ATR 2019 – 24ème Congrès National de Réanimation

Hypercapnie dans le SDRA
- Tolérée ou non -

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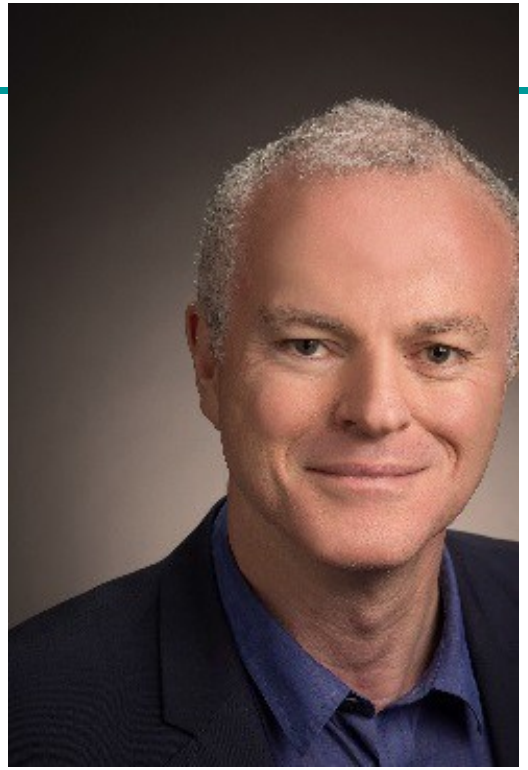
srlf SOCIÉTÉ DE RÉANIMATION DE LANGUE FRANÇAISE

R3S

Liens d'intérêt

Contrats de recherche, expertise, exposés, inscription à des congrès

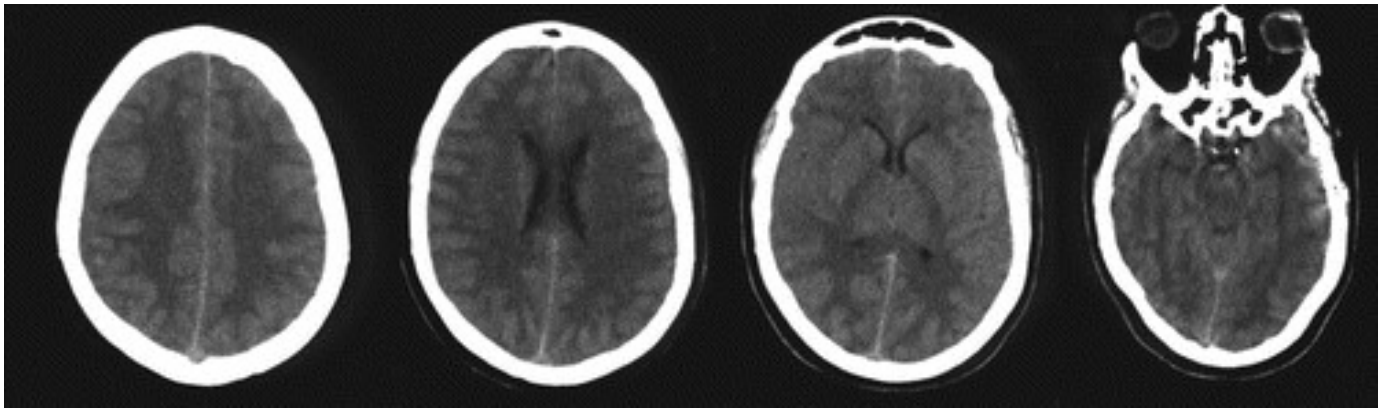
- Philips: contrat de recherche
- Getinge: intervention
- Air Liquide santé: contrat de recherche
- Baxter : expertise, intervention
- Hamilton : intervention
- Respinor : contrat de recherche
- Lungpacer : contrat de recherche, expertise
- Fisher & Paykel : congrès, intervention



Brian P Kavanagh (1962 – 2019)

L’hypercapnie est elle par elle-même létale ?

- **Massive brain edema (hypercapnia alone ?)**

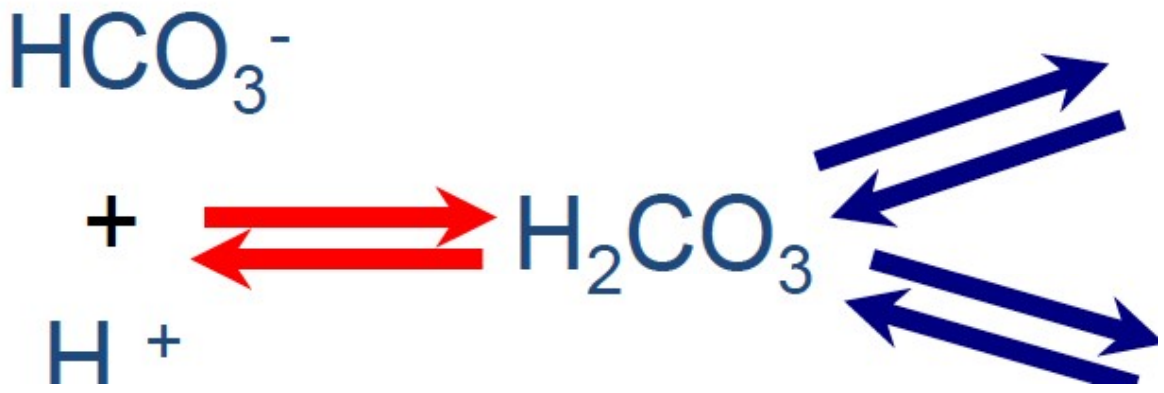


- **Full recovery without sequelae**
  - $PaCO_2$ = 293 mmHg, pH = 6.77 (asthma)

    Mazzeo et al. Paedriatr Anaesth 2004
  - $PaCO_2$ = 375 mmHg, pH = 6.60 (anesthesia)

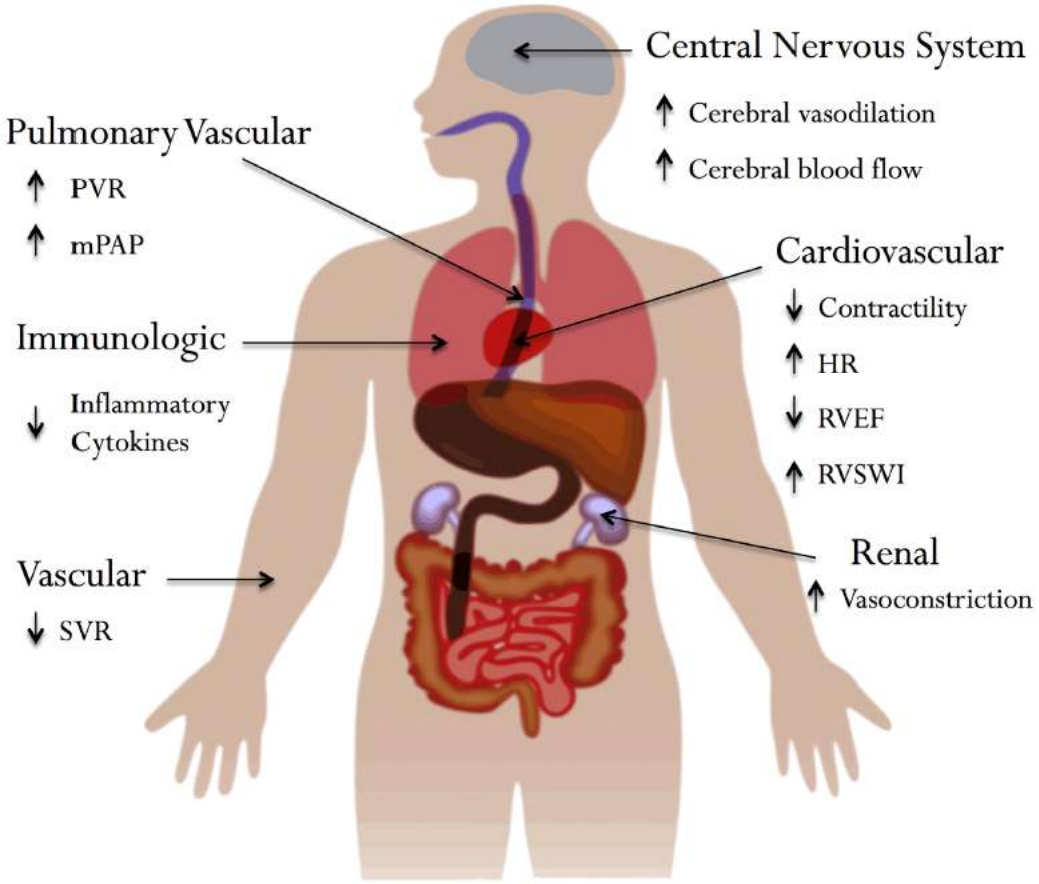
    Potkin et al. Chest 1992

Hypercapnie vs. Acidose hypercapnique



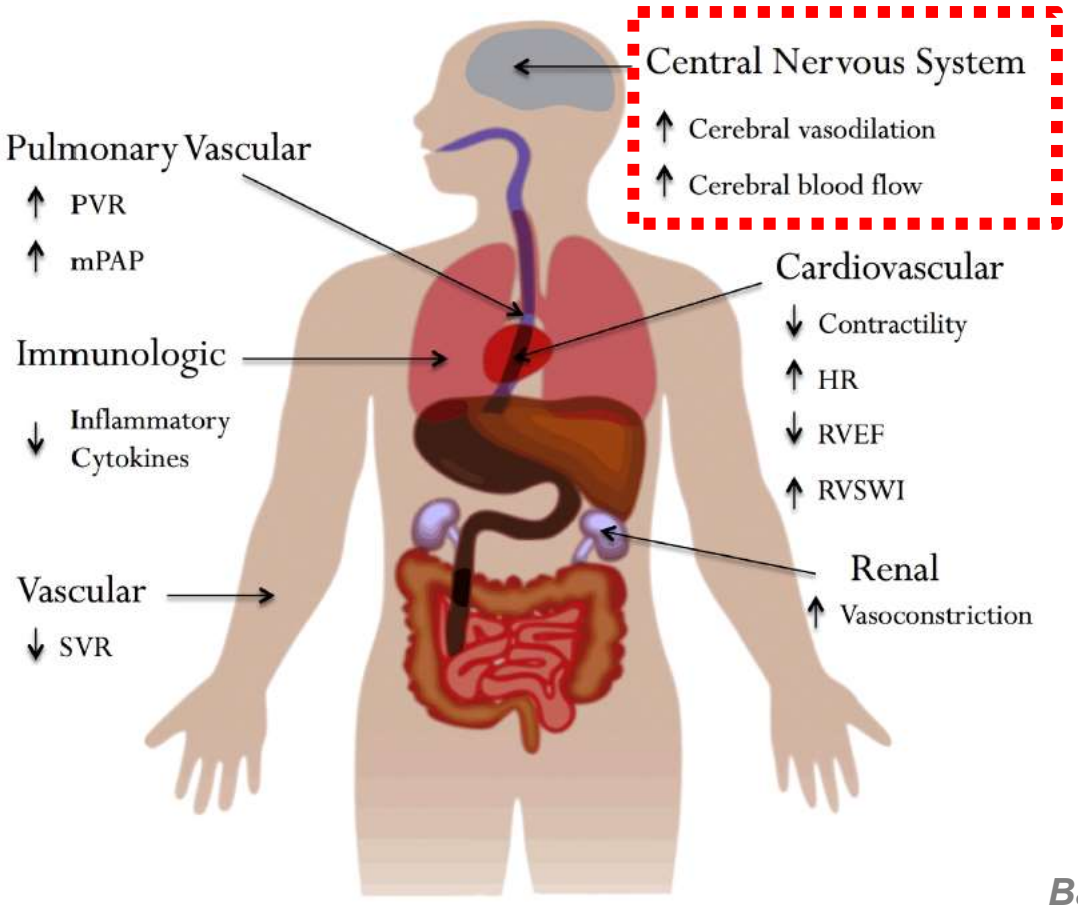
- **Hypercapnie : $PaCO_2$ > 45 mmHg**
- **Acidose hypercapnique : $PaCO_2$ > 45 mmHg and pH < 7.35**
- **Hypercapnie “tamponnée” : $PaCO_2$ > 45 and pH > 7.35**

Hypercapnie – Impact physiologique



Barnes et al. Chest 2017

Hypercapnie – Impact physiologique



Barnes et al. Chest 2017

L'hypercapnie permissive

- A concept born 35 years ago, in Lausanne (Switzerland)
- For patients on MV for severe asthma

Mechanical Controlled Hypoventilation in Status Asthmaticus[1,2]

R. DARIOLI and C. PERRET

AM REV RESPIR DIS 1984; 129:385-387

L’hypercapnie permissive dans le SDRA

- Applied in ARDS 6 years later in Christchurch (New Zealand)

Low mortality associated with low volume pressure limited ventilation with permissive hypercapnia in severe adult respiratory distress syndrome

K. G. Hickling, S. J. Henderson and R. Jackson

Departments of Intensive Care and Radiology, Christchurch Hospital, Christchurch, New Zealand

Intensive Care Med (1990) 16:372 – 377

- Confounding effect of reduced V_T (reduced VILI) ??

L'hypercapnie protège les poumons

Citation	Model[M]/ Investigation[I]	Major
Kogan *et al.* Vopr Med Khim 1996 [29]	M: *In vitro* study on human blood phagocytes and alveolar macrophages I: Direct effects of CO_2 on production of reactive oxygen species	Hypercapnia reduces th ide and other free ra cells
Laffey *et al.* Am J Respir Crit Care Med 2000 [11]	M: *In vivo* rabbit model of lung ischemia/reperfusion (IR) injury I: Protective effects of therapeutic hypercapnia on protection from lung IR injury	Therapeutic hypercapn nary inflammation lung mechanics
Laffey *et al.* Am J Respir Crit Care Med 2000 [13]	M: Isolated perfused rabbit lung IR I: Therapeutic effects of hypercapnia versus acidosis and the effects of buffering acidosis	Hypercapnic acidosis is ry; buffering the acic
Sinclair *et al.* Am J Respir Crit Care Med 2002 [30]	M: *In vivo* rabbit model of ventilator-induced lung injury (VILI) I: Protection of Hypercapnic acidosis against VILI	Hypercapnic acidosis i ventilator-induced lu
Takeshita *et al.* Am J Respir Cell Mol Biol 2003 [31]	M: Isolated perfused rabbit, endotoxin-induced lung injury I: Cellular mechanisms of the effects of hypercapnic acidosis	Hypercapnic acidosis a reducing inflammati κB activity
Laffey *et al.* Am J Respir Crit Care Med 2004 [32]	M: *In vivo* rat model; endotoxin-induced lung injury I: Effects of therapeutic hypercapnia and hyper	Hypercapnic acidosis a reducing the produ species and neutroph

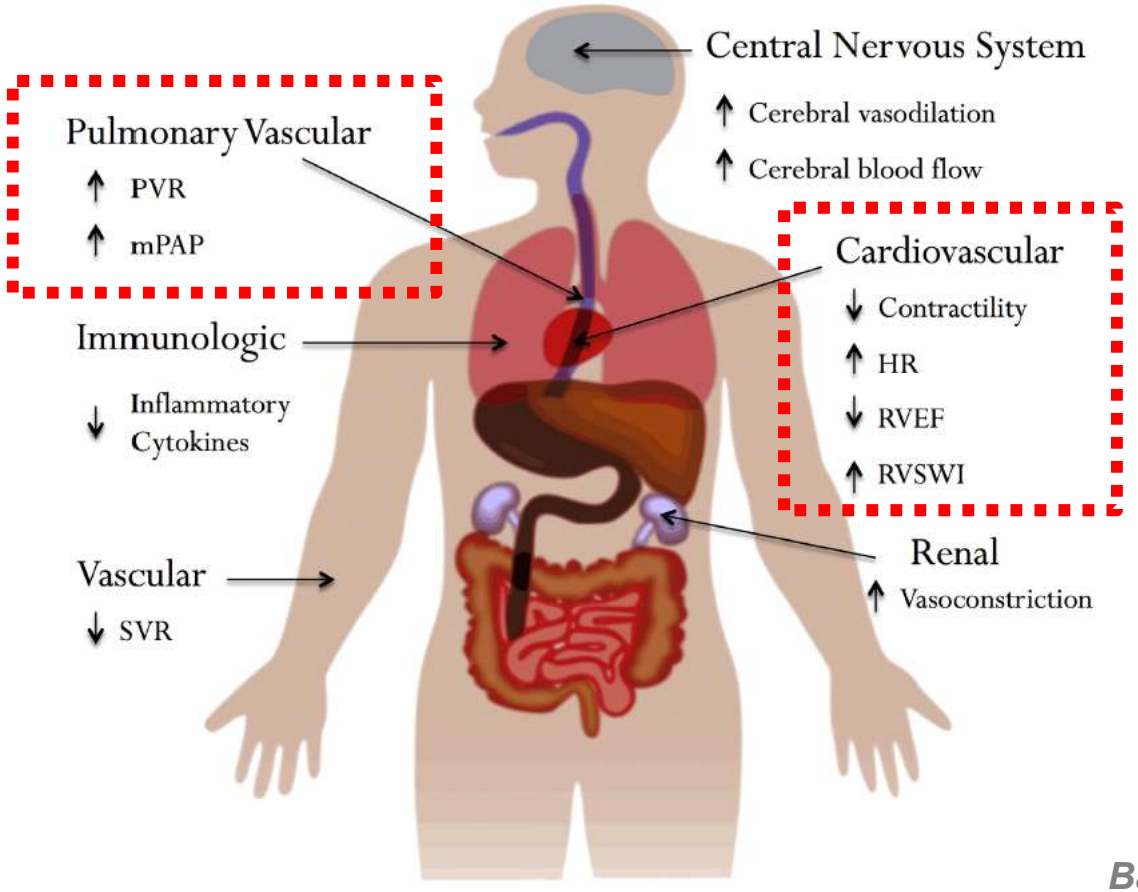
L'hypercapnie induit des lésions pulmonaires

Citation	Model[M]/Investigation[I]	Major F
Pedoto *et al.* Am J Respir Crit Care Med 1999 [54]	M: In vivo rat model; I: Effects of intravenous HCl infusion on nitric oxide production and hemodynamic stability	Hypercapnic acidosis w creasing the producti tion and causes severe
Lang *et al.* Am J Physiol Lung Cell Mol Physiol 2000 [55]	M: In vitro model of fetal rat alveolar epithelial cells treated with hypercapnia (15% CO_2); I: Effect of therapeutic hypercapnia on modifying the production of NO	Hypercapnic acidosis i cells by increasing the
Doerr *et al.* Am J Respir Crit Care Med 2005 [56]	M: Ex vivo perfused rat lung model of ventilator-induced lung injury; I: Effects of hypercapnic acidosis on lung cell injury and repair	Hypercapnic acidosis re wound repair in alveo
Briva *et al.* PLoS ONE 2007 [57]	M: Isolated rat lung model; isolated rat alveolar epithelial cells treated with hypercapnia (5% CO_2); I: Effects of hypercapnia on Na+/K+ ATPase function in fluid reabsorption	Hypercapnia impairs alv tion by causing the ATPase
O'Croinin *et al.* Crit Care Med 2008 [53]	M: In vivo rat model of acute lung injury by in- tratracheal E. coli instillation; sustained hyper-	Hypercapnic acidosis w ing pulmonary barri

Hypercapnie et poumons – Au total

- **Effet protecteur**
  - ↓ agression oxydante, ↓ cytokines pro-inflammatoires
  - ↓ recrutement des PNN
  - ↓ œdème dans le SDRA, ↓ VILI
- **Effet délétère**
  - ↓ bactéricidie médiée par l'immunité
  - Dysfonction des PNN, risque bactérien
  - ↓ capacités de réparation de l'épithélium alvéolaire
  - ↓ réabsorption de l'œdème

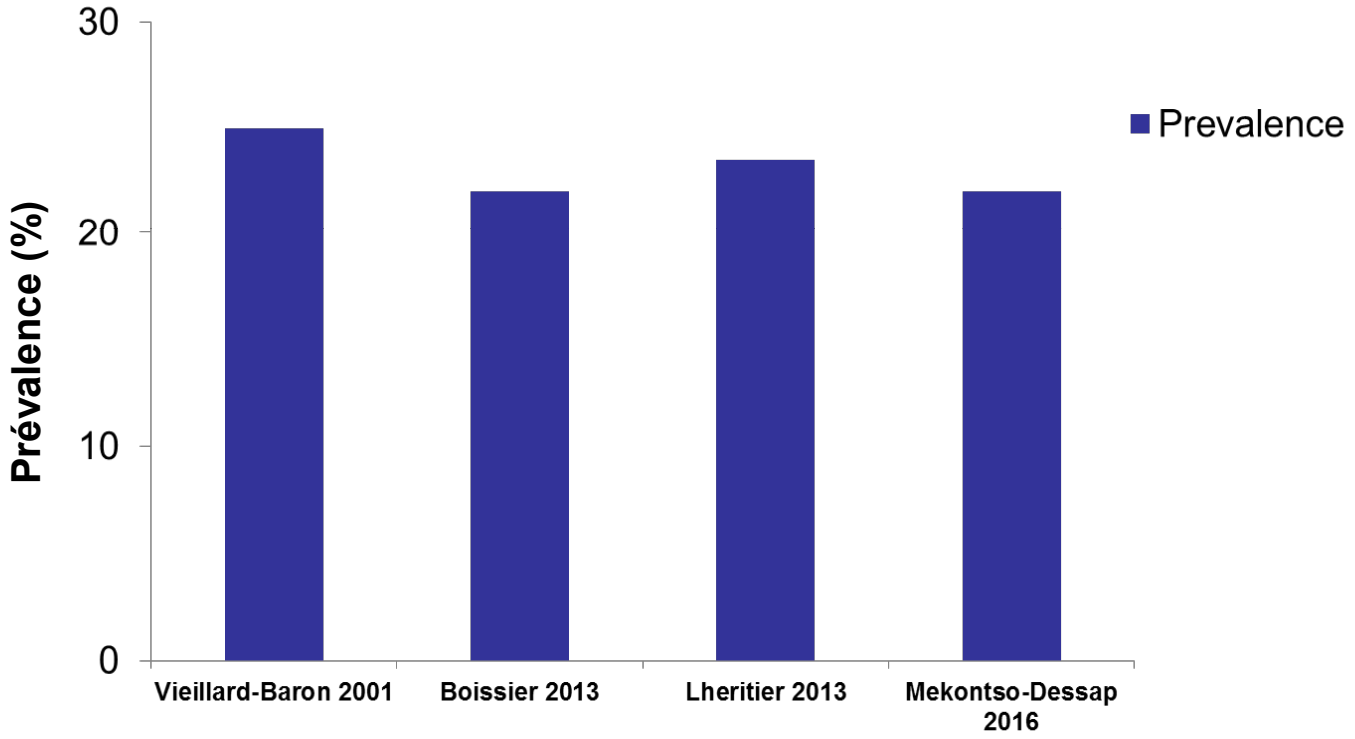
Hypercapnie – Impact physiologique



Barnes et al. Chest 2017

Cœur pulmonaire aigu

Prévalence du cœur pulmonaire aigu



Armand Mekontso Dessap
Florence Boissier
Cyril Charron
Emmanuelle Bégot
Xavier Repessé
Annick Legras
Christian Brun-Buisson

Acute cor pulmonale during prot ventilation for acute respiratory syndrome: prevalence, predictors impact

- 752 pts with moderate or severe ARDS
- 22 % with Acute Cor Pulmonale (echo)

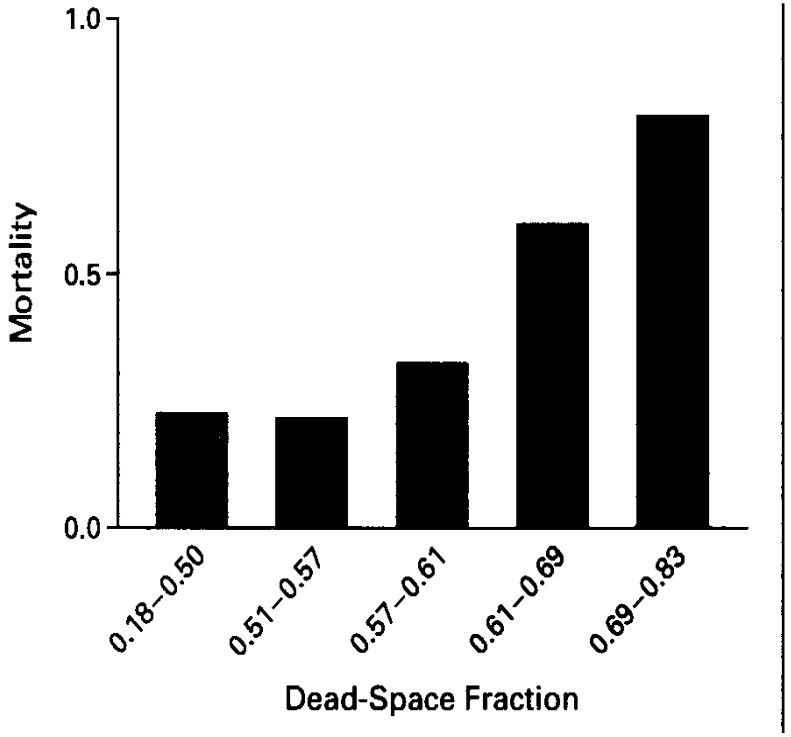
Variable	Odds ratio (95 % CI) by logistic regression	
	Univariate	Multivariab
Pneumonia as cause of ARDS	2.54 (1.79–3.62), $p < 0.01$	2.73 (1.84–
Respiratory settings on TEE da		
Tidal volume <7 mL/kg	1.70 (1.17–2.47), $p < 0.01$	I/NR
Respiratory rate ≥30 breaths/1	1.70 (1.11–2.60), $p = 0.02$	I/NR
Plateau 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	2.16 (1.51–3.10), $p < 0.01$	2.28 (1.53–

Intensive Care Med (2016) 42:862–870

Hypercapnie et pronostic

A very difficult question

- **$PaCO_2$ depends on**
  - minute ventilation
  - **VD/VT**
- **VD/VT is**
  - independently and strongly
  - **associated with outcome**
- Effect of $PaCO_2$ per se ???



N Engl J Med 2002 ; 346 : 1281-6

VOLUME 342 MAY 4, 2000

VENTILATION WITH LOWER TIDAL VOLUMES AS COMI TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG AND THE ACUTE RESPIRATORY DISTRESS SYND

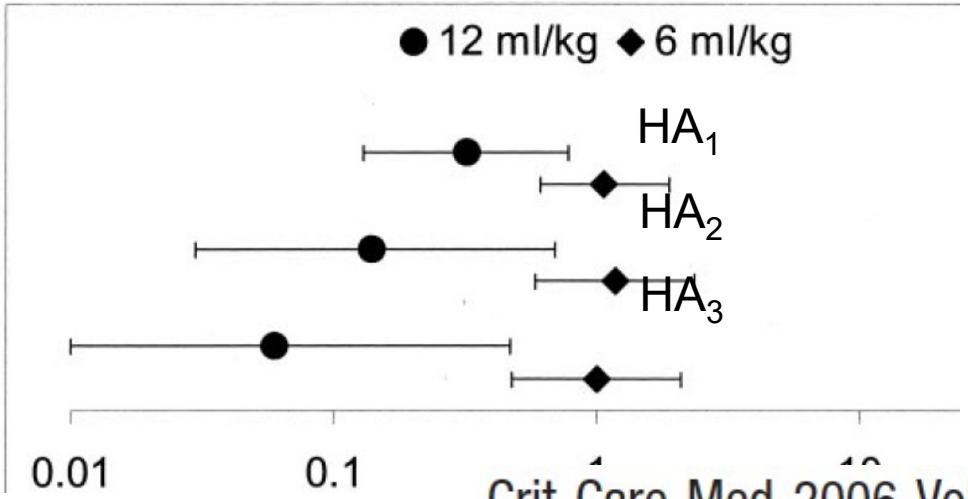
VARIABLE	DAY 1		DAY 3	
	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES
Tidal volume (ml/kg of predicted	6.2±0.9	11.8±0.8	6.2±1.1	11.8±0.8
Respiratory rate (breaths/min)	29±7	16±6	30±7	17±7
Minute ventilation (liters/min)	12.9±3.6	12.6±4.5	13.4±3.5	13.4±4.8
$PaCO_2$ (mm Hg)	40±10	35±8	43±12	36±9

Hypercapnic acidosis and mortality in acute lung

David A. Kregenow, MD; Gordon D. Rubenfeld, MD; Leonard D. Hudson, MD; Er

Hypercapnia : ↓ mortality in pts receiving a high VT (12 ml/kg)

Definition	pH	P_a (mı
HA_1	< 7.40	>
HA_2	< 7.35	>



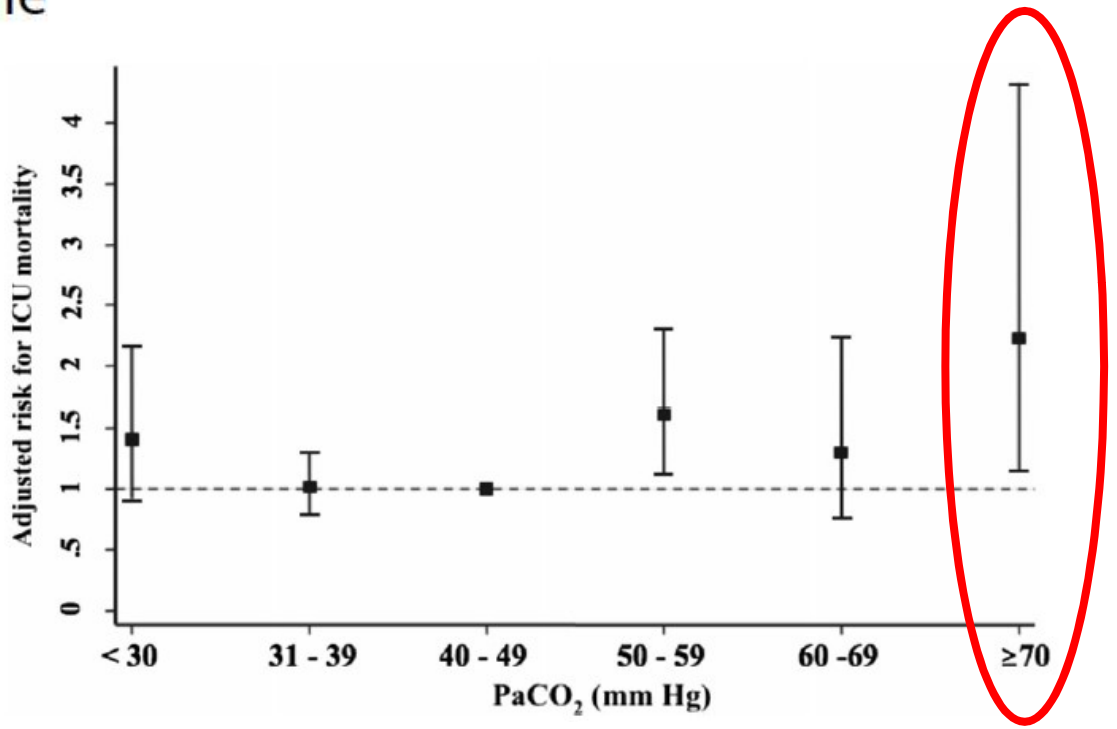
Crit Care Med 2006 Vol. 34.

Severe hypercapnia and outcome of mechanically ventilated patients with moderate or severe acute respiratory distress syndrome

- **Post hoc analysis** of the databases of Esteban studies on MV
- **1899 patients** with ARDS
- **Relationship between hypercapnia and outcome**
- **Adjustment** for age, APACHE II, acidosis, PaO_2/FiO_2, dead space, respiratory rate, protective ventilation or not

Intensive Care Med (2017) 43:200–208

Severe hypercapnia and outcome of mechanically ventilated patients with moderate or severe acute respiratory distress syndrome



Intensive Care Med (2017) 43:200–208

Effects of Hypercapnia and Hypercapnic Acidosis on Hospital Mortality in Mechanically Ventilated Patients*

Ravindranath Tiruvoipati, FCICM[1–3]; David Pilcher, FCICM[3]; Hergen Buscher, FCICM[4,5]; John Botha, FCICM[1,2]; Michael Bailey, PhD[3]

- **Pos hoc analysis** of the database of the ANZICS
- **14** year period (2000 – 2013), 171 ICUs
- **252 812 MV pts** for **ARF whatever the cause (<u>not only ARDS</u>)**
- Worst pH/$PaCO_2$ recorded during the first 24 hour of MV
- **Normocapnia vs Compensated hypercapnia vs Hypercapnic acidosis**
- **Hospital mortality**

Crit Care Med 2017; 45:e649–e656

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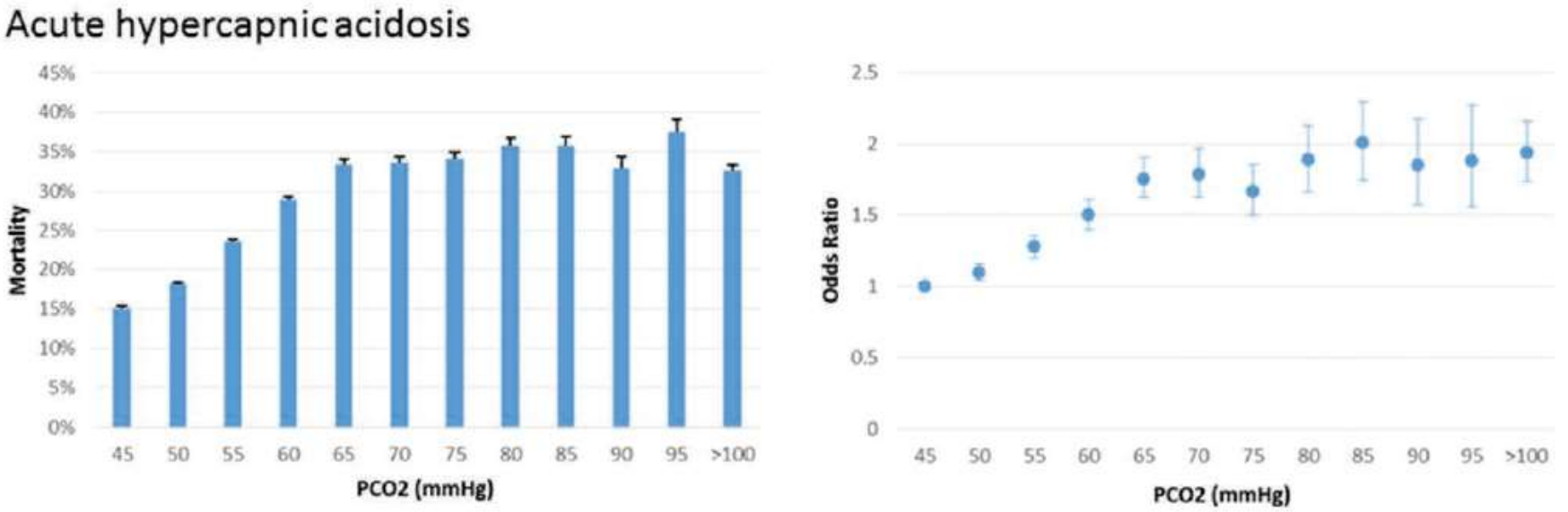

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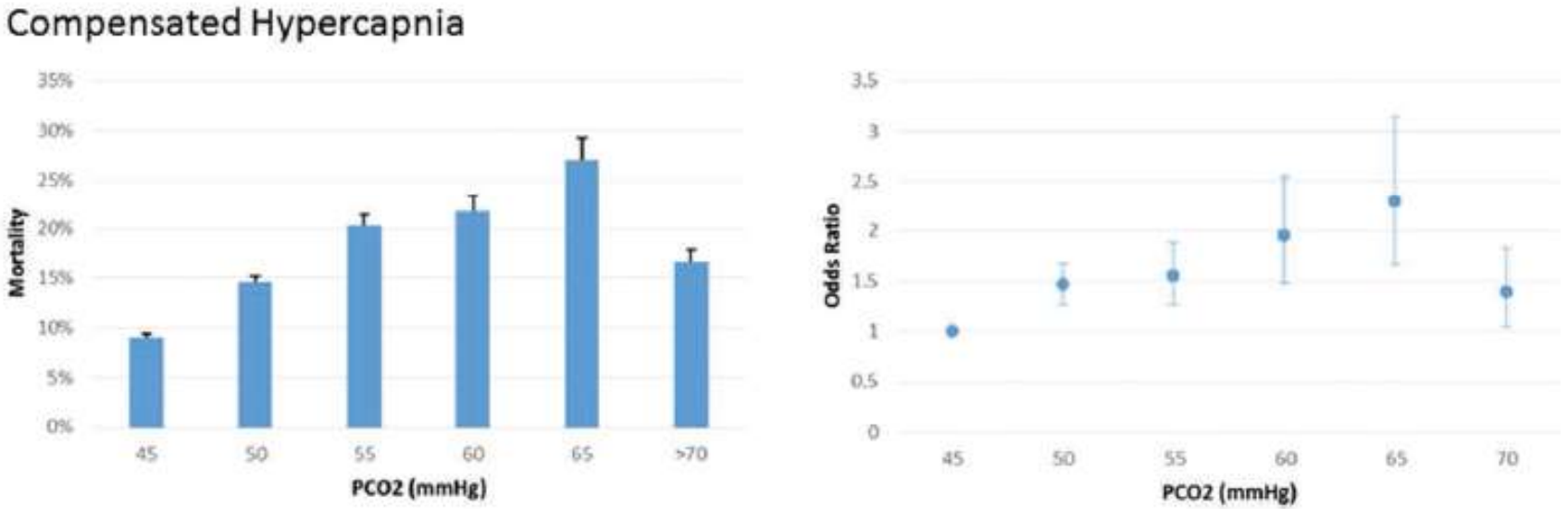

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Rôle de l'hypoxémie

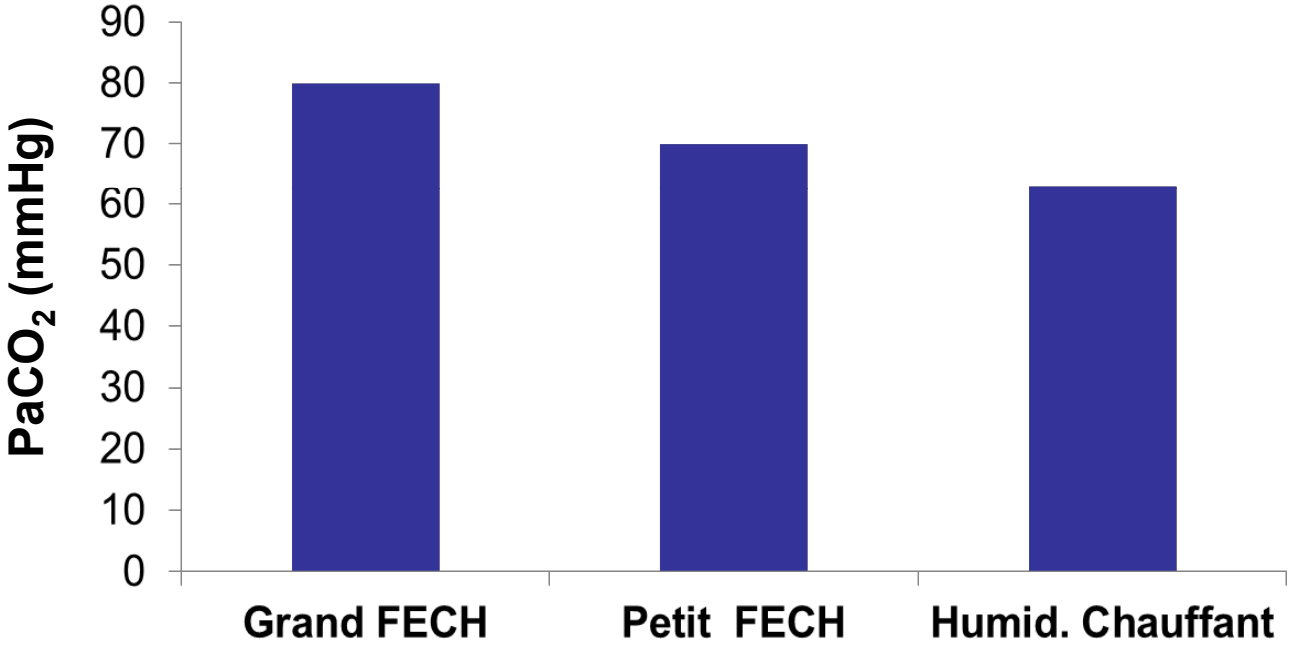
TABLE 3. Multivariate Analysis of Odds Ratio for Hospital Mortality Based on P/F Ratios

P/F Ratio	Normocapnia and Normal pH, OR (95% CI)	Compensated Hypercapnia, OR (95% CI)	Hypercapnic Acidosis, OR (95% CI)	*p*
P/F ratio, < 100	1.66 (1.50–1.84)	2.03 (1.75–2.36)	2.66 (2.51–2.82)	< 0.001
P/F ratio, 100–200	1.12 (1.40–1.20)	1.69 (1.53–1.87)	1.78 (1.69–1.88)	
P/F ratio, 200–300	1.00 (0.94–1.08)	1.20 (1.07–1.35)	1.46 (1.38–1.55)	
P/F ratio, > 300	Reference category (1.00)	1.00 (0.88–1.13)	1.37 (1.29–1.46)	

Crit Care Med 2017; 45:e649–e656

Diminuer la $PaCO_2$

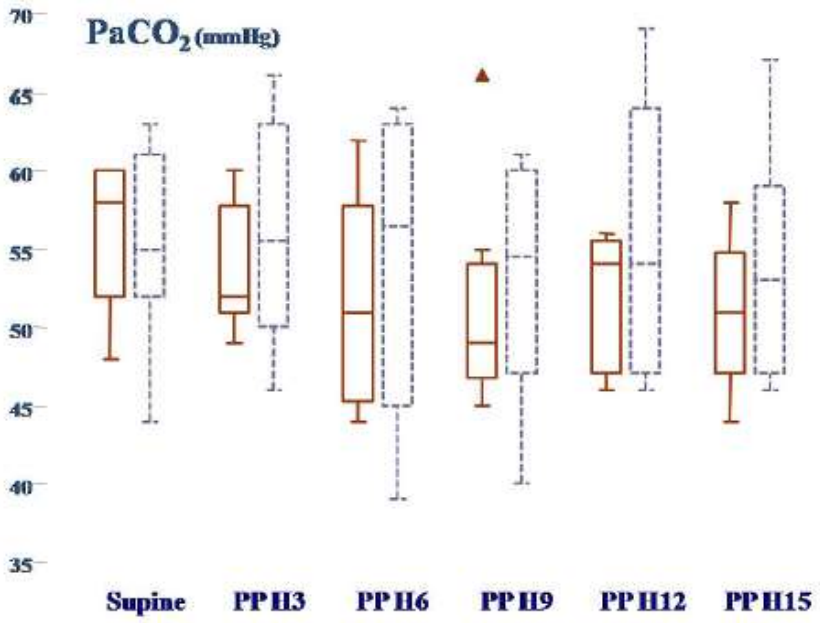
Espace mort instrumental



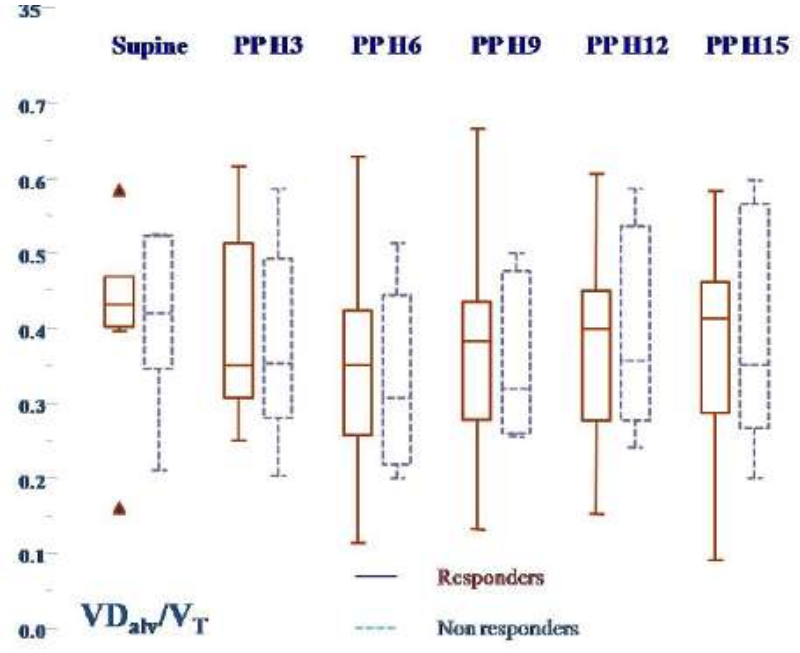
Prat et coll. IntensiveCare Med 2016

Décubitus ventral

PaCO2



VD/VT

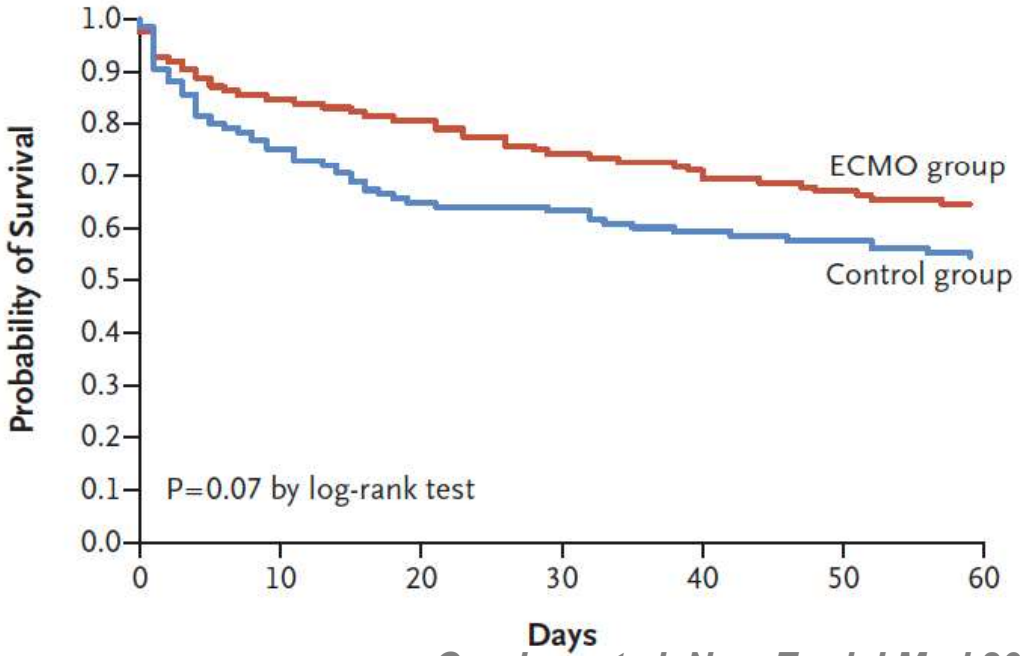


Charron et coll. Crit Care 2011

ECMO – $ECCO_2R$

EOLIA – SDRA

- **pH < 7.25 avec $PaCO_2$ > 60 mmHg**
  for more than 6 hours
- **PaO_2/FiO_2 < 50 mmHg**
  for more than 3 hours
- **PaO_2/FiO_2 < 80 mm Hg**
  for more than 6 hours



Combes et al. New Engl J Med 2018

Conclusion

Hypercapnie : permissive, oui, mais pas trop

- **Une hypercapnie modérée peut être tolérée**
  - $PaCO_2 < 60$ mmHg
  - pH > 7,25 ou 7,30
- **Une hypercapnie sévère est associée à une surmortalité**
  - Cause ou conséquence ? VD/VT est un facteur confondant
  - Rôle de l'acidose ?
- **Corriger les hypercapnies majeures**
  - ↑ FR, ↓ espace mort instrumental, décubitus ventral
  - ECMO, ECCOR ?

Thanks for your attention

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