Pulmonary vascular dysfunction during ARDS

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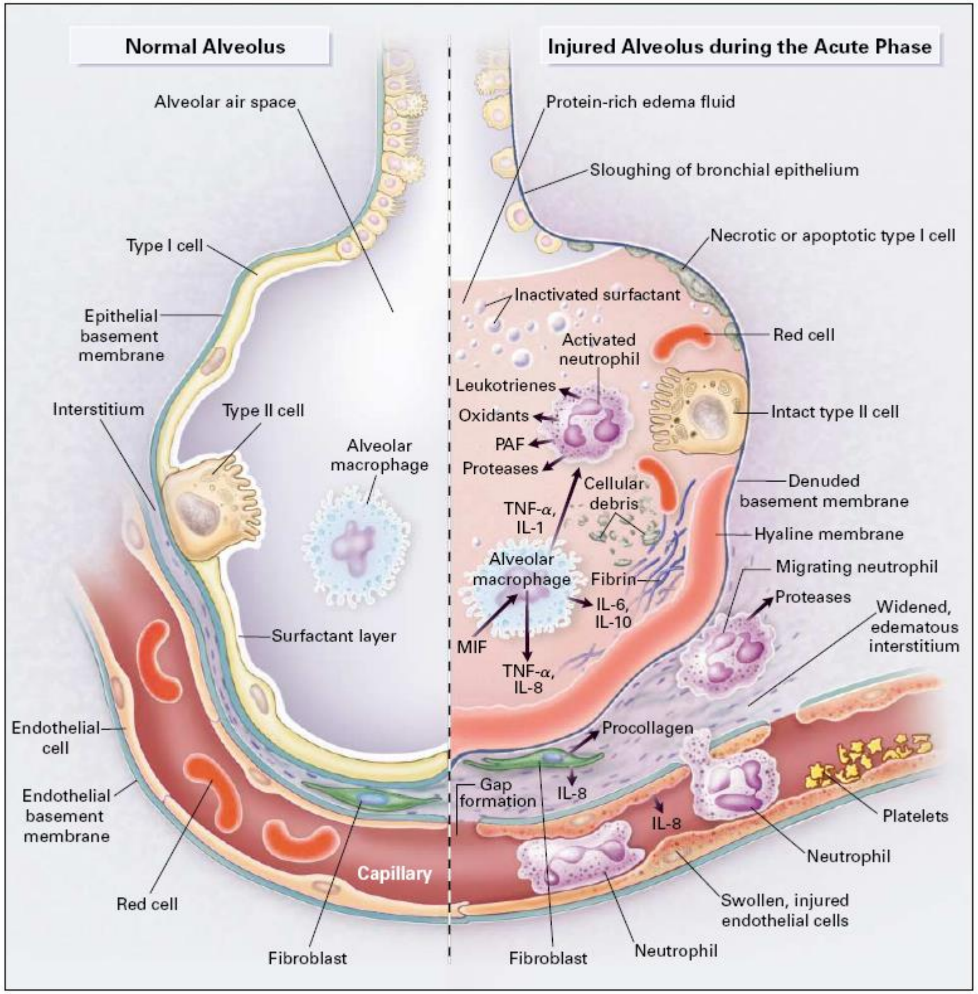
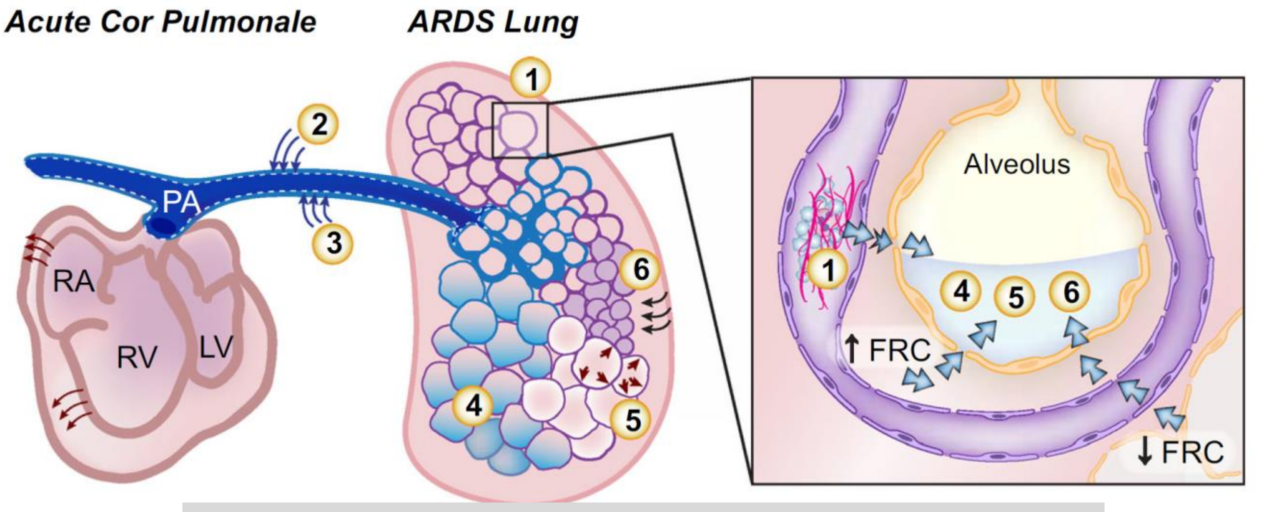
Pathophysiology
Diagnosis
Prognosis
Treatment

ARDS is a disease of the pulmonary alveoli AND capillaries



Ware, NEJM 2000

Factors associated with lung vascular dysfunction during ARDS



VASO-OCCLUSION

1. Endothelial lesions, thrombosis, remodeling

VASOCONSTRICTION

2. Hypoxemia, hypercapnia

3. Endogenous mediators (Tx, LT, ET…)

VESSEL COMPRESSION

4. Edema

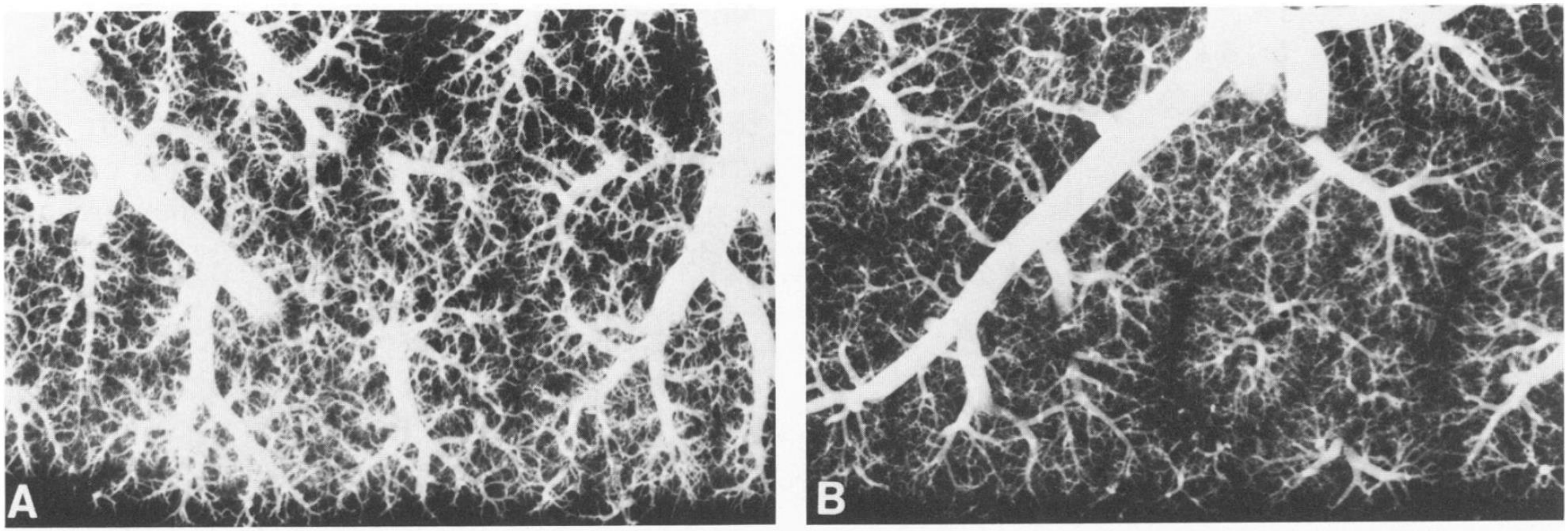
5. Overdistension

6. Lung collapse

Adapted from Guerin, ICM 2016

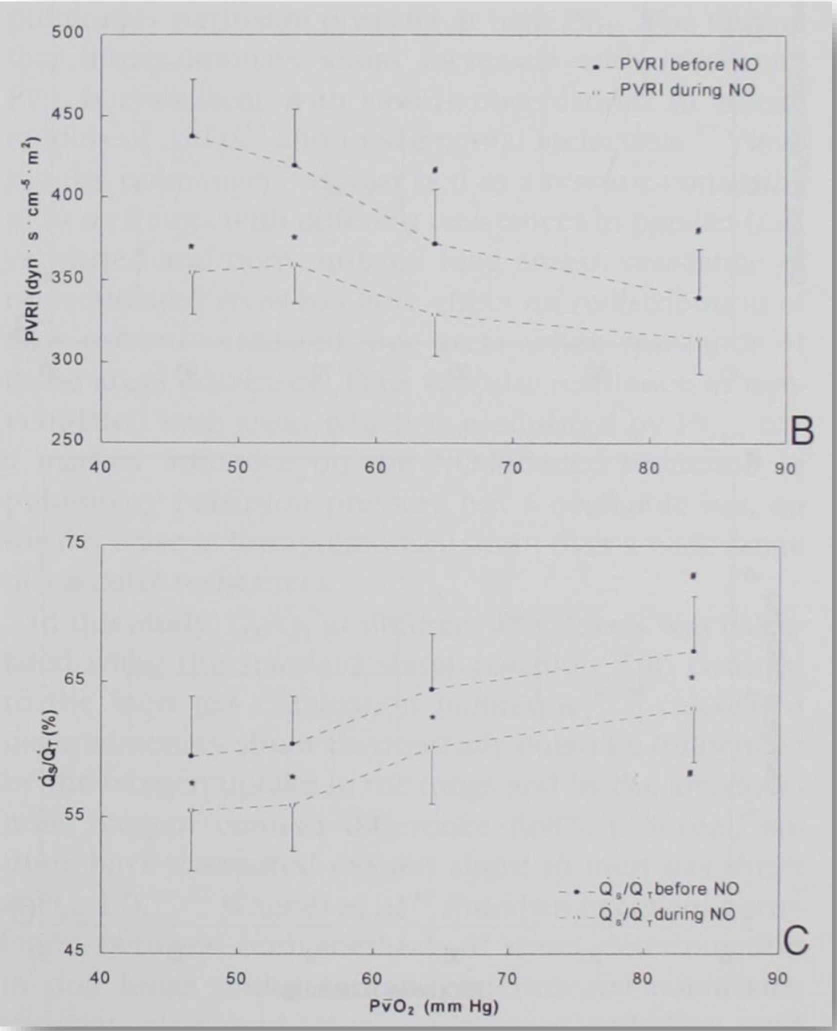
Vaso-occlusion

Normal adult **Early ARDS**



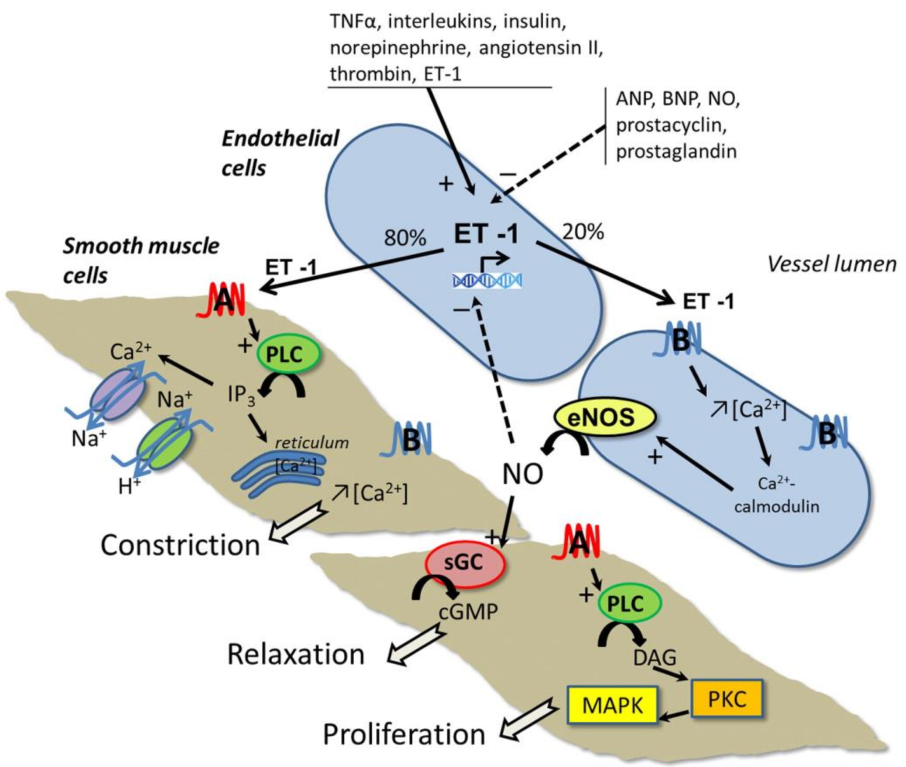
Tomashefski, Am J Pathol 1983

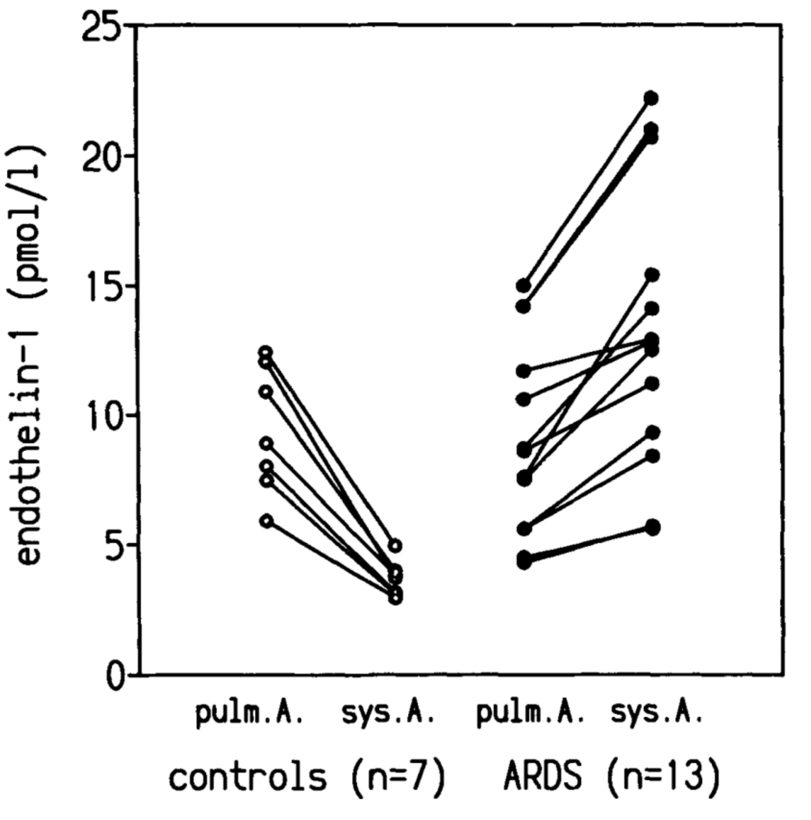
Hypoxic pulmonary vasoconstriction



Benzing, Anesthesiology 1997

Endothelins





Nicolas Vignon-Zellwegera, Life Sci 2012

Druml, ARRD 1993

Role of ventilation

VASO-OCCLUSION
1. Endothelial lesions, thrombosis, remodeling

VASOCONSTRICTION
2. Hypoxemia, hypercapnia
3. Mediators (Tx, LT, ET…)

VESSEL COMPRESSION
4. Edema
5. Overdistension
6. Lung collapse

Lung injury

Lung vascular dysfunction

Mechanical ventilation

VASO-OCCLUSION
1. Endothelial lesions, thrombosis, remodeling

VASOCONSTRICTION
2. Hypoxemia, permissive hypercapnia
3. Mediators (Tx, LT, ET…)

VESSEL COMPRESSION
4. Edema (VILI)
5. Overdistension
6. Lung collapse

Intrathoracic pressures alteration: effect on RV function

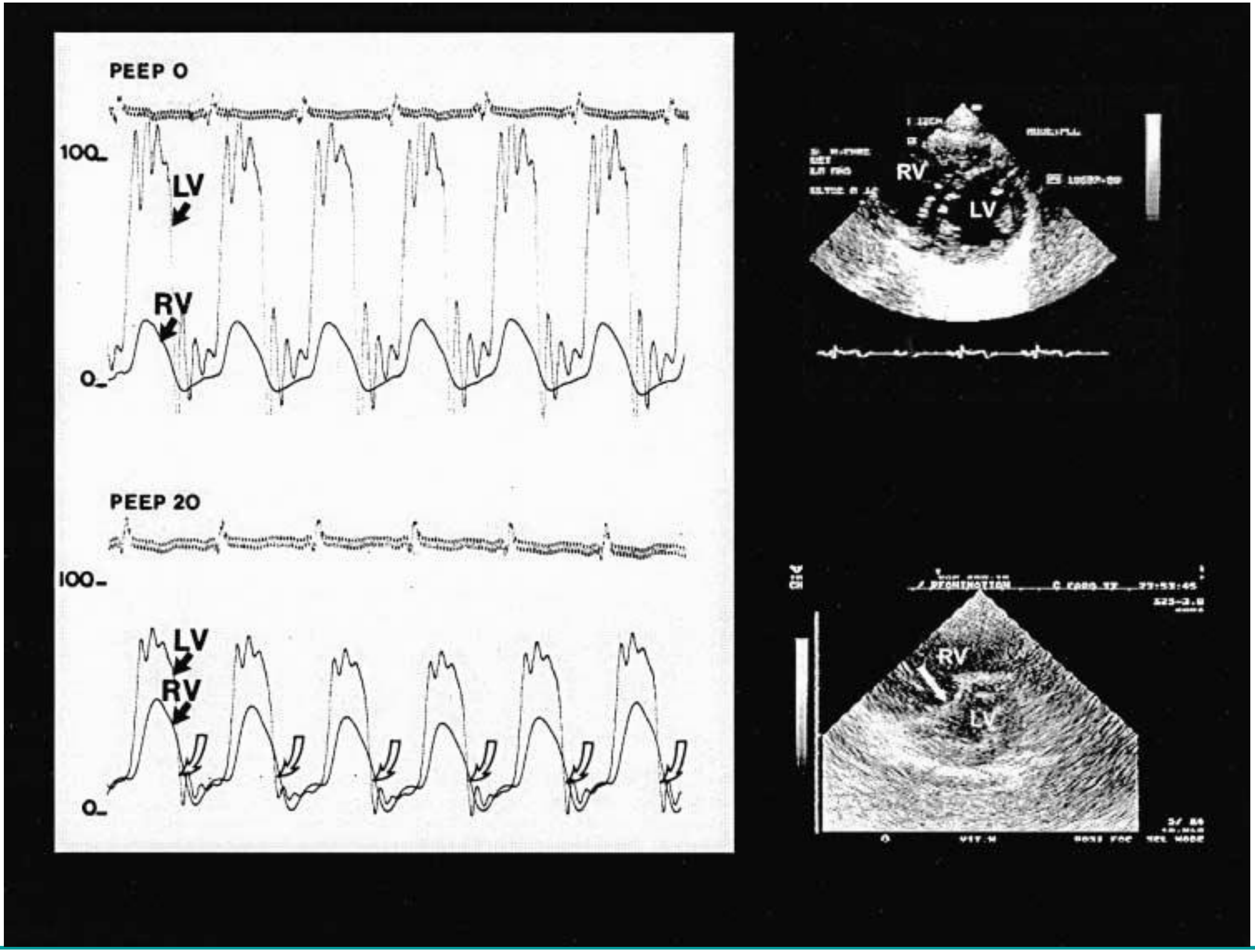
- ↑ pleural pressure
  - ↓ pressure gradient of venous return ?
  - ↓ conductance of venous return (collapsible zone)

  ➡ ↓ **RV preload** (<u>preload effect</u>)

- ↑ transpulmonary pressure
  - ↓ pulmonary capillaries conductance

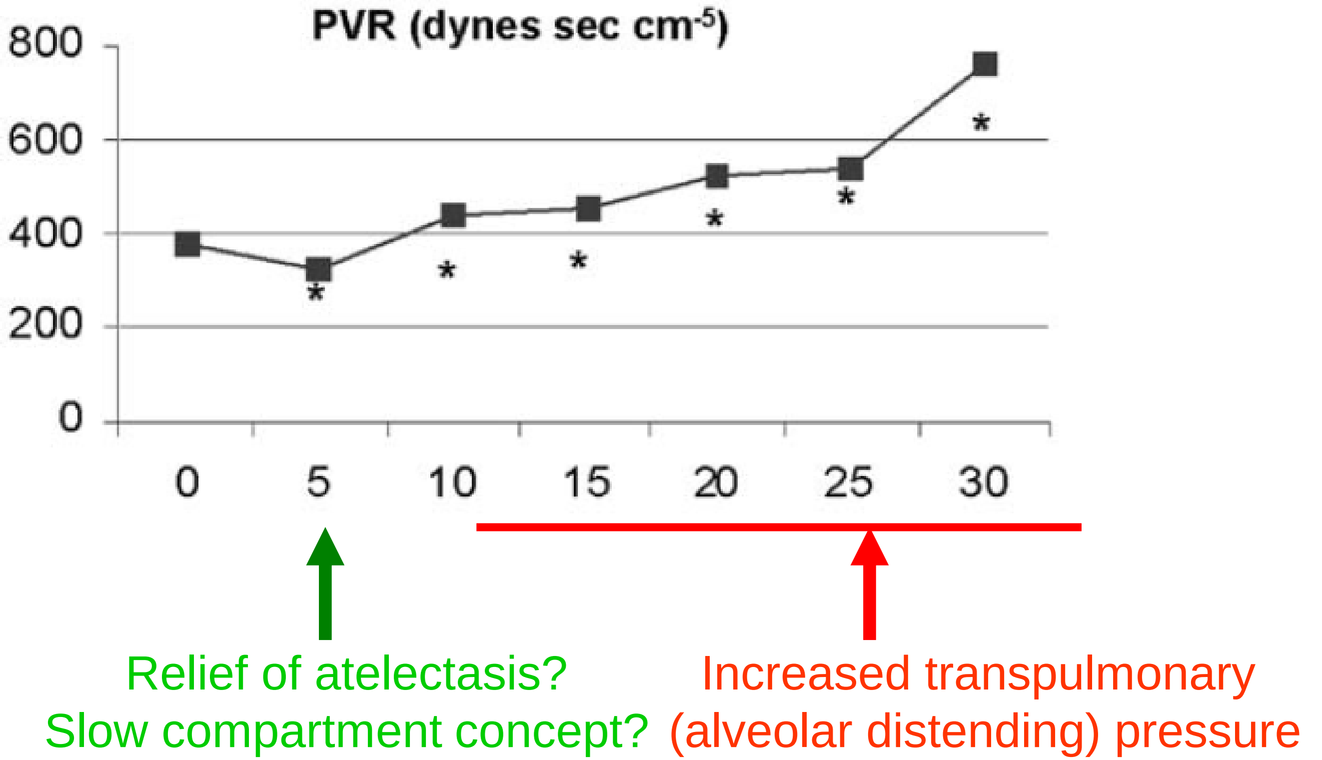
  ➡ ↑ **RV afterload** (<u>afterload effect</u>)

RV afterload effect and ventricular coupling



Vieillard-Baron, AJRCCM 2002

Dual effect of PEEP on RV afterload



Jellinek JAP 2000

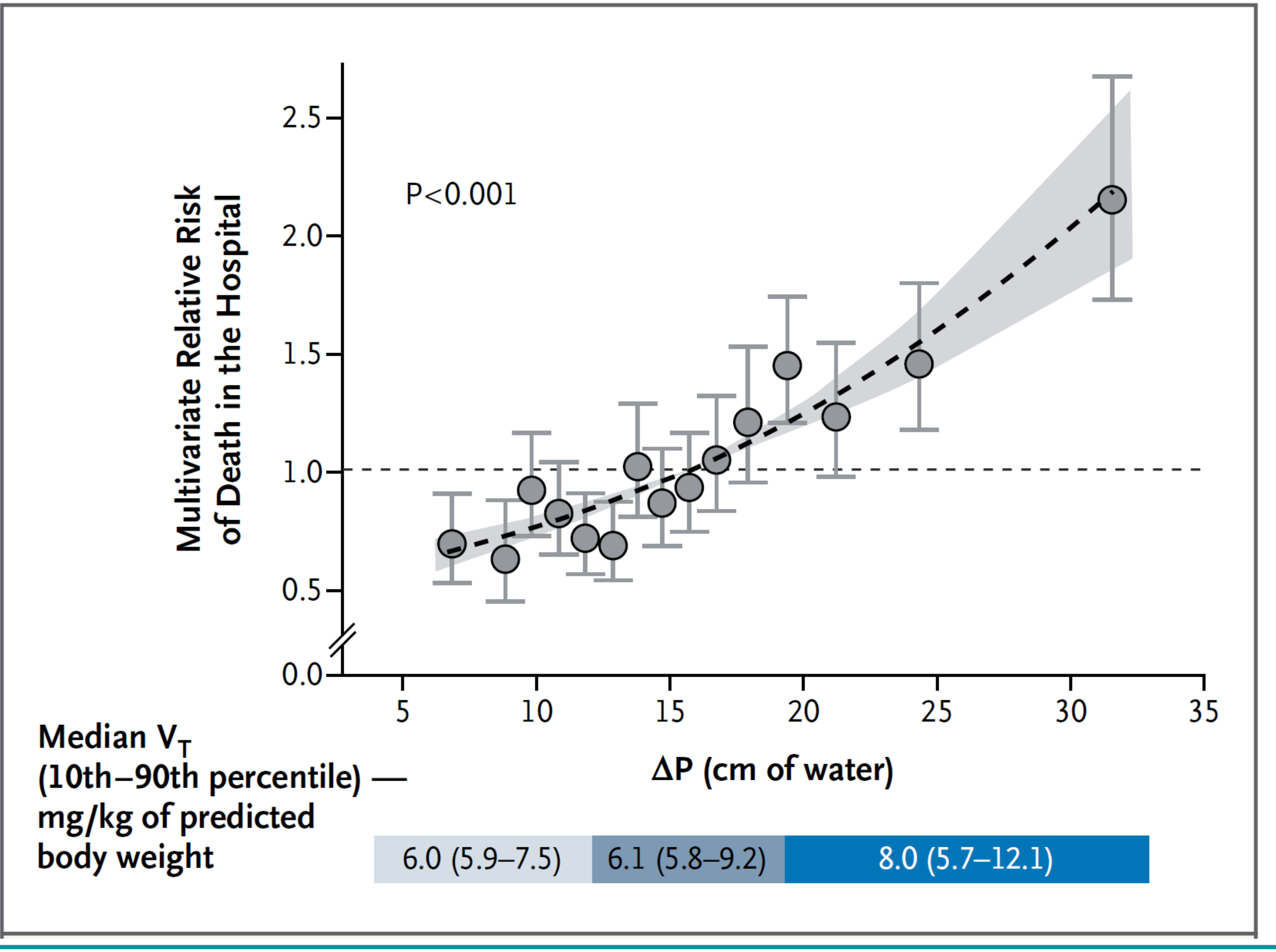
Role of respiratory settings

Table 2 Factors associated with acute cor pulmonale in patients with acute respiratory distress syndrome

Variable	Odds ratio (95 % CI) by logistic regression	
	Univariate	Multivariable[a]
Pneumonia as cause of ARDS	2.54 (1.79–3.62), $p < 0.01$	2.73 (1.84–4.05), $p < 0.01$
Respiratory settings on TEE day		
Tidal volume <7 mL/kg	1.70 (1.17–2.47), $p < 0.01$	I/NR
Respiratory rate ≥30 breaths/min	1.70 (1.11–2.60), $p = 0.02$	I/NR
Plateau pressure ≥27 cmH_2O	1.91 (1.33–2.73), $p < 0.01$	I/NR
Compliance <30 ml/cmH_2O	1.91 (1.33–2.73), $p < 0.01$	I/NR
Driving pressure ≥18 cmH_2O[b]	2.16 (1.51–3.10), $p < 0.01$	2.28 (1.53–3.38), $p < 0.01$
Arterial blood gases on TEE day		
PaO_2/FiO_2 ratio <150 mmHg	2.41 (1.49–3.92), $p < 0.01$	2.60 (1.50–4.52), $p < 0.01$
$PaCO_2$ ≥48 mmHg	2.95 (2.06–4.21), $p < 0.01$	2.39 (1.62–3.52), $p < 0.01$

Mekontso Dessap, ICM 2016

Driving pressure and ARDS prognosis



Amato, NEJM 2015

Pathophysiology

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How to detect lung vascular dysfunction ?

- Biology
  - ↑blood marker of endothelial injury

    eg: ↑ angiopoietin-2/angiopoietin-1 ratio

    (►*may reflect systemic rather than pulmonary endothelial injury*)

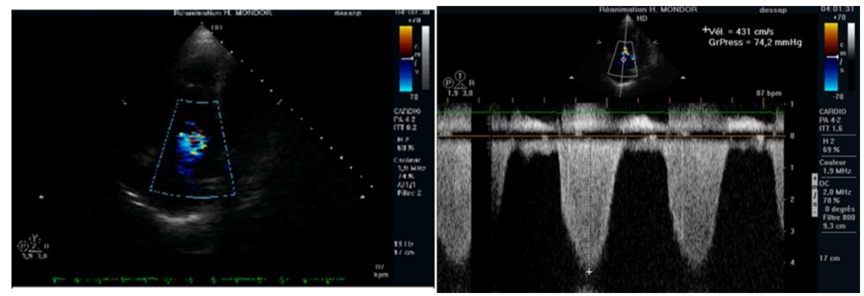
- Dead space calculation
  - ↑alveolar dead space

- Pulmonary artery catheter
  - ↑PAP and PVR
  - ↑Transpulmonary gradient (PAPm - PAOP)
  - CVP > PAOP

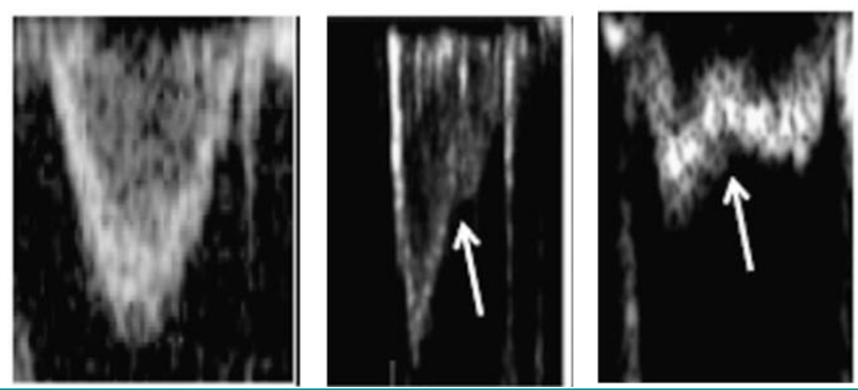
Echocardiography to detect lung vascular dysfunction

↑ RV afterload

- ↑PAP



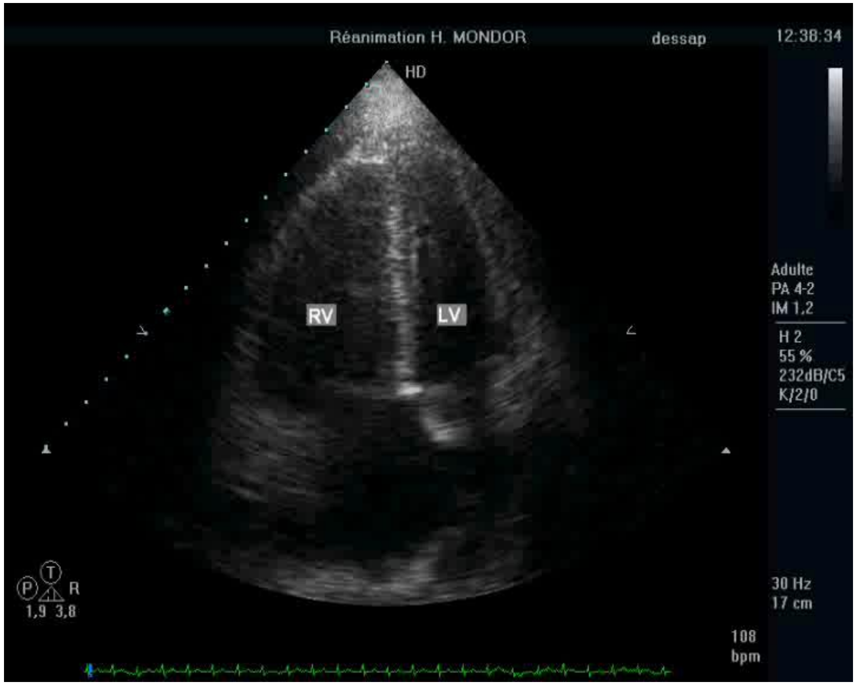
- Alteration of pulmonary ejection flow



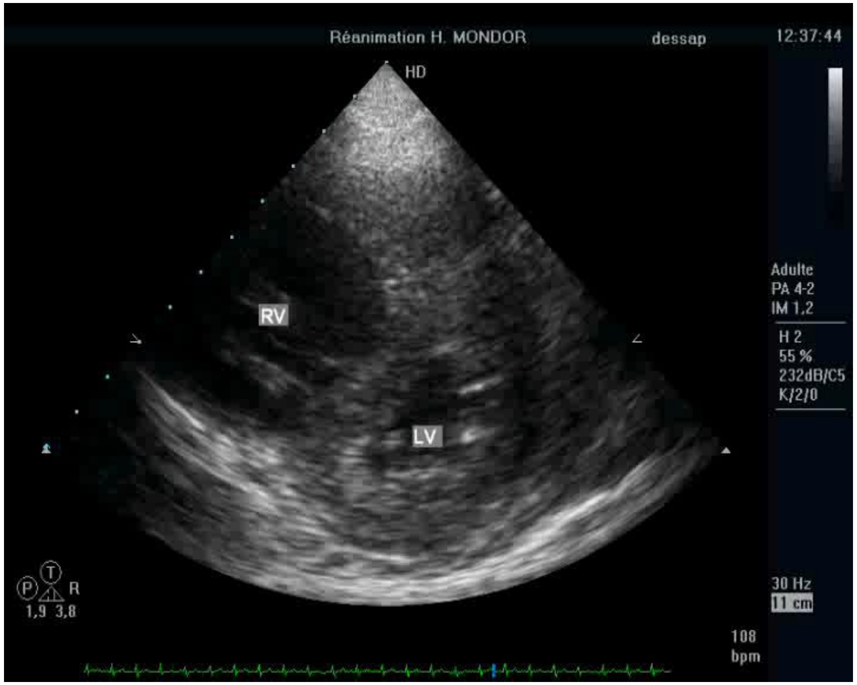
Arkles, AJRCCM 2011

Cor pulmonale

RV dilatation



Septal dyskinesia



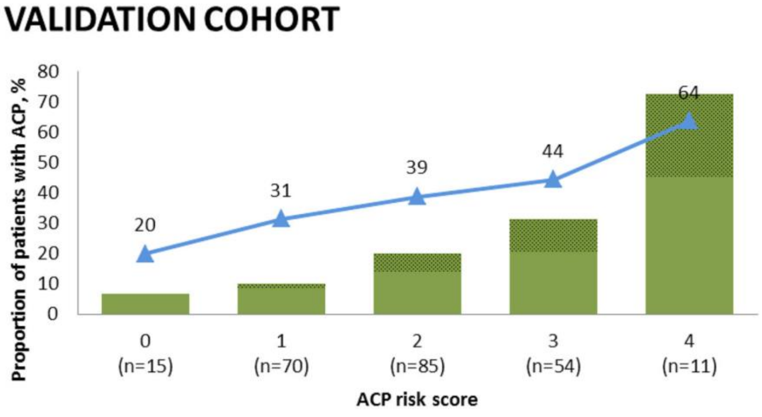
Risk factors for cor pulmonale

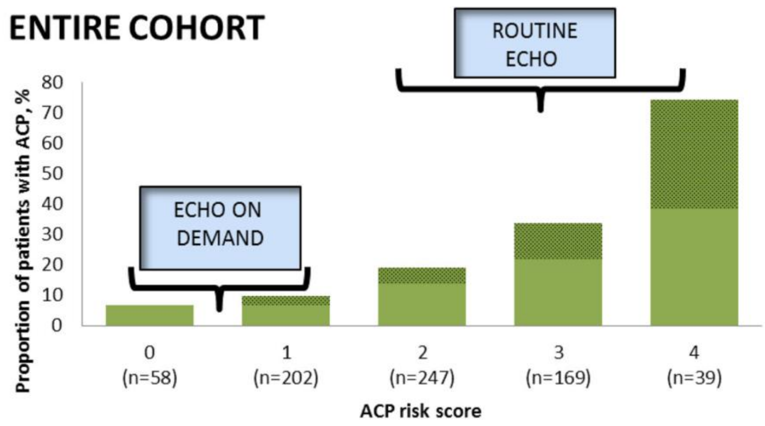
Table 3 The acute cor pulmonale risk score

Parameter	Score
Pneumonia as cause of ARDS	1
Driving pressure $\geq$18 cmH_2O[a]	1
PaO_2/FiO_2 ratio <150 mmHg	1
$PaCO_2$ $\geq$48 mmHg	1
Total score	0–4

Mekontso Dessap, ICM 2015

ACP risk score

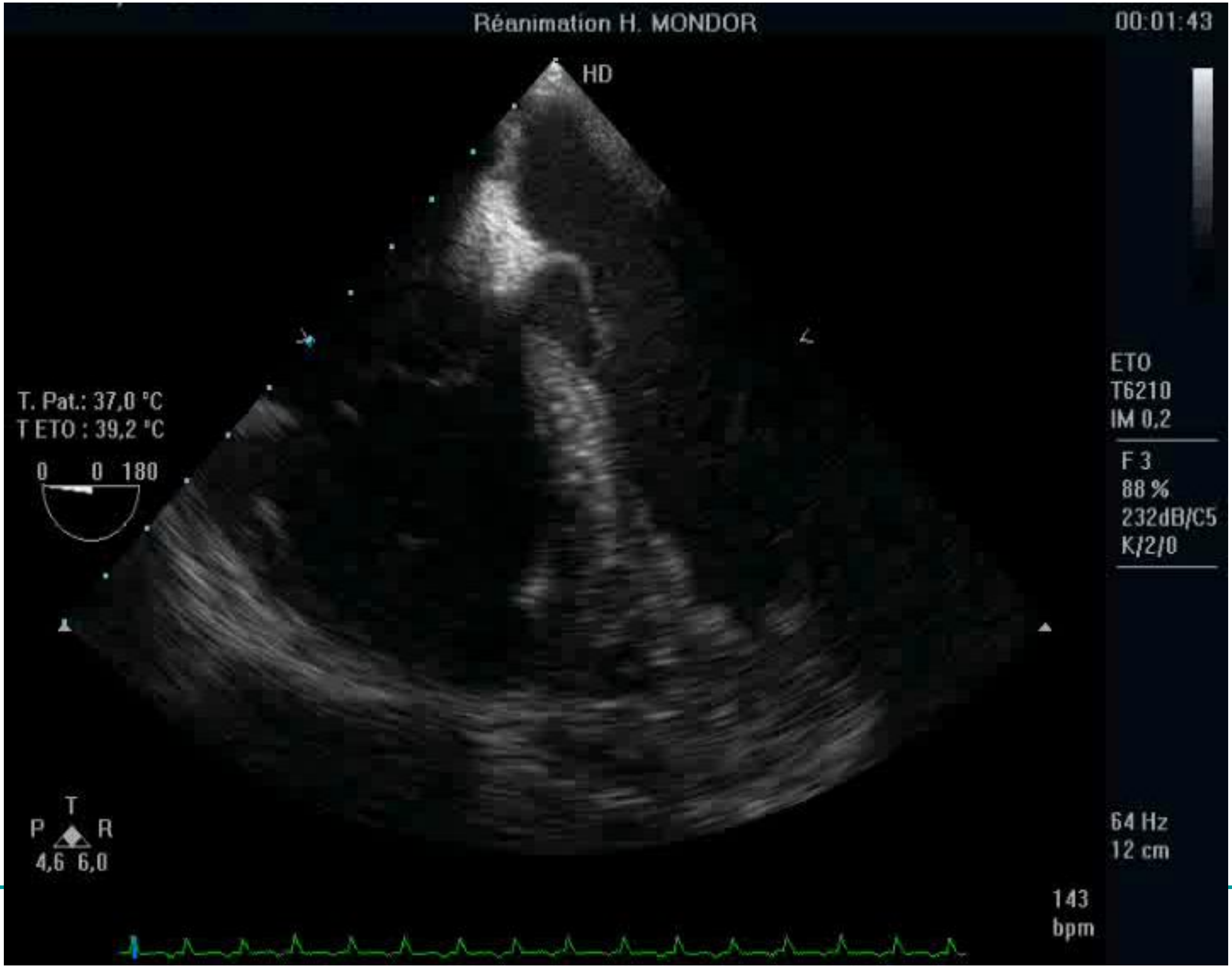




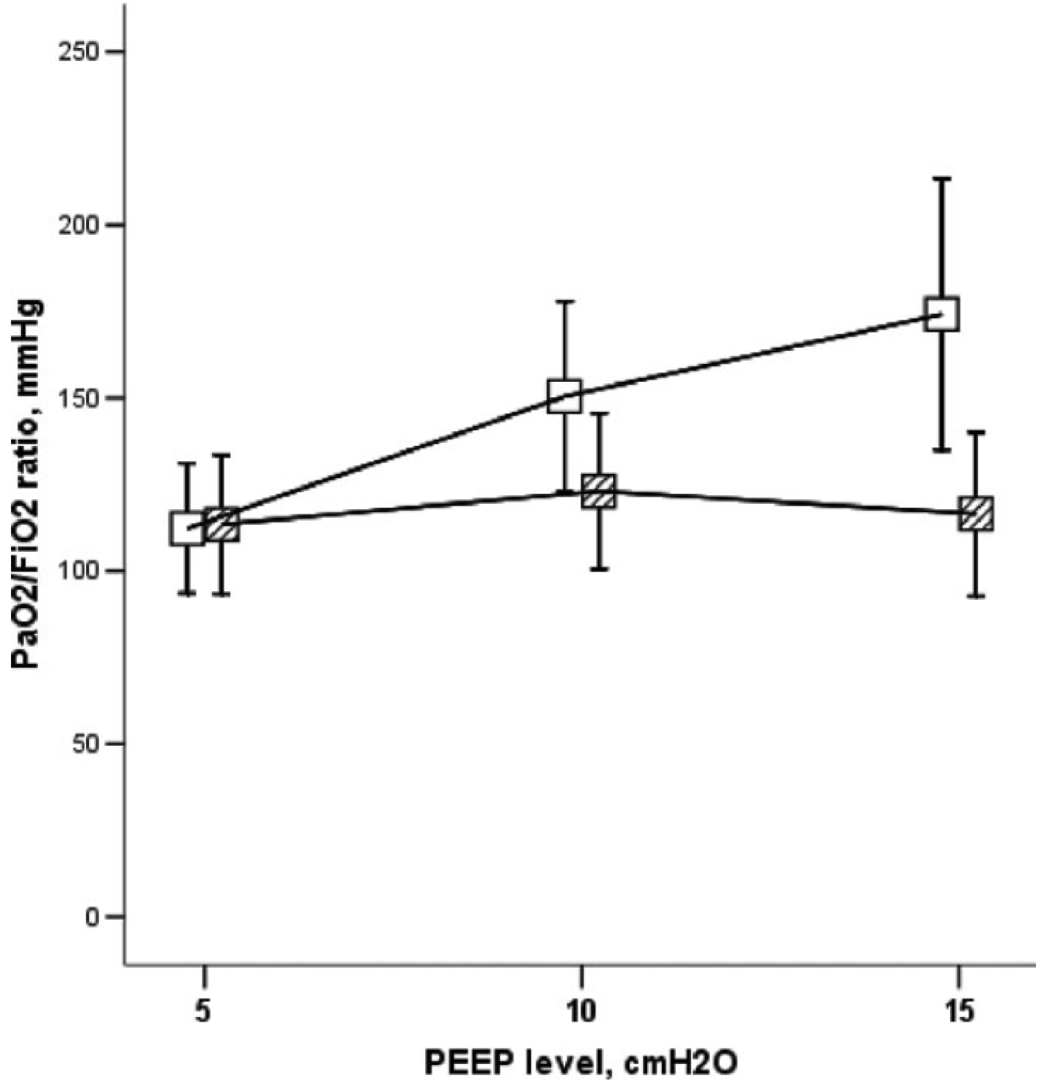
Mekontso Dessap, ICM 2015

Clinical implications of lung vascular dysfunction during ARDS

- Hemodynamics (RV failure)
- Oxygenation (PFO shunting)


Réanimation H. MONDOR
00:01:43
HD
T. Pat.: 37,0 °C
T ETO : 39,2 °C
0 0 180
ETO
T6210
IM 0,2
F 3
88 %
232dB/C5
K/2/0
T
P R
4,6 6,0
64 Hz
12 cm
143
bpm

PFO and PEEP



Mekontso Dessap, CCM 2010

Pathophysiology

Diagnosis

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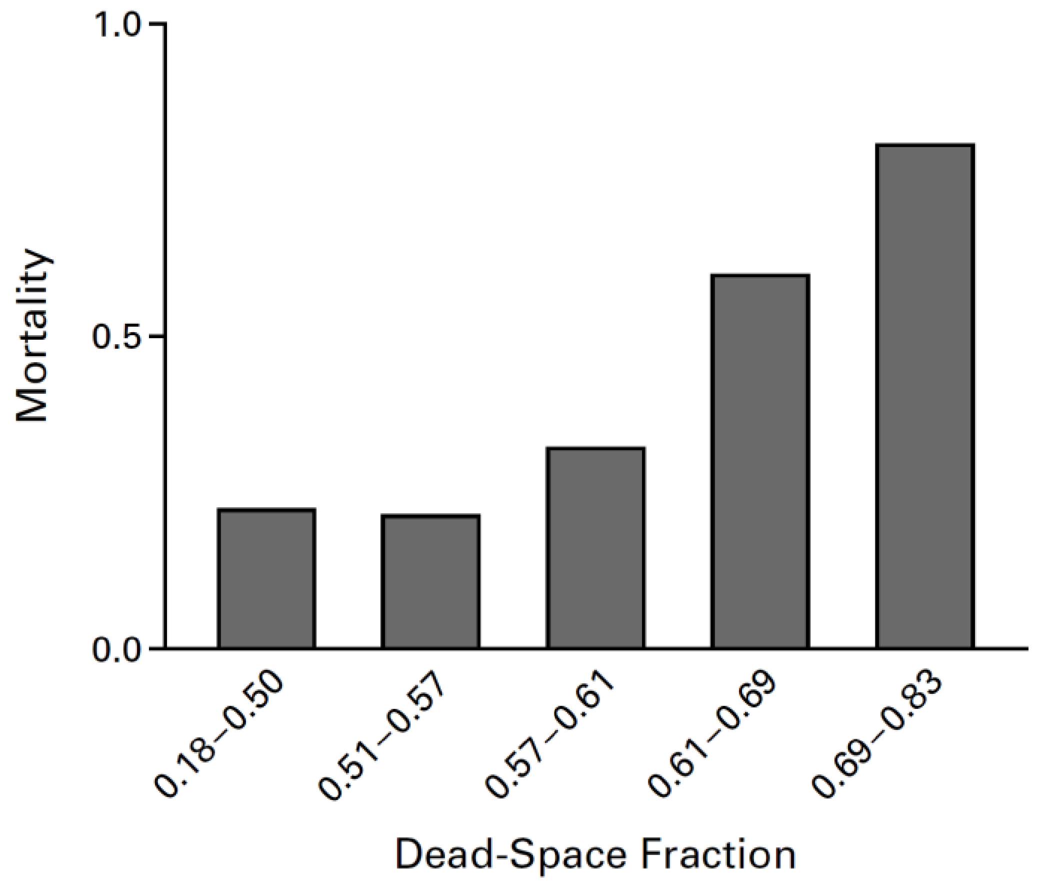
Prognosis of dead space fraction

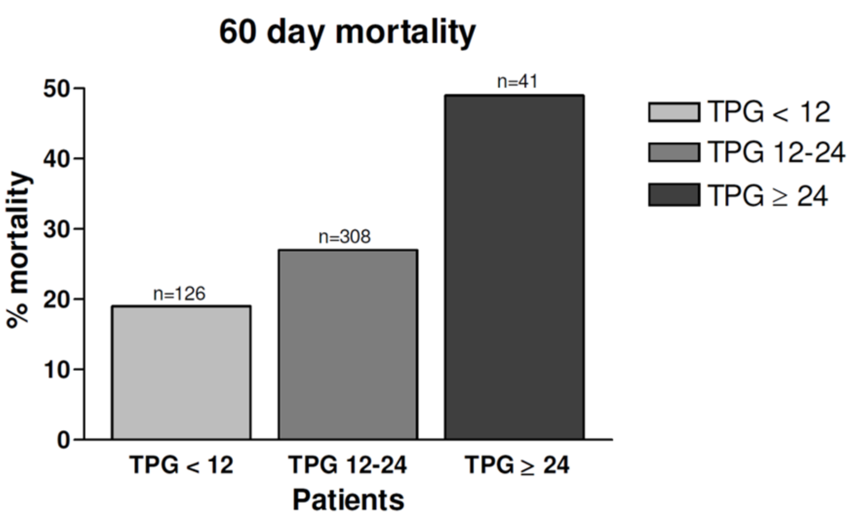


Nuckton, NEJM 2002

Prognosis of PAC indexes

	Survive (n=47)	Dead (n=98)	p
PAPm, mmHg	27	28	0.49
PVRi	350	367	0.60
CVP>PAOP	**19%**	**33%**	**<0.05**
RVF	9%	10%	0.98

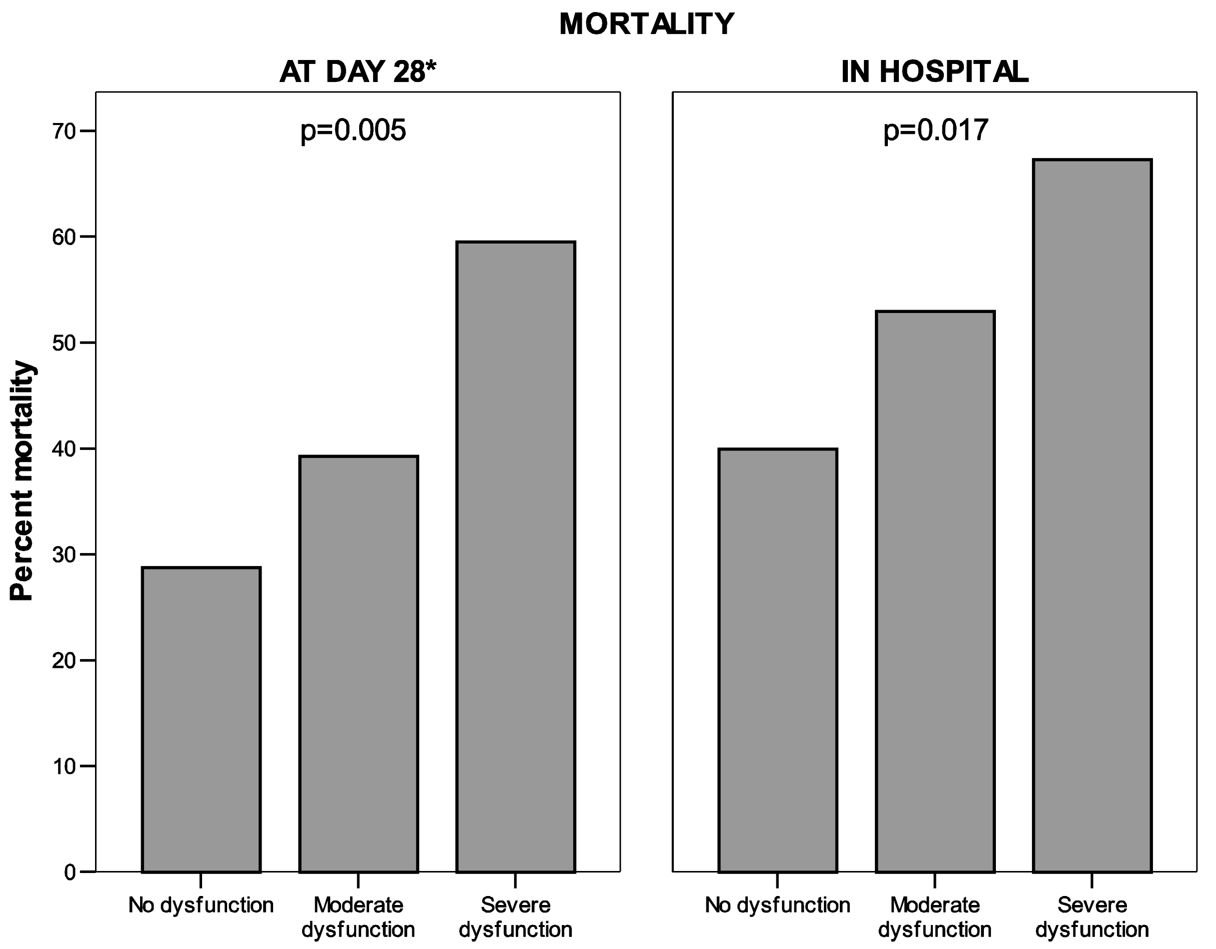
	Survive (n=348)	Dead (n=127)	P
TPG	**14.3**	**15.7**	**0.009**
PVRI	**299.9**	**326.4**	**0.03**



Osman, ICM 2009

Bull, AJRCCM 2010

Prognosis of lung vascular dysfunction



Boissier, ICM 2013

Pathophysiology

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Intravenous vasodilators

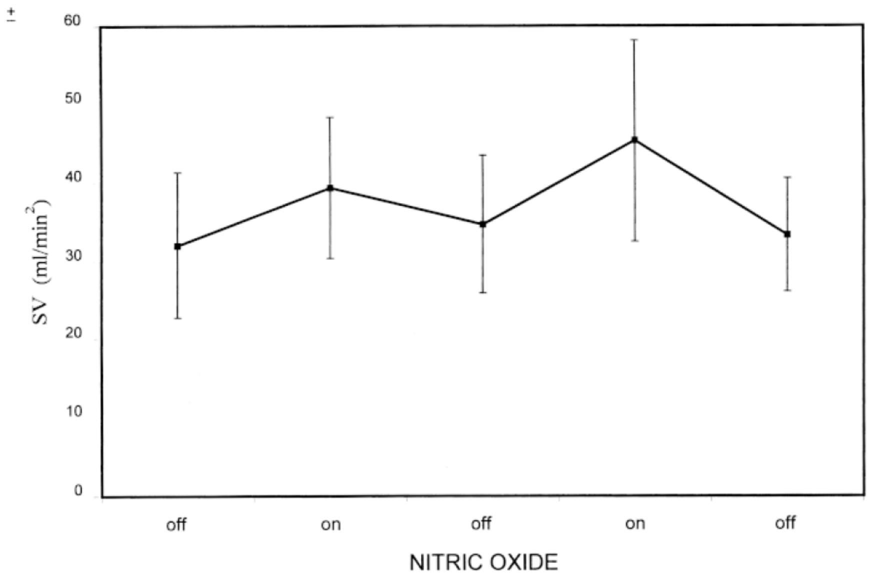
EXAMPLES

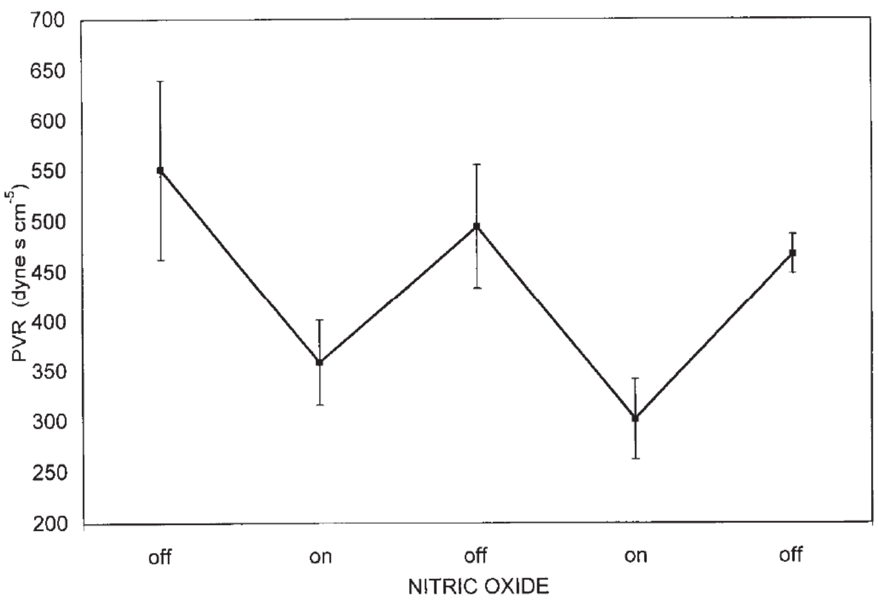
- PGE1
- PGI2 (prostacyclin)
- Nitroprusside
- Isoproterenol
- Diltiazem

DRAWBACKS

- Lack of selectivity for the pulmonary circulation
  - Systemic hypotension
- Act on ventilated and non ventilated pulm.vessels
  - ↑ shunt fraction and ↓ PaO_2
- **No clinical benefit in randomized trials**

Inhaled NO



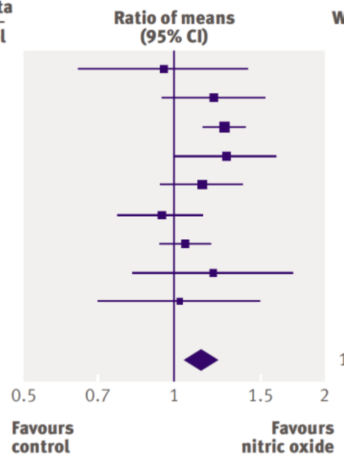


Human RV failure
Bohrade, AJRCCM 1999

Inhaled NO

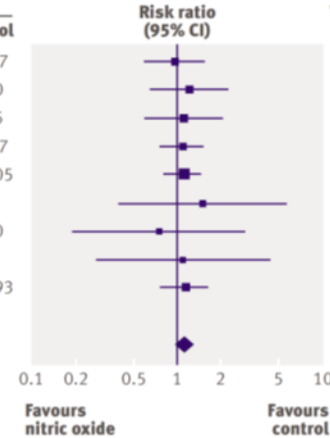
P/F RATIO

Study	No of patients with data: Nitric oxide	Control	Weight (%)	Ratio of means (95% CI)
Day[w1]	11	10	3.8	0.95 (0.64 to 1.42)
Schwebel[w2]	9	10	8.5	1.20 (0.94 to 1.54)
Dellinger[w3]	120	57	24.9	1.27 (1.14 to 1.41)
Michael[w4]	16	16	9.1	1.28 (1.01 to 1.62)
Troncy[w5]	15	15	12.4	1.14 (0.94 to 1.39)
Dobyns[w6]	49	50	11.9	0.94 (0.77 to 1.15)
Lundin[w7]	78	66	21.1	1.05 (0.93 to 1.19)
Mehta[w9]	8	6	4.2	1.20 (0.82 to 1.75)
Park[w11]	11	6	4.1	1.03 (0.70 to 1.51)
Total	312	236	100.0	1.13 (1.04 to 1.23)



SURVIVAL

Study	Deaths/patients randomised: Nitric oxide	Control	Weight (%)	Risk ratio (95% CI)
Dellinger[w3]	35/120	17/57	11.2	0.98 (0.60 to 1.59)
Michael[w4]	11/20	9/20	6.8	1.22 (0.65 to 2.29)
Troncy[w5]	9/15	8/15	6.7	1.13 (0.60 to 2.11)
Lundin[w7]	41/93	35/87	22.5	1.10 (0.78 to 1.55)
Payen[w8]	48/98	46/105	30.3	1.12 (0.83 to 1.50)
Mehta[w9]	4/8	2/6	1.5	1.50 (0.40 to 5.65)
Gerlach[w10]	3/20	4/20	1.4	0.75 (0.19 to 2.93)
Park[w11]	4/11	2/6	1.4	1.09 (0.28 to 4.32)
Taylor[w12]	44/192	39/193	18.2	1.13 (0.77 to 1.66)
Total	577	509	100.0	1.10 (0.94 to 1.30)



Adhikari, BMJ 2007

Ventilatory strategy: primum non nocere:

- Avoid excessive hypoxemia / hypercapnia
- Avoid lung vascular stretch
  - Limit driving pressure
  - Limit recruitment maneuvres
- Prone position

Ventilatory strategy: RV protective approach

- Avoid excessive hypoxemia / hypercapnia
- Avoid lung vascular stretch
  - Limit driving pressure
  - Limit recruitment maneuvres
- Prone position

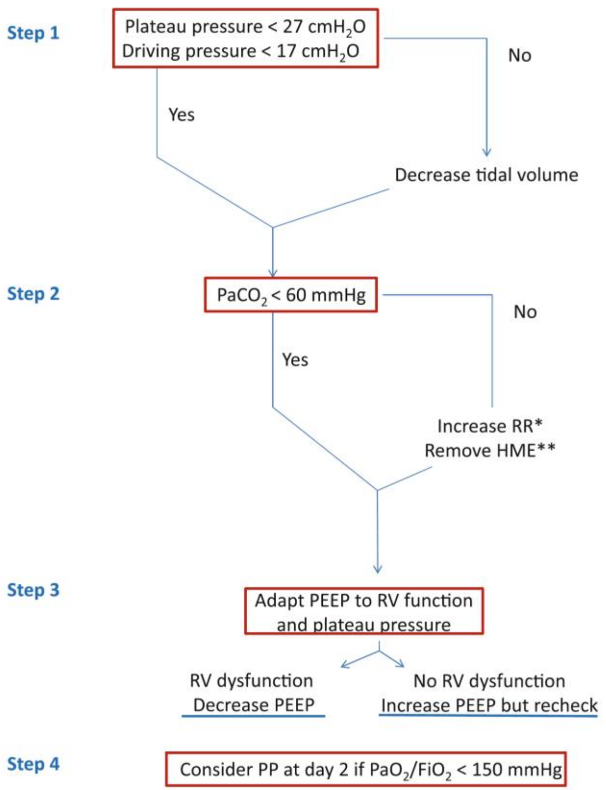
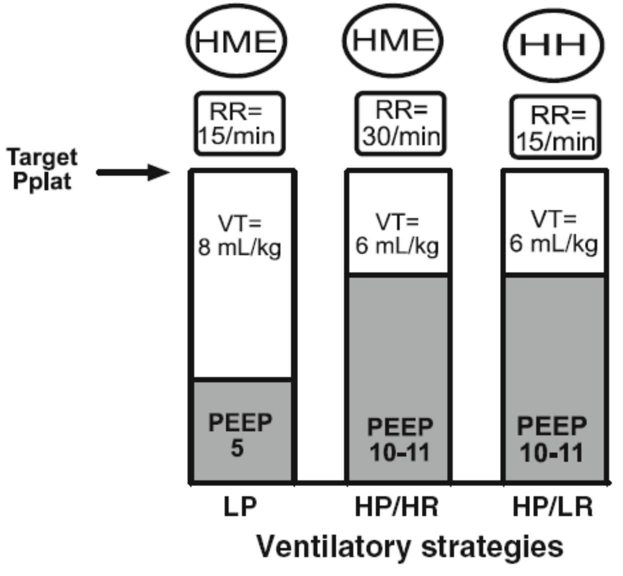
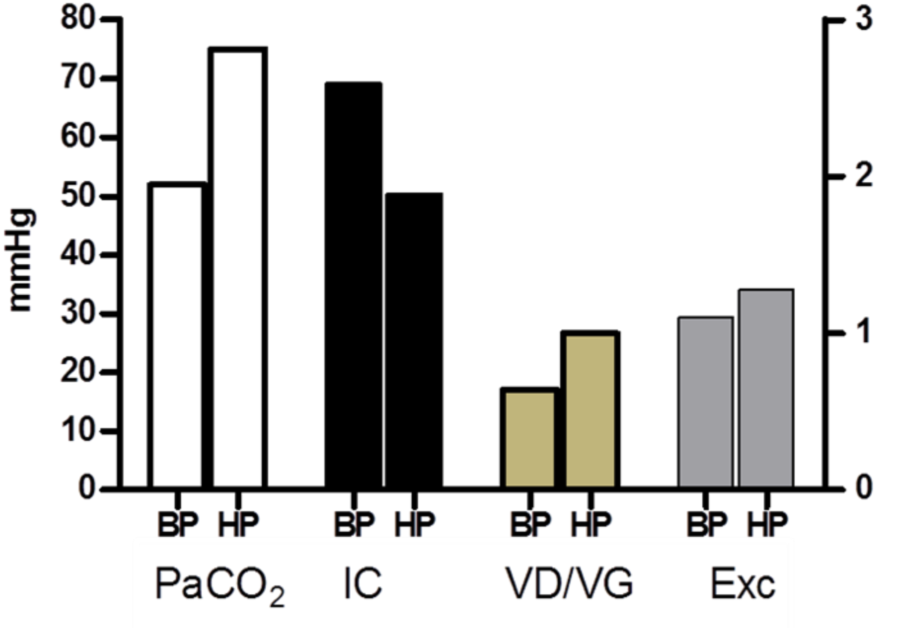


Fig. 1 Proposed approach to preventing acute cor pulmonale and limiting its consequences: a *right* ventricular protective approach. *RR* respiratory rate, *RV* right ventricular, *HME* heat and moisture exchanger, *PP* prone positioning, *PEEP* positive end-expiratory pressure. *Avoid any intrinsic PEEP. **Replace HME by a heated humidifier

Vieillard-Baron, ICM 2013

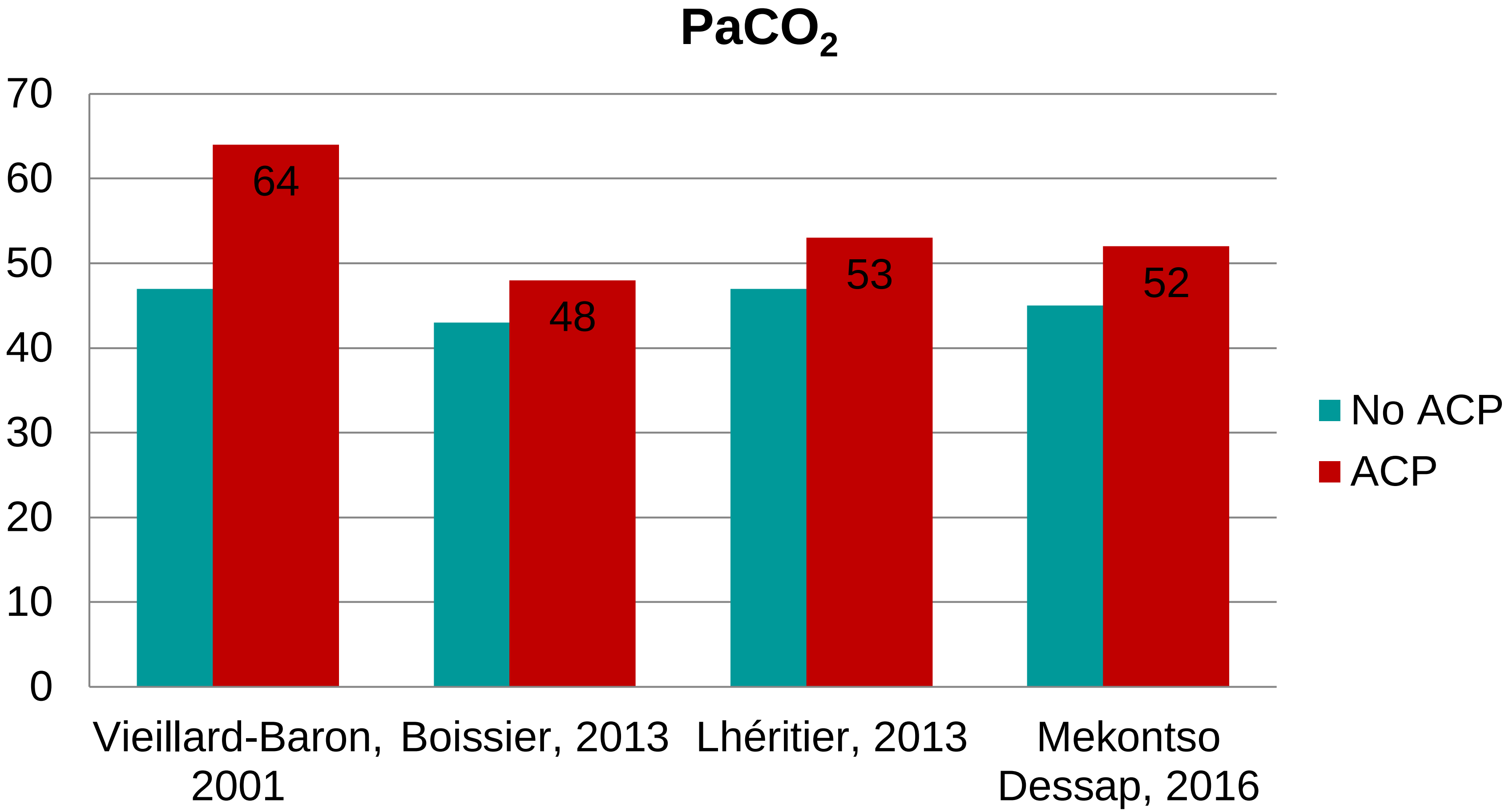
Hypercapnia and lung vascular dysfunction



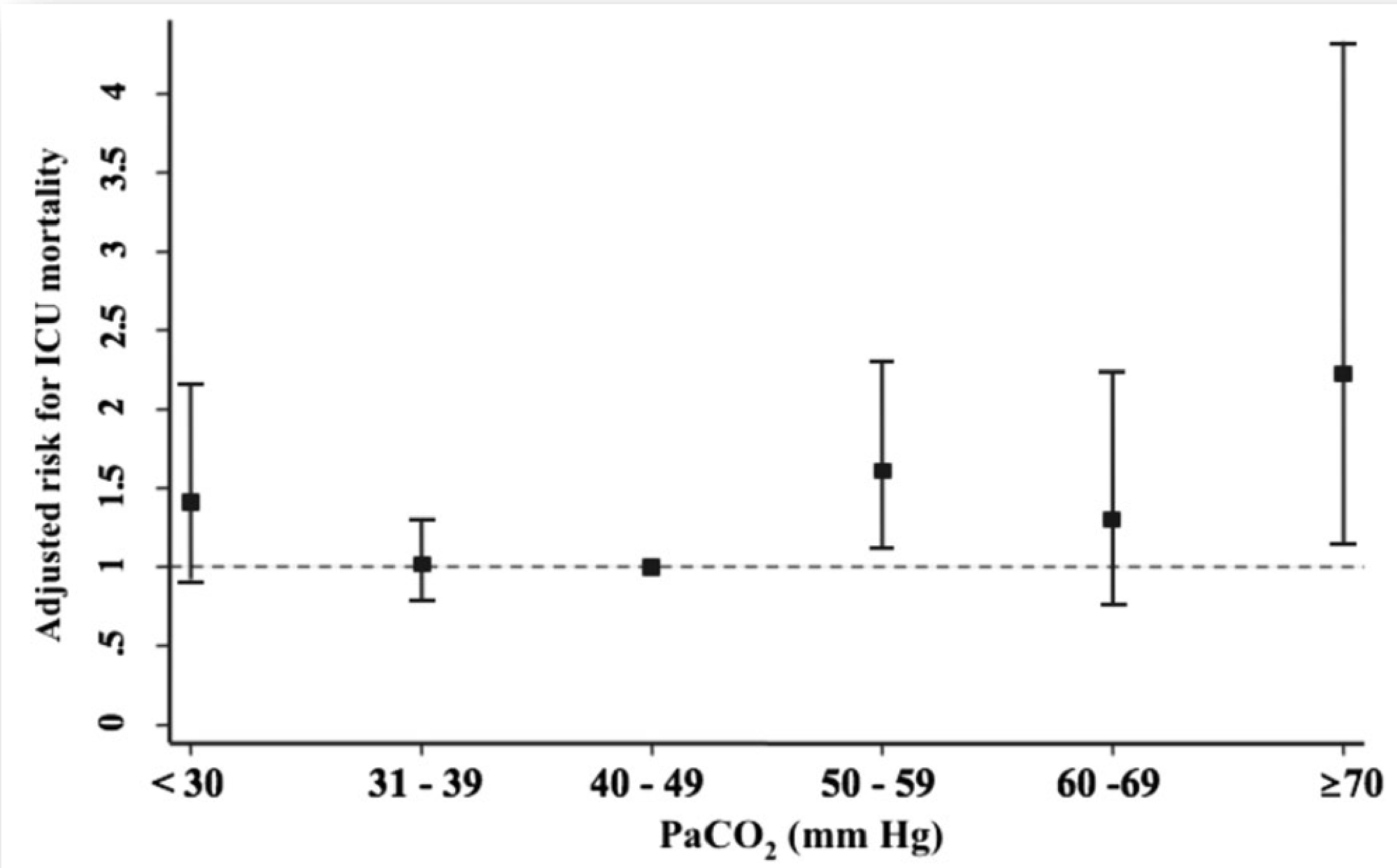


Mekontso Dessap, ICM 2009

Hypercapnia and lung vascular dysfunction

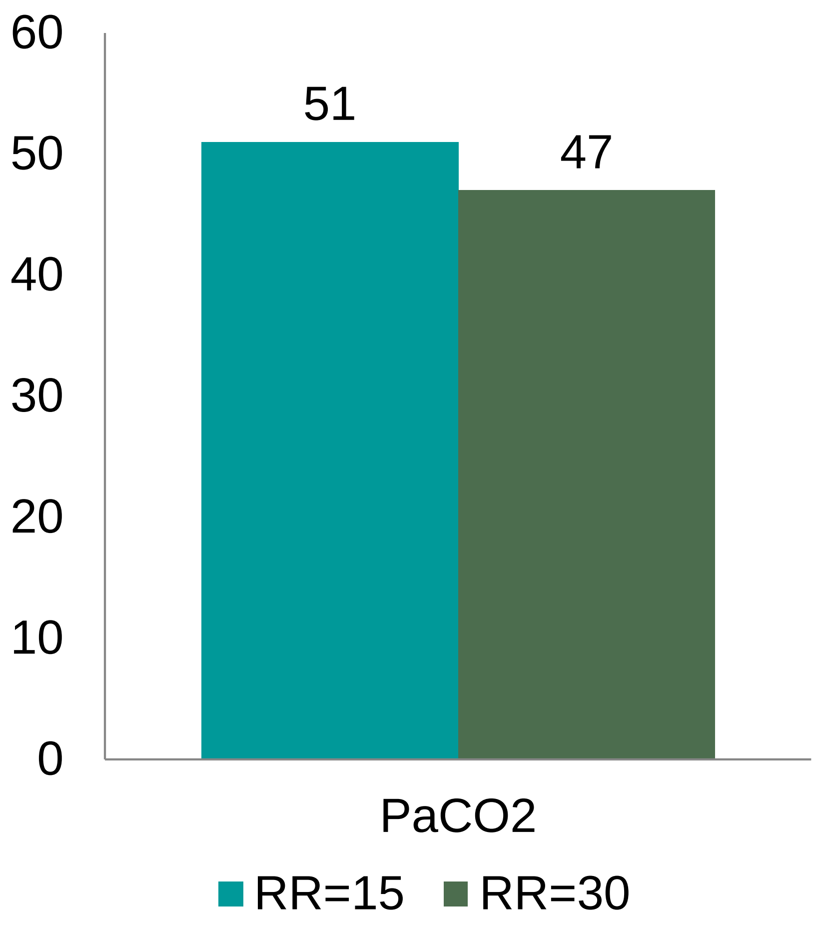


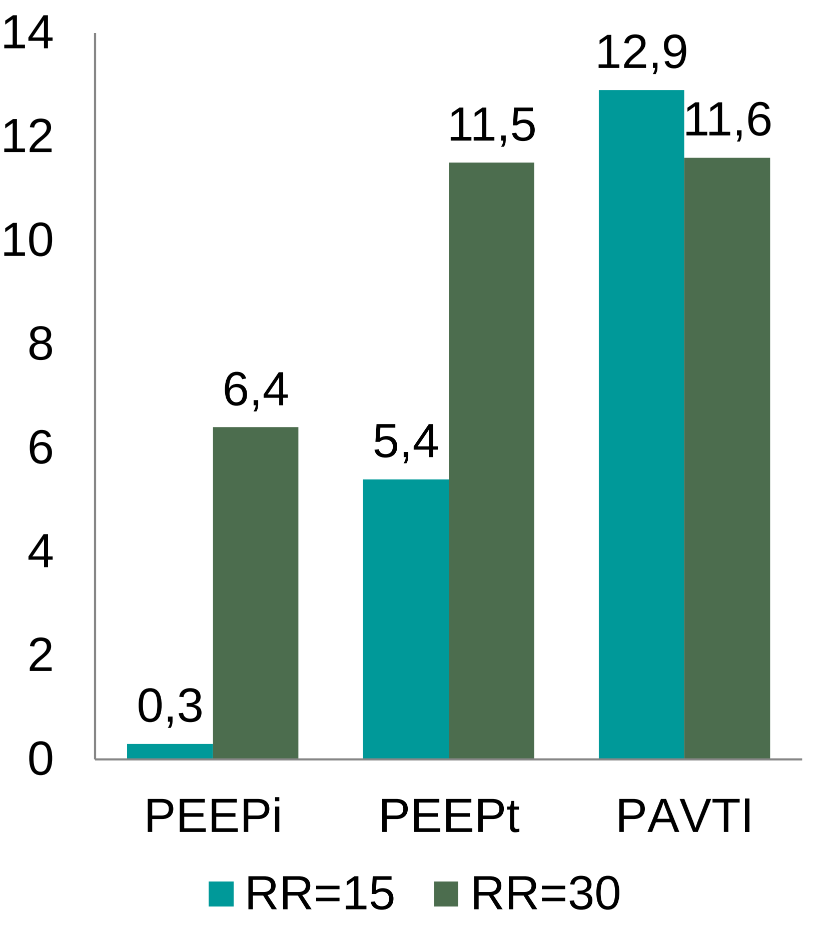
Hypercapnia and mortality of ARDS



Nin, ICM 2017
(n=1899)

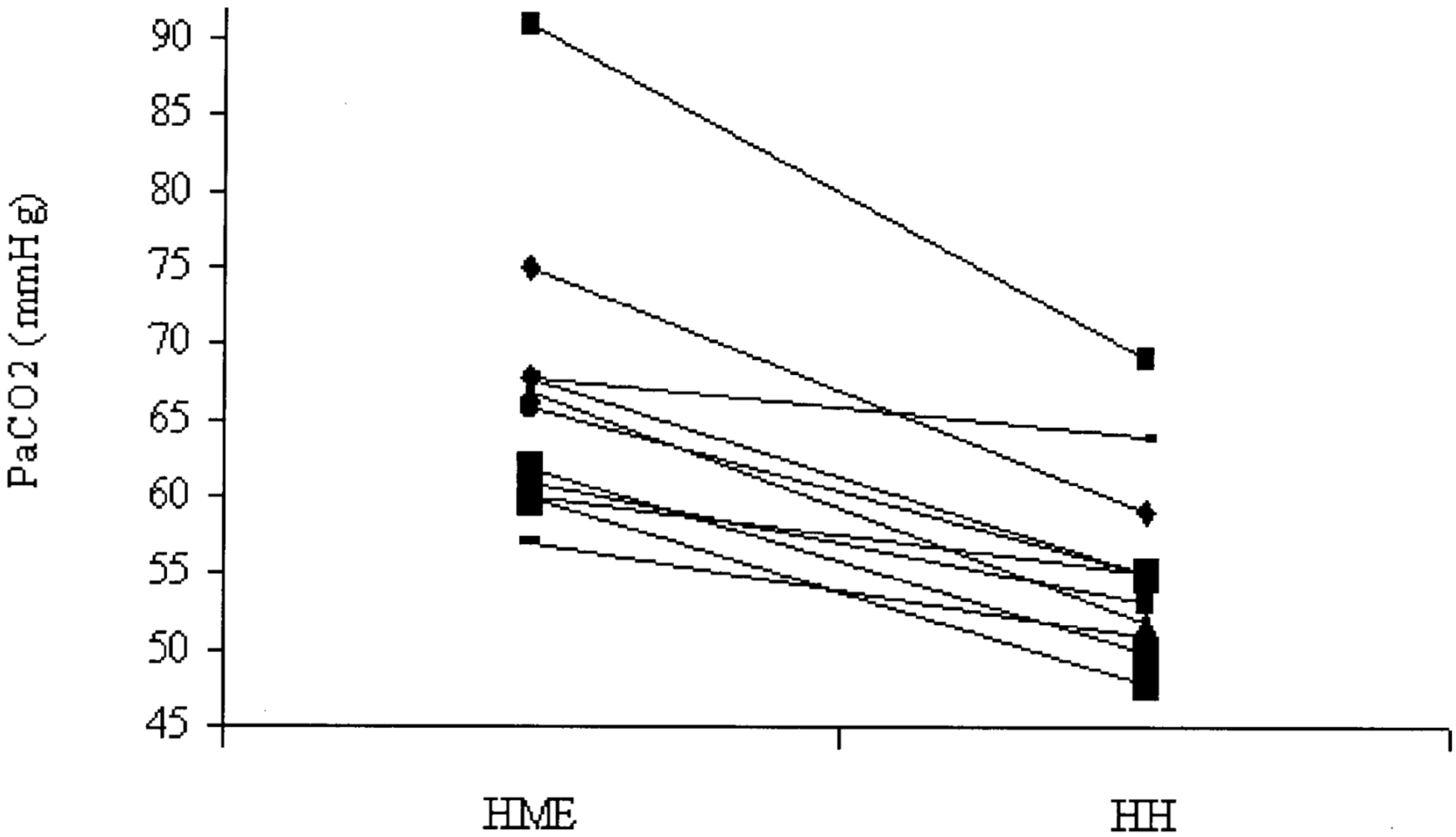
$PaCO_2$ and RR





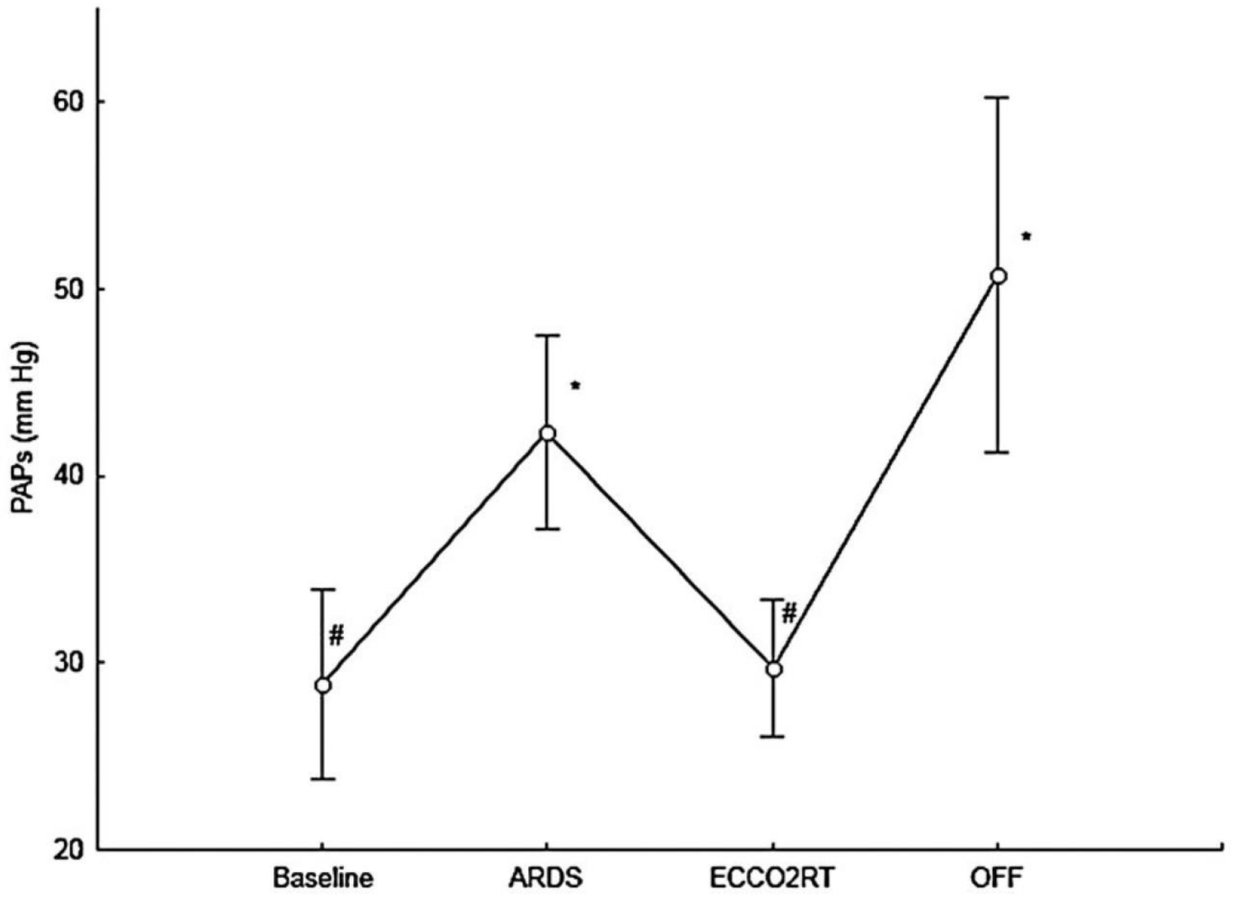
Vieillard-Baron, CCM 2002

Heated humidifier



Prin, ICM 2002

$ECCO_2$-R ?



Porcine ARDS
Morimont, Anesthesiol Scand 2015

Expert opinion

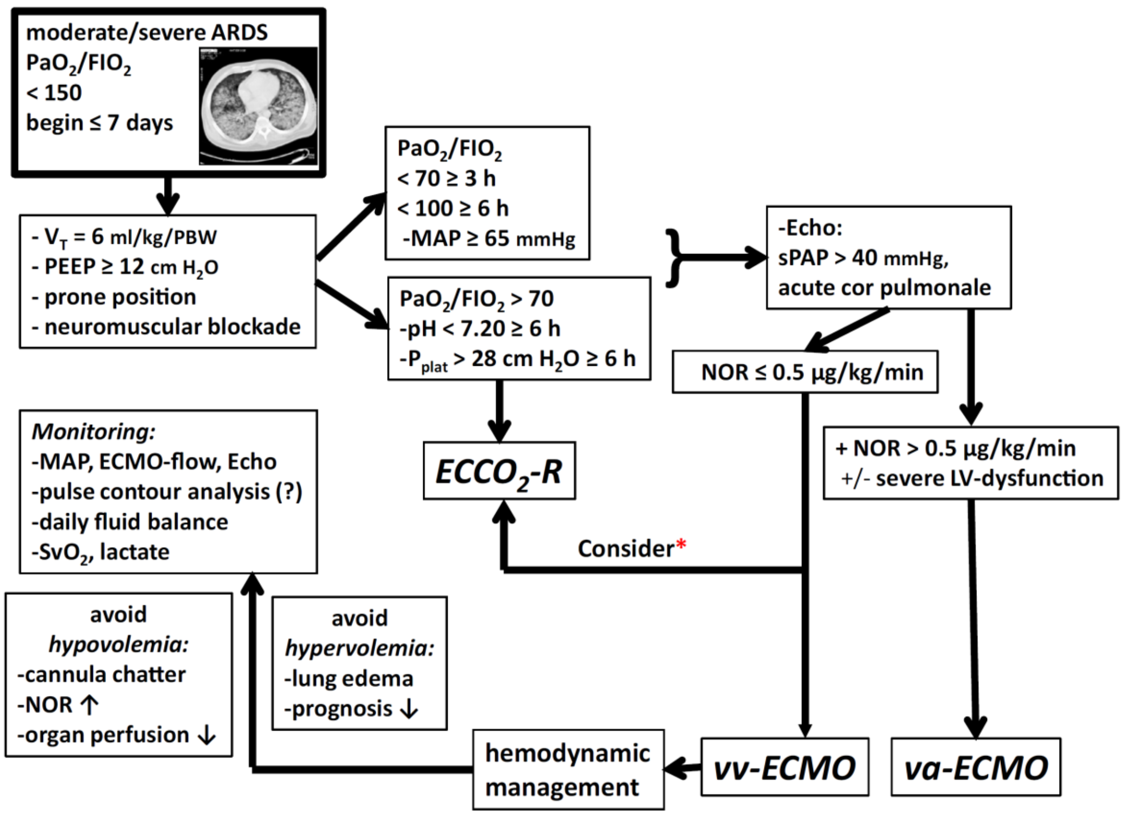
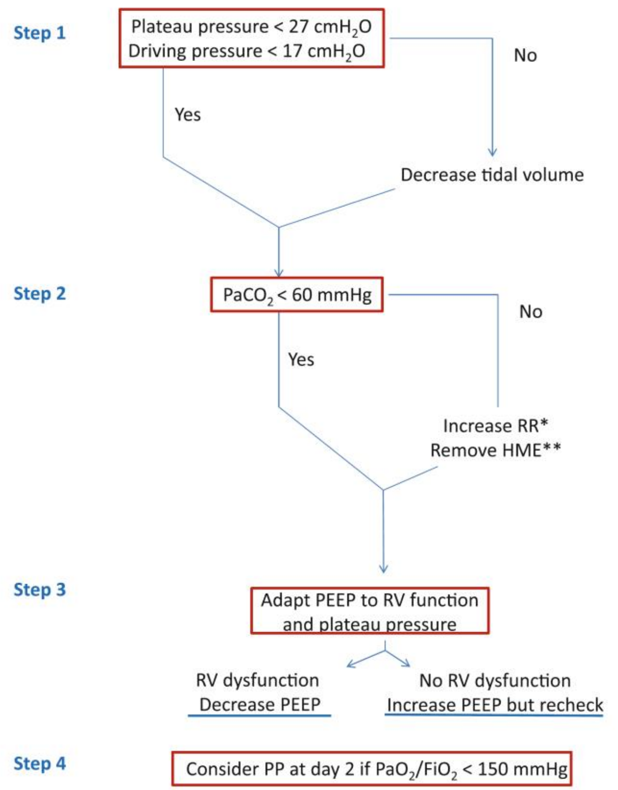


Fig. 3 Proposed algorithm regarding indications for ECMO/$ECCO_2R$ and hemodynamic management during ECMO/$ECCO_2R$ in patients with severe ARDS at risk of hemodynamic instability. Readers have to be cautioned that this algorithm was not previously validated. V_T tidal volume, P_{plat} inspiratory plateau pressure, *MAP* mean arterial pressure, *NOR* norepinephrine, SvO_2 central venous oxygen saturation. *Asterisk* as re-emphasized in the text, this is currently not evidence-based data

Vieillard-Baron, ICM 2016

RV protective approach



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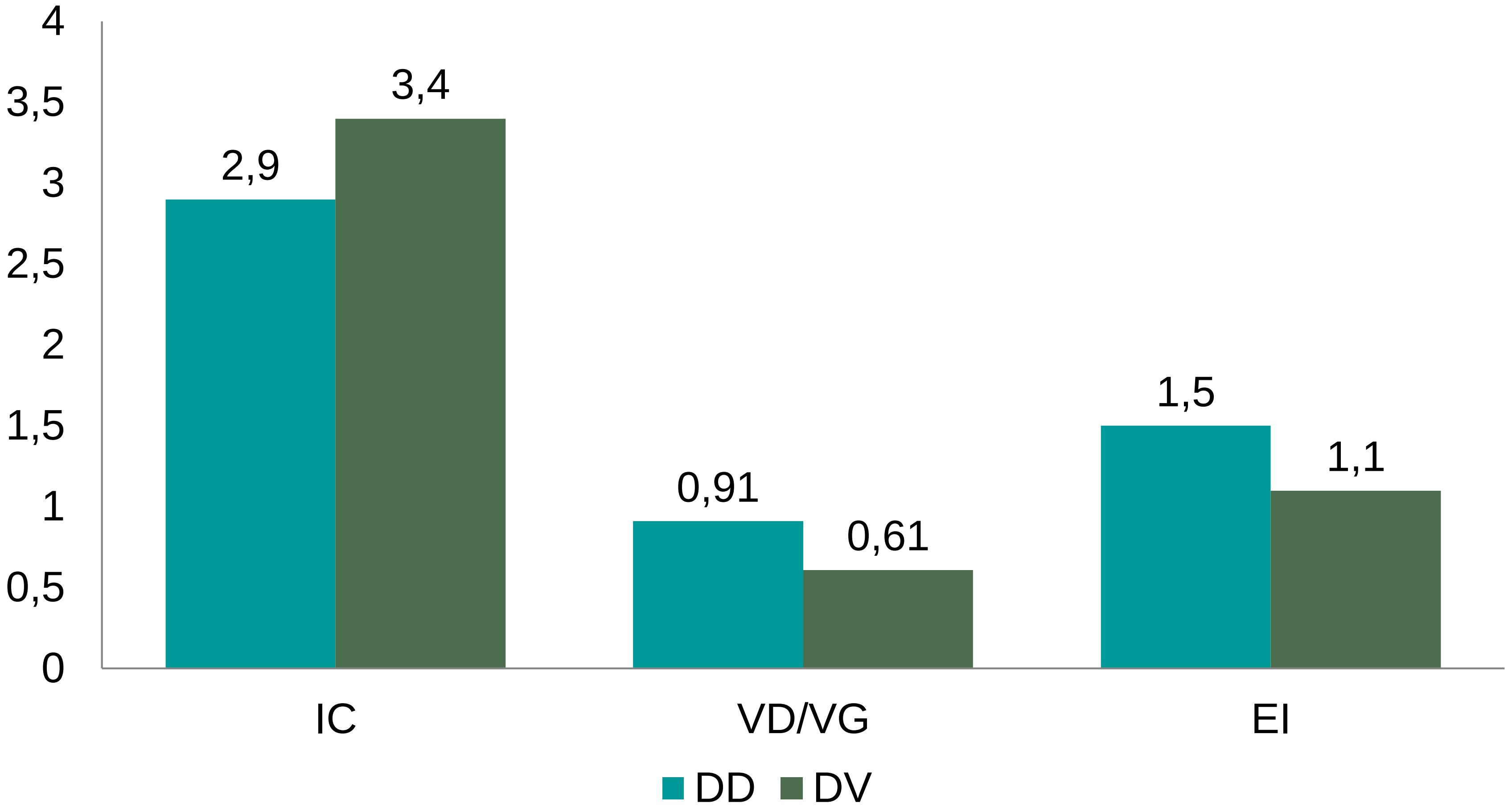
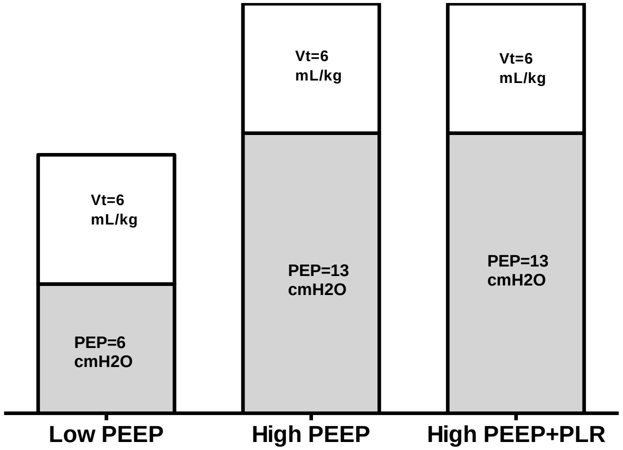
Vieillard-Baron, ICM 2013

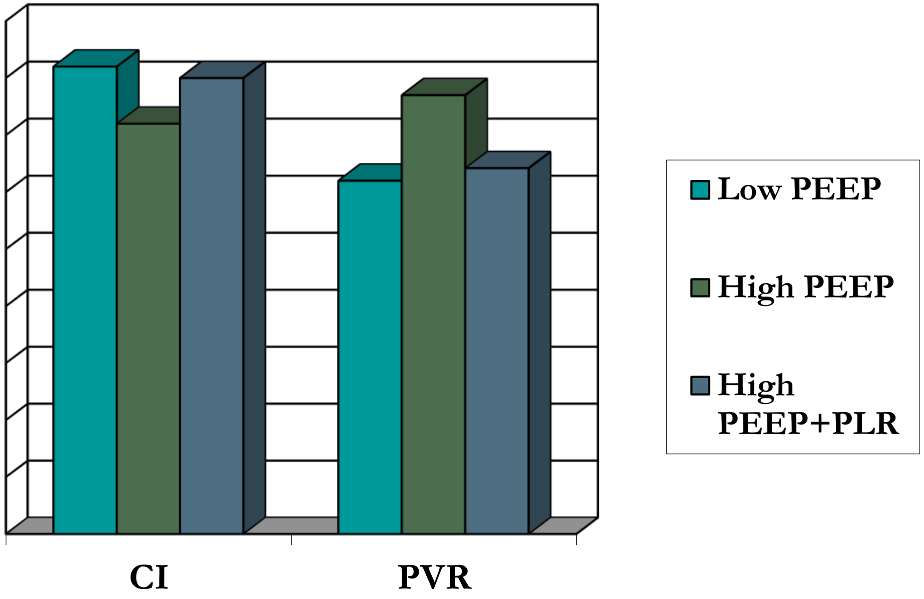
Prone position



Vieillard-Baron, Chest 2007

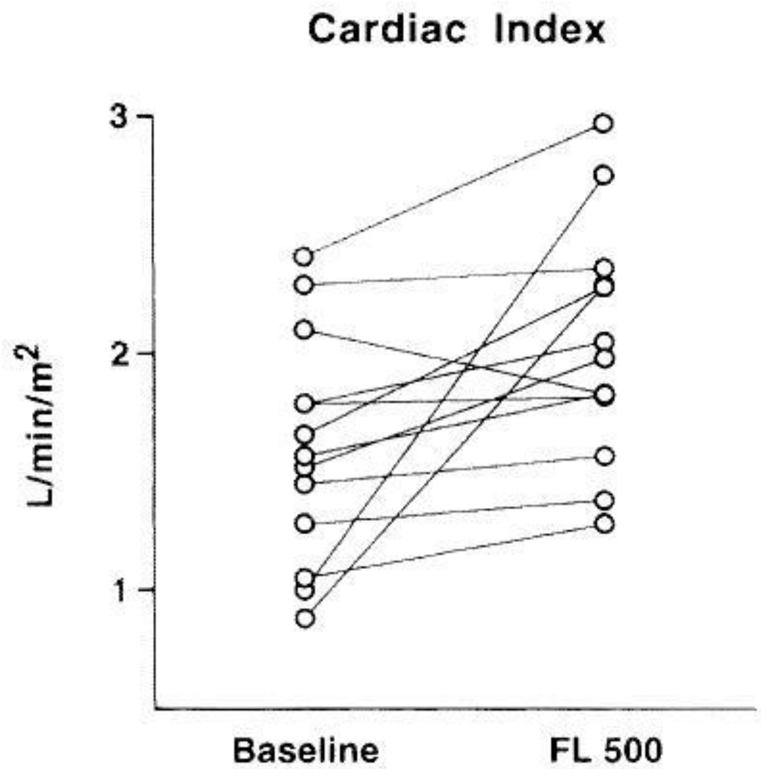
Fluid loading

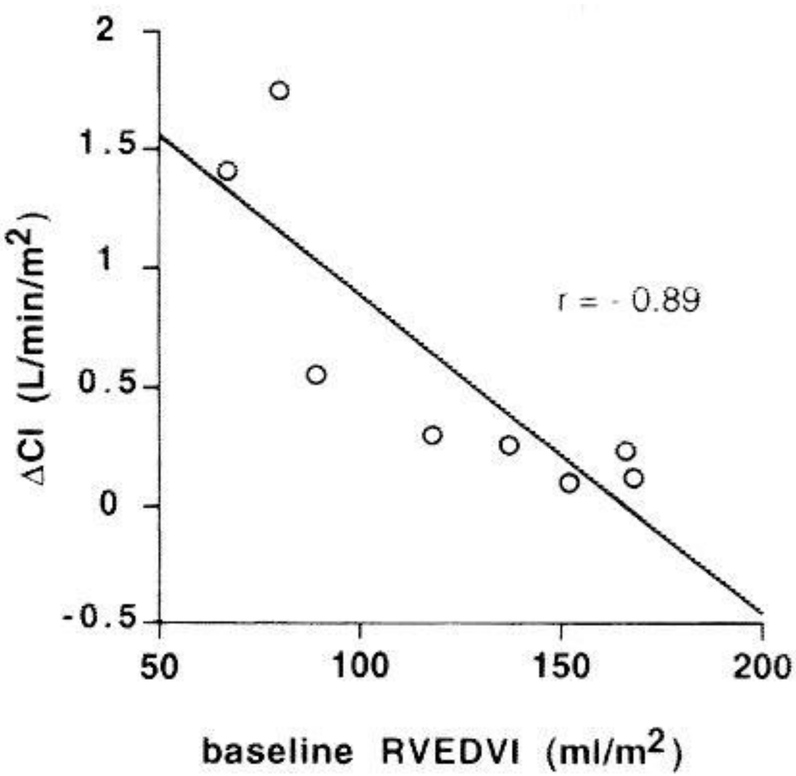




Fougères, CCM 2009

Fluid loading





Massive PE
Mercat, CCM 1999

Conclusions

- Lung vascular dysfunction :
  - is present in a significant number of ARDS patients
  - alters prognosis
  - can be detected with various tools, especially echocardiography
  - should prompt a specific ventilatory management