
# Impact of drainage cannula size and blood flow in VV-ECMO

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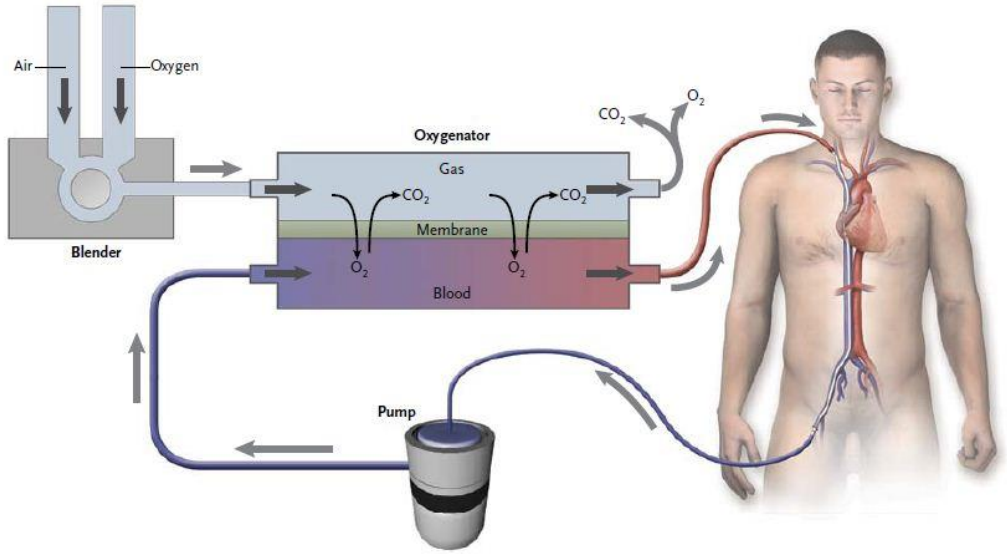
Plug group

the PLUG

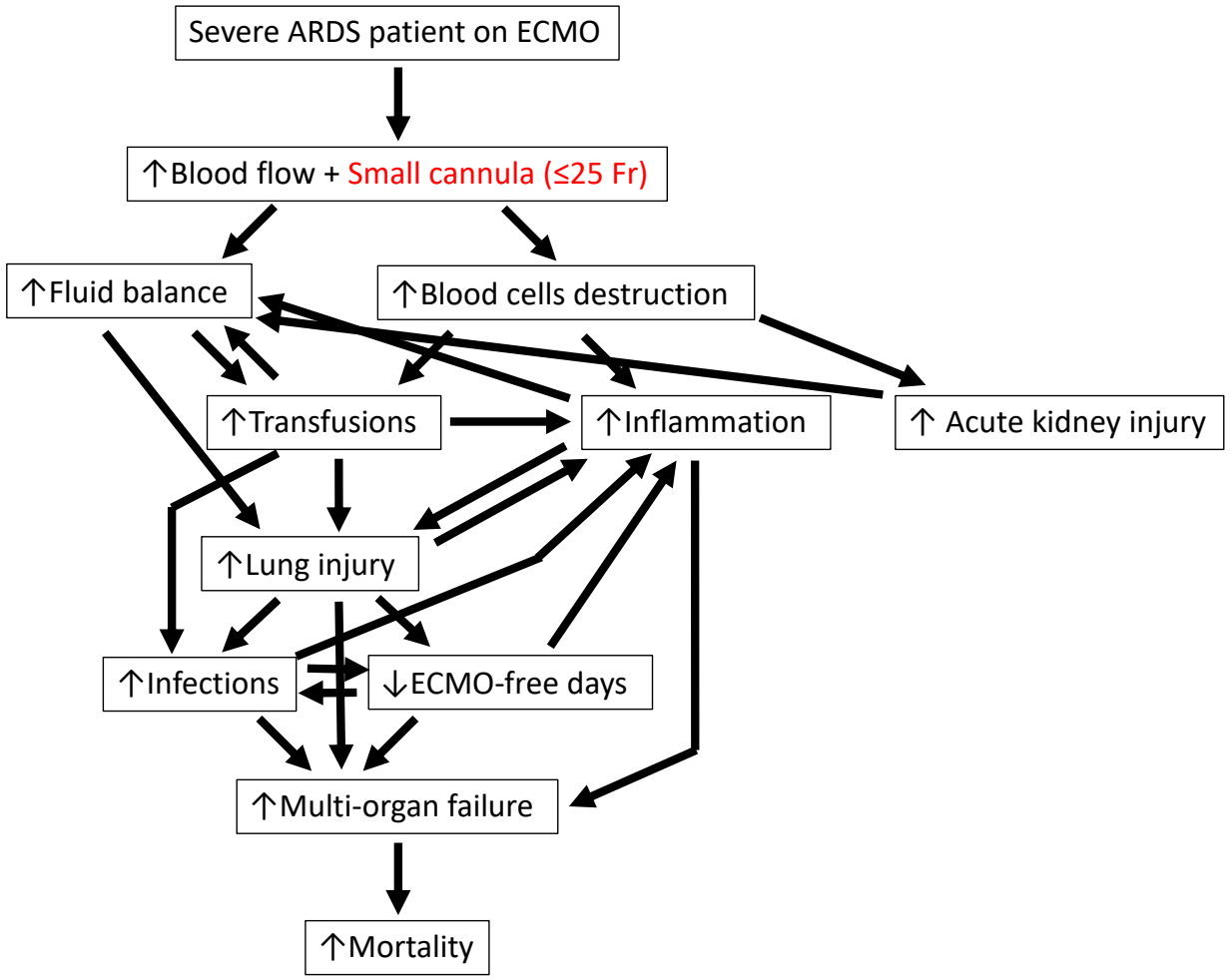
# ECMO: a powerful modulator of physiology

Physiologic effects of ECMO are not limited to improved gas exchange:

1. *Ventilation* can be modulated to avoid VILI and PSILI
2. *Drainage cannula size* can impact inflammation and fluid balance
3. *Blood flow* could impact V/Q mismatch and pulmonary circulation

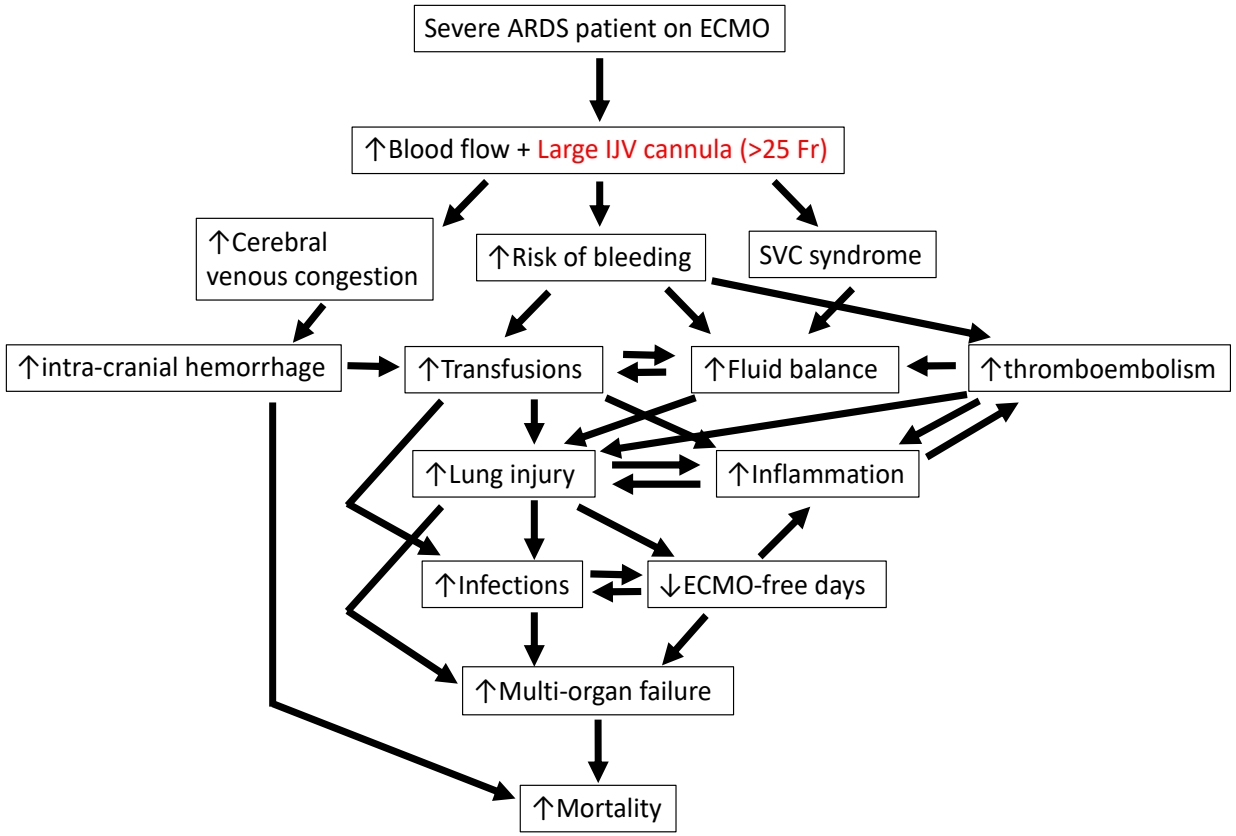


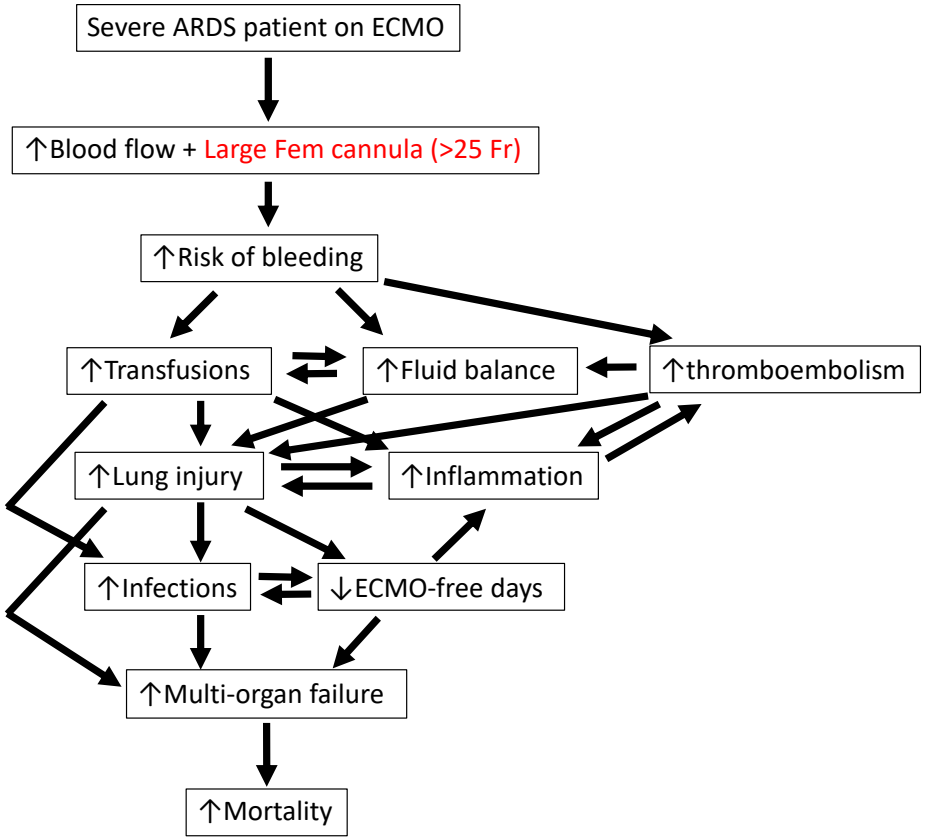
# Risks of small drainage cannula size




Specific risks: need of higher volemia to maintain blood flow, very low negative drainage pressure causing hemolysis

# Risks of large drainage cannula size




Specific risks: bleeding, cerebral venous congestion for jugulo-femoral or single site IJV

LARGE vs SMALL: EQUIPOISE??

# Cannula size is associated with mortality

**Extracorporeal membrane oxygenation network organisation and clinical outcomes during the COVID-19 pandemic in Greater Paris, France: a multicentre cohort study**

*Guillaume Lebreton, Matthieu Schmidt, Maharajah Ponnaiah, Thierry Folliguet, Marylou Para, Julien Guihaire, Emmanuel Lansac, Edouard Sage, Bernard Cholley, Bruno Mégarbane, Pierrick Cronier, Jonathan Zarka, Daniel Da Silva, Sebastien Besset, Igor Lacombat, Nicolas Mongardon, Christian Richard, Jacques Duranteau, Charles Cerf, Gabriel Saiydoun, Romain Sonneville, Jean-Daniel Chiche, Patrick Nataf, Dan Longrois, Alain Combes, Pascal Leprince, and the Paris ECMO-COVID-19 investigators**

| | All patients (n=302) | Survival status 90 days after ECMO | | p value |
|---|---|---|---|---|
| | | Alive (n=138) | Dead (n=164) | |
| Venovenous ECMO | 288 (95%) | 133 (96%) | 155 (95%) | 0·44 |
| Femoro–jugular | 273 (90%) | 130 (94%) | 143 (87%) | 0·43 |
| Femoro–femoral | 15 (5%) | 3 (2%) | 12 (7%) | 0·020 |
| Diameter of the admission cannula, Fr | 25 (25–29) | 29 (25–29) | 25 (24–29) | 0·017 |
| Diameter of the return cannula, Fr | 21 (19–21) | 21 (19–21) | 21 (19–21) | 0·28 |
| Venoarterial or venoarterial–venous ECMO | 14 (5%) | 5 (4%) | 9 (5%) | 0·44 |
| Femoro–femoral venoarterial ECMO | 10 (3%) | 3 (2%) | 7 (4%) | 0·21 |
| Femoro–subclavian venoarterial ECMO | 1 (<1%) | 1 (1%) | 0 | NA |
| Femoro–femoro–jugular venoarterial–venous ECMO | 3 (1%) | 1 (1%) | 2 (1%) | 0·56 |
| ECMO blood flow, L/min | 5·0 (4·4–5·5); n=287 | 5·0 (4·3–5·4); n=134 | 5·0 (4·5–5·4); n=153 | 0·38 |
| Sweep gas flow, L/min | 6 (4–8); n=285 | 5 (4–7); n=130 | 6 (4–8); n=155 | 0·0098 |

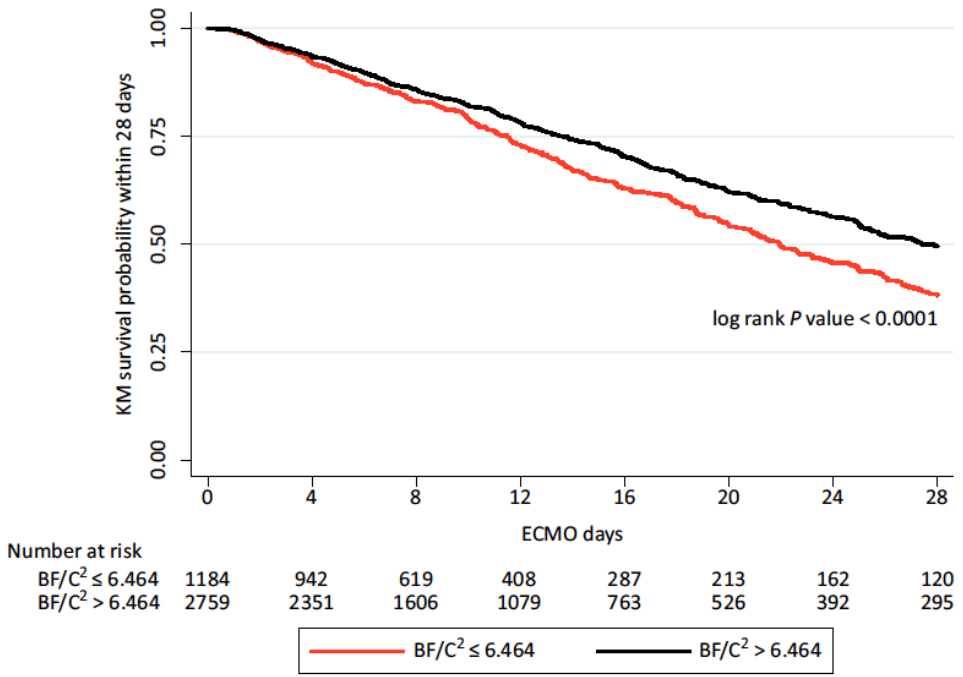
| | Odds ratio (95% CI) | p value |
|---|---|---|
| Age, years | .. | 0·012 |
| ≤48 | 2·89 (1·41–5·93) | .. |
| 49–56 | 2·01 (1·01–3·99) | .. |
| ≥57 | 1 (ref) | .. |
| Pre-ECMO renal component of the SOFA-II score, per point increase | 0·67 (0·55–0·83) | 0·0003 |
| Time between intubation and ECMO, per day decrease | 0·91 (0·84–0·99) | 0·022 |
| Centre with ≥30 venovenous ECMOs in previous year | 2·98 (1·46–6·04) | 0·0026 |

ECMO for COVID in Paris: survivors had larger drainage cannula size, same blood flow, lower gas flow (lower VCO2 or lower dead space of the NL?)

In multivariate analysis, cannula size disappeared inside centre experience?

*Lebreton et al Lancet Resp Med 2021*

# Cannula size vs. blood velocity within the cannula




| Outcome: In-Hospital Mortality within 28 d | Adjusted HR (95% CI) | *P* Value |
|---|---|---|
| $BF/C^2$, per 10-ml/(min*$F^2$) increase | 0.53 (0.28–0.99) | 0.046 |
| Cannula size, per 1-F increase | 1.00 (0.95–1.06) | 0.979 |
| Age, per 10-yr increase | 1.20 (1.12–1.28) | <0.001 |
| Female sex | 0.90 (0.74–1.10) | 0.294 |
| BMI, per 5-kg/$m^2$ increase | 0.95 (0.90–1.01) | 0.076 |
| Days of ventilation before ECMO start | 1.00 (0.98–1.01) | 0.592 |
| Pre-ECMO $Pa_{O_2}/FI_{O_2}$, per 25-unit increase | 1.01 (0.97–1.04) | 0.719 |
| $Pa_{O_2}/FI_{O_2}$ at 24 h, per 25-mm Hg increase | 1.00 (0.98–1.01) | 0.588 |
| Use of vasoactive drugs before ECMO | 1.10 (0.90–1.35) | 0.339 |
| Geographical location | | |
| North America (reference category) | 1 | – |
| Latin America | 0.95 (0.58–1.57) | 0.850 |
| Europe | 0.73 (0.57–0.95) | 0.017 |
| Asia-Pacific | 0.96 (0.71–1.30) | 0.804 |
| Southwest Asia | 1.11 (0.79–1.55) | 0.558 |
| Year of enrollment | | |
| 2012–2016 (reference category) | 1 | – |
| 2017 | 1.18 (0.82–1.71) | 0.373 |
| 2018 | 1.30 (0.91–1.85) | 0.153 |
| 2019 | 0.85 (0.59–1.22) | 0.382 |
| 2020 | 1.45 (1.00–2.09) | 0.049 |
| 2021 | 1.12 (0.72–1.74) | 0.612 |

*Mauri T et al Am J Resp Crit Care Med 2021*

ml/min/$Fr^2$ → 5 l/min with 27 Fr → 5000/729 = 6.85 (proxy for distance/time inside the cannula)

ELSO registry, 3535 ARDS patients, dual site cannulation, no COVID

$BF/C^2$ but not cannula size was an independent predictor of mortality after adjustment for age, sex, BMI, days of MV before ECMO, PF ratio before ECMO, shock, world region, calendar year

Interestingly, Europe was protective and year 2020 was more dangerous

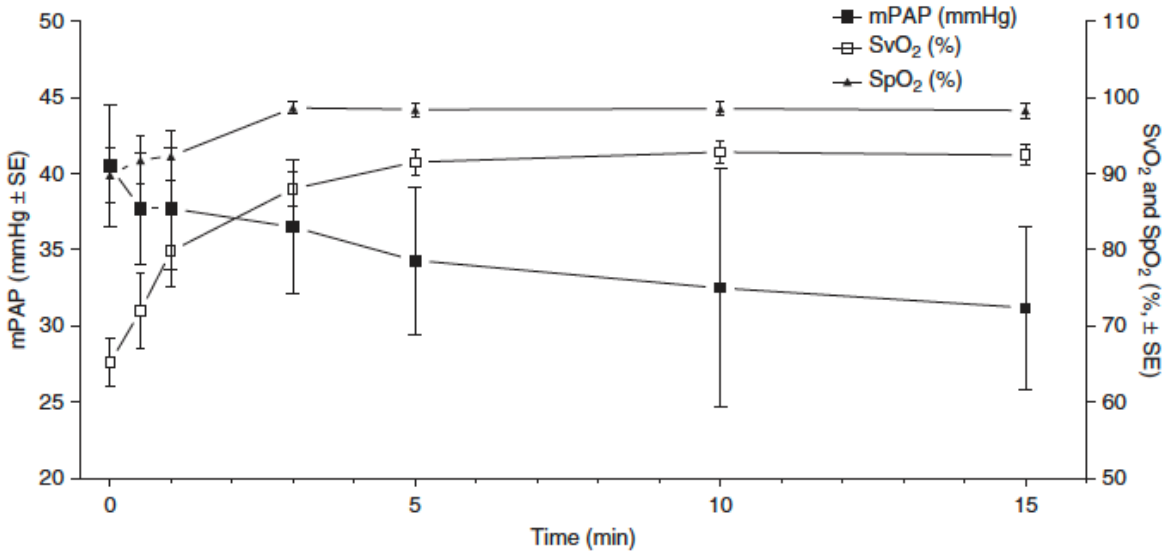
# Cannula size or ECMO blood flow?

- Both large and smaller cannulas carry intrinsic risks
- The key could be blood flow
- Once you choose your drainage cannula size, try to increase the blood flow as much as possible
- To obtain $BF/C^2 > 6.464$:

| Cannula size (Fr) | Minimal blood flow (l/min) |
|---|---|
| 21 | 2.85 |
| 23 | 3.42 |
| 25 | 4.04 |
| 27 | 4.71 |
| 29 | 5.44 |
| 31 | 6.21 |

# «Positive» effects of ECMO blood flow?

Reis Miranda D, AJRCCM 2015




Spinelli E, ASAIO J 2020

**Table 3. Changes in Clinical Parameters Associated with ECMO Initiation**

| Characteristic | Before ECMO (N = 20) | At Day 1 (N = 20) | *p*-values |
|---|---|---|---|
| Arterial pH | 7.249 (7.208–7.353) | 7.380 (7.363–7.425) | <0.001 |
| $PaCO_2$ (mmHg) | 65±19 | 46±8 | <0.001 |
| $PaO_2$ (mmHg) | 69 (63–87) | 86 (67–111) | 0.009 |
| Arterial lactate (mmol/l) | 1.5 (1.2–2.4) | 1.6 (1.1–3.0) | 0.298 |
| Shunt venous admixture (%) | 41±13 | 54±18 | 0.005 |
| $SvO_2$ (%) | 68±11 | 84±7 | 0.001 |
| Tidal volume—ml/kg PBW | 6.5±1.5 | 3.9±2.1 | 0.005 |
| Respiratory rate (bpm) | 25±5 | 9±2 | <0.001 |
| PEEP (cm $H_2O$) | 13±4 | 17±4 | 0.001 |
| Plateau pressure (cm $H_2O$) | 31±3 | 28±3 | <0.001 |
| Driving pressure (cm $H_2O$) | 18±4 | 11±4 | <0.001 |
| $FiO_2$ (ventilator) (%) | 86±17 | 75±20 | 0.016 |
| Respiratory-system compliance (ml/cm $H_2O$) | 21 (18–24) | 21 (16–30) | 0.146 |
| PAPs (mmHg) | 46±11 | 40±12 | 0.001 |
| PAPm (mmHg) | 34±9 | 31±8 | 0.042 |
| PAPd (mmHg) | 26±6 | 24±7 | 0.062 |
| Wedge pressure (mmHg) | 17±4 | 16±4 | 0.906 |
| Cardiac output (L/min) | 7.4±2.1 | 7.7±1.9 | 0.276 |

ECMO, extracorporeal membrane oxygenation; PAPd, diastolic pulmonary artery pressure; PAPm, mean pulmonary artery pressure; PAPs, systolic pulmonary artery pressure; PBW, predicted body weight; PEEP, positive end-expiratory pressure.

After ECMO start, PAPs could decrease

However, upon start of ECMO, there are a number of mechanisms that could impact PAPs: $SvO_2$, $PvCO_2$ and pH directly improve PAPs, decreased driving and mean airways pressure lowers RV afterload and pulmonary vascular compression

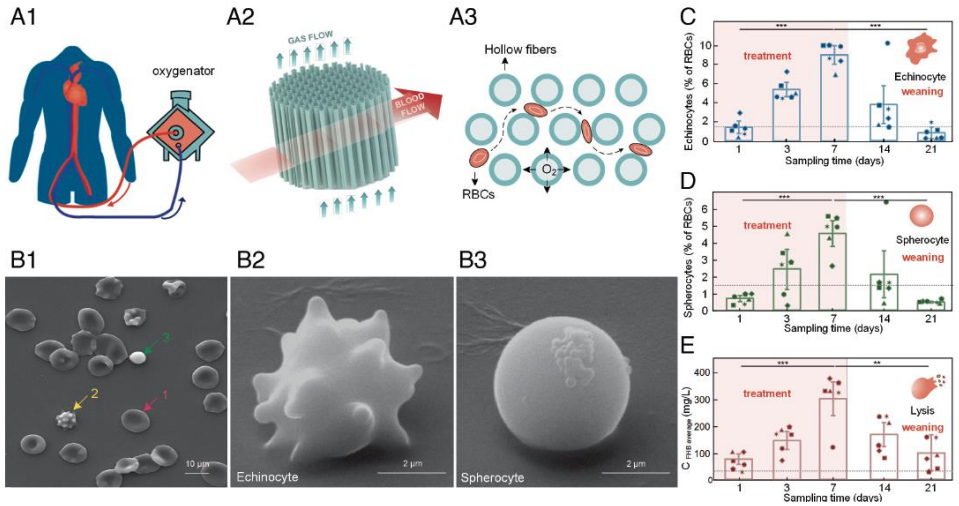
# «Negative» effects of ECMO blood flow?

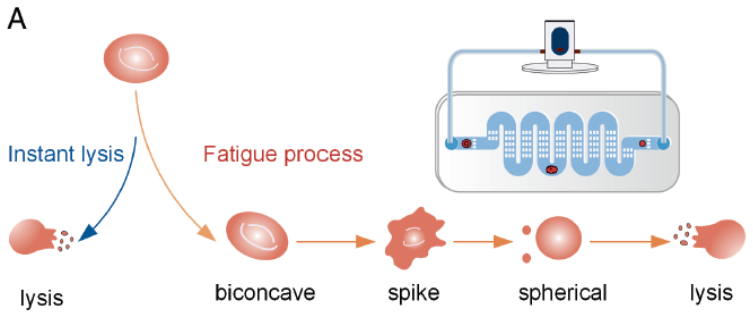
PNAS RESEARCH ARTICLE | ENGINEERING MEDICAL SCIENCES

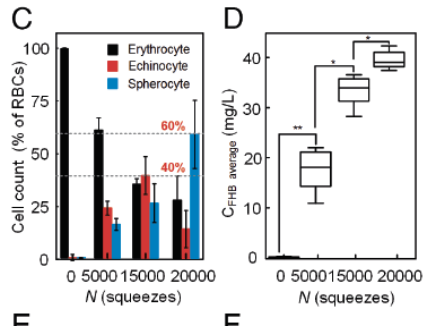
## Fatigue of red blood cells under periodic squeezes in ECMO

Yunfan Pan[a,1], Yan Li[a,1], Yongjian Li[a], Jiang Li[b], and Haosheng Chen[a,2]

Edited by David Weitz, Harvard University, Cambridge, MA; received June 25, 2022; accepted October 26, 2022



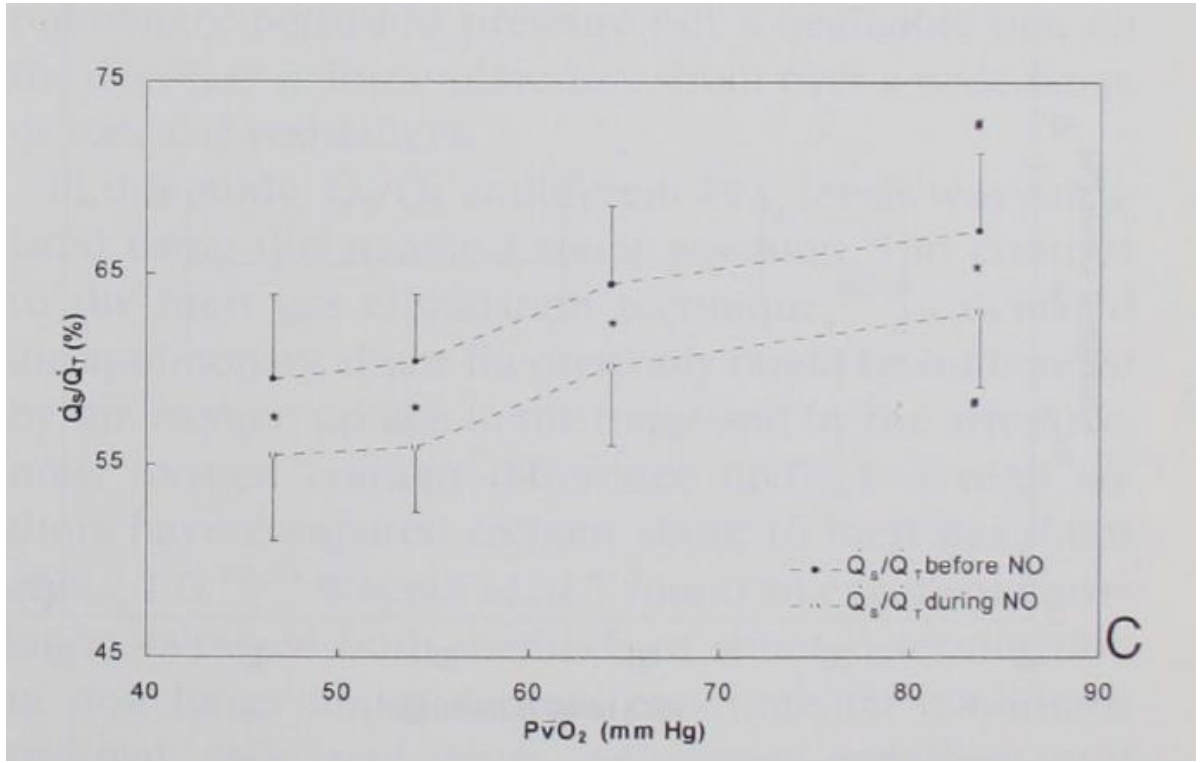




Periodic squeeze of RBCs by the oxygenator fibres induces reduction of intracellular ATP, transformation in spherocytes and lysis → inflammation → lung injury and multiorgan failure

The more the squeezes (higher blood flow vs. prolonged time on ECMO) the more lysis

# «Negative» effects of ECMO blood flow?




Benzing A, Anesthesiology 1997

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Spinelli E, ASAIO J 2020

Higher $PvO_2$ blunts hypoxic pulmonary vasoconstriction and could increase intrapulmonary shunt

Pulmonary function (oxygenation and $CO_2$ removal) could worsen on ECMO?

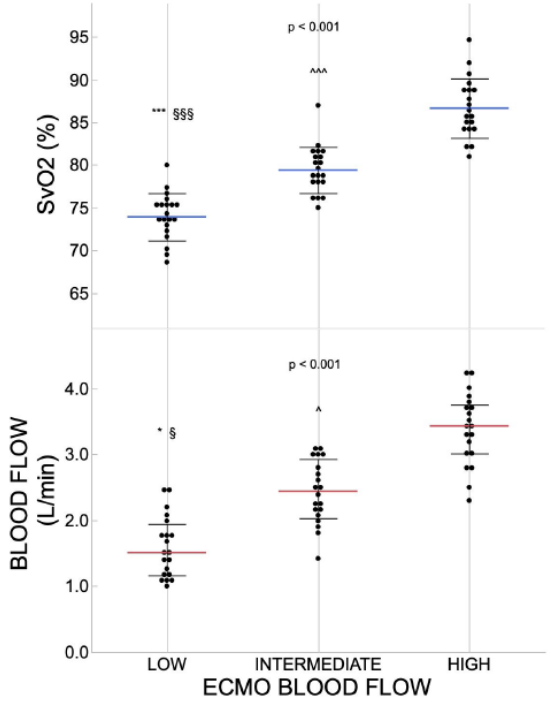
# Phsyiologic effects of ECMO blood flow

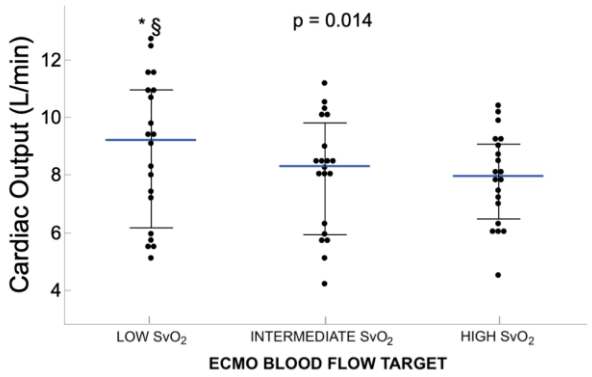
- ARDS patients on ECMO
- No shock, no severe RV failure
- EIT + Swan Ganz monitoring
- 2 centers (Milan Policlinico, Monza San Gerardo)
- Clinical PEEP, DP 12-14, RR 10-12
- Unchanged equal $FiO_2$ and $FdO_2$, ECMO gas flow
- 3 blood flow for 20 minutes: target $SvO_2$ 70-75, 75-80, >80%
- Complete physiologic assesment

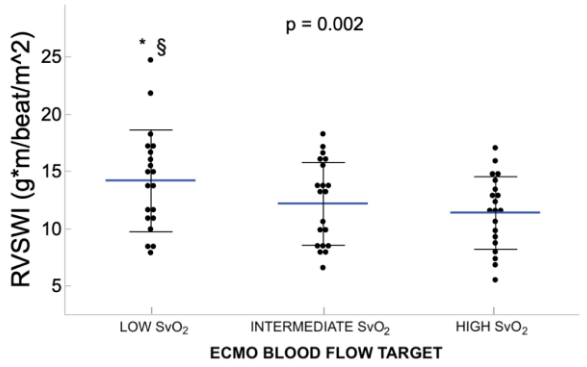
*Spinelli et al AJRCCM 2024*

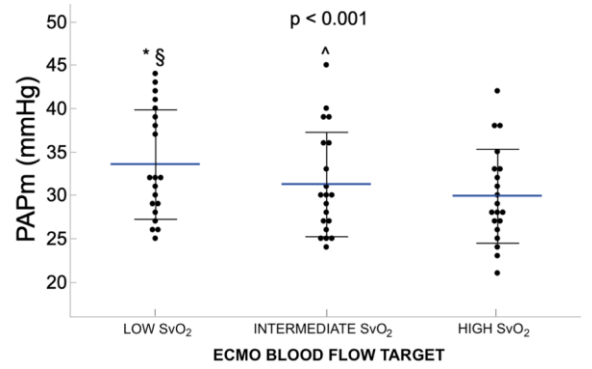
# ECMO blood flow and pulmonary hemodynamics

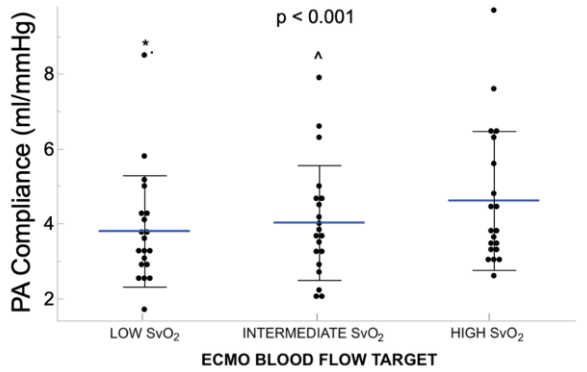
Methods




No change in MV, blood flows of 1.5, 2.4, 3.5 l/min ($BF/C^2$ of 2.56, 3.90, 5.49 ml/min/$Fr^2$)

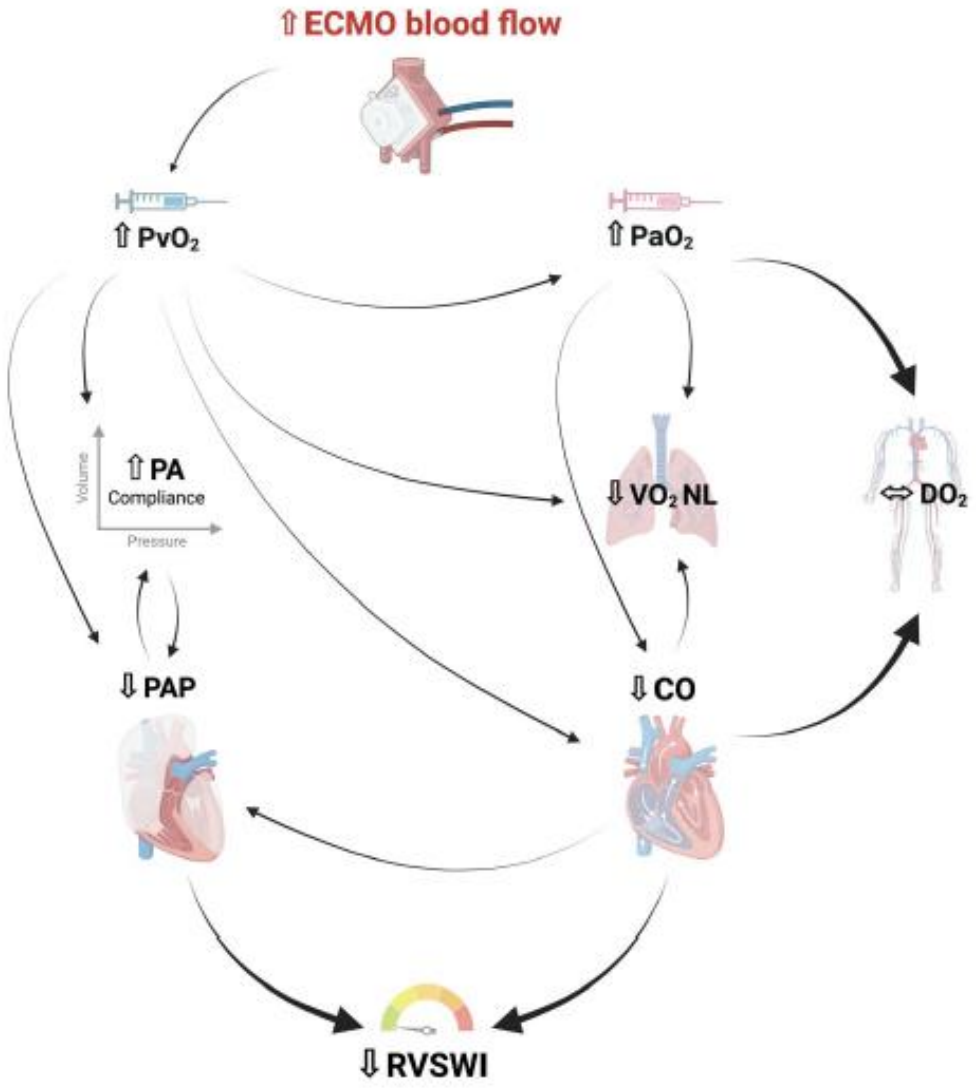
Minimal change in PVR: 180 → 170 → 159 dyn*s*$cm^{-5}$ p=0.064

Minimal decrease in $DO_2$: 1110 → 1027 → 1041 ml/min p=0.044

*Spinelli et al AJRCCM 2024*

Lower RV work, stable hemodynamic/oxygenation balance efficiency

# Mechanisms of RV protection by ECMO blood flow

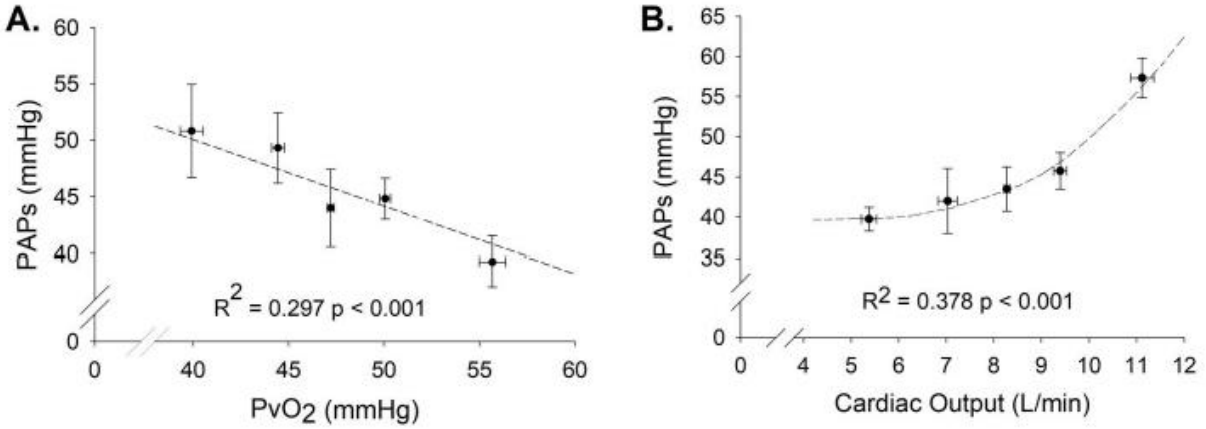


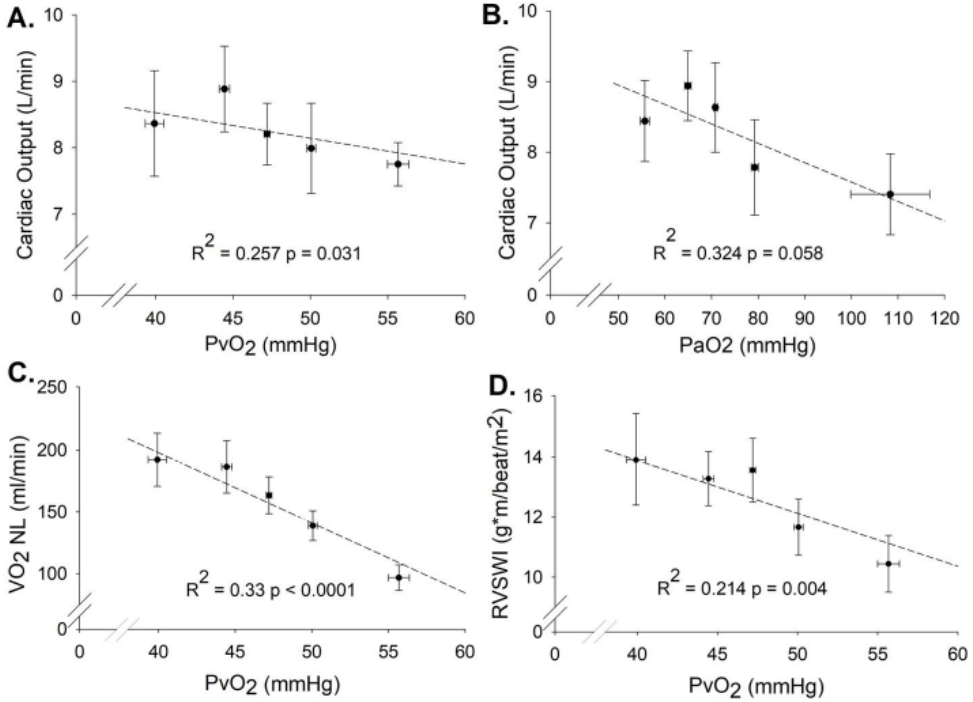

Increased $PvO_2$ → ↓PAP, ↑PA compliance, ↓$VO_2$NL, ↓CO, ↑$PaO_2$

vvECMO <u>provides hemodynamic support</u> by allowing lower RV work with stable $DO_2$

*Spinelli et al AJRCCM 2024*

# Physiologic determinants for RV protection




PAPs correlated with $PvO_2$ (linear) and CO (treshold effect)

Cardiac output correlated with $PvO_2$ and $PaO_2$

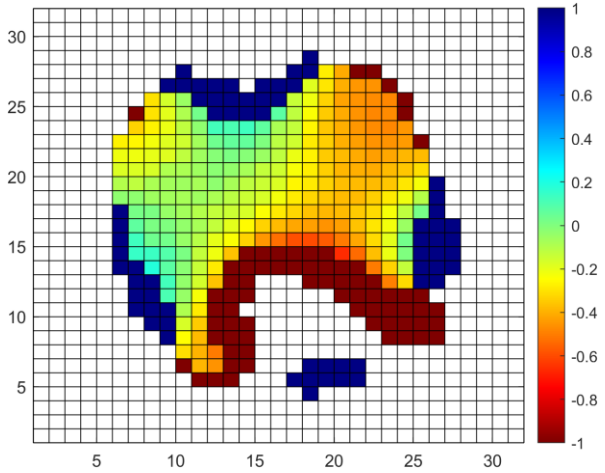
RV workload correlated with $PvO_2$

$PvO_2$ increase is the real target (more positive effects) rather than CO decrease?

*Spinelli et al AJRCCM 2024*

# What about VQ mismatch?

| Variables | ECMO Blood Flow Target | | | p-value |
|---|---|---|---|---|
| | Low $SvO_2$ | Intermediate $SvO_2$ | High $SvO_2$ | |
| **Blood gases** | | | | |
| $SvO_2$ (%) | 73.9 ± 2.8 * § | 79.4 ± 2.7 ^ | 86.7 ± 3.5 | < 0.001 |
| $PvO_2$ (mmHg) | 42 ± 3 *** §§§ | 47 ± 3 ^^^ | 53 ± 4 | < 0.001 |
| $PvCO_2$ (mmHg) | 53 ± 5 | 50 ± 5 | 48 ± 5 | <0.001 |
| $PaO_2$ | 63 [57-70] * § | 70 [62-81] ^ | 83 [72-99` | < 0.001 |
| $PaCO_2$ (mmHg) | 52 ± 6 *** §§§ | 49 ± 5 ^^ | 47 ± 6 | <0.001 |
| Intrapulmonary shunt (%) | 51.5 [41.9-64.6] | 50.9 [40.2-60.2]^ | 52.6 [45.3-64.9] | 0.638 |
| Arterial pH | 7.39 ± 0.05 | 7.41 ± 0.05 | 7.42 ± 0.05 | < 0.001 |
| **EIT ventilation and perfusion** | | | | |
| Ventral Ventilation (%) | 28 [21-34] | 29 [24-36] | 29 [24-35] | 0.511 |
| Middle Ventilation (%) | 60 [43-69] | 56 [43-69] | 58 [44-68] | 0.443 |
| Dorsal Ventilation (%) | 11 [7-25] | 16 [6-25] | 15 [5-24] | 0.511 |
| Ventral Perfusion (%) | 21 [15-29] | 21 [15-28] | 21 [15-27] | 0.520 |
| Middle Perfusion (%) | 67 [53-69] | 65 [56-67] | 64 [54-70] | 0.336 |
| Dorsal Perfusion (%) | 15 [10-20] | 16 [13-22] | 15 [13-19] | 0.115 |
| **EIT V/Q mismatch** | | | | |
| Only ventilated units (%) | 10.7 [4.7-14.5] * | 6.7 [3.8-10.9] | 10.9 [5.5-19.6] | 0.016 |
| Only perfused units (%) | 16.7 [7.9-22.5] | 17.3 [12.2-22.5] | 16.6 [12.8-21.2] | 0.212 |
| Unmatched units (%) | 25.2 [10.3-27.7] | 23.1 [19.6-31.8] | 27.8 [24.7-31.3] | 0.086 |

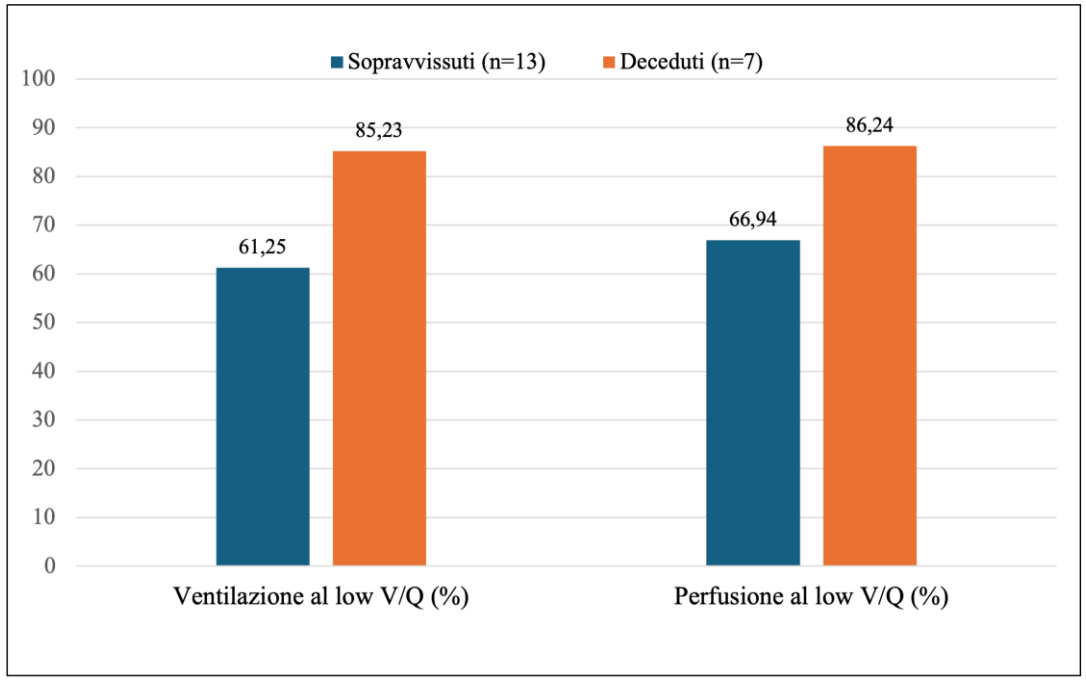


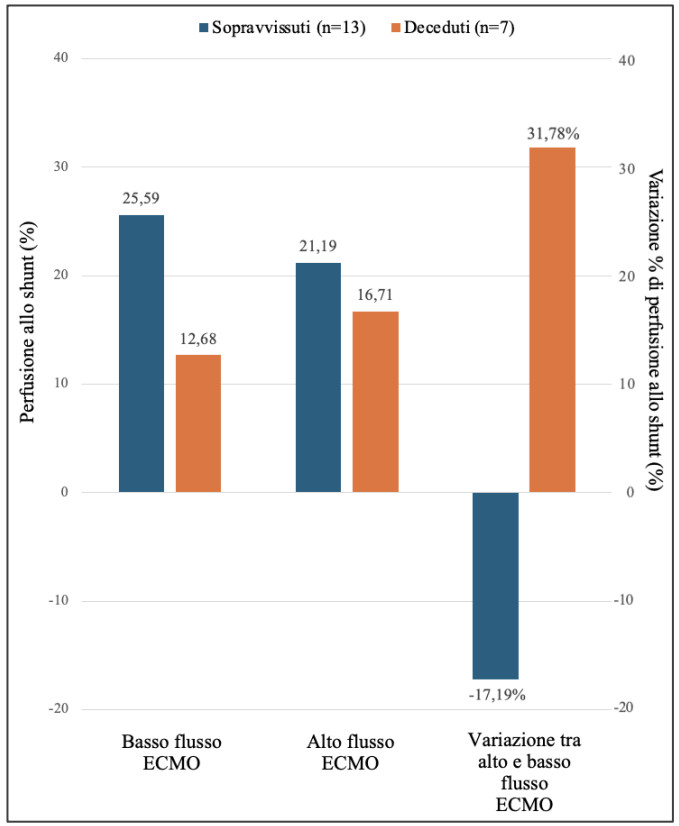

No apparent effect on calculated shunt and EIT-based VQ mismatch (macroscopic analysis)

PvO2 range not wide enough to see differences? Stable not so “inflamed” patients?

*Spinelli et al AJRCCM 2024*

# Loss of shunt compensation as a sign of severity?




At lowest blood flow rate, non-survivors had larger ventilation and perfusion to the low VQ compartment

When blood flow and $SvO_2$ increase, survivors decrease shunt (active compensation) while non-survivors decrease shunt (“passive” behaviour?)

# Work in progress..

Personalised ECMO to improve physiology (and outcomes?):

- Blood flow → highest allowed by drainage cannula size ($BF/C^2$ >6.464), monitor hemolysis
- $SvO_2$ >80% and $PvO_2$ >45 mmHg to protect the right heart and the pulmonary circulation
- Larger low VQ and compensation of shunt to identify more severe patients

Still a lot of work to understand physiology and translate into clinical practice..