Management des atteintes respiratoires sévères et intérêt de l'$ECCO_2R$

Management of severe respiratory failure and the rationale for $ECCO_2R$

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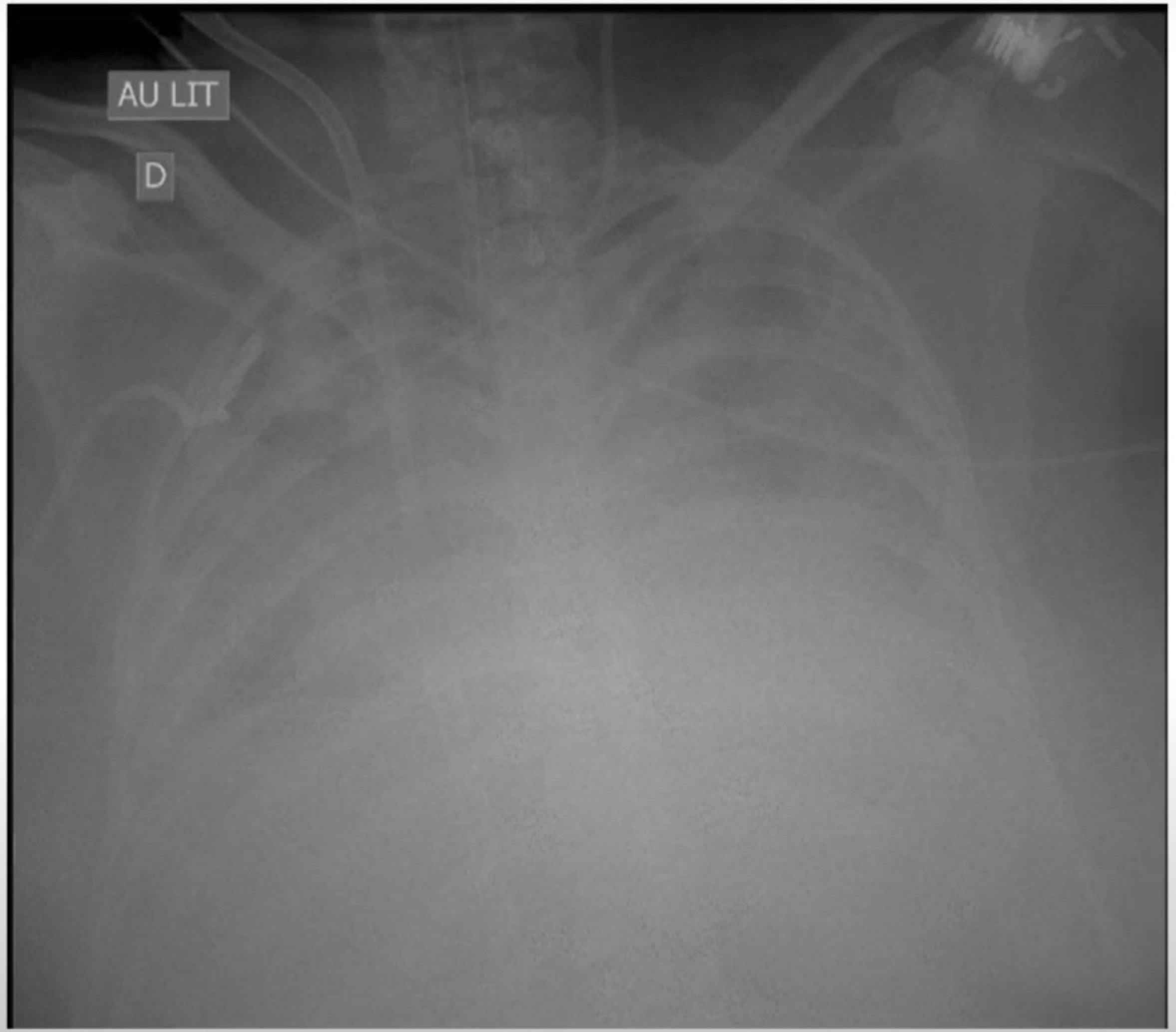
Conflicts of interest

- Invitation by Baxter laboratory for the « CAPSO 2021 »
- No other conflict of interest

Acute respiratory distress syndrome (ARDS)



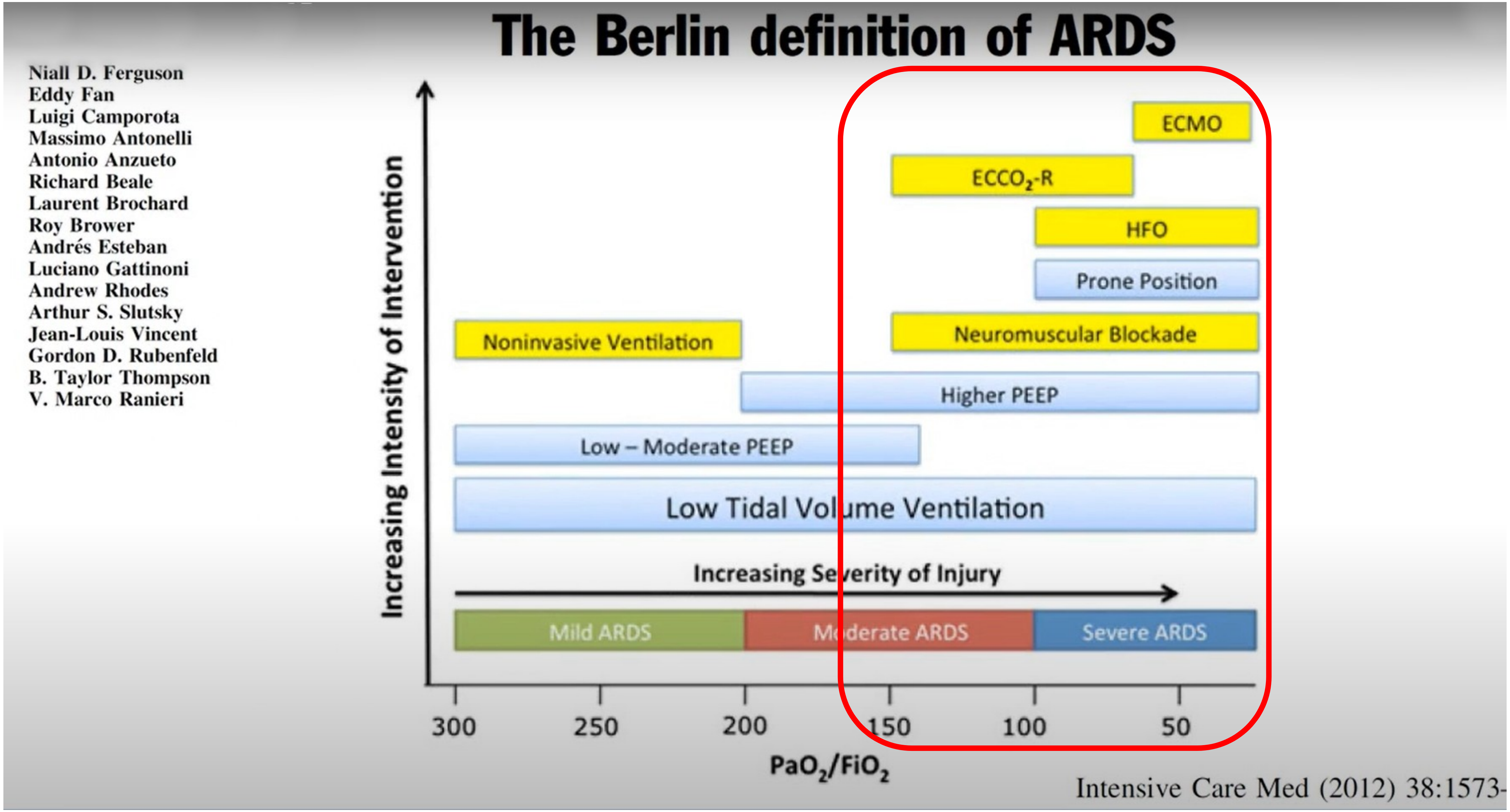
Acute respiratory distress syndrome (ARDS)

Table 3 The Berlin definition of ARDS (with permission from [22])

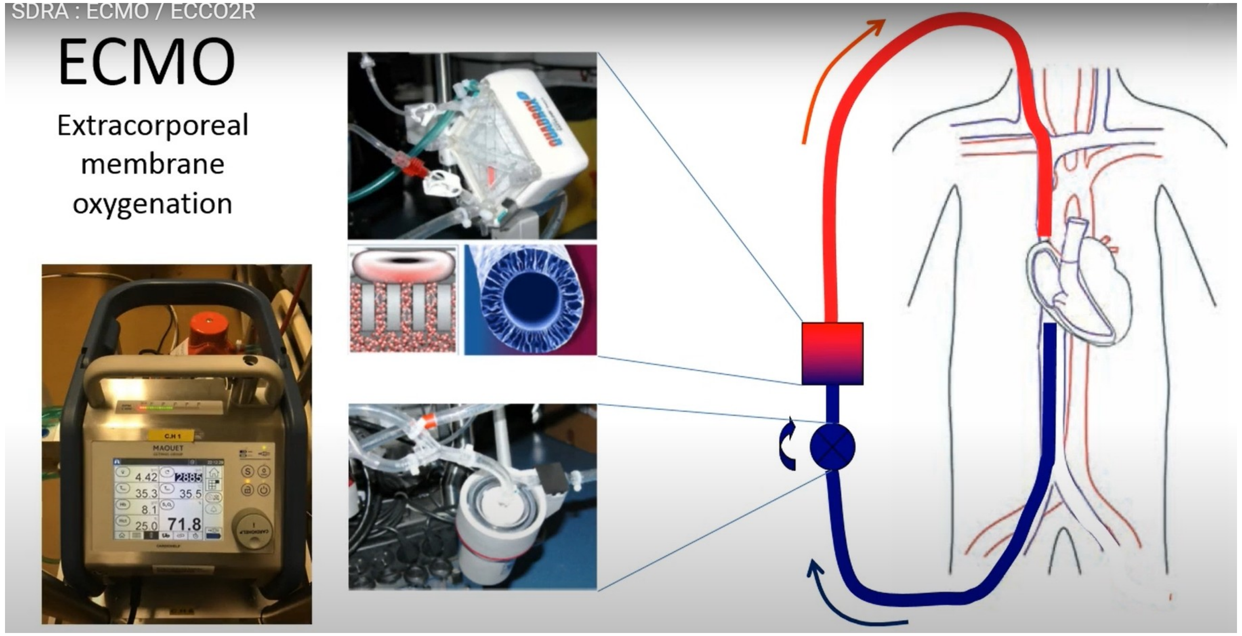
Ferguson ICM 2012

	Acute respiratory distress syndrome		
Timing	Within 1 week of a known clinical insult or new/worsening respiratory symptoms		
Chest imaging[a]	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules		
Origin of Edema	Respiratory failure not fully explained by cardiac failure or fluid overload; Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present		
	Mild	Moderate	Severe
Oxygenation[b]	$200 < PaO_2/FiO_2 \leq 300$ with PEEP or CPAP ≥ 5 cmH_2O[c]	$100 < PaO_2/FiO_2 \leq 200$ with PEEP ≥ 5 cmH_2O	PaO_2/FiO2 ≤ 100 with PEEP ≥ 5 cmH_2O

ARDS Treatment



Characteristics ECMO *vs* $ECCO_2R$

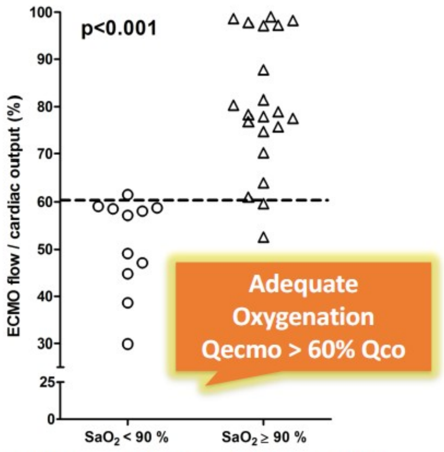


ECMO

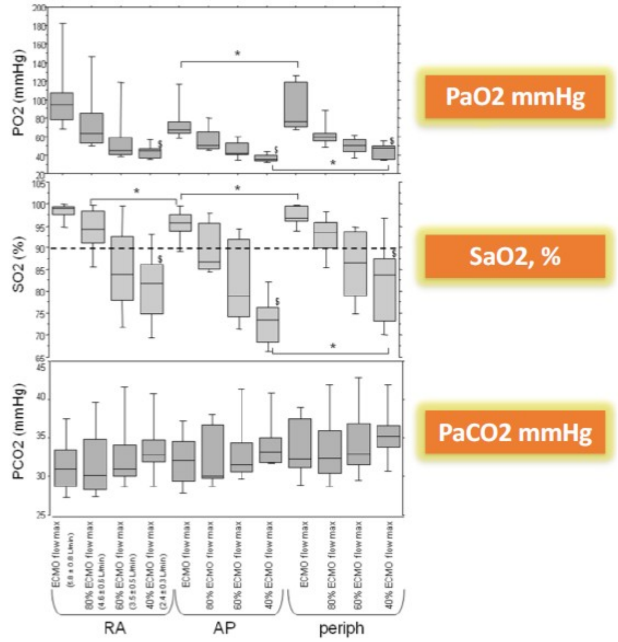
- Large cannulas
- High extracorporeal flow (> 4000 mL/min)
- Large membrane oxygenator
- Full blood oxygenation
- Full blood decarboxylation
- High technicity, ECMO center

Characteristics ECMO *vs* $ECCO_2R$

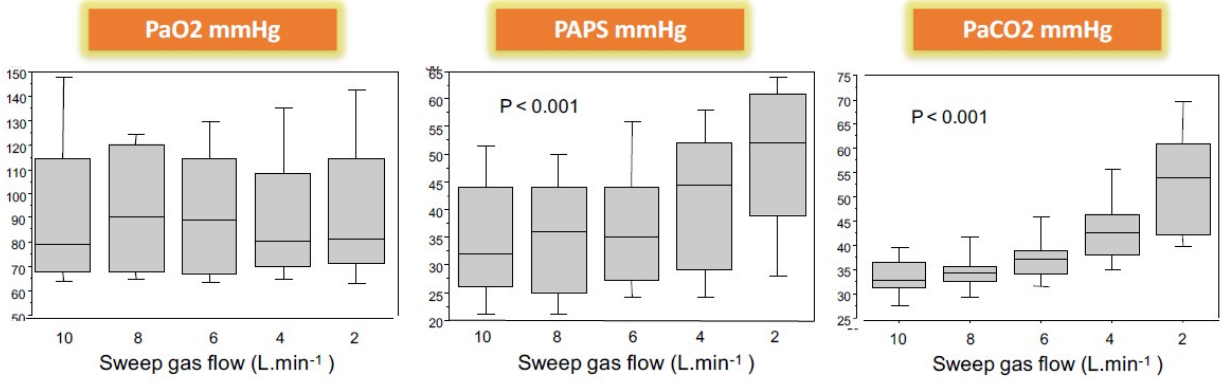
Influence of ECMO flow



Schmidt et al, Intensive Care Med, 2013



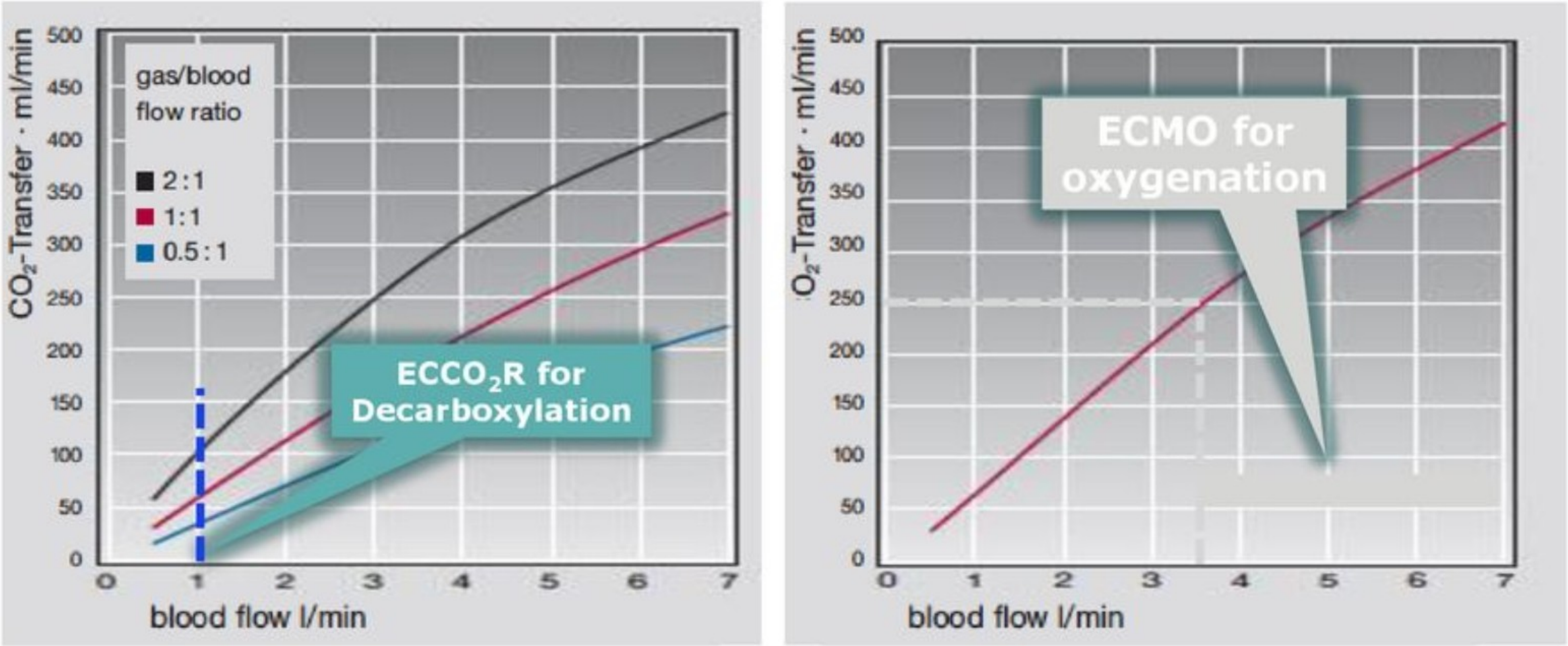
Influence of Sweep Gas Flow



Schmidt et al, Intensive Care Med, 2013

Characteristics ECMO *vs* $ECCO_2R$

Membrane lung O2/CO_2 transfer



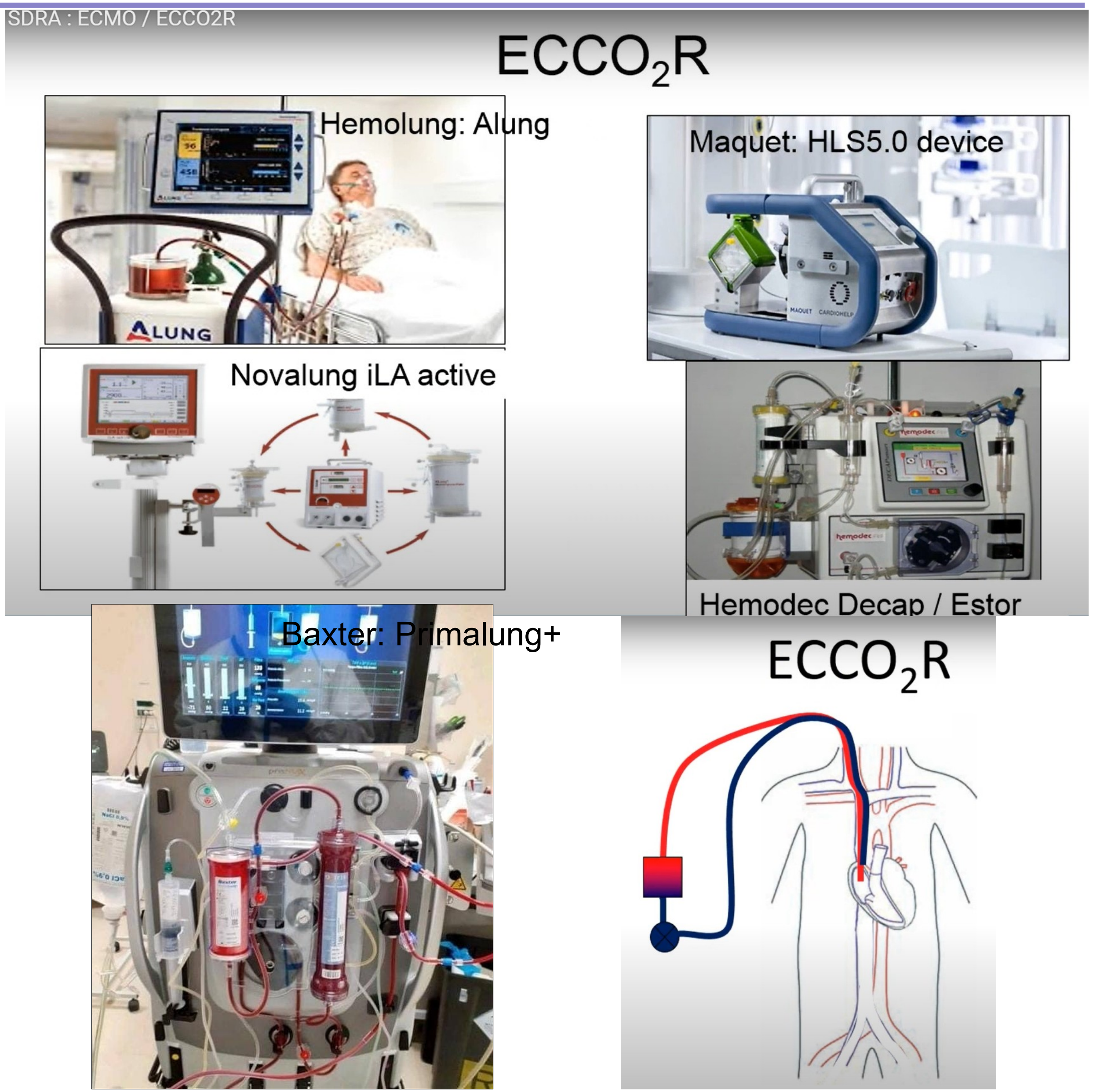
CO_2 transfer

O_2 transfer

Characteristics ECMO *vs* $ECCO_2R$

$ECCO_2R$ (respiratory dialysis)

- Double lumen catheter
- Low-flow, resiratory dialysis (300-1000 mL/min)
- Medium size oxygenator
- No blood oxygenation
- Partial blood decarboxylation
- Regular ICU



Characteristics ECMO *vs* $ECCO_2R$

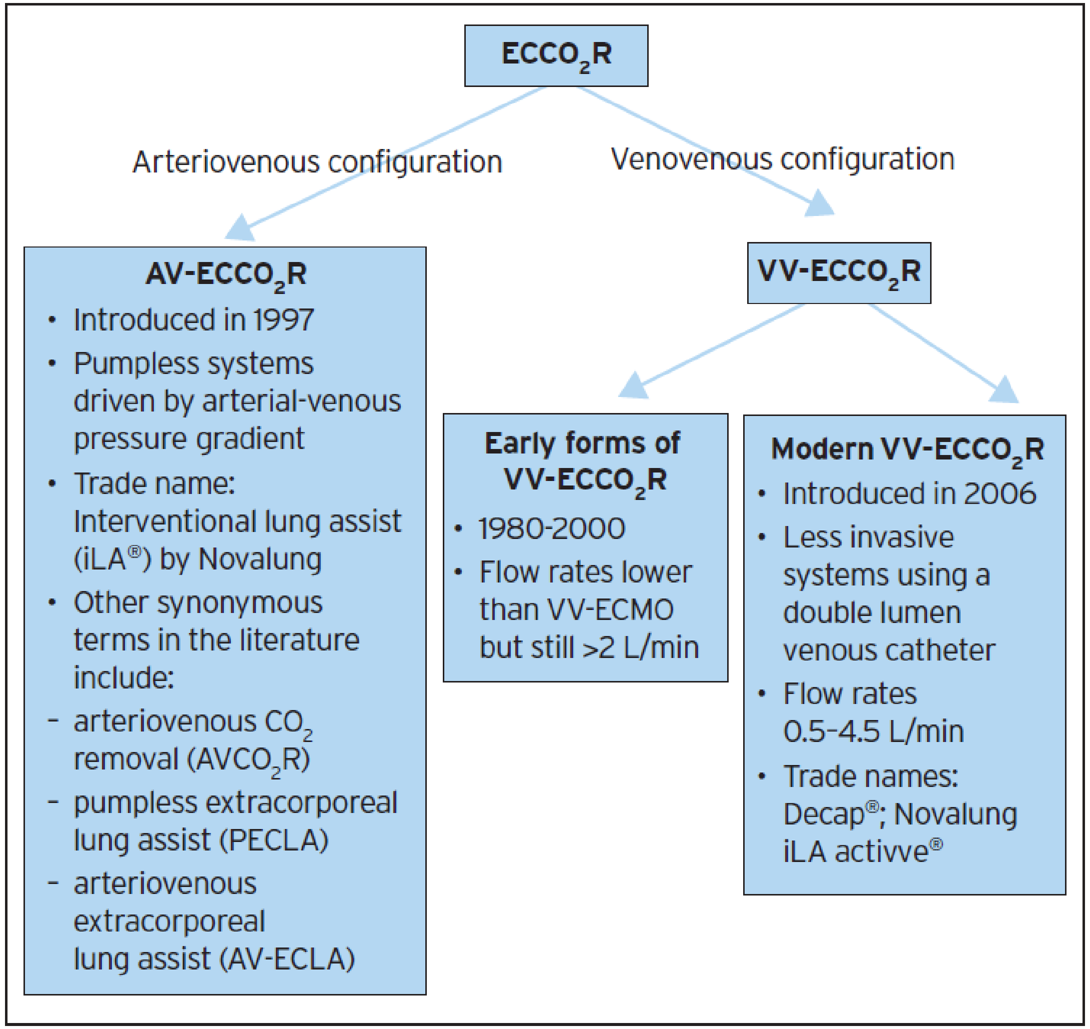


Figure 1 Classification of $ECCO_2R$ systems

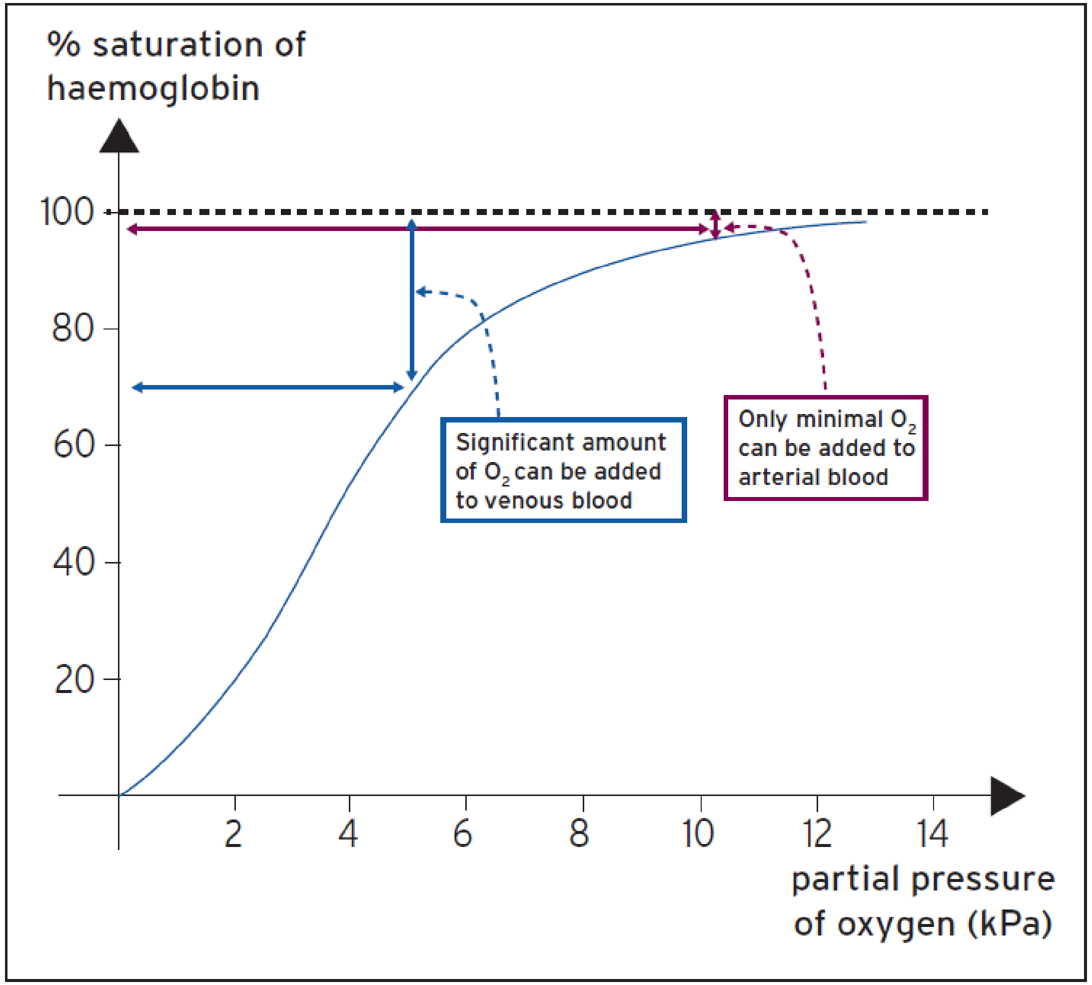


Figure 3 Oxyhaemoglobin dissociation curve illustrating why AV-$ECCO_2R$ can only make a small contribution to oxygenation.

Baker, JICS 2012

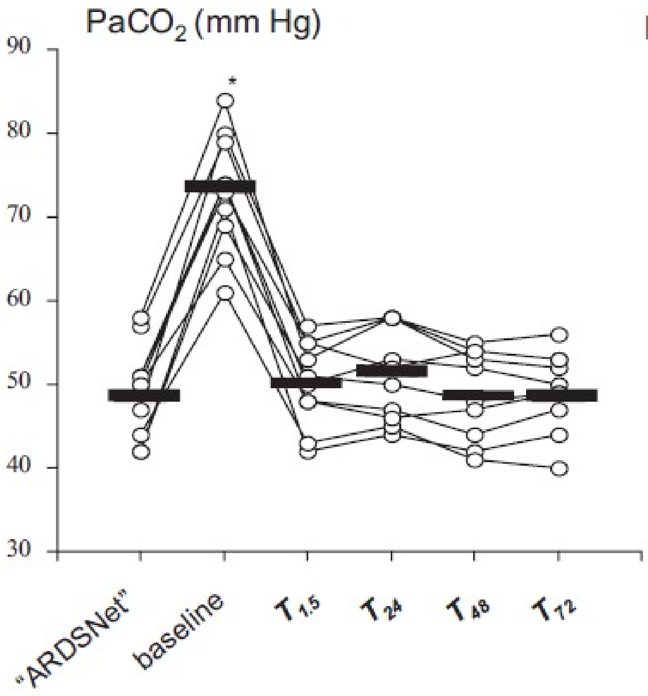
Ultraprotective ventilation – Extra-corporeal decarboxylation

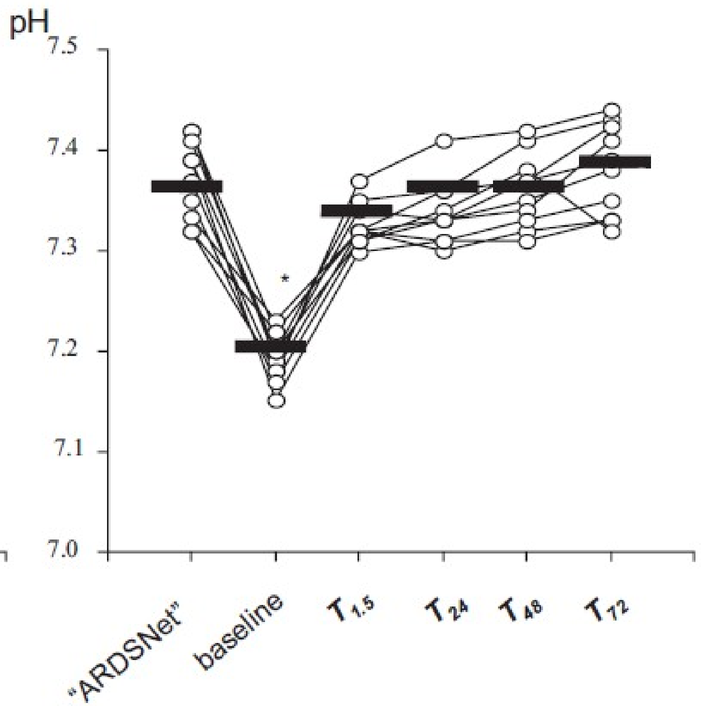
Anesthesiology 2009; 111:826–35

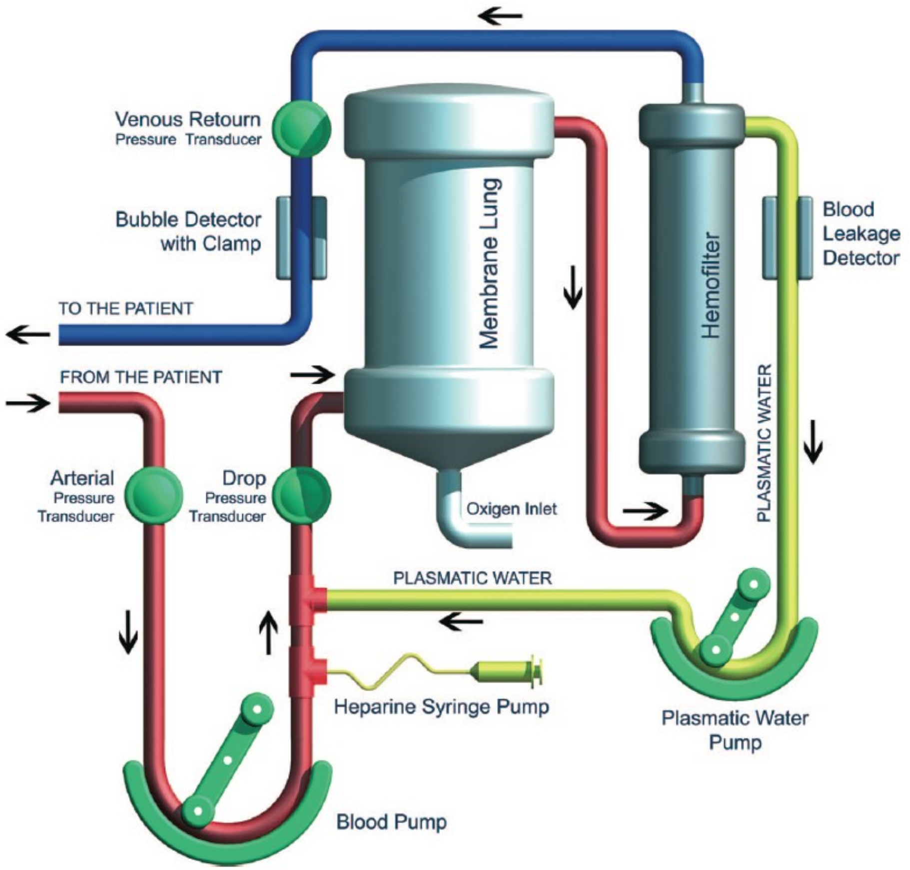
Tidal Volume Lower than 6 ml/kg Enhances Lung Protection

Role of Extracorporeal Carbon Dioxide Removal

Pier Paolo Terragni, M.D., Lorenzo Del Sorbo, M.D.,* Luciana Mascia, M.D., Ph.D.,* Rosario Urbino, M.D.,* Erica L. Martin, Ph.D.,* Alberto Birocco, M.D.,† Chiara Faggiano, M.D.,† Michael Quintel, M.D.,‡ Luciano Gattinoni, M.D.,§ V. Marco Ranieri, M.D.||*







ARDS and right ventricular dysfunction

Diagnosis of right ventricular dysfunction in 20-25% of ARDS

<u>Factors associated with protective ventilation</u>

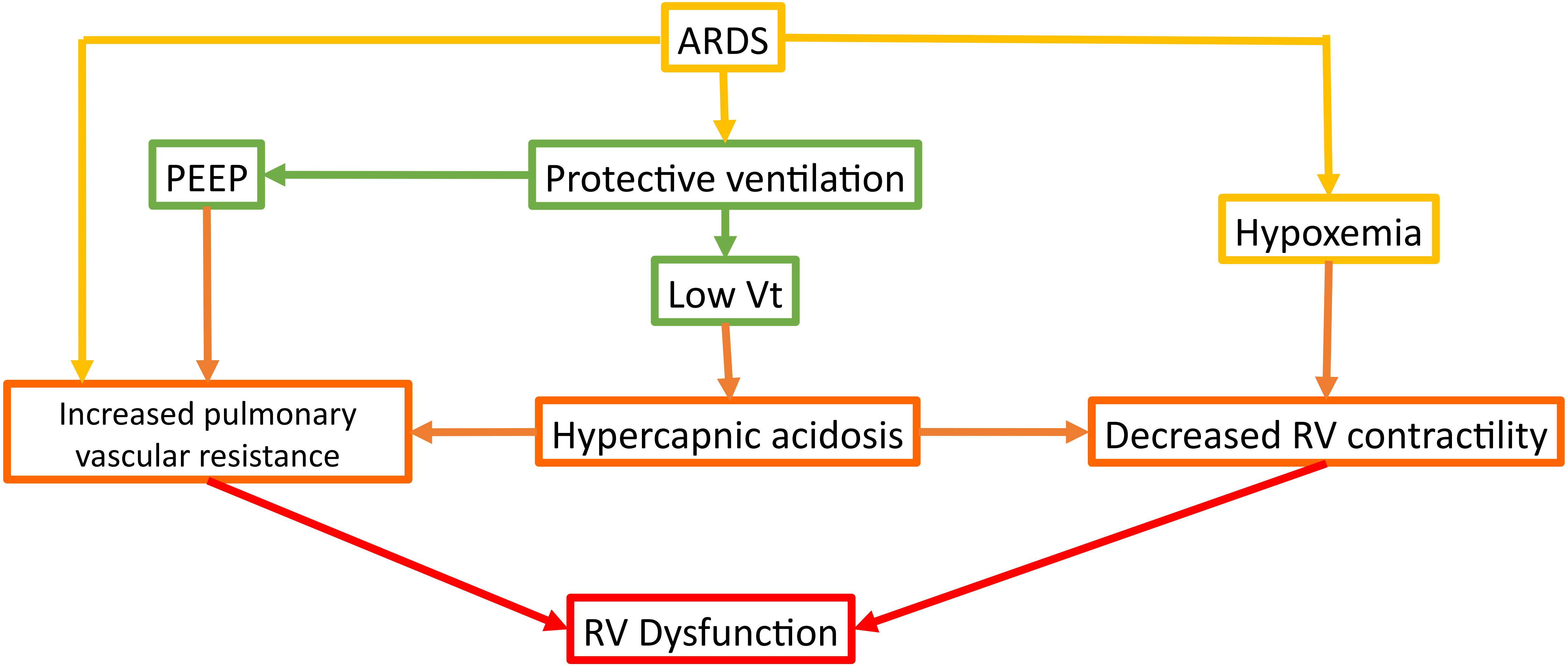
- Vt — Vieillard-Baron. *J Appl Physiol* 1999
- P_{Plat} — Jardin. *ICM*. 2007
- PEEP — Mekontso Dessap. *ICM*. 2007

<u>Rôle of hypercapnia and acidosis</u>

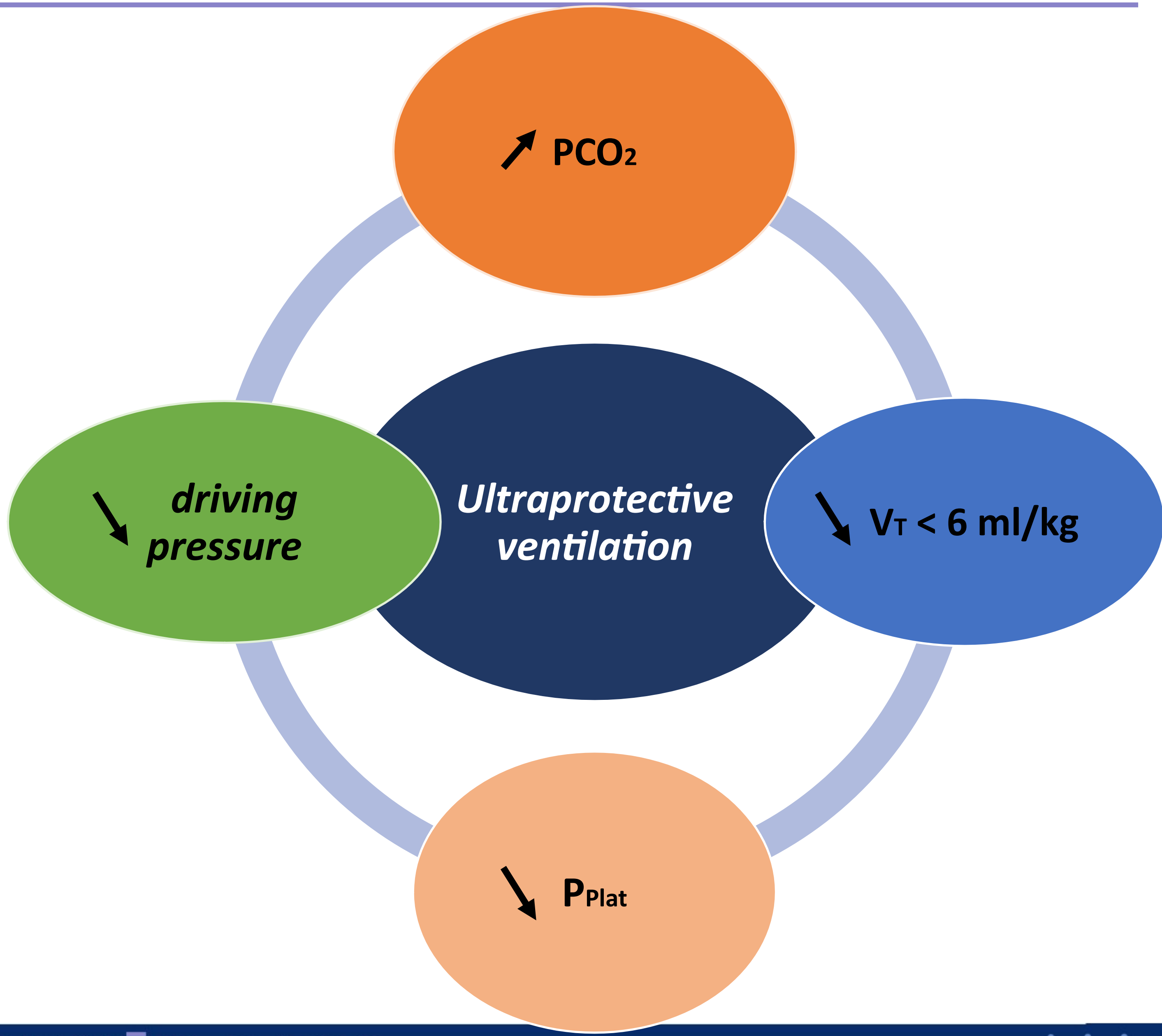
<u>Target: Avoiding acute cor pulmonale</u>

- Poor prognosis

ARDS and right ventricular dysfunction



ARDS and right ventricular dysfunction



ARDS and right ventricular dysfunction

Goursaud *et al. Ann. Intensive Care* (2021) 11:3
https://doi.org/10.1186/s13613-020-00784-3

Annals of Intensive Care

RESEARCH **Open Access**

Ultraprotective ventilation allowed by extracorporeal CO_2 removal improves the right ventricular function in acute respiratory distress syndrome patients: a quasi-experimental pilot study

Suzanne Goursaud[1,2*], Xavier Valette[1], Julien Dupeyrat[1], Cédric Daubin[1] and Damien du Cheyron[1]

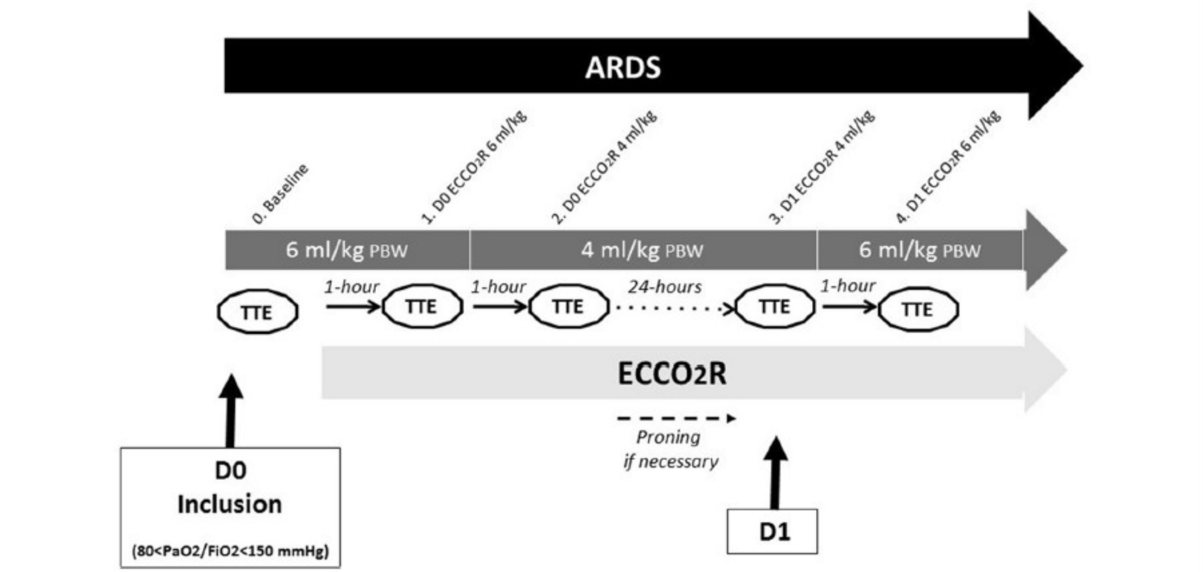


Fig. 1 Study protocol. Transthoracic echocardiography (TTE), extracorporeal CO_2 removal ($ECCO_2R$), predictive body weight (PBW), day (D)

ARDS and right ventricular dysfunction

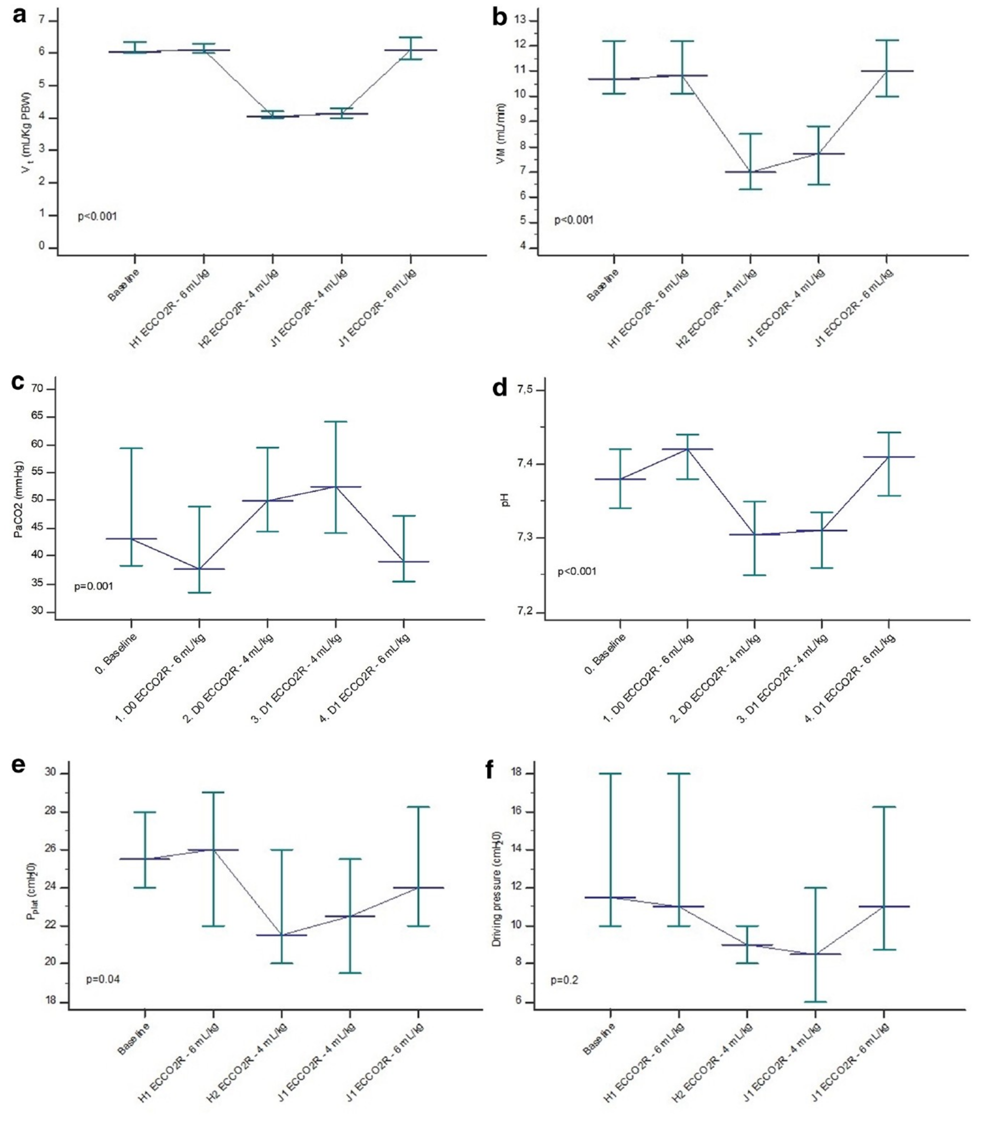


Fig. 2 Time course of ventilation parameters during the study period. Tidal volume (V_T) (**a**); minute ventilation (VM) (**b**); $PaCO_2$, partial alveolar carbon dioxide pressure (**c**); pH (**d**); plateau pressure (P_{plat}) (**e**); driving pressure (DP) (**f**)

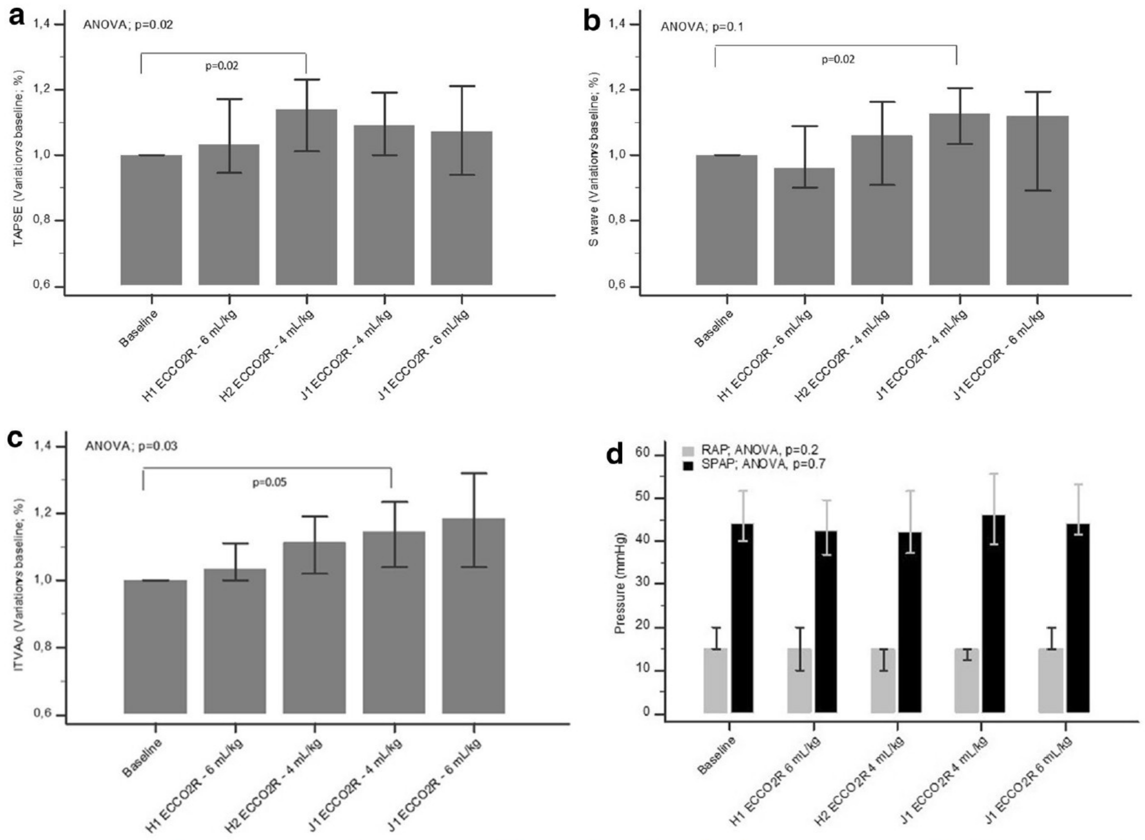
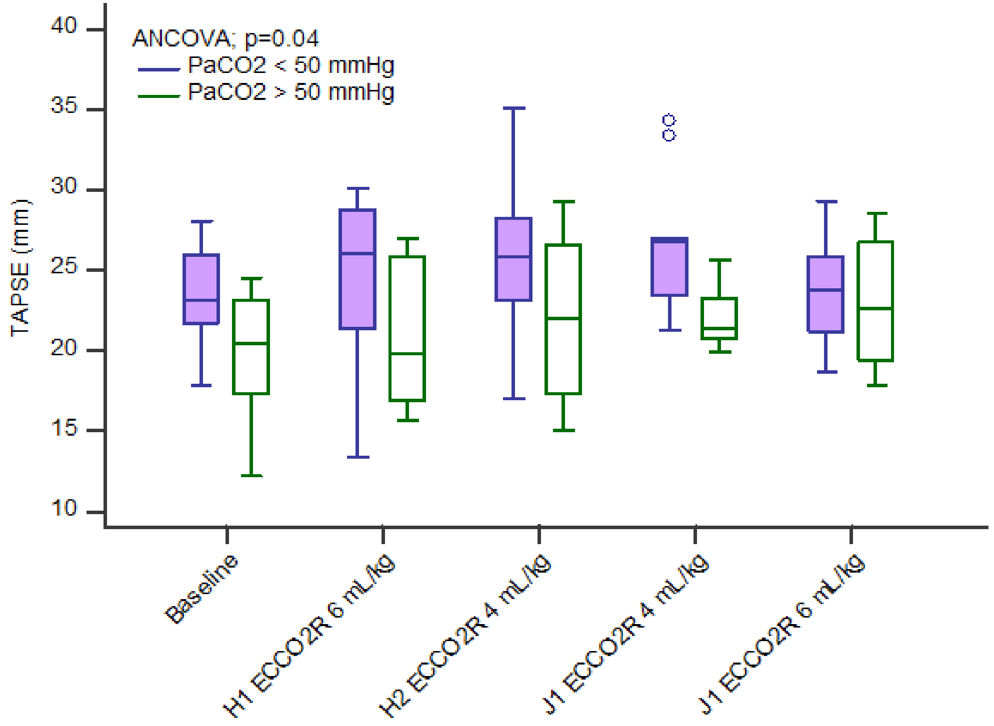
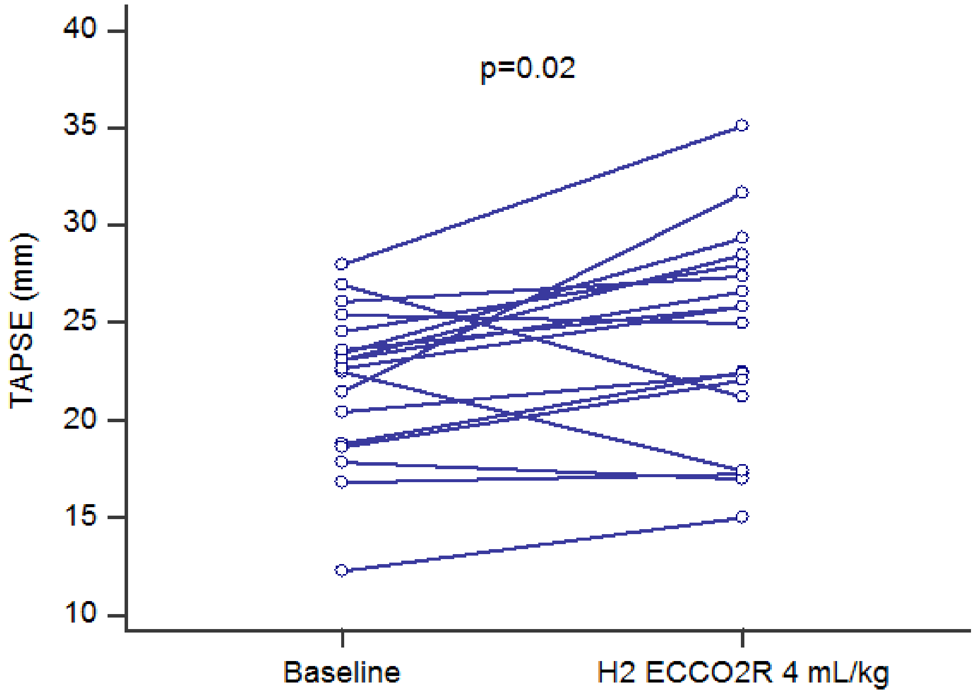


Fig. 3 Time course of echocardiography variables during the study period. Tricuspid annular plane systolic excursion (TAPSE) (**a**); right ventricle systolic excursion velocity (*S'*) (**b**); aortic velocity time integral (VTIAo) (**c**); right atrial estimation pressure (RAP) and pulmonary systolic arterial pressure (sPAP) (**d**)

ARDS and right ventricular dysfunction





$ECCO_2R$

Parameter	Baseline	$ECCO_2R$			
	V_T 6 mL/kg (n=18)	V_T 6 mL/kg (n=18)	V_T 4 mL/kg (n=18)	V_T 4 mL/kg (n=16)	V_T 6 mL/kg (n=17)
	Day 0			Day 1	
Blood flow (mL/min)	NA	400 (400-400)	400 (400-400)	400 (400-400)	400 (400-400)
Sweep gas flow (L/min)	NA	10 (10-10)	10 (10-10)	10 (10-10)	10 (10-10)
Time of utilization (hours)	34.5 (24.5-49.5)				
Heparin bolus at $ECCO_2R$ starting (IU/kg)	87 (68-97)				
Heparin (IU/kg/day)	408 (348-494)			348 (275-400)	
AntiXa activity (UI/ml)	0.16 (0.12-0.19)	0.75 (0.48-1.30)		0.54 (0.45-0.81)	

$ECCO_2R$-related adverse events	n (%)
Membrane lung clotting , n (%)	5 (28)
Bleeding	
At cannula insertion, n (%)	0
Significant, n (%)	1 (6)
Infectious complication, n (%)	0
Thrombocytopénia, n (%)	0
Clinical outcomes	
Death in ICU (n, %)	8 (44)
28-day mortality, n (%)	8 (44)
Lenght of stay in ICU (days)	15 (11-20)
Lenght of stay in ICU after inclusion (days)	11 (7-17)
Duration of mechanical ventilation in ICU survivors (days)	12 (8.3-15.8)
Duration of mechanical ventilation after inclusion in ICU survivors (days)	7.5 (6-12)
SOFA score with $ECCO_2R$	8 (5-9)
Duration of catecholamines (days)	3 (1.3-4)
Duration of catecholamine after inclusion (days)	2 (0-3)
Patient requiring RRT after inclusion, n (%)	3 (17)
RRT at ICU discharge, n (%)	2 (11)
Creatinine level at ICU discharge (µmol/l)	59 (38-101)

ARDS and right ventricular dysfunction

ARDS

Lung protective approach

Right ventricular protective approach

$ECCO_2R$

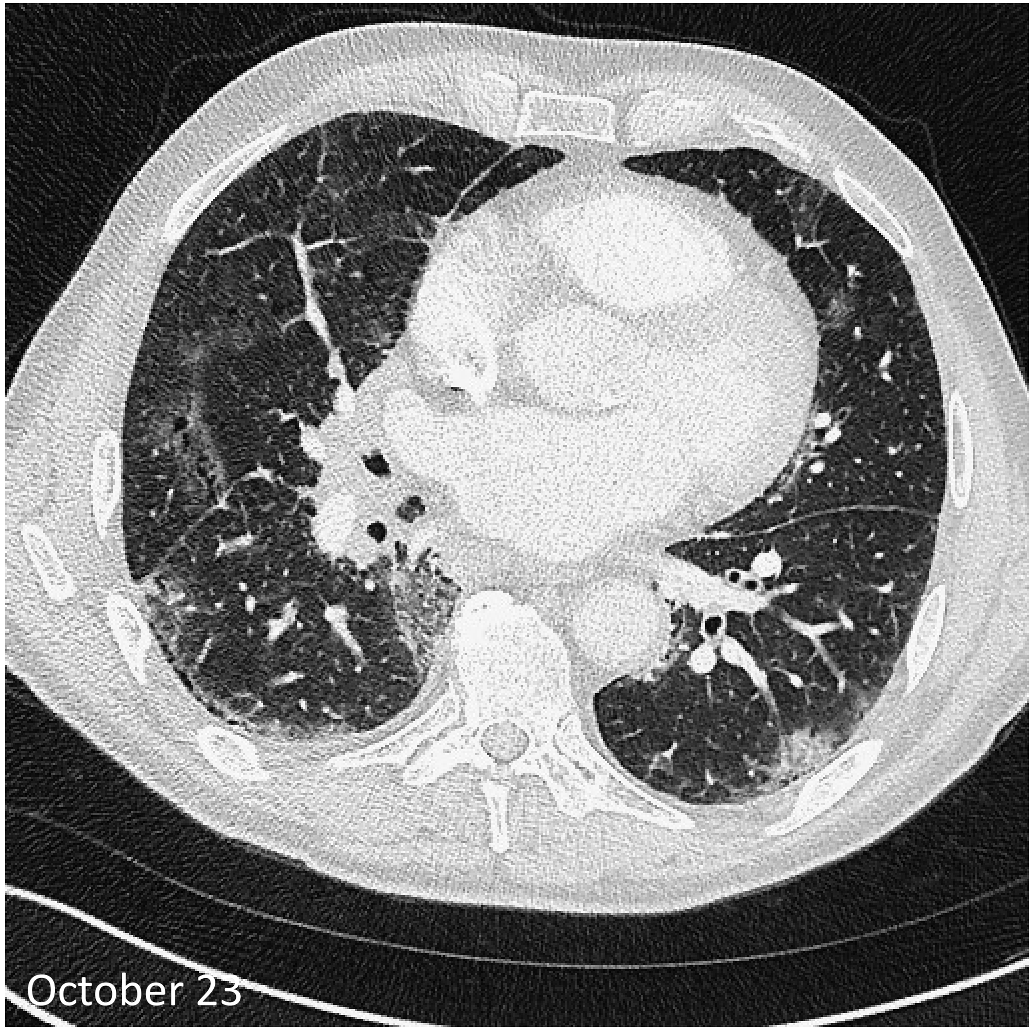
Case vignette 1, Mr L.

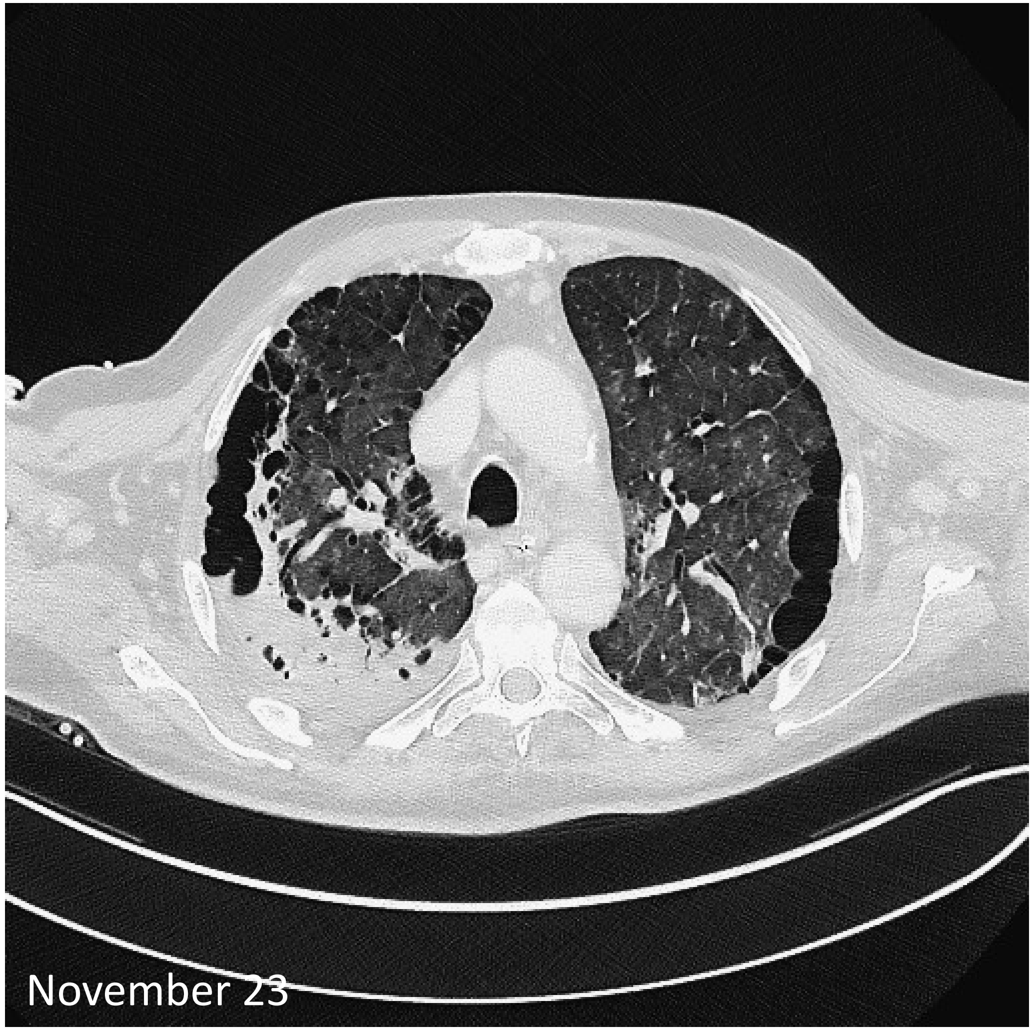
A previously healthy patient, 54 years old, with obesity (BMI 36 Kg/m^2) presents with critical COVID-19

- First line treatment with high flow nasal cannula: Q 50 L/min; FiO_2 80% then 100%
- At day 1, hypoxemia increased with SpO_2 < 90%. The patient was intubated and treated with mechanical ventilation, Vt 6 mL/Kg (PBW), sedation and neuromuscular blockers, prone position
    - FiO_2 of 1.0 and PEEP 14 cmH_2O, RR 30/min
    - Pplat = 29 cmH_2O
    - Driving pressure = 15 cmH_2O
    - PaO_2/FiO_2 = 125
    - pH is 7.25, $PaCO_2$ = 64 mmHg
- Echocardiography shows right ventricular dysfunction and SPAP 55 mmHg without ACP

- Decision to extracorporeal decarboxylation to get ultraprotective ventilation and controlled $PaCO_2$

Case vignette 1, Mr L.





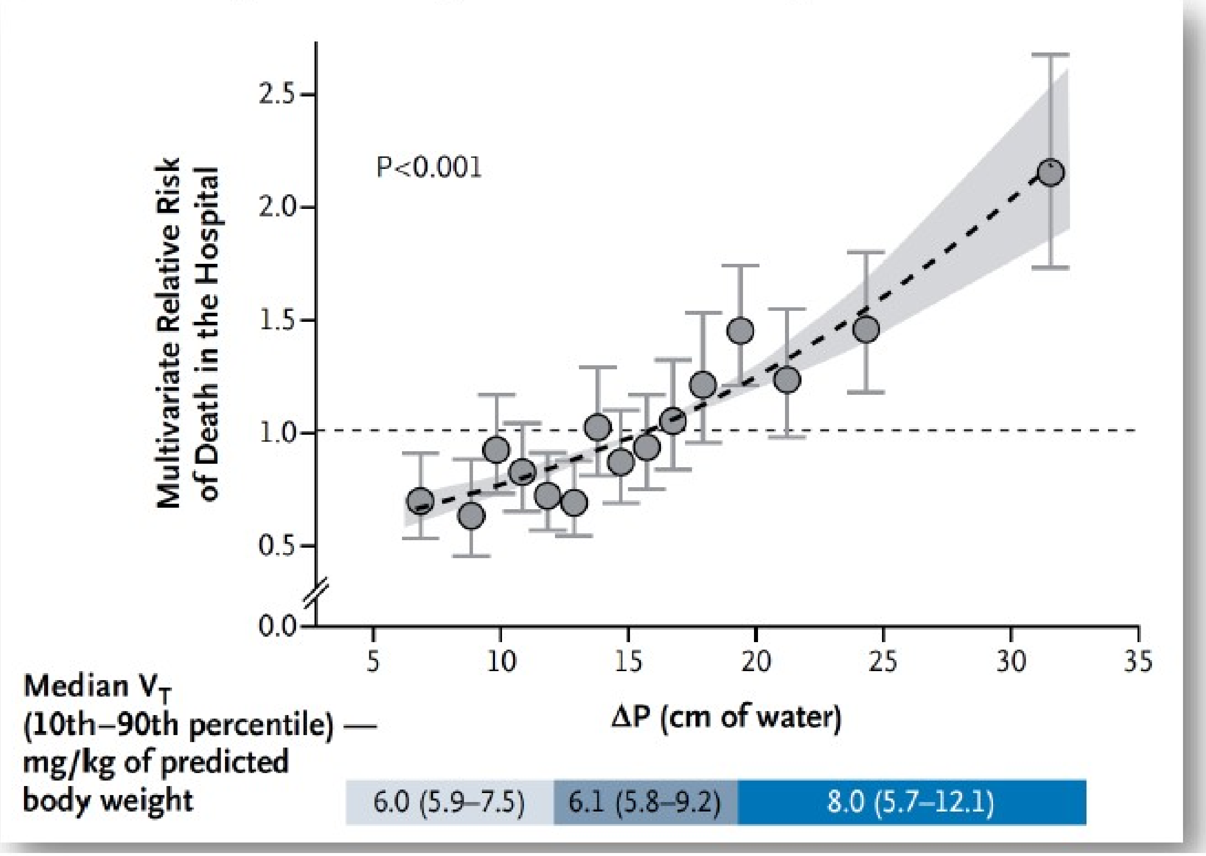

PHILIPS

ARDS and driving pressure

SPECIAL ARTICLE

N ENGL J MED 372;8 NEJM.ORG FEBRUARY 19, 2015

Driving Pressure and Survival in the Acute Respiratory Distress Syndrome



Amato et al.

Case vignette 1, Mr L.

	Set 1 (72 hours)			Set 2 (72 hours)		No set	Set 3 (56 hours)	
	H-1	H1	H2	H-1	H2	Transport	H-1	H2
Vt (mL/kg)	6	5	4	6	4	6	6	4
RR (/min)	30	30	24	24	24	28	28	22
Pplat (cmH_20)	29	26	23	28	22	27	27	22
PEEP (cmH_2O)	14	15	15	15	15	14	15	13
DP (cmH_2O)	15	11	8	13	7	13	12	9
Blood gas								
pH	7.24	7.34	7.3	7.32	7.29	7.32	7.34	7.36
$PaCO_2$ (mmHg)	66	47	52	56	48	54	55	48
PaO_2 (mmHg)	94	95	93	88	90	82	84	80
PaO_2/FiO_2	105	112	116	176	138	136	145	200

Case vignette 1, Mr L.

Outcomes

- $ECCO_2R$ from day 2 to Day 11 = 9 days
  - Double lumen dialysis catheter, 13 FR, 14 cm, right internal jugular vein
  - 3 sets of Prismalung+ (Q_p 400 mL/min; S_{memb} 0.8 m^2)
  - 1 filter clotting, probably due to prone position associated with $ECCO_2R$
  - No acute bleeding event
  - Mean AntiXa activity = 0.54 UI/mL
- SPAP Improvement in echocardiography at day 3 (SPAP below 40 mmHg)
- Alive at Day 28
- One ventilator associated pneumonia with lung abscess (*pseudomonas aeruginosa*) and septic shock
- Favorable outcome despite decreased in lung compliance
- Tracheostomy for weaning from mechanical ventilation …

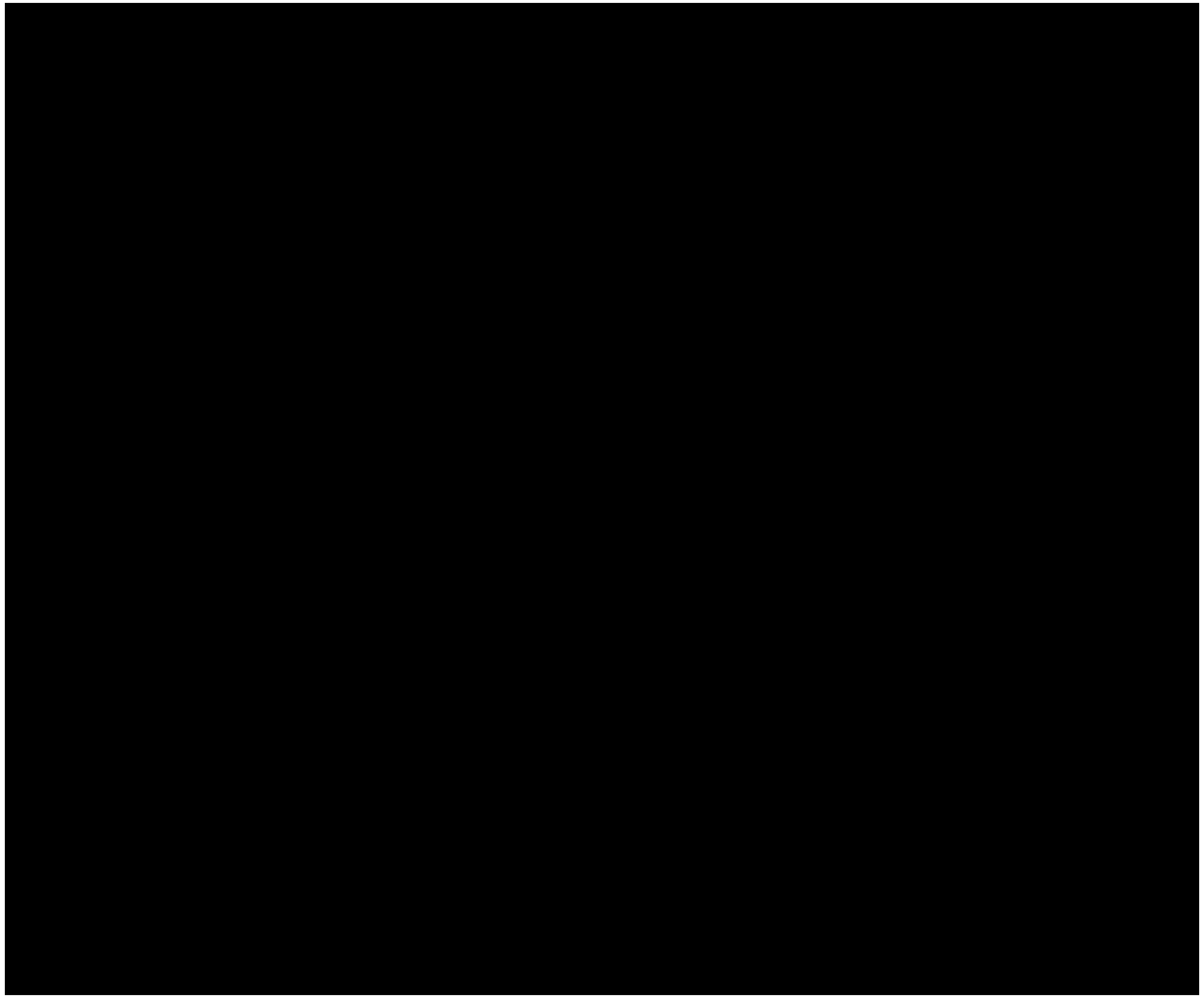
Case vignette 2, Mr K.

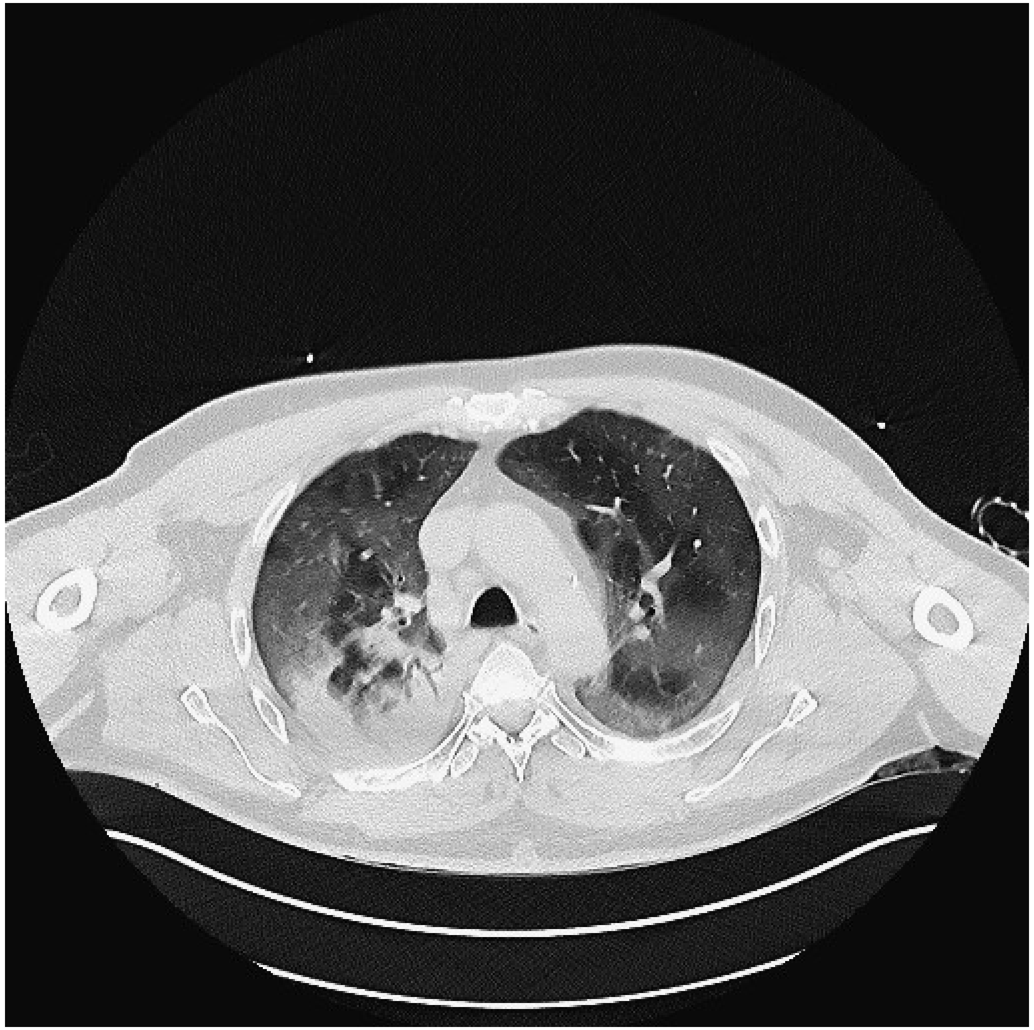
A patient, 62 years old, with hypertension presents with pneumococcal pneumonia-induced ARDS, septic shock and AKI KDIGO3

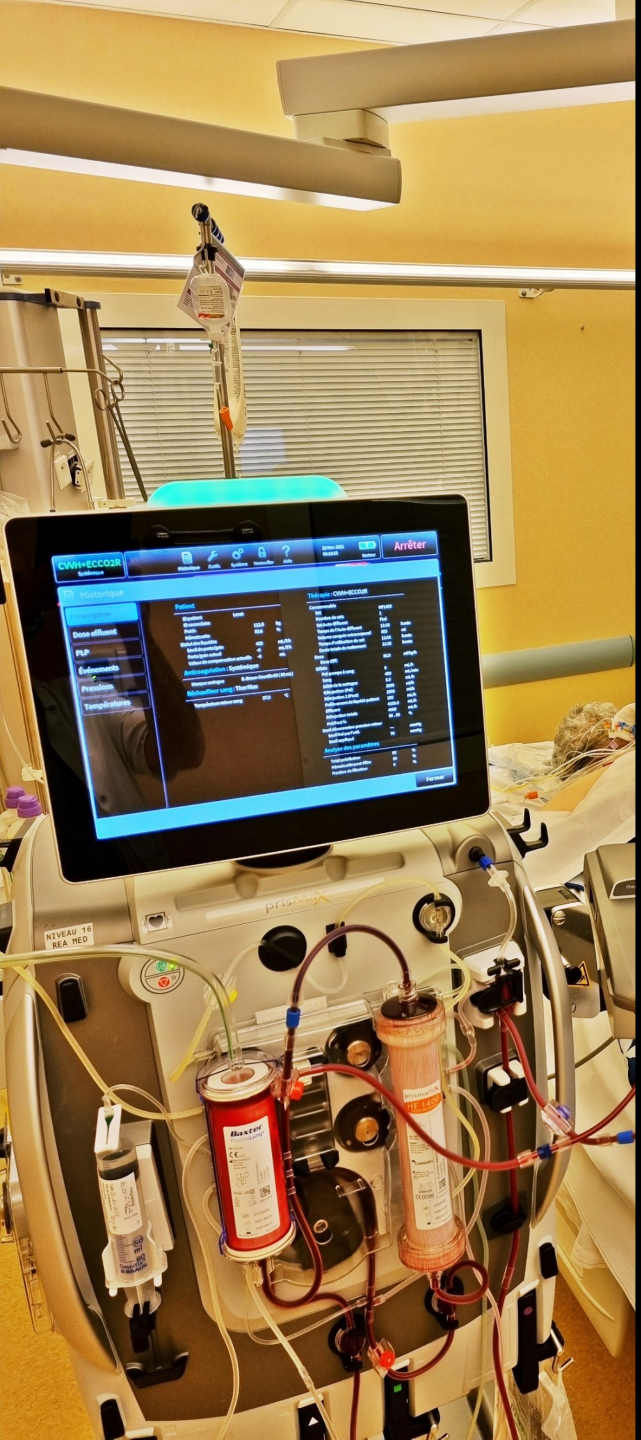
- The patient was intubated and treated with mechanical ventilation, Vt 6 mL/Kg (PBW), sedation and neuromuscular blockers, prone position
    - FiO_2 of 1.0 and PEEP 15 cmH_2O, RR 30/min
    - Pplat = 30 cmH_2O
    - Driving pressure = 15 cmH_2O
    - PaO_2/FiO_2 = 116
    - pH is 7.22, $PaCO_2$ = 59 mmHg
    - Serum creatinine = 321 µmol/L and urine output < 0.3 mL/kg/h during 12 hours
    - Serum potassium = 6.1 mmol/L

- Decision to start renal replacement therapy
- Decision to extracorporeal decarboxylation to get ultraprotective ventilation and controlled $PaCO_2$
- **Combined CVVH-$ECCO_2R$**

Case vignette 2, Mr K.







CWH+ECCO2R
Arrêter
Historique
Fermer
NIVEAU 16
REA MED
Baxter

ATTENTION
PATIENT (E)
CURARISÉ (E)
CWH+ECCO2R
Arrêter
Fermer
Baxter

Case vignette 2, Mr K.

	Set 1 (72 hours)		Set 2 (49 hours)	
	H-1	H2	H-1	H2
Vt (mL/kg)	6	4	5	4
RR (/min)	30	24	30	22
Pplat (cmH_20)	30	24	27	23
PEEP (cmH_2O)	14	15	15	15
DP (cmH_2O)	16	9	12	8
Blood gas				
pH	7.28	7.32	7.30	7.34
$PaCO_2$ (mmHg)	60	66	55	51
PaO_2 (mmHg)	89	95	81	86
PaO_2/FiO_2	111	105	135	172
Creatinine (µmol/L)	346	265	126	118

Outcomes

- $ECCO_2R$ from day 2 to Day 7 = 5 days
  - Double lumen dialysis catheter, 13 FR, 14 cm, right internal jugular vein
  - 2 sets of Prismalung+ (Q_p 400 mL/min; S_{memb} 0.8 m²)
  - 1 filter clotting
  - No acute bleeding event
  - Mean AntiXa activity = 0.48 UI/mL
- Renal function improved 8 days after ICU admission, with increased daily urine output and normalization of serum creatinine. No more session of dialysis
- Weaning from mechanical ventilation at day 22
- Alive at Day 28

Combes et al. Critical Care (2020) 24:490
https://doi.org/10.1186/s13054-020-03210-z

Critical Care

RESEARCH Open Access

$ECCO_2R$ therapy in the ICU: consensus of a European round table meeting

Alain Combes[1,2*], Georg Auzinger[3,4†], Gilles Capellier[5,6†], Damien du Cheyron[7†], Ian Clement[8†], Guglielmo Consales[9†], Wojciech Dabrowski[10†], David De Bels[11†], Francisco Javier González de Molina Ortiz[12,13†], Antje Gottschalk[14†], Matthias P. Hilty[15†], David Pestaña[16,17†], Eduardo Sousa[18†], Redmond Tully[19†], Jacques Goldstein[20] and Kai Harenski[21]

Table 1 $ECCO_2R$ treatment criteria for patients with ARDS

Parameter	Target	Score	
Initiation criteria			
Driving pressure	≥ 14 cmH_2O	31	Consensus
P_{plat}	≥ 25 cmH_2O	22	Consensus
$PaCO_2$	> 60–80 mmHg	21	Majority agreement
pH	< 7.25	20	Majority agreement
Reduce V_T to < 6 mL/PBW	–	18	Majority agreement
Respiratory rate	≥ 25 to > 30	14	Majority agreement
PaO_2/FiO_2	100–200	10	Majority agreement
PEEP	–	8	No agreement
Treatment targets			
Driving pressure	< 14 cmH_2O	66*	Consensus
P_{plat}	< 25 cmH_2O	57*	Majority agreement[†]
Respiratory rate	< 25 or < 20 breaths/min	44*	Consensus
pH	> 7.30	39*	Majority agreement
V_T	≤6 mL/PBW	39*	Majority agreement
$PaCO_2$	< 50–55 mmHg	30	Majority agreement

Criteria for $ECCO_2R$ treatment considered to be of importance and selected from the provided list. Target describes any potential target values identified, with '–' indicating that no target parameter was provided or considered relevant. Score indicates the combined total score, with higher scores indicating a higher perceived importance. Consensus means a consensus threshold (≥ 80%) was reached, majority agreement means ≥ 50% agreed but consensus level was not reached, and no agreement means < 50% agreed

*Based on the post-meeting survey. [†]Note, for P_{plat}, a consensus threshold of 80% was not reached in the meeting; in the post-meeting survey, it was rated as the second most important target

Table 2 Typical characteristics for initiating $ECCO_2R$ for rescue therapy and to facilitate ultra-protective ventilation in ARDS

Parameter	Target for initiation in: Rescue	Target for initiation in: Ultra-protective ventilation
Driving pressure	> 15 to 20 cmH_2O	> 13 to 15 cmH_2O
P_{plat}	> 30 to 35 cmH_2O	≥ 25 cmH_2O
$PaCO_2$	≥ 60 mmHg	≥ 60 mmHg
pH	< 7.25–7.30	< 7.25–7.30
Respiratory rate	> 20 to 30 breaths/min	> 20 breaths/min
PaO_2/FiO_2	< 150	< 150
PEEP	> 8 to 15	≥ 8

Responses were captured during the post-meeting survey (Round 3) and general themes were identified

Table 3 $ECCO_2R$ weaning protocol for patients with ARDS

Weaning criteria and steps for weaning for $ECCO_2R$ in ARDS*
$ECCO_2R$ will be applied for at least 48 h
PaO_2/FiO_2 > 200 mmHg before testing weaning possibility
Set V_T at 6 mL/PBW and PEEP 5–10 cmH_2O
Driving pressure should be < 14 cmH_2O
Respiratory rate should be 20–30 breaths/min
Reduce gas flow to zero, using 2 L/min decremental steps
While weaning, pH should remain > 7.30 and respiratory rate < 25 breaths/min
Patient will be weaned off $ECCO_2R$ therapy after a minimum of 12 h of stability under these settings (including pH > 7.30 and respiratory rate < 25 breaths/min)

*A consensus was reached for all of these criteria and steps

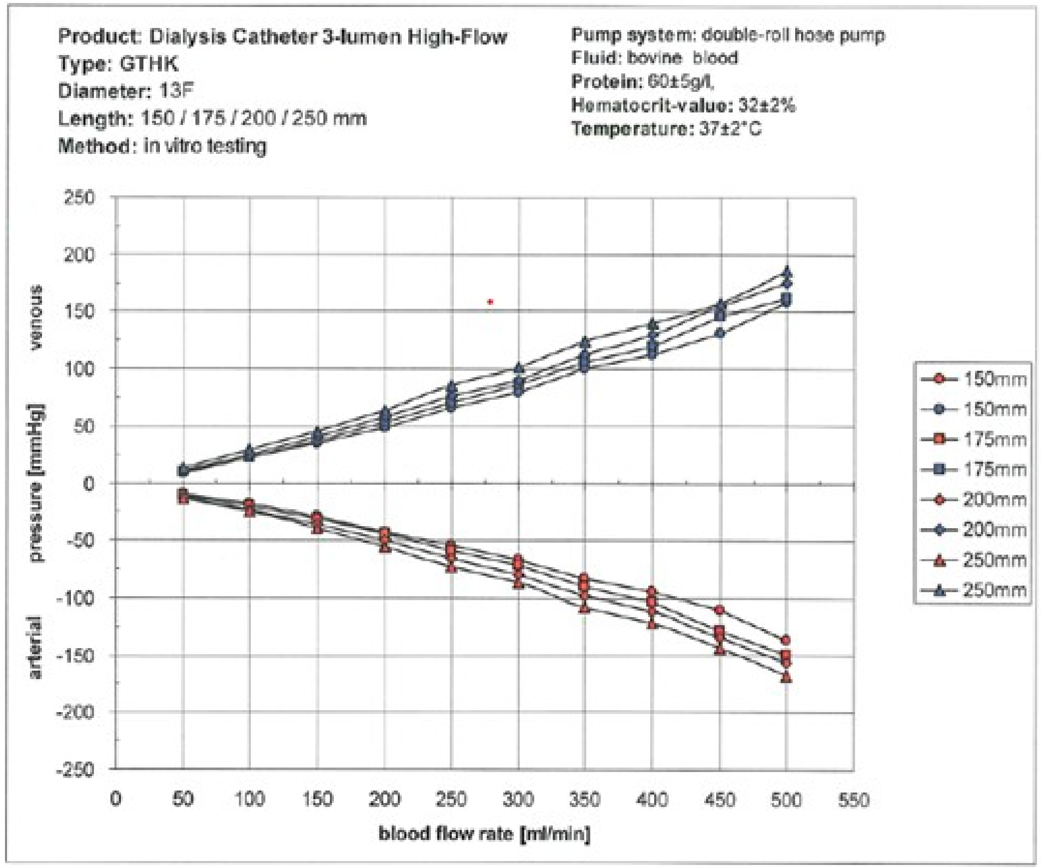
Table 6 Heparin anticoagulation strategy

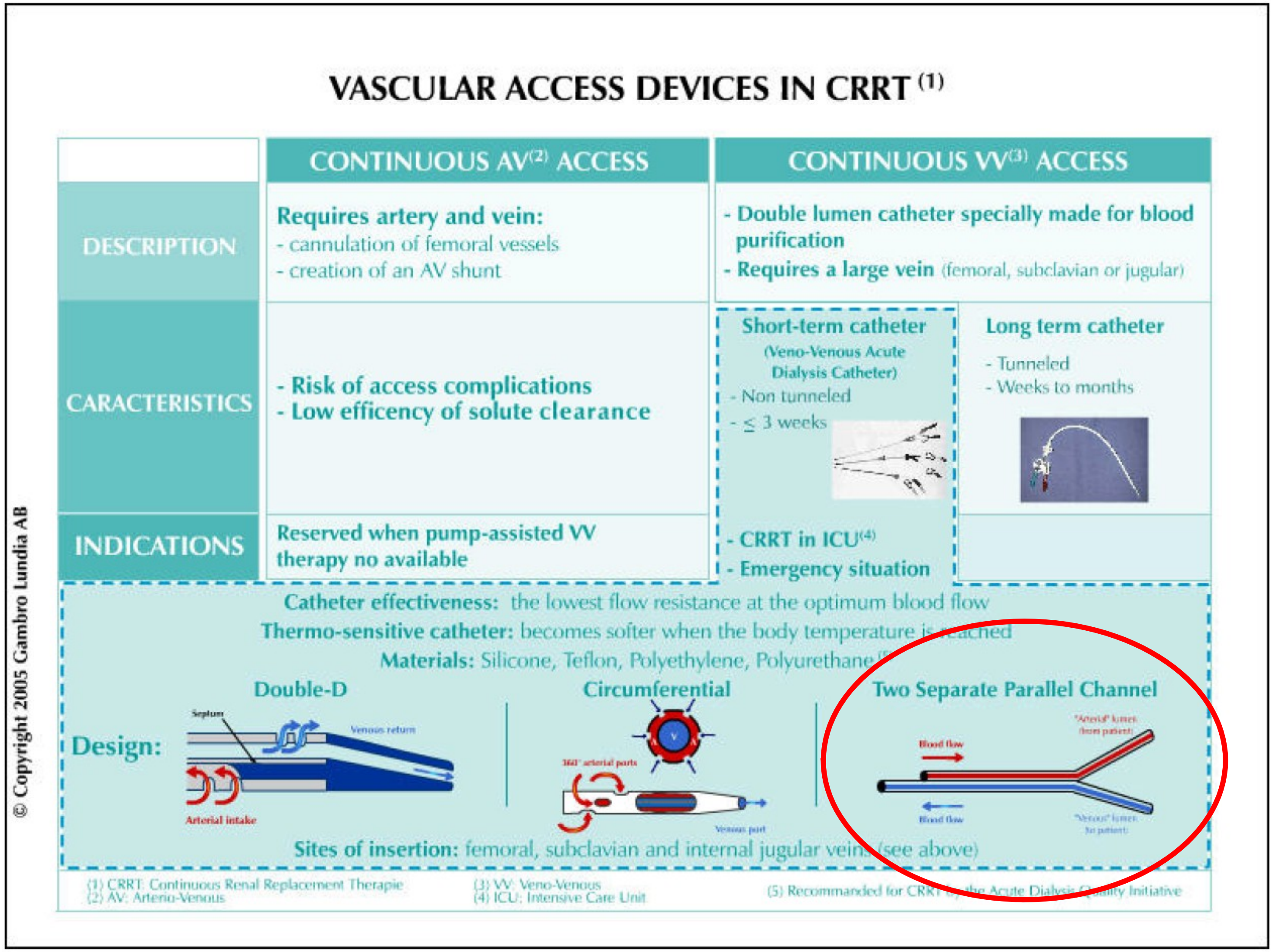
1. Anticoagulation with intravenous unfractionated heparin, preferably applied to the extracorporeal circuit
2. Monitor aPTT or anti-Xa or both
a. To obtain an aPTT of 1.5–2.0 times normal baseline (45–70 s), or anti-Xa activity of 0.3–0.5 UI/mL
3. Initial bolus of heparin
a. 40–80 units/kg PBW
b. Bolus will not be performed in patients already on full anticoagulation
c. Bolus routinely performed when guidewires have been inserted/or after catheter insertion
4. Patients with proven HIT-2
a. Argatroban protocol, e.g. 0.5–2.0 μg/kg/min

Vascular access and $ECCO_2R$

Double lumen catheter insertion

- 13 or 14 FR
- Right internal jugular vein preferentially
- Blood flow > 300 mL/min





VASCULAR ACCESS DEVICES IN CRRT [1]

	CONTINUOUS AV[2] ACCESS	CONTINUOUS VV[3] ACCESS	
DESCRIPTION	**Requires artery and vein:** - cannulation of femoral vessels - creation of an AV shunt	- **Double lumen catheter specially made for blood purification** - **Requires a large vein** (femoral, subclavian or jugular)	
CARACTERISTICS	- **Risk of access complications** - **Low efficency of solute clearance**	**Short-term catheter** (Veno-Venous Acute Dialysis Catheter) - Non tunneled - ≤ 3 weeks	**Long term catheter** - Tunneled - Weeks to months
INDICATIONS	Reserved when pump-assisted VV therapy no available	- CRRT in ICU[4] - Emergency situation	

Catheter effectiveness: the lowest flow resistance at the optimum blood flow
Thermo-sensitive catheter: becomes softer when the body temperature is reached
Materials: Silicone, Teflon, Polyethylene, Polyurethane[5]

Design: Double-D | Circumferential | Two Separate Parallel Channel

Sites of insertion: femoral, subclavian and internal jugular veins (see above)

(1) CRRT: Continuous Renal Replacement Therapie
(2) AV: Arterio-Venous
(3) VV: Veno-Venous
(4) ICU: Intensive Care Unit
(5) Recommanded for CRRT by the Acute Dialysis Quality Initiative

Conclusion

An evolving paradigm for management of ARDS …

- ARDSnet strategy might not protect lung against tidal hyperinflation and ventilator-induced lung injury
  - Pplat 28-30 cmH20 is probably not the graal …

- There is **a need to decrease tidal volume to reduce VILI**
  - From 6 to 4 or less mL/kg PBW **(« ultraprotective » ventilation concept)**
  - With Pplat < 25 cmH2O
  - With DeltaP < 15 cmH20
  - With high level of PEEP to prevent lung derecruitment
  - With reduced RR …

- Ultraprotective ventilation might be obtain
  - With **extracorporeal decarboxylation (vv-ECCO2R), moderate ARDS**
  - With **extracorporeal oxygenation and decarboxylation (vv-ECMO), severe ARDS**

RCT – $ECCO_2R$

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Lower Tidal Volume Ventilation Facilitated by Extracorporeal Carbon Dioxide Removal vs Standard Care Ventilation on 90-Day Mortality in Patients With Acute Hypoxemic Respiratory Failure
The REST Randomized Clinical Trial

August 2021

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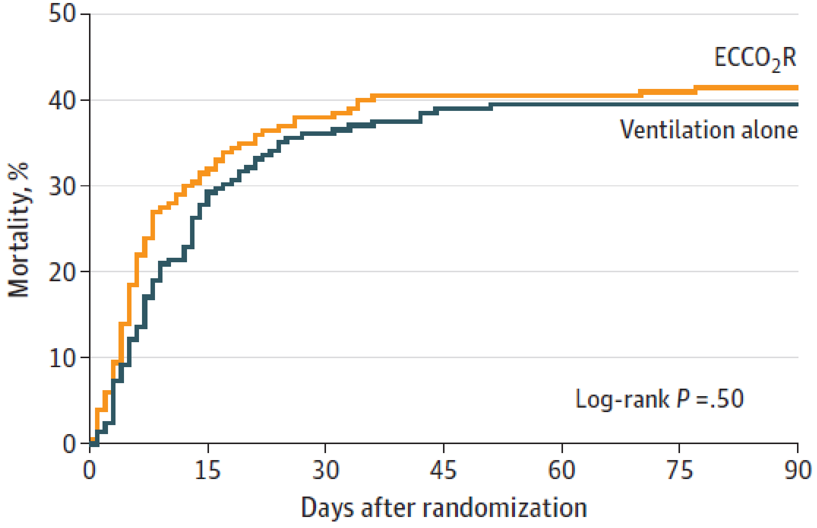
Figure 2. Kaplan-Meier Curve of the Time to Death by Treatment Group in a Study of Lower Tidal Volume Facilitated by Extracorporeal Carbon Dioxide Removal in Patients With Acute Hypoxemic Respiratory Failure



No. at risk							
$ECCO_2R$	200	137	124	119	119	118	117
Ventilation alone	205	148	131	125	124	124	124

Table 3. Adverse Events in a Study of Lower Tidal Volume Facilitated by Extracorporeal Carbon Dioxide Removal in Patients With Acute Hypoxemic Respiratory Failure

	$ECCO_2R$ (n = 202)		Ventilation alone (n = 210)	
Adverse event	No. of events	No. (%) of patients	No. of events	No. (%) of patients
Adverse events[a]	168	106 (52.5)	61	48 (22.9)
Related to study intervention[a,b]	65	51 (25.3)	0	0
Serious adverse events[c,d]	70	62 (30.7)	20	18 (8.6)
Related to study intervention[b]	22	21 (10.4)	0	0
Adverse events of specific interest				
Bleeding at other site (excluding intracranial hemorrhage)	18	17 (8.4)	3	3 (1.4)
Intracranial hemorrhage	10	10 (5.0)	2	2 (1.0)
Device failure causing adverse event	9	9 (4.5)	0	0
Bleeding at cannula site	8	8 (4.0)	0	0
Infectious complications[e]	7	7 (3.5)	1	1 (0.5)
Heparin-induced thrombocytopenia	4	4 (2.0)	0	0
Hemolysis	3	3 (1.5)	0	0
Ischemic stroke	1	1 (0.5)	3	3 (1.4)
Serious adverse events of specific interest[f]				
Bleeding at other site (excluding intracranial hemorrhage)	6	6 (3.0)	1	1 (0.5)
Intracranial hemorrhage	9	9 (4.5)	0	0
Infectious complications[e]	5	5 (2.5)	0	0
Device failure causing serious adverse event	2	2 (1.0)	0	0
Heparin-induced thrombocytopenia	1	1 (0.5)	0	0
Ischemic stroke	1	1 (0.5)	3	3 (1.4)

Conclusion

Low-flow ECCO2R may help to obtain ultraprotective ventilation, but:

- Need expertise with the device and adequate vascular access
    - Double lumen catheter ≥ 13 FR or more, right jugular internal vein
- Need high level of systemic anticoagulation
- Need to take care with pressure regimen in the extracorporeal circuit (transmembrane-, in- and out-flow pressure sensor)
    - One of the main identified problem is the association of prone position and $ECCO_2R$ = risk of filter clotting
- Need to take into account the cost …
- Best timing remains unknow
- Need further large randomized trial to test impact on morbi/mortality in moderate-to-severe ARDS

Conclusion and prospectives

$ECCO_2R$ in AE-COPD

- An other potential indication …
- Case-control ECLAIR study
  - 25 cases with AE-COPD and NIV
  - Intubation avoided in 56% of patients with NIV
  - Adverse events in 36% of patients
  - No difference in IMV, MV-free days, LOS in ICU and mortality
  - Braune *et al.* ICM 2017
- Impact on morbi/mortality needs to be tested
- Best timing is unknown
- Adverse events …
- Costs …
- Need for further large randomized trial

Table 4 $ECCO_2R$ treatment initiation criteria for patients with ae-COPD

Initiation criteria for patients at risk of NIV failure	
Parameter	
No decrease in $PaCO_2$ while on NIV	Consensus
No decrease in respiratory rate while on NIV	Consensus
Clinical signs of respiratory failure	Majority agreement
pH 7.25–7.30	Majority agreement
Baseline $PaCO_2$	No agreement
Baseline respiratory rate	No agreement
Initiation criteria for patients who are already intubated	
- Patients who look like they will not be extubated early without $ECCO_2R$	
○ Previous intubation for ae-COPD	
○ Has failed a spontaneous breathing trial due to increased dyspnoea	
○ Reintubation after first extubation attempt despite NIV	
○ Patients with severe bronchospasm who are difficult/impossible to ventilate adequately or otherwise not responding to medical treatment	
○ Patients who remain hypercapnic and not improving with MV	
- No hypoxemia preventing extubation	
- MV < 72 h	
- Patients with home NIV and good quality of life	

Thank you for your attention