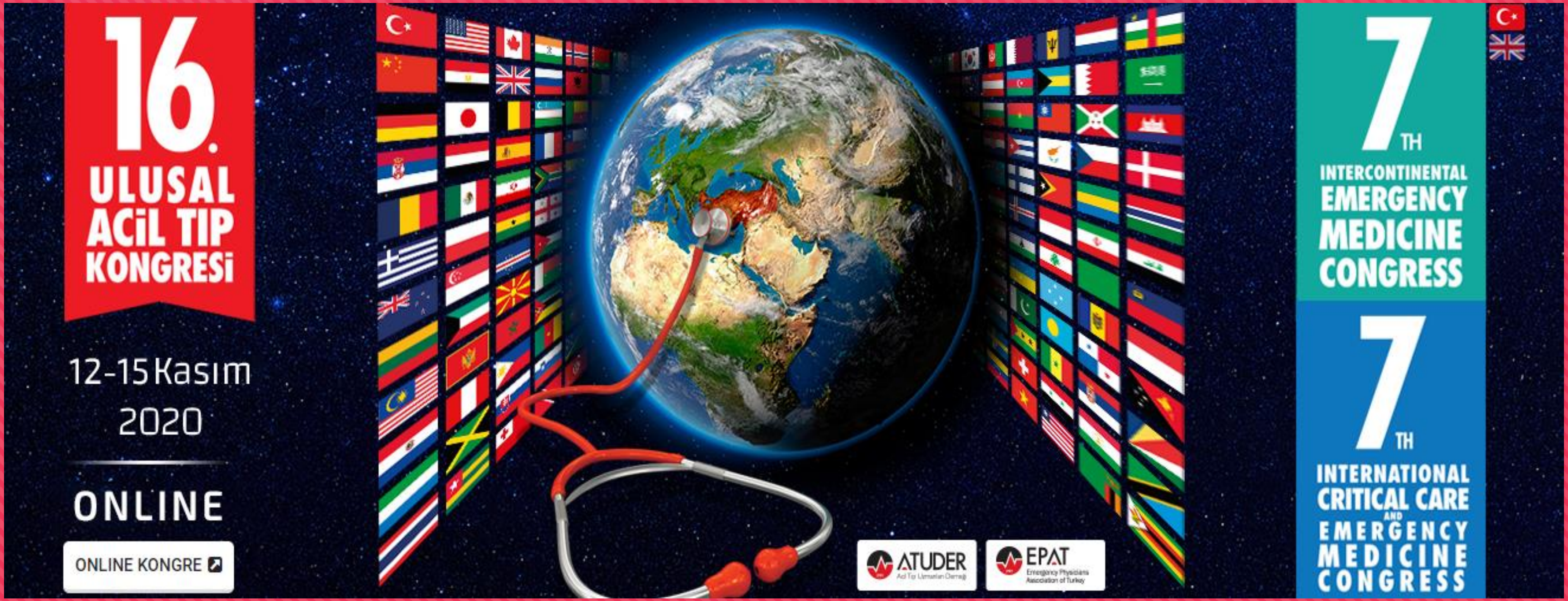
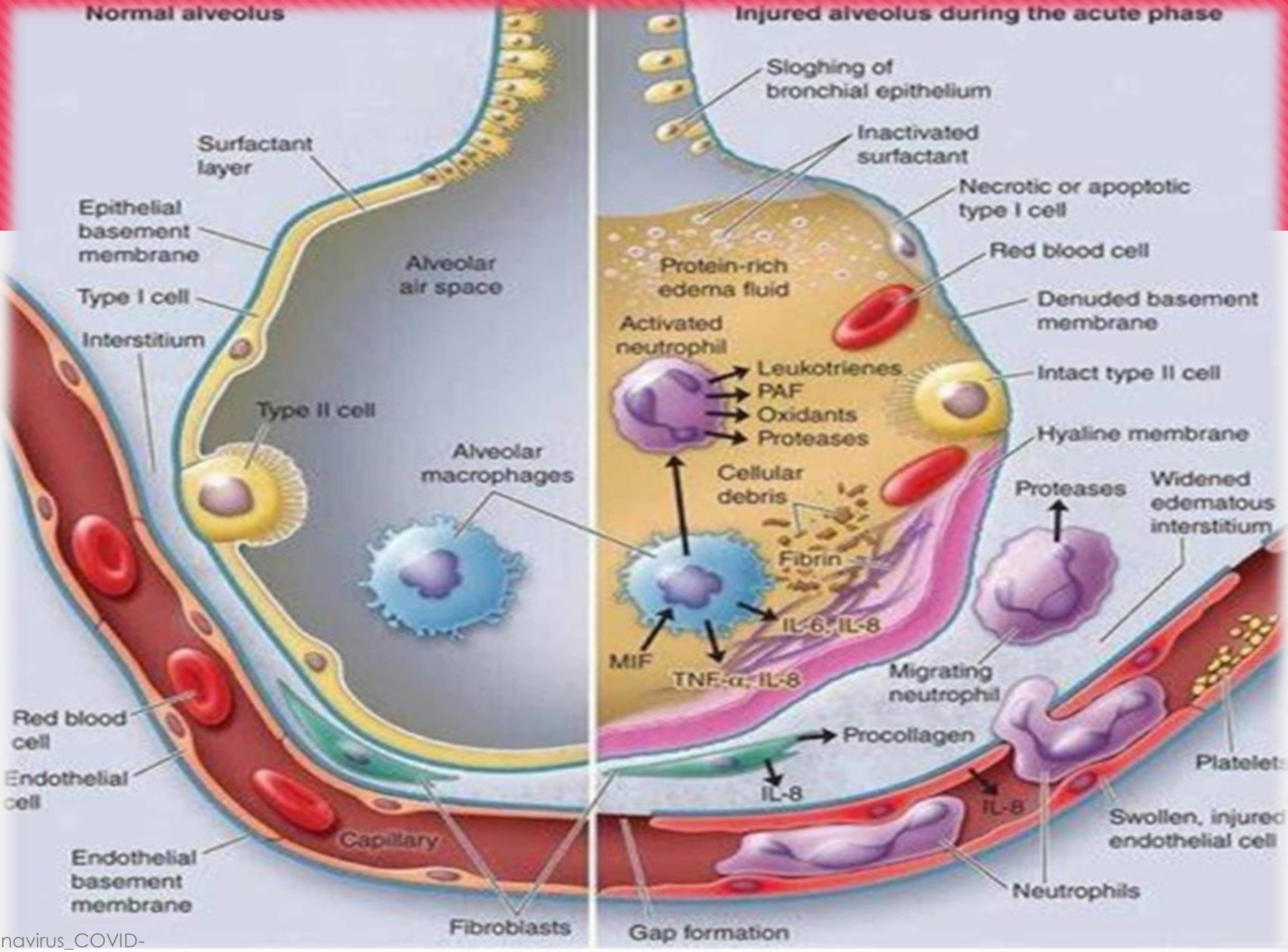


Permissive hypercapnia in ARDS

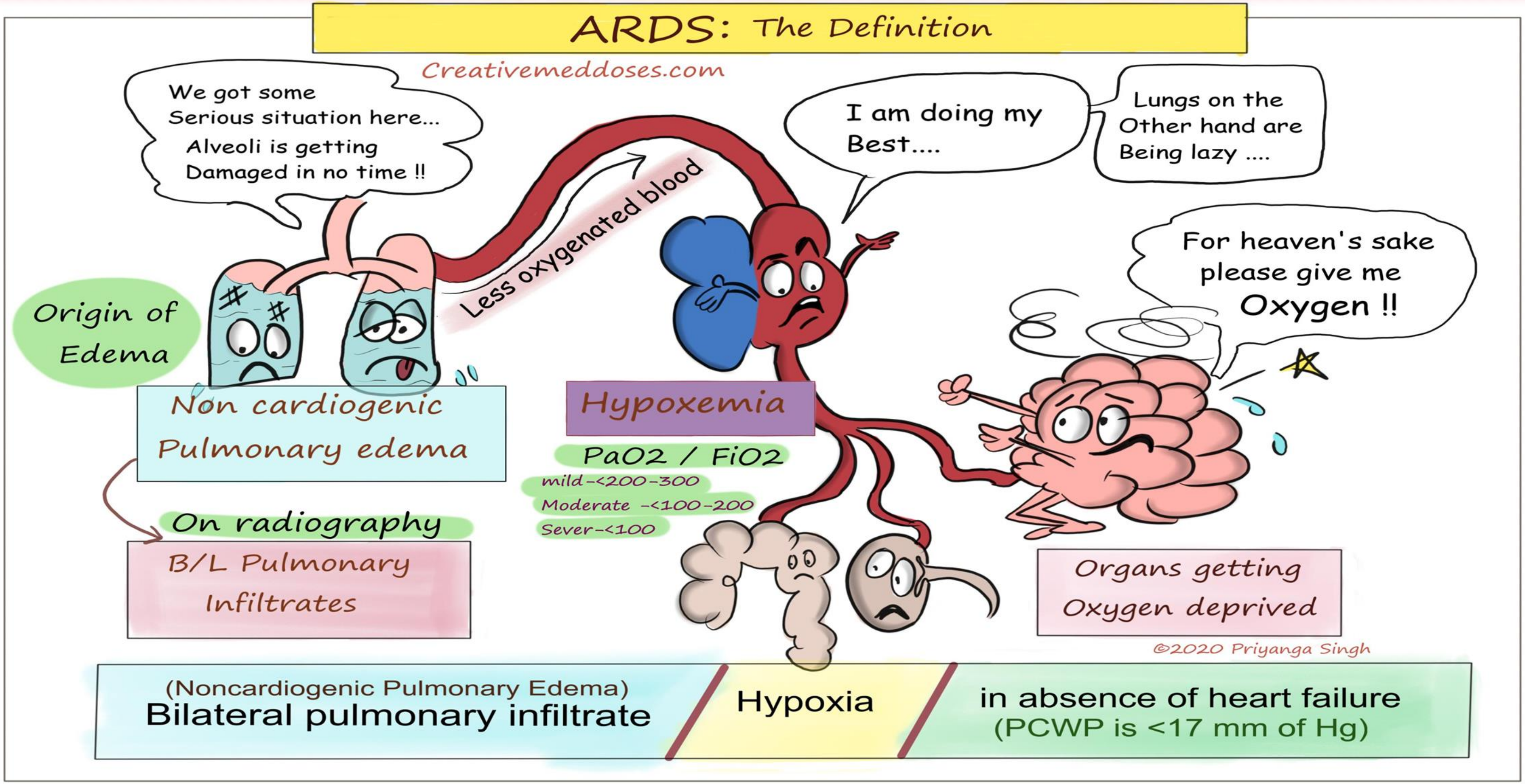
Asts. Prof. Dr. Gülşah ÇIKRIKÇI IŞIK

November - 2020



- PATHOPHYSİOLOGY

https://www.researchgate.net/publication/342432932_Coronavirus_COVID-19_Fulminant_Myopericarditis_and_Acute_Respiratory_Distress_Syndrome_ARDS_in_a_Middle-Aged_Male_Patient/figures?lo=1

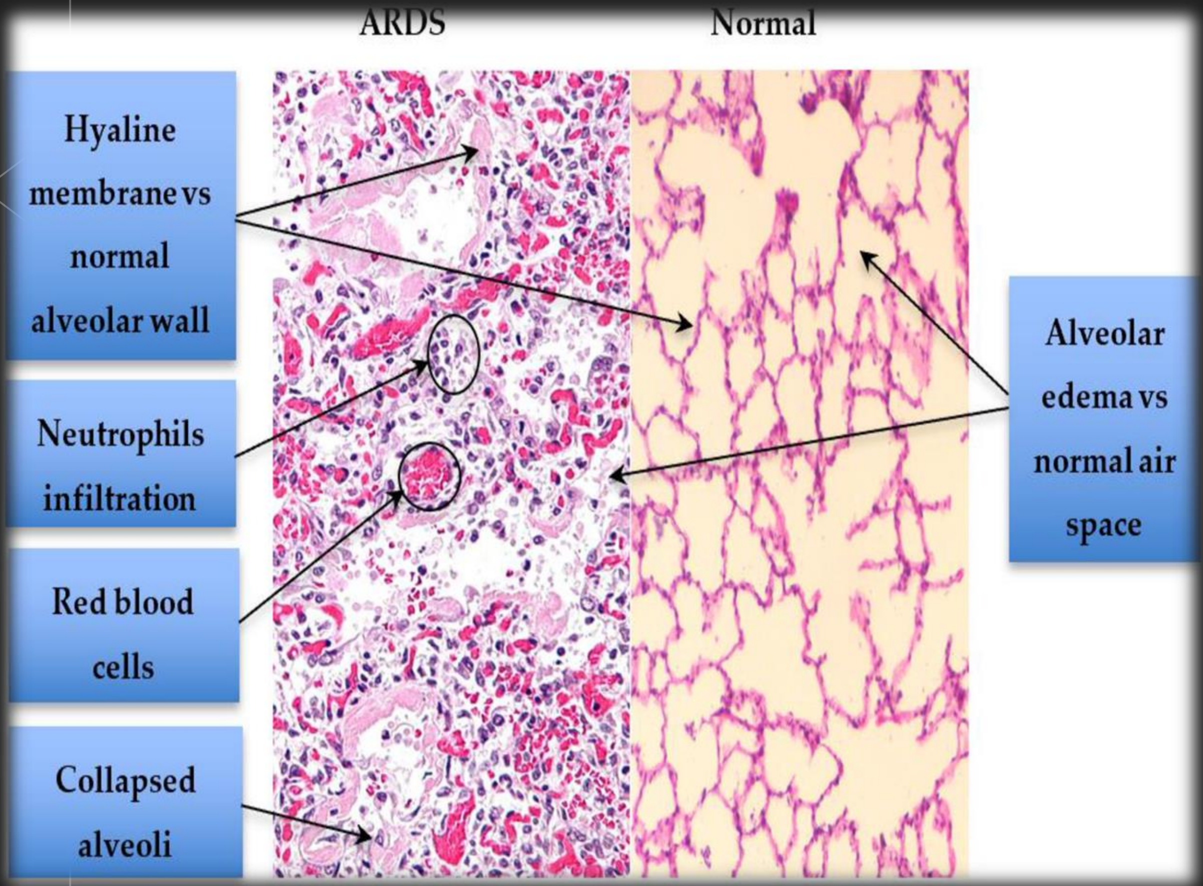


https://creativemeddoses.com/topics-list/acute-respiratory-distress-syndrome-ards/

IS IT THAT MUCH EASY?

VENTILATOR-INDUCED LUNG INJURY

- Barotrauma
- Oxygen toxicity
- Volutrauma
- Atelectrauma
- Biotrauma



Bates JHT, Smith BJ. Ventilator-induced lung injury and lung mechanics. Ann Transl Med. 2018 Oct;6(19):378.

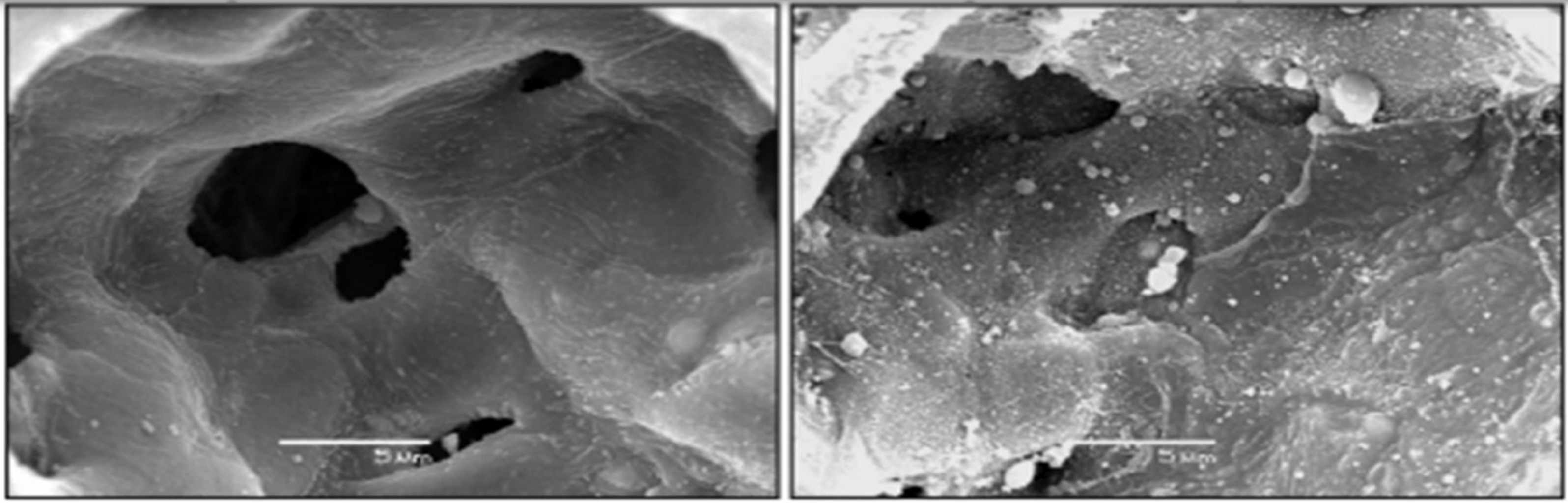


Figure 3 Scanning electron micrograph depicting an undamaged alveolar surface (right panel) and fragmented alveolar epithelium (left panel) caused by two hours of ventilation at high tidal volumes and zero end expiratory pressure. Reproduced with permission from Hamlington *et al.* (88).

Bates JHT, Smith BJ. Ventilator-induced lung injury and lung mechanics. Ann Transl Med. 2018 Oct;6(19):378.

Ventilate for adequate oxygenation and normal CO_2 levels

Prevent ventilator induced lung injury

NHLBI ARDS NETWORK
Mechanical Ventilation Protocol

- Low tidal volume ventilation = 6cc/kg (of ideal body weight)
- Pplat (airway pressure) = determined by a 1-second hold maneuver with the ventilator of less than 30 mm Hg
- Utilization of higher PEEP (minimum of 14 at 48 hours) and low FIO2 strategies
- Goal SpO2 88% to 95% and avoidance of hyperoxemia

Young M, DiSilvio B, Rao S, Velliyattikuzhi S, Balaan M. Mechanical Ventilation in ARDS. Crit Care Nurs Q. 2019 Oct/Dec;42(4):392-399.

ARDSnet

NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary

INCLUSION CRITERIA: Acute onset of

1. $PaO_2/FiO_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT

1. Calculate predicted body weight (PBW)
   Males = 50 + 2.3 [height (inches) - 60]
   Females = 45.5 + 2.3 [height (inches) -60]
2. Select any ventilator mode
3. Set ventilator settings to achieve initial V_T = 8 ml/kg PBW
4. Reduce V_T by 1 ml/kg at intervals $\leq$ 2 hours until V_T = 6ml/kg PBW.
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust V_T and RR to achieve pH and plateau pressure goals below.

OXYGENATION GOAL: PaO_2 55-80 mmHg or SpO_2 88-95%
Use a minimum PEEP of 5 cm H_2O. Consider use of incremental FiO_2/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/higher FiO2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

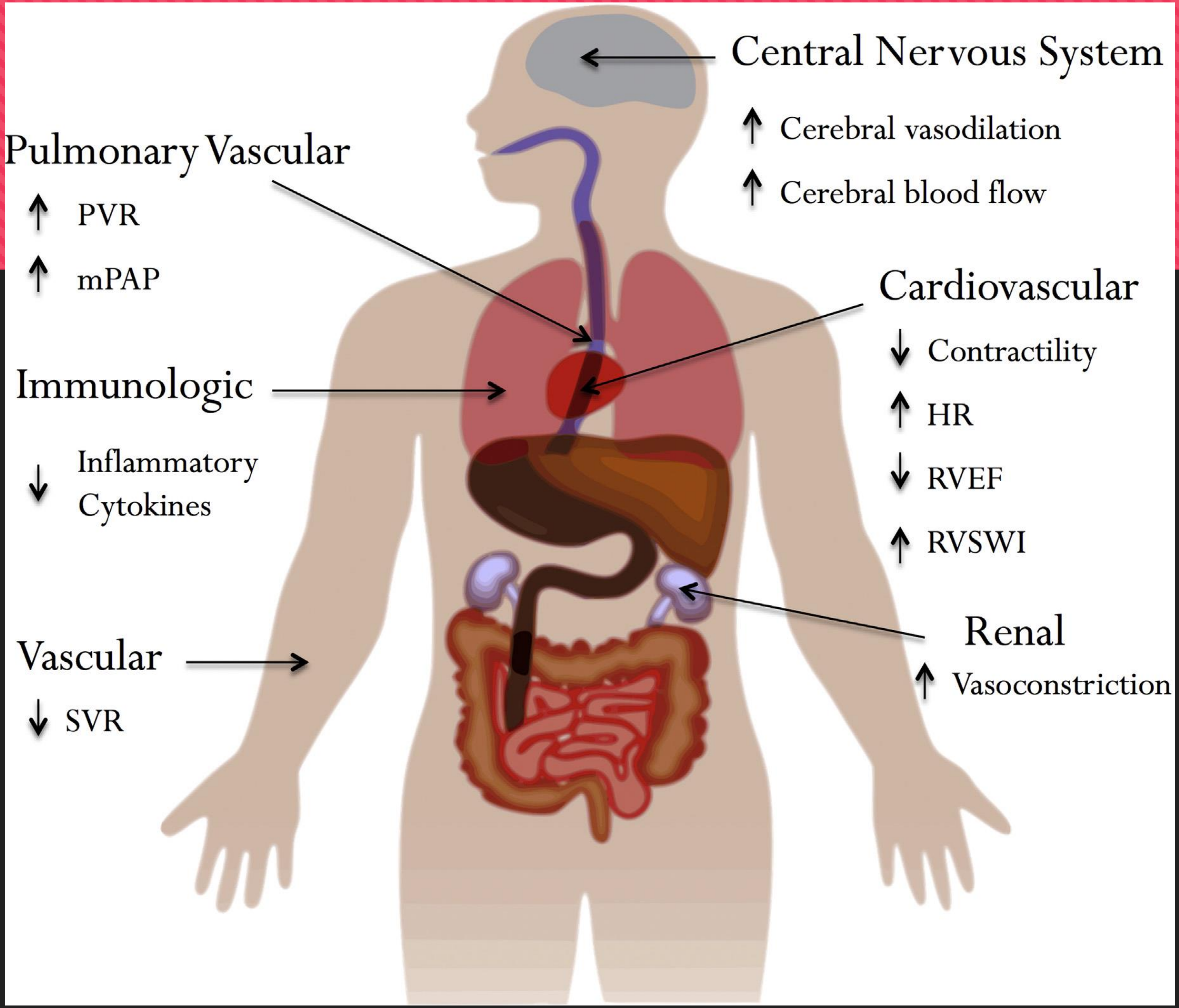
PLATEAU PRESSURE GOAL: $\leq$ 30 cm H_2O
Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T.
If Pplat > 30 cm H_2O: decrease V_T by 1ml/kg steps (minimum = 4 ml/kg).
If Pplat < 25 cm H_2O and V_T< 6 ml/kg, increase V_T by 1 ml/kg until Pplat > 25 cm H_2O or V_T = 6 ml/kg.
If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains $\leq$ 30 cm H_2O.

PERMİSSİVE HYPERCAPNİA

- PaCO2 levels should rise by less than 10 mmHg/h and
- Normally allowed to rise a level of 45 to 65 mmHg.
- Ph levels of 7.25 or more seem to be the most common target
- Buffering agents
  - sodium bicarbonate
  - tromethamine

Young M, DiSilvio B, Rao S, Velliyattikuzhi S, Balaan M. Mechanical Ventilation in ARDS. Crit Care Nurs Q. 2019 Oct/Dec;42(4):392-399.

Is it harmless?



It is still unclear whether hypercapnic acidosis carries survival benefits independent of using low tidal volumes

Morales-Quinteros L, Camprubí-Rimblas M, Bringué J, Bos LD, Schultz MJ, Artigas A. The role of hypercapnia in acute respiratory failure. Intensive Care Med Exp. 2019 Jul 25;7(Suppl 1):39. doi: 10.1186/s40635-019-0239-0. PMID: 31346806; PMCID: PMC6658637.

Multicenter Study > Intensive Care Med. 2017 Feb;43(2):200-208.
doi: 10.1007/s00134-016-4611-1. Epub 2017 Jan 20.

Severe hypercapnia and outcome of mech ventilated patients with moderate or seve respiratory distress syndrome

Abstract

Purpose: To analyze the relationship between hypercapnia developing within the first 48 h after the start of mechanical ventilation and outcome in patients with acute respiratory distress syndrome (ARDS).

Patients and methods: We performed a secondary analysis of three prospective non-interventional cohort studies focusing on ARDS patients from 927 intensive care units (ICUs) in 40 countries. These patients received mechanical ventilation for more than 12 h during 1-month periods in 1998, 2004, and 2010. We used multivariable logistic regression and a propensity score analysis to examine the association between hypercapnia and ICU mortality.

Main outcomes: We included 1899 patients with ARDS in this study. The relationship between maximum $PaCO_2$ in the first 48 h and mortality suggests higher mortality at or above $PaCO_2$ of ≥50 mmHg. Patients with severe hypercapnia ($PaCO_2$ ≥50 mmHg) had higher complication rates, more organ failures, and worse outcomes. After adjusting for age, SAPS II score, respiratory rate, positive end-expiratory pressure, PaO_2/FiO_2 ratio, driving pressure, pressure/volume limitation strategy (PLS), corrected minute ventilation, and presence of acidosis, severe hypercapnia was associated with increased risk of ICU mortality [odds ratio (OR) 1.93, 95% confidence interval (CI) 1.32 to 2.81; p = 0.001]. In patients with severe hypercapnia matched for all other variables, ventilation with PLS was associated with higher ICU mortality (OR 1.58, CI 95% 1.04-2.41; p = 0.032).

Conclusions: Severe hypercapnia appears to be independently associated with higher ICU mortality in patients with ARDS.

The incidence of severe hypercapnia increased significantly with the time (1998, 2004, and 2010) as a consequence of the diverse respiratory strategies practiced over the years, which may reflect the feeling of many intensivists that hypercapnia could be beneficial, however…

Nin et al. Severe hypercapnia and outcome of mechanically ventilated patients with moderate or severe acute respiratory distress syndrome. Intensive Care Med. 2017 Feb;43(2):200-208.

Multicenter Study > Crit Care Med. 2017 Jul;45(7):e649-e656.
doi: 10.1097/CCM.0000000000002332.

Effects of Hypercapnia and Hypercapnic Acid[...] Hospital Mortality in Mechanically Ventilated Patients

Abstract

Objectives: Lung-protective ventilation is used to prevent further lung injury in patients on invasive mechanical ventilation. However, lung-protective ventilation can cause hypercapnia and hypercapnic acidosis. There are no large clinical studies evaluating the effects of hypercapnia and hypercapnic acidosis in patients requiring mechanical ventilation.

Design: Multicenter, binational, retrospective study aimed to assess the impact of compensated hypercapnia and hypercapnic acidosis in patients receiving mechanical ventilation.

Settings: Data were extracted from the Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation Adult Patient Database over a 14-year period where 171 ICUs contributed deidentified data.

Patients: Patients were classified into three groups based on a combination of pH and carbon dioxide levels (normocapnia and normal pH, compensated hypercapnia [normal pH with elevated carbon dioxide], and hypercapnic acidosis) during the first 24 hours of ICU stay. Logistic regression analysis was used to identify the independent association of hypercapnia and hypercapnic acidosis with hospital mortality.

Interventions: Nil.

Measurements and main results: A total of 252,812 patients (normocapnia and normal pH, 110,104; compensated hypercapnia, 20,463; and hypercapnic acidosis, 122,245) were included in analysis. Patients with compensated hypercapnia and hypercapnic acidosis had higher Acute Physiology and Chronic Health Evaluation III scores (49.2 vs 53.2 vs 68.6; $p < 0.01$). The mortality was higher in hypercapnic acidosis patients when compared with other groups, with the lowest mortality in patients with normocapnia and normal pH. After adjusting for severity of illness, the adjusted odds ratio for hospital mortality was higher in hypercapnic acidosis patients (odds ratio, 1.74; 95% CI, 1.62-1.88) and compensated hypercapnia (odds ratio, 1.18; 95% CI, 1.10-1.26) when compared with patients with normocapnia and normal pH ($p < 0.001$). In patients with hypercapnic acidosis, the mortality increased with increasing PCO_2 until 65 mm Hg after which the mortality plateaued.

Conclusions: Hypercapnic acidosis during the first 24 hours of intensive care admission is more strongly associated with increased hospital mortality than compensated hypercapnia or normocapnia.

In another retrospective analysis including ov[...] ventilation showed that patients who develo[...] 65 mmHg) during the first 24 h of mechanic[...] than those who had compensated hypercap[...]

Tiruvoipati R, Pilcher D, Buscher H, Botha J, Bailey M. Effects of Hypercapnia and Hypercapnic Acidosis on Hospital Mortality in Mechanically Ventilated Patients. Crit Care Med. 2017 Jul;45(7):e649-e656.

Table 3 Randomized controlled studies in lung-protective ventilation and $PaCO_2$ levels

Study	Mortality benefit	$PaCO_2$ in control arm (mmHg ± SD)	$PaCO_2$ in LPV arm (mmHg ± SD)	Buffer used
ARDSNet [2]	Yes	35.8 ± 8.0	40.0 ± 10.0	Yes
Amato et al. [66]	Yes	36.0 ± 1.5	58.0 ± 3.0	No
Brochard et al. [46]	No	41.0 ± 7.5	59.5 ± 19.0	No
Brower et al. [67]	No	40.1 ± 1.6	50.3 ± 3.5	Yes
Stewart et al. [68]	No	46.1 ± 10	54.5 ± 15	No

LPV lung-protective ventilation

Different studies, different results…

Morales-Quinteros L, Camprubí-Rimblas M, Bringué J, Bos LD, Schultz MJ, Artigas A. The role of hypercapnia in acute respiratory failure. Intensive Care Med Exp. 2019 Jul 25;7(Suppl 1):39.

Extracorporeal CO2 removal

- ECCO2R facilitated ventilation with ultralow tidal volumes near to 3 mL/kg PBW, while preventing hypercapnic acidosis*
- One currently recruiting randomized clinical trial evaluates whether ultraprotective ventilation by employing ECCO2R affects 90-day mortality in patients with hypoxemic acute respiratory failure**

*Strategy of UltraProtective Lung Ventilation With Extracorporeal CO2 Removal for New-Onset Moderate to seVere ARDS (SUPERNOVA)
**pRotective vEntilation With Veno-venouS Lung assisT in Respiratory Failure (REST)

Adverse effects…

- It can be associated to adverse effects such worsening hypoxemia and increased FiO2 requirements due to a decrease in mean airway pressure, low ventilation-perfusion ratio, and lower partial pressure of alveolar oxygen secondary to a decreased lung respiratory quotient.
- Besides, because of the low flow system of ECCO2R, higher anticoagulation requirements are needed in order to maintain ECCO2R efficiency and performance. Therefore, significant complications may occur as a consequence of anticoagulation or catheter insertion with hemodynamic instability and a higher number of red blood cell transfusions needed.

Morales-Quinteros L, Camprubí-Rimblas M, Bringué J, Bos LD, Schultz MJ, Artigas A. The role of hypercapnia in acute respiratory failure. Intensive Care Med Exp. 2019 Jul 25;7(Suppl 1):39.

In conclusion

- What the exact impact of high carbon dioxide levels on the outcome of ARDS patients remains uncertain.
- More importantly, whether it should be accepted or whether it should be prevented or treated with invasive techniques for extracorporeal removal remains highly uncertain.

Thanks for listening….