up to the common iliac artery with systemic insertion of a reperfusion cannula (7 Fr) for the ipsilateral superficial femoral artery. The initial output is adjusted to the theoretical cardiac output (70/mL/kg/min) then to a target MAP ≥ 65 mmHg (after volume loading and vasopressors, if necessary). Inotrope support with dobutamine could be continued to maintain an aortic valve opening. Curative anticoagulation was started by intravenous unfractionated heparin for a target anti-Xa level between 0.2 and 0.4 IU/mL. The decision to wean the patient from VA-ECMO depends on a set of clinic-biological and ultrasound criteria assessed by daily weaning trial at a minimum VA-ECMO output of 1.5-2 L/min.

Characteristics of left heart decompression used (9)

The IABP (AutoCAT 2 Wave TELEFLEX®) is implanted in the descending aorta then connected to an electrocardiogram in order to inflate the balloon with helium during protodiastole and deflate it during telediastole, thereby reducing the LV afterload while increasing diastolic blood pressure (DBP) and thus coronary and cerebral perfusion.

The micro-axial flow pump Impella (Abiomed, Danvers, MA, USA) is a catheter-based LV assist device which is inserted into the LV cavity via arterial access (axillary or subclavian access in case of Impella 5.0, and femoral access in case of Impella CP). From that position, it actively drains blood from the LV and propels it into the proximal ascending aorta, thereby decreasing LV preload and increasing cardiac output.

Percutaneous atrioseptostomy (PA) involves creating a left-right shunt through perforation of the interatrial septum after femoral vein catheterization. PA was performed under fluoroscopic guidance in the hemodynamical or electrophysiological laboratories, with the help of trans-oesophageal echocardiography when needed. After femoral venous catheterization, transseptal puncture was performed according to usual techniques (10) with a SLO sheath (St Jude Medical™) and Brokenbrough needle, under common fluoroscopic landmarks and/or pressure monitoring. Of note that transseptal puncture was sometimes especially tricky in this situation, due to the presence of the ECMO venous canula, anticoagulation and dilated/distorted cardiac anatomy. Then an aortic valvuloplasty balloon (diameter 10 to 18 mm) was mounted over a 0.32 mm guidewire positioned in the left superior pulmonary vein. The sheath was then removed into the right atrium and the balloon was inflated at the level of the transseptal puncture in order to create an inter-atrial communication and thus maintain a significant left-right shunt (11).

The surgical decompression is the addition of a left intraventricular cannula to the venous circuit of the VA-ECMO by surgical approach: a transvalvular aortic cannula by a subclavian artery or axillary approaches, or directly through the LV by transapical thoracotomy or sternotomy.

The different LHD techniques were implemented and checked under x-ray and/or ultrasound guidance (transesophageal echo (TEE) or transthoracic echo (TTE)).
Table S1. Comparison of characteristics of cardiogenic shock or refractory cardiac arrest VA-ECMO patients with vs without left heart decompression

|                              | General population n=163 | Non-LHD group n=100 (61%) | LHD group n=63 (39%) | p-value |
|------------------------------|---------------------------|---------------------------|----------------------|---------|
| **Demographic data**        |                           |                           |                      |         |
| Male                         | 113 (69%)*                | 65 (65%)                  | 48 (76%)             | 0.133   |
| Age (years)                  | 55 (42 – 61) †            | 52 (36 – 62)              | 57 (47 – 60)         | 0.091   |
| BMI (kg/m²)                  | 25.9 (22.8 – 29.4)        | 25.3 (22 – 29)            | 26.6 (24 – 30)       | 0.071   |
| **Previous known heart disease** |                         |                           |                      |         |
| Ischemic                     | 61 (37%)                  | 29 (29%)                  | 32 (51%)             | 0.053   |
| Dilated                      | 20 (12%)                  | 11 (11%)                  | 9 (14%)              | 0.535   |
| Hypertrophic                 | 12 (7%)                   | 10 (10%)                  | 2 (3%)               | 0.105   |
| Valvular                     | 11 (7%)                   | 8 (8%)                    | 3 (5%)               | 0.424   |
| Tachycardia induced cardiomyopathy | 17 (10%)                  | 9 (9%)                    | 8 (13%)              | 0.453   |
| None                         | 50 (31%)                  | 32 (32%)                  | 18 (29%)             | 0.645   |
| **Cardiovascular risk factors** |                         |                           |                      |         |
| Hypertension                 | 54 (33%)                  | 32 (32%)                  | 22 (36%)             | 0.648   |
| Diabetes                     | 24 (15%)                  | 15 (15%)                  | 9 (14%)              | 0.901   |
| Smoking                      | 87 (53%)                  | 49 (49%)                  | 38 (60%)             | 0.160   |
| Dyslipidemia                 | 40 (25%)                  | 23 (23%)                  | 17 (27%)             | 0.527   |
| **Indication for VA-ECMO**   |                           |                           |                      |         |
| RCS / RCA                    | 110 (68%) / 53 (32%)      | 68 (68%) / 32 (32%)       | 42 (67%) / 21 (33%)  | 0.269   |
| **Etiology of the RCS**      |                           |                           |                      |         |
| End-stage heart failure      | 18 (11%)                  | 10 (10%)                  | 8 (13%)              | 0.799   |
| Recent myocardial infarction | 44 (27%)                  | 16 (16%)                  | 28 (44%)             | <0.001  |
| Drug overdose                | 13 (8%)                   | 13 (13%)                  | 0 (0%)               | 0.002   |
| Electrical storm             | 24 (15%)                  | 15 (15%)                  | 9 (14%)              | 0.999   |
| Other (pulmonary embolism, ARDS, etc.) | 31 (19%)                  | 24 (24%)                  | 7 (11%)              | 0.069   |
### Severity score at initiation

| Score | ENCOURAGE | SOFA | SAPS2 |
|-------|-----------|------|-------|
| Severity | 22 (14.2 – 27.8) | 21 (14 – 27) | 23 (17 – 28) | 0.425 |
| SOFA | 11 (9 – 13) | 12 (9 – 13) | 10 (9 – 12) | 0.192 |
| SAPS2 | 68.5 (55 – 79) | 68 (54 – 78) | 70 (57 – 80) | 0.571 |

### Therapeutics at initiation

| Therapeutics | ENCOURAGE | SOFA | SAPS2 | p-value |
|--------------|-----------|------|-------|---------|
| Noradrenaline | 94 (58%) | 62 (62%) | 32 (51%) | 0.144 |
| Adrenaline | 104/161 (65%) | 60/98 (61%) | 44 (70%) | 0.245 |
| Dobutamine | 60 (37%) | 32 (32%) | 28 (44%) | 0.135 |
| RRT | 7 (4%) | 7 (7%) | 0 (0%) | 0.146 |
| Mechanical ventilation | 149 (91%) | 94 (94%) | 55 (87%) | 0.132 |

### RCA before initiation of VA-ECMO

| RCA | ENCOURAGE | SOFA | SAPS2 | p-value |
|-----|-----------|------|-------|---------|
| Prior cardiac arrest | 93 (57%) | 56 (56%) | 37 (59%) | 0.747 |
| Out-of-hospital RCA | 36 (22%) | 25 (25%) | 11 (17%) | 0.342 |
| No flow > 5 min | 9/87 (10%) | 6/51 (12%) | 3/36 (8%) | 0.727 |
| Bilateral mydriasis at initiation | 35/149 (23%) | 28/94 (30%) | 7/55 (13%) | 0.018 |

### Clinical and biological data at initiation of VA-ECMO

| Parameter | ENCOURAGE | SOFA | SAPS2 | p-value |
|-----------|-----------|------|-------|---------|
| HR (bpm) | 73.5 (0 – 111) | 57 (0 – 115) | 90 (0 – 110) | 0.627 |
| MAP (mmHg) | 50 (0 – 67) | 50 (0 – 65) | 55 (0 – 70) | 0.383 |
| LVEF (%) | 10 (5 – 20) | 10 (5 – 25) | 10 (5 – 15) | 0.009 |
| Arterial blood pH | 7.21 (7.05 – 7.35) | 7.19 (7.03 – 7.35) | 7.22 (7.1 – 7.33) | 0.815 |
| PaO2 (mmHg) | 108 (74.7 – 267.5) | 113 (77 – 255) | 105 (72.7 – 279) | 0.947 |
| PaCO2 (mmHg) | 39.6 (30 – 49) | 39.2 (30.9 – 50.3) | 40 (29 – 47) | 0.593 |
| Lactatemia (mmol/L) | 7.1 (3.2 – 14.3) | 6.7 (3.8 – 14) | 8.3 (3 – 14.9) | 0.903 |
| Serum creatinine (µmol/L) | 135 (103 – 171.5) | 138 (103 - 177) | 127.5 (103 – 164) | 0.648 |
| ASAT (IU/L) | 184 (62.5 – 611.5) | 184 (79 – 612) | 229 (47 – 647) | 0.935 |
| ALAT (IU/L) | 107.5 (56 – 370.5) | 105 (48 – 403) | 112 (57 – 338) | 0.877 |
PT (%)  
\[ 55 \ (39 - 69) \quad 52.5 \ (40 - 69) \quad 55 \ (36 - 71) \ 0.977 \]

Hemoglobin (g/dL)  
\[ 12.5 \ (10.1 - 15.0) \quad 12.3 \ (10.2 - 14) \quad 12.6 \ (10.1 - 15.2) \ 0.508 \]

**Blood product transfusions during hospitalization**

| Blood product        | N (25% - 75%) | P (25% - 75%) | Q (25% - 75%) | p-value |
|----------------------|---------------|---------------|---------------|---------|
| pRBCs                | 8 (3 - 13)    | 6 (2 - 11)    | 10 (5 - 17)   | <0.001  |
| Fresh frozen plasma  | 2 (0 - 6)     | 0.5 (0 - 6)   | 3 (0 - 6)     | 0.063   |
| Platelet concentrates| 1 (0 - 8)     | 1 (0 - 7)     | 3 (0 - 12)    | 0.006   |

**Complications**

| Complication          | N (25%) | P (25%) | Q (25%) | p-value |
|-----------------------|---------|---------|---------|---------|
| Neurological complications | 40 (25%) | 23 (23%) | 17 (27%) | 0.583   |
| Sepsis                | 122 (75%) | 70 (70%) | 52 (83%) | 0.181   |
| RRT                   | 56 (34%) | 29 (29%) | 27 (43%) | 0.094   |
| LV thrombus           | 13 (8%)  | 7 (7%)   | 6 (10%)  | 0.768   |

**Evolution**

| Evolution                     | N (25% - 75%) | P (25% - 75%) | Q (25% - 75%) | p-value |
|-------------------------------|---------------|---------------|---------------|---------|
| Duration of ICU stay (days)   | 16.5 (11 – 28) | 13 (9 – 21) | 28 (15 – 40) | 0.007   |
| Length of hospital stay (days)| 36.5 (23.3 – 53.3) | 35 (21 – 51) | 41 (29 – 58) | 0.251   |
| Duration of VA-ECMO (days)    | 6 (4 - 10)    | 5 (3 – 7)    | 10 (6.3 – 16) | <0.001  |
| Weaning VA-ECMO               | 88 (54%)      | 54 (54%)     | 34 (54%)      | 0.9969  |
| Transplant or chronic assistance at 3 months | 15/160 (9%) | 9/98 (9%) | 6/62 (10%) | 0.921   |
| Death at D90                 | 101 (62%)     | 56 (56%)     | 45 (71%)      | 0.066   |

*Copied result N (%), N being the number of cases and (%) the ratio of cases over the total number, expressed as a percentage
† Copied result M (25 – 75P), M being the median and 25 – 75P the interquartile range
‡ When data are missing, the case/total ratio is indicated before the percentage ()

ALAT: alanin aminotransferase; ASAT: aspartate aminotransferase; ARDS: acute respiratory distress syndrome; bpm: beats per minute; BMI: body mass index; D: day; HR: heart rate; ICU: intensive care unit; LHD: left heart decompression; LV: left ventricle; LVEF: left ventricular ejection fraction; MAP: mean arterial pressure; pRBCs: packed red blood cells; PACO2: partial pressure of carbon dioxide; PaO2: partial pressure of oxygen; PT: prothrombin time; RCA: refractory cardiac arrest; RCS: refractory cardiogenic shock; RRT: renal replacement therapy; SAPS2: simplified acute physiology score 2; SOFA: sequential organ failure assessment; VA-ECMO: veno-arterial extracorporeal membrane oxygenation
Table S2. Progression of the variables of interest during the first 48 hours after introduction of the left heart decompression

|                      | Total LHD population (n=63) | Atrioseptostomy (n=26) | Other LHD (n=37) |
|----------------------|-----------------------------|------------------------|-----------------|
|                      | M(25-75p)                   | Friedmann test         | Friedmann test  | Friedmann test |
|                      | p                           | p<0.05 between variables | p<0.05 between variables | p<0.05 between variables |
| Lactatemia (mmol/L)  |                             |                        |                 |                 |
| H0†                 | 4.5 (1.7-8.8)               | (H48)                  | 3.0 (1.7 – 9.7) | NA‡             |
|                     |                             |                        | 2.8 (2 – 4.4)   | 3.8 (1.7 – 6.0) |
|                     |                             |                        | 1.9 (1.5 – 2.8) | 2.1 (1.5 – 4.3) |
| H24                 | 3.2 (1.7-4.9)               | **0.012**              | **0.103**       | NA              |
|                     |                             |                        | 2.8 (2 – 4.4)   | **0.017**       |
|                     |                             |                        | 2.1 (1.5 – 4.3) | NS              |
|                     |                             |                        | 2.1 (1.5 – 4.3) |
| H48                 | 2.1 (1.5-3.5)               | (H0)                   | 1.9 (1.5 – 2.8) | (H0)            |
|                     |                             | (H24)                  | 2.1 (1.5 – 4.3) | (H0)            |
| Arterial blood pH   |                             |                        |                 |                 |
| H0                  | 7.31 (7.23 - 7.430)         | (H24)                  | 7.31 (7.23 – 7.43) | 7.23 (7.12 – 7.34) |
|                     |                             | (H48)                  | 7.31 (7.23 – 7.43) | (H48)           |
|                     |                             |                        | 7.37 (7.34 – 7.44) | NS              |
|                     |                             |                        | 7.38 (7.29 – 7.42) | **0.011**       |
|                     |                             |                        | 7.42 (7.36 – 7.47) | (H0)            |
| H24                 | 7.38 (7.34 - 7.440)         | <**0.001**             | **0.029**       | 7.38 (7.29 – 7.42) |
|                     |                             |                        | 7.38 (7.29 – 7.42) | (H0)            |
|                     |                             |                        | NS              | (H0)            |
| H48                 | 7.43 (7.35 - 7.475)         | (H0)                   | 7.44 (7.38 – 7.48) | (H0)            |
|                     |                             | (H24)                  | 7.44 (7.38 – 7.48) | (H0)            |
| Total bilirubin (mmol/L) |                             |                        |                 |                 |
| H0                  | 13.2 (6.5 - 23.8)           | (H24)                  | 18.2 (11.8 – 34.6) | 14.3 (6.5 – 20.9) |
|                     |                             | (H48)                  | 18.2 (11.8 – 34.6) | (H48)           |
|                     |                             |                        | 23.9 (13 – 50.2)  | NS              |
|                     |                             |                        | 26.1 (14.5 – 36.1) | <**0.001**     |
|                     |                             |                        | 32.4 (21.5 – 45)  | (H48)           |
| H24                 | 18.2 (12.7 - 35.1)          | <**0.001**             | <**0.001**      | 26.1 (14.5 – 36.1) |
|                     |                             |                        | 26.1 (14.5 – 36.1) | (H24)           |
|                     |                             |                        | NS              | <**0.001**     |
|                     |                             |                        | 32.4 (21.5 – 45)  | (H48)           |
| H48                 | 24.5 (15.5 - 57.8)          | (H0)                   | 57.8 (21.8 – 89)  | (H0)            |
|                     |                             | (H24)                  | 57.8 (21.8 – 89)  | (H48)           |
| Hemoglobin (g/dL)   |                             |                        |                 |                 |
| H0                  | 11.6 (9.7 – 14)             | (H24)                  | 10.8 (9.2 – 12.8) | 12.4 (10.8 – 14.9) |
|                     |                             | (H48)                  | 10.8 (9.2 – 12.8) | (H48)           |
|                     |                             |                        | 12.4 (10.8 – 14.9) | (H48)           |
| H24                 | 10.0 (8.7 – 11.0)           | (H0)                   | 10.0 (8.7 – 11.0) | 9.9 (8.5 – 11.7) |
|                     |                             | (H24)                  | 9.9 (8.5 – 11.7)  | (H0)            |
|                     |                             |                        | 9.9 (8.5 – 11.7)  | (H0)            |
|                | H0       | H24      | H48       | H0       | H24      | H48       |
|----------------|----------|----------|-----------|----------|----------|-----------|
| **Platelets (G/L)** |          |          |           |          |          |           |
| H0             | 140 (107 – 219) | (H24)    | 121 (98 – 79) | (H48)    | 217 (155 – 335) | (H24)    |
| H24            | 108 (75 – 171)  | <0.001   | 103 (71 – 171) | 0.004    | NS       | <0.001    |
| H48            | 93 (76 – 119)   | (H0)     | 93 (85 – 121) | (H0)     | 94 (73 – 115)   | (H0)     |
| **Serum creatinine (µmol/L)** |          |          |           |          |          |           |
| H0             | 122 (91 – 161)  | NA       | 124 (78 – 168) | NA       | 124 (99 – 159) | NA       |
| H24            | 144 (87 – 201)  | 0.626    | 153 (99 – 205) | 0.781    | NA       | 0.715     |
| H48            | 131 (97 – 225)  | NA       | 129 (108 – 216) | NA       | 131 (87 – 259) | NA       |
| **Diuresis during the last 24 hours** |          |          |           |          |          |           |
| H0             | 1350 (275-2400) | (H24)    | 1350 (720 – 2455) | NA       | 413 (65 – 1495) | NA       |
| H24            | 1700 (809-2740) | 0.027    | 1540 (848 – 2425) | 0.277    | NA       | 1835 (615 – 2893) | 0.047† |
| H48            | 1308 (968-1850) | (H24)    | 1355 (998 – 2413) | NA       | 1550 (1005 – 2366) | NA       |

* H0; H24; H48: data at the time of LHD introduction; 24 hours after; 48 hours after
† Copied result M (25 – 75P), M being the median and 25 – 75P the interquartile range
‡ NA: not applicable
§ NS: non-significant
† Significant Friedman test but multiple comparisons of non-significant pairs
Table S3. Characteristics that affect 90-day mortality for VA-ECMO patients with left heart decompression based on multivariable Cox proportional-hazard model

| Covariate                                      | Exp(b)* | 95% CI of Exp(b) | p-value |
|------------------------------------------------|---------|------------------|---------|
| Percutaneous atrioseptostomy (vs others LHD)   | 2.53    | 1.17 to 5.45     | 0.019   |
| Prior cardiac arrest                           | 0.80    | 0.42 to 1.53     | 0.504   |
| Tachycardia induced cardiomyopathy             | 1.50    | 0.50 to 4.44     | 0.469   |
| BMI (kg/m²)                                    | 1.01    | 0.95 to 1.08     | 0.781   |

BMI, body mass index; CI confidence interval; LHD, left heart decompression

*For a continuous covariate, Exp(b) is the increase of the hazard ratio for 1 unit change of the continuous variable. Note that when b is negative, then Exp(b) is less than 1 and Exp(b) is the decrease of the hazard ratio for 1 unit change of the continuous variable. For a dichotomous covariate, Exp(b) is the hazard ratio.*
Table S4. Characteristics that affect 90-day mortality for VA-ECMO patients with left heart decompression based on multivariable Cox proportional-hazard model 2

| Covariate                                    | Exp(b) | 95% CI of Exp(b) | p-value |
|----------------------------------------------|--------|------------------|---------|
| Percutaneous atrioseptostomy (vs others LHD) | 1.99   | 1.03 to 3.85     | 0.041   |
| Time under MV before LHD performance (days)  | 0.99   | 0.61 to 1.61     | 0.982   |
| Recent myocardial infarction                 | 1.16   | 0.63 to 2.16     | 0.637   |
| Curative LHD indication (vs prophylactic)    | 1.05   | 0.55 to 2.04     | 0.876   |

CI confidence interval; LHD, left heart decompression; MV, mechanical ventilation

*For a continuous covariate, Exp(b) is the increase of the hazard ratio for 1 unit change of the continuous variable. Note that when b is negative, then Exp(b) is less than 1 and Exp(b) is the decrease of the hazard ratio for 1 unit change of the continuous variable. For a dichotomous covariate, Exp(b) is the hazard ratio.)*
Figure S1. Kaplan-Meier curves describing 90-day survival for patients on VA-ECMO for cardiogenic shock or refractory cardiac arrest with (red) vs without (blue) left heart decompression.

Decompressed patients associated each patient one or more left heart decompression technique used during VA-ECMO support. Time is provided in days. “p-value” is unadjusted. LHD, left heart decompression.
Figure S2. Kaplan-Meier curves describing survival at 90-day for patients on VA-ECMO according to curative (blue) vs prophylactic (green) left heart decompression indication for decompressed patients

In case of refractory and critical pulmonary congestion, a “curative” LHD was introduced. In case of severely depressed left ventricular ejection fraction (LVEF), low differential arterial pressure (<5-10 mmHg), major distention of the left ventricle, or absence of aortic valve opening, a “preventive” LHD was considered. Time is provided in days. “p-value” is unadjusted. LHD, left heart decompression.