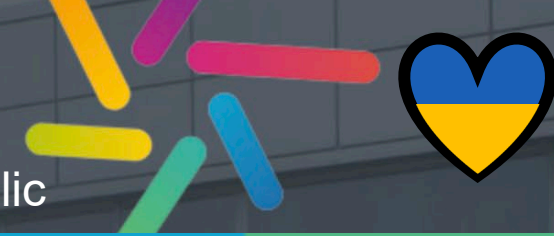


# COLOURS OF SEPSIS

January 24 – 28th 2022, Ostrava Czech Republic



Hot Topics in Intensive Care

## Ventilatory management of C-ARDS: Lessons from the Pandemic

Fernando Suarez Sipmann  
Servicio de Medicina Intensiva  
Hospital Universitario de La Princesa  
Universidad Autonoma de Madrid  
Madrid, Spain  
[fsuarezsipmann@gmail.com](mailto:fsuarezsipmann@gmail.com)

Dept. Surgical Sciences  
Hedenstierna Laboratory  
University of Uppsala  
[Fsuarez.sipmann@surgsci.uu.se](mailto:Fsuarez.sipmann@surgsci.uu.se)



# Disclosures



## Advisor + Research Support/Grants

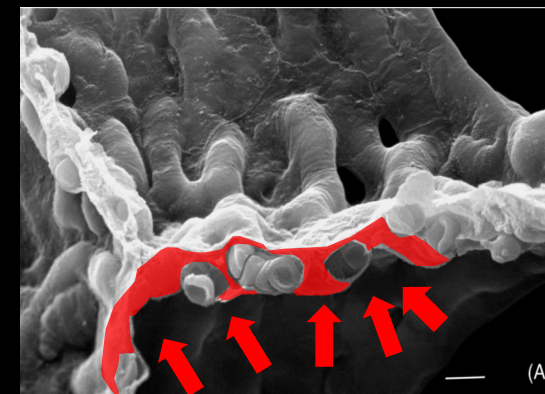
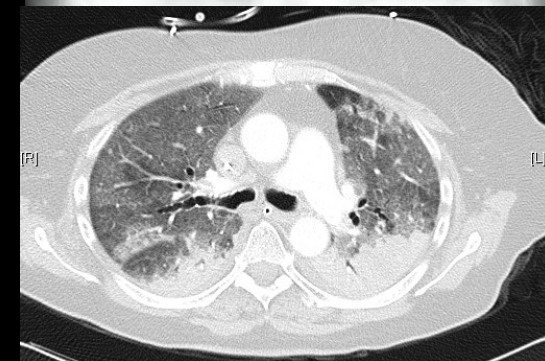
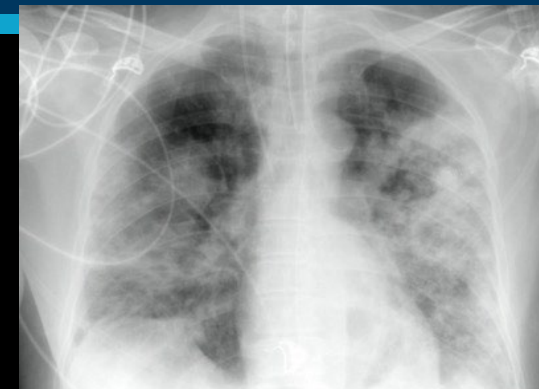
Maquet Critical Care  
Timpel Medical

## Speaker fees

Philips  
Air Liquide

# “Differential” Characteristics of C-ARDS

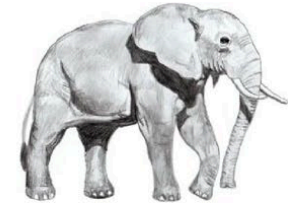
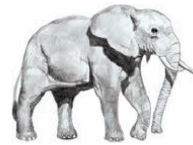
- Diffuse bilateral patchy infiltrates  
Ground glass opacifications  
Sparing of aerated spaces
- Initial Hypoxemia out of proportion from the derangement in lung mechanics and radiologic expresión
- Profound derangement in gas exchange  
Increased shunt and later stages Dead space
- Angiocentric Pathophysiology  
Involment: endothelium >> endothelium  
Vascular dysfunction (thrombosis  
Perfusion mal-distribution  
Vasodilation- vascular shunt



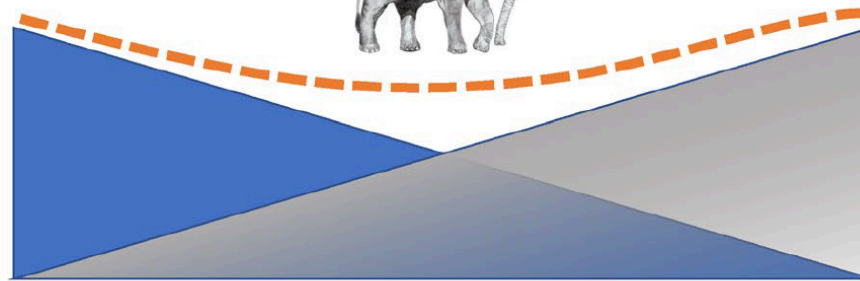
# Integrating the evidence: confronting the COVID-19 elephant

*Intensive Care Med (2020) 46:1904–1907*

John J. Marini<sup>1\*</sup> , R. Phillip Dellinger<sup>2</sup> and Daniel Brodie<sup>3</sup>



Better Lung Compliance  
Ineffective Recruitment  
Atypical PEEP Response  
V/Q Mismatching  
Gas Filled Lungs  
'Ground Glass' Infiltrates  
Adequate Organ Function  
Limited Inflammation  
Immune Suppression (?)




Time

Worse Lung Compliance  
Usual PEEP & Prone Responses  
Extensive Shunting  
Edematous Lungs  
Consolidating Infiltrates  
Multi-Organ Dysfunction  
Extensive Thrombogenesis  
Inflammation and Fibrosis  
Cytokine Release (?)



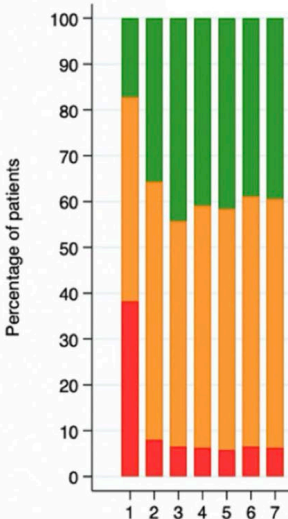


# Clinical features, ventilatory management, and outcome of ARDS caused by COVID-19 are similar to other causes of ARDS

Carlos Ferrando<sup>1,2\*</sup> , Fernando Suarez-Sipmann<sup>2,3,4</sup>, Ricard Mellado-Artigas<sup>1</sup>, María Hernández<sup>5</sup>, Alfredo Gea<sup>6</sup>, Egoitz Arruti<sup>7</sup>, César Aldecoa<sup>8</sup>, Graciela Martínez-Pallí<sup>1</sup>, Miguel A. Martínez-González<sup>9,10</sup>, Arthur S. Slutsky<sup>11,12</sup> and Jesús Villar<sup>2,11,13</sup>

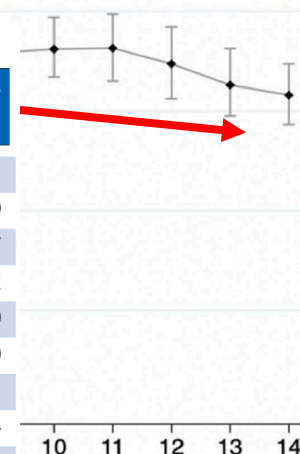
## Take-home message

COVID-19 patients with ARDS predominantly presented a typical moderate-to-severe ARDS. Ventilatory management, and 28-day outcome did not differ from other causes of ARDS.

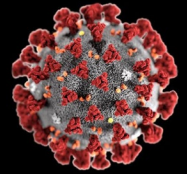


**Table 2 Ventilation and outcomes according to ARDS severity**

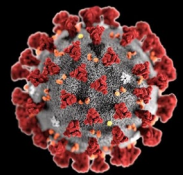
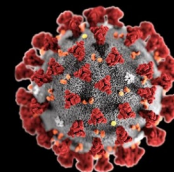
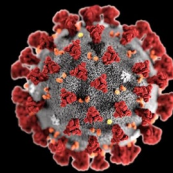
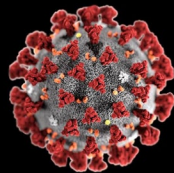
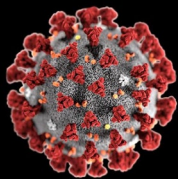
	All (n = 742)	Severe ARDS (n = 283)	Moderate ARDS (n = 331)	Mild ARDS (n = 128)	p value
<b>Outcomes</b>					
Ventilation-free days	4 [0–18]	0 [0–16]	6 [0–18]	8 [0–21]	0.069
Discharged from ICU	401/742 (54%)	136/283 (48%)	185/331 (55%)	80/128 (62%)	0.017
Length of time on the ventilator	14 [7–24]	14 [8–24]	14 [7–24]	13 [7–24]	0.582
Still in ICU	100 (13%)	36 (12%)	47 (14%)	17 (13%)	0.880
Still under invasive MV	72 (9.7%)	26 (9.1%)	34 (10%)	12 (9.3%)	1.000
28-day mortality	241 (32%)	111 (39%)	99 (29%)	31 (24%)	0.005
ICU length of stay	19 [11–37]	19 [12–35]	19 [11–39]	19 [11–36]	0.894
ICU length of stay of discharge patients	17 [11–28]	17 [12–28.5]	17 [11–30]	17.5 [10–27]	0.940
ICU length of stay of deceased patients	17 [10–25]	17 [11–27]	17 [9–26]	17 [10–21]	0.803



# Lessons (I..) Learned From the Pandemic



- Lung Protection is key
- Reappraisal of the use of Adjuvant interventions: Sinergies!
- PEEP Individualization is Key
- Dangerous transition to spontaneous breathing



# Ventilatory Management of C-ARDS



## Lung Protective Ventilation

VT limitation to 4 - 8 mL/kg ideal 6-mL/kg

Pplat limitation ideal  $\leq 28$  cmH<sub>2</sub>O max  $\leq 30$  cmH<sub>2</sub>O

Driving Pressure limitation  $\leq 15$  cmH<sub>2</sub>O

RR minimum necessary to ensure sufficient CO<sub>2</sub> elimination

PEEP individualized to minimize lung collapse and overdistension

## Adjuvant measures

Muscle relaxation

Prone positioning

Recruitment maneuvers

Nitric oxide



And so... the Paella is ready



# But....



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

## International Journal of Gastronomy and Food Science

journal homepage: [www.elsevier.com/locate/ijgfs](http://www.elsevier.com/locate/ijgfs)

### A nightmare glocal discussion. What are the ingredients of Paella Valenciana?

P. Vidal-González<sup>a,\*</sup>, P. Medrano-Ábalos<sup>b</sup>, E.J. Sáez Álvarez<sup>b</sup>

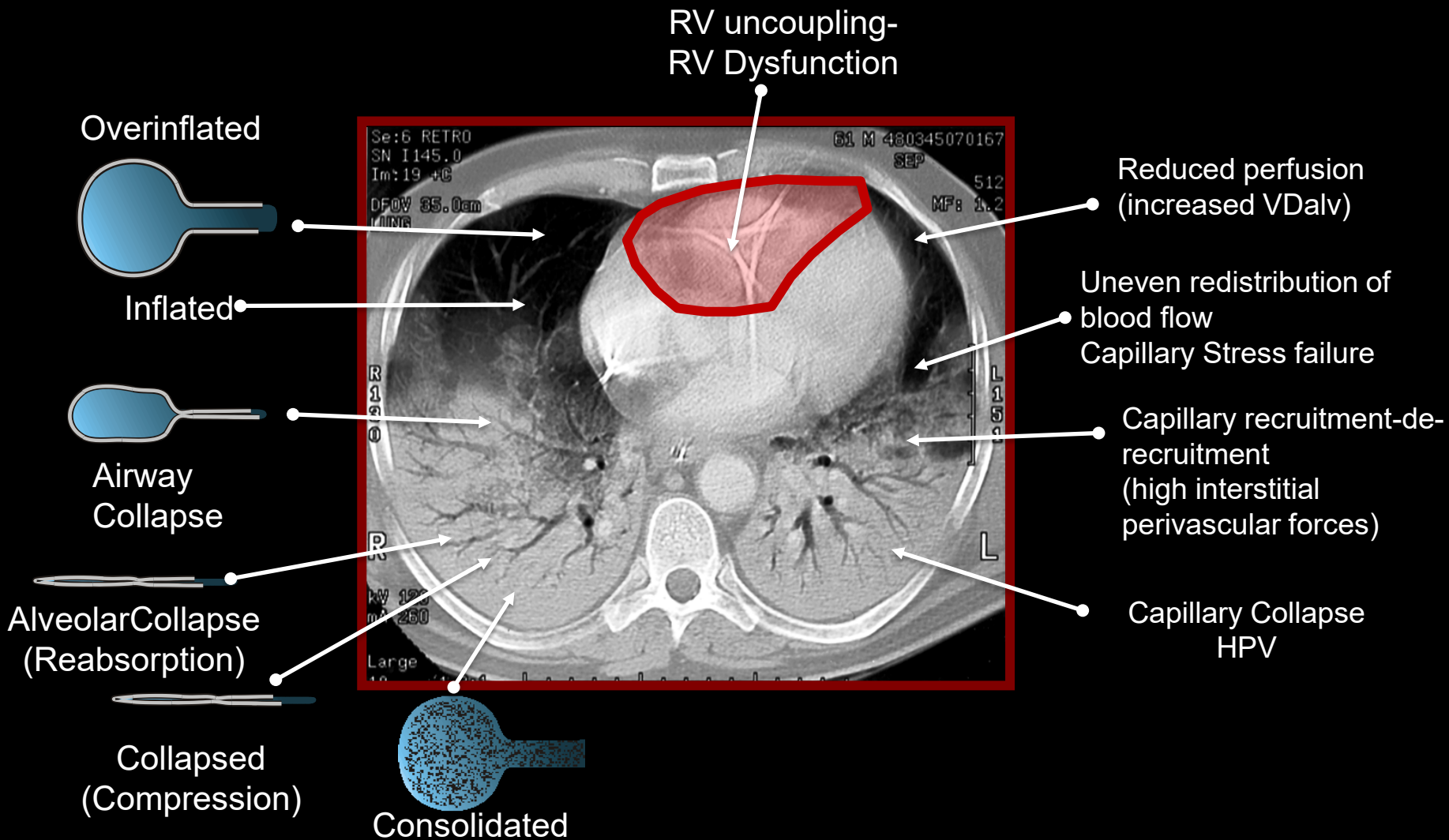
<sup>a</sup> Anthropology Research Institute, Universidad Católica de Valencia, Spain

<sup>b</sup> Nursing School, Universidad Católica de Valencia, Spain, Guillem de Castro, 94, 46003, Valencia, Spain

After a quantitative investigation among non-professional chefs from the 266 towns in the province of Valencia, we found that 10 ingredients are repeated with a very high frequency and that we consider to be the basic ingredients. Fifty other ingredients were identified that are used occasionally, as a sign of the diversity and richness of the dish. This study is provided to offer guidelines to focus debate and social discussion on what the ingredients of a “true Paella Valenciana” should be.



# The complex heterogeneous ARDS lung





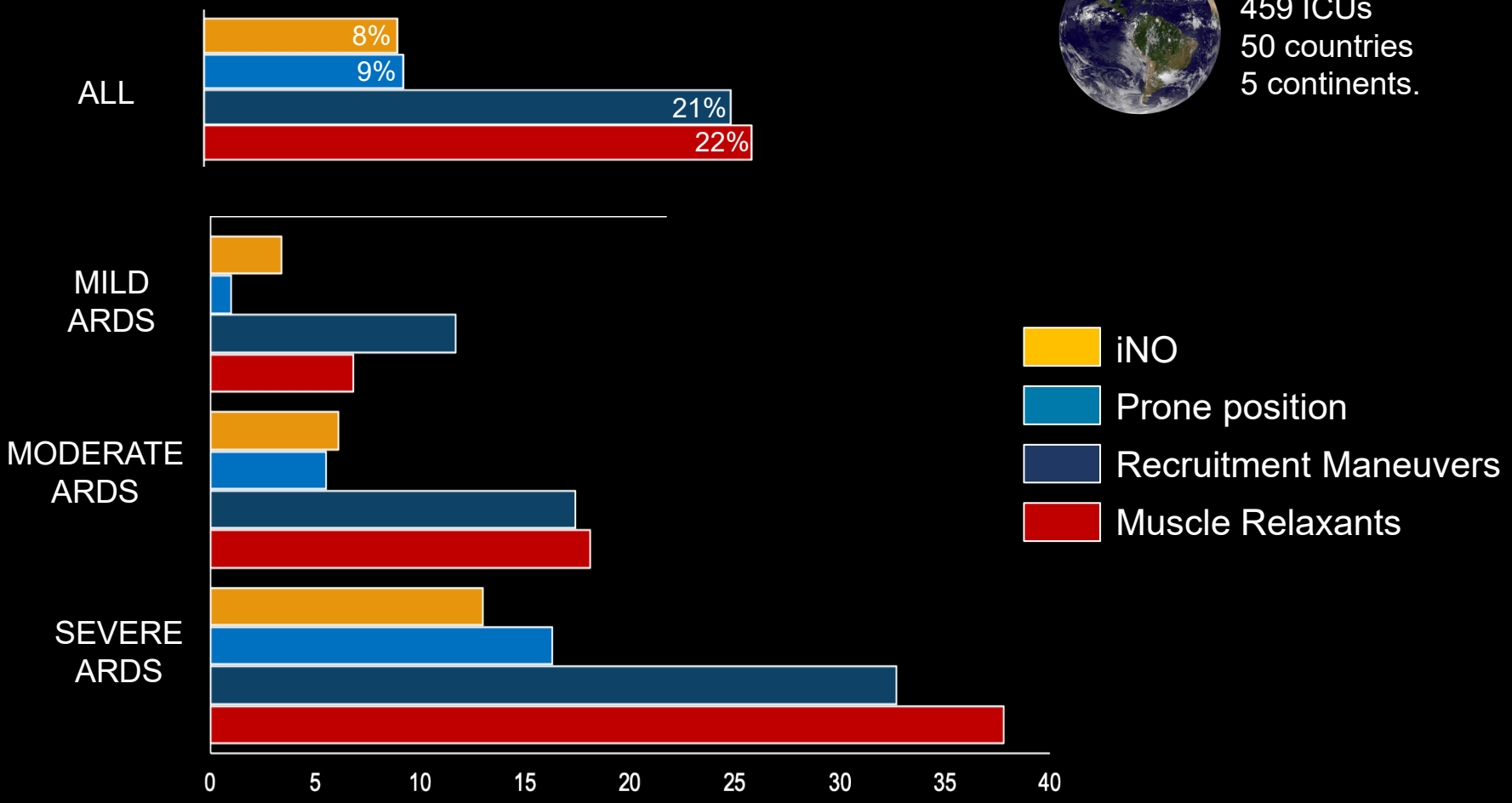
# Use of Adjunctive Measures in ARDS

## Status Before the Pandemic

## LUNG SAFE Study



2377 ARDS patients  
459 ICUs  
50 countries  
5 continents.



# Synergies

The search and use of synergistic effects is common (and necessary) in clinical medicine

## Oncology

- Chemotherapy (adjuvant, early consolidation)

## Infectious diseases

- Antibiotics

(early)

..... M



## Ventilatory Management of ARDS?

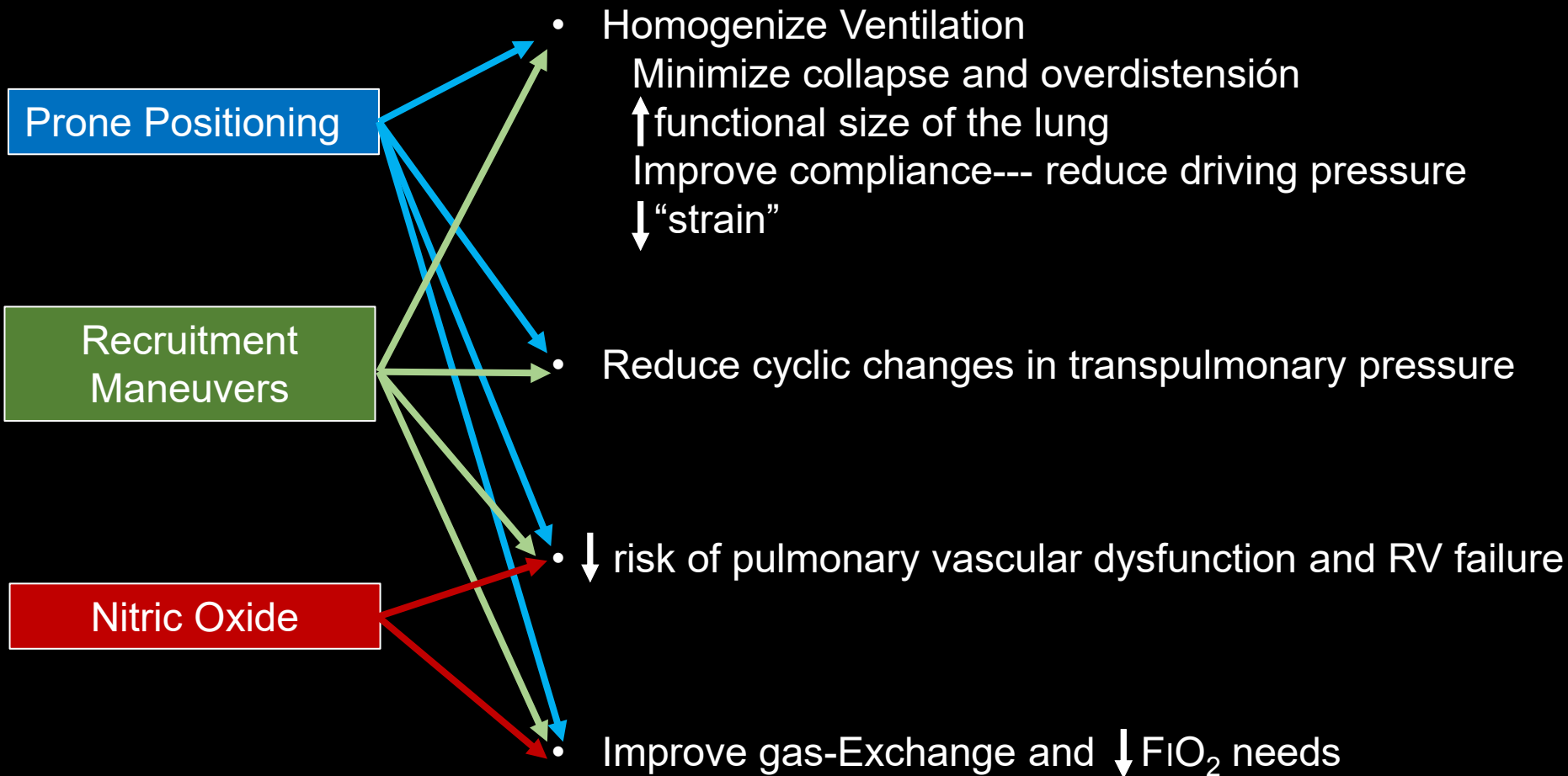


Knowledge of mechanisms of action and predominant pathophysiological aspects of each stage of the in the evolution is critical for applying the correct therapeutic strategies

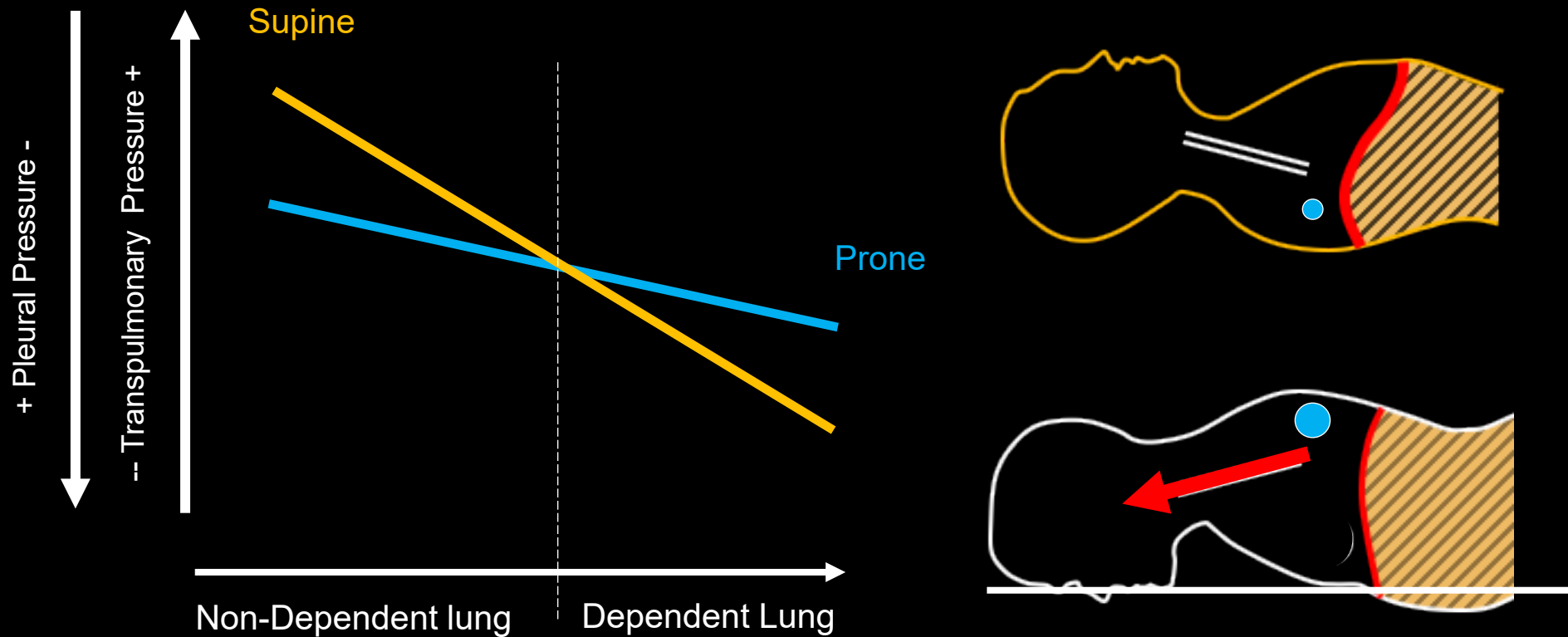
# Adjuvant Measures- Sinergies

## Adjuvant Measures

## Objectives



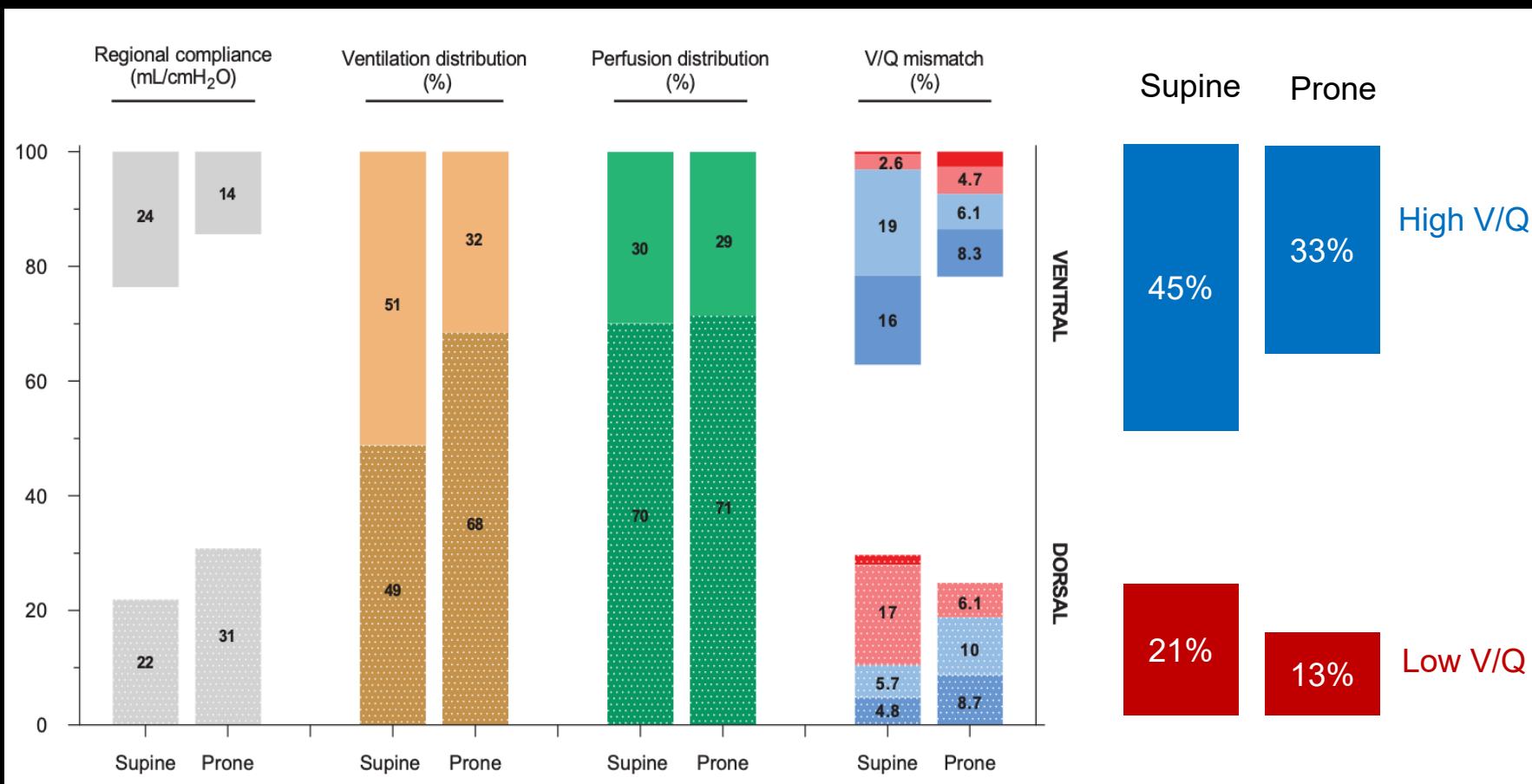
# Effects of Prone Positioning



Re-aeration of dorsal lung regions that maintain a greater perfusion

# Effects of proning measured by EIT

## 9 C-ARDS patients



Perier F et al AJRCCM 2020 epub)

# Changing the Prone Positioning Paradigm

Carsetti et al. Critical Care (2020) 24:225  
https://doi.org/10.1186/s13054-020-02956-w

Critical Care

Open Access

RESEARCH LETTER

## Prolonged prone position ventilation for SARS-CoV-2 patients is feasible and effective

Andrea Carsetti<sup>1,2</sup>, Agnese Damia Paclirini<sup>2</sup>, Benedetto Marini<sup>2</sup>, Simona Pantanetti<sup>2</sup>, Erica Adriano<sup>1,2</sup> and Abele Donati<sup>1,2\*</sup>

**Keywords:** SARS-CoV-2, Prone position ventilation

**Background:** Recently, novel coronavirus 2019 (nCoV-19) is spreading all around the world causing severe acute respiratory syndrome (SARS-CoV-2) requiring mechanical ventilation in about 5% of infected people [1, 2]. Prone position ventilation is an established method to improve oxygenation in severe acute respiratory distress syndrome (ARDS), and its application was able to reduce mortality rate [3]. Although the severity of critically ill patients with SARS-CoV-2 may require intensive care unit (ICU) management, it may create management problems due to the limited number of healthcare workers compared to the number of patients. Often, sustained oxygenation improvement can only be achieved after several cycles of prone position, with a work overload for healthcare staff. To face these problems, we implemented a prone protocol that allows to extend the time for the prone position beyond 16 h, aiming to reduce the number of prone cycles per patient. Thus, the aim of this report was to assess the feasibility and efficacy of prone position ventilation beyond the usual 16 h.

**Methods:** We retrospectively collected data from 10 critically ill patients intubated and mechanically ventilated for SARS-CoV-2. Six patients underwent both standard and prolonged prone position, the latter after one standard cycle

**Results:** All patients were intubated and mechanically ventilated for SARS-CoV-2. Six patients (54.4%) were obese. All standard prone position cycles lasted for 16 h whereas the median duration of prolonged prone position was 36 h (IQR 33.5–39). Oxygenation significantly improved during prolonged prone position (p = 0.034). On the other hand, the gain in oxygenation was not maintained after prolonged prone position (p = 0.423). Static compliance of the respiratory system did not change significantly during prolonged prone position (p > 0.05). Application of prone position did not expose patients to an increased incidence of skin pressure lesions, and other complications were not reported.

**Conclusions:** Our report showed that prone position beyond 16 h may probably be safely performed in patients with SARS-CoV-2 and severe hypoxemia not responsive to conventional mechanical ventilation. This approach might have several potential advantages. First, oxygenation improvement might be higher during prolonged prone position than during standard prone position, and the gain

**Abstract**  
**Background:** Prone position ventilation (PPV) has been shown to improve oxygenation in patients with moderate to severe ARDS. However, the duration of PPV is often limited by the need for patient repositioning. We aimed to assess the feasibility and efficacy of prolonged prone position ventilation (PPV) in SARS-CoV-2 patients.

**Methods and results:** This study was performed in 10 patients (ICUs) with moderate to severe ARDS. All patients were intubated and mechanically ventilated. Enrollment occurred between 12/2020 and 1/2021. Patients were divided into two groups: Group 1 (n = 4) received standard PPV (16 h) and Group 2 (n = 6) received prolonged PPV (36 h). Primary endpoint was the need for rescue tracheostomy. Secondary endpoints were mortality, ventilator-free days (VFDs), and days on mechanical ventilation (DMMV).

**Conclusions:** Prolonged PPV was feasible and effective in SARS-CoV-2 patients. It allowed for a significant increase in VFDs and a reduction in DMMV compared to standard PPV.

**Keywords:** Prone position ventilation, Acute respiratory distress syndrome, SARS-CoV-2

**Background**  
Prone position (PP) has been shown to improve oxygenation in patients with moderate to severe ARDS. However, the duration of PP is often limited by the need for patient repositioning. We aimed to assess the feasibility and efficacy of prolonged prone position ventilation (PPV) in SARS-CoV-2 patients.

**Methods and results**  
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Prolonged PPV was feasible and effective in SARS-CoV-2 patients. It allowed for a significant increase in VFDs and a reduction in DMMV compared to standard PPV.

**Keywords**  
Prone position ventilation, Acute respiratory distress syndrome, SARS-CoV-2

**Figure 1** Timeline of PPV: A, alive; D, dead; MV, mechanical ventilation.

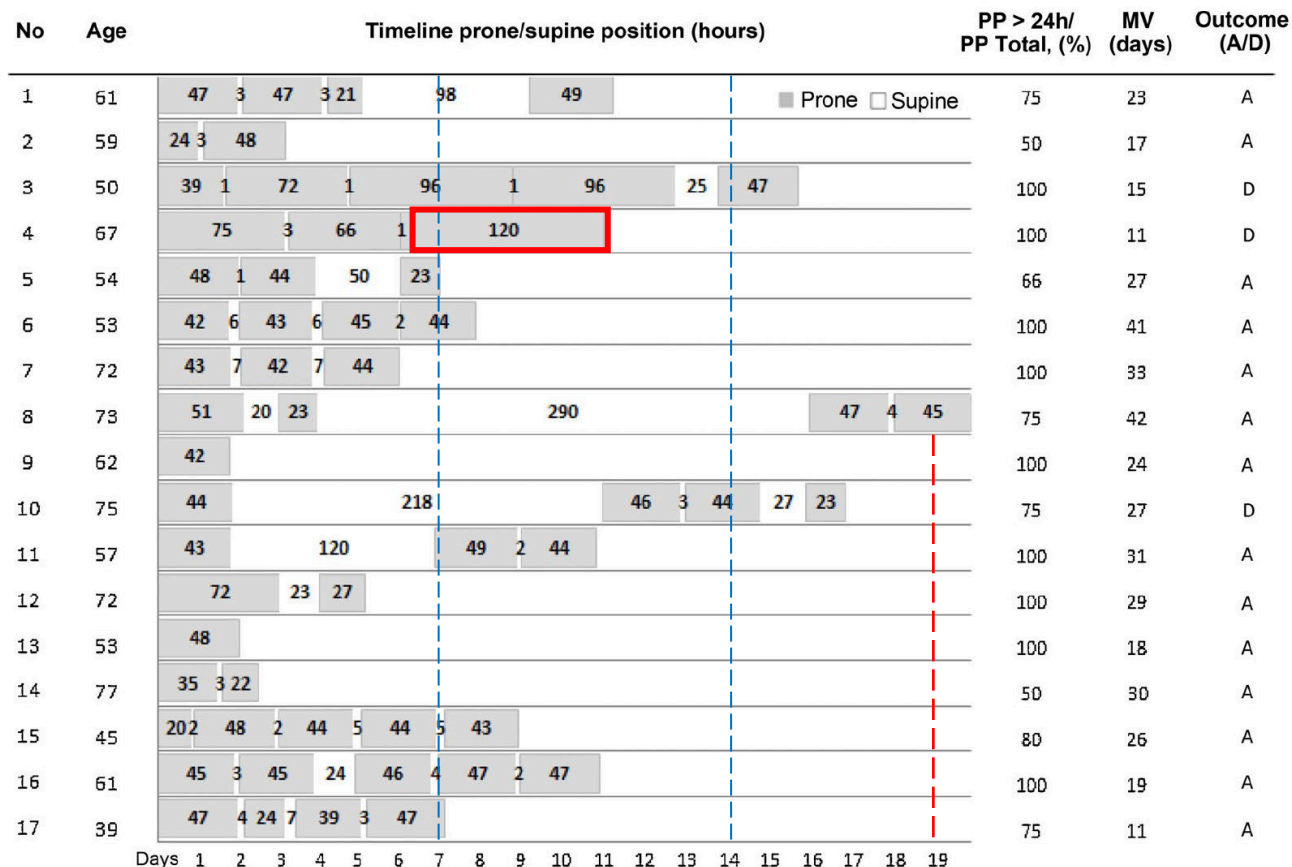
**Springer**

## Prolongued/Delayed Prone Positioning

- Feasible
- Safe (Low incidence of adverse events)
- Potential clinical – organizational benefits



# Prolongued/Delayed Prone sessions

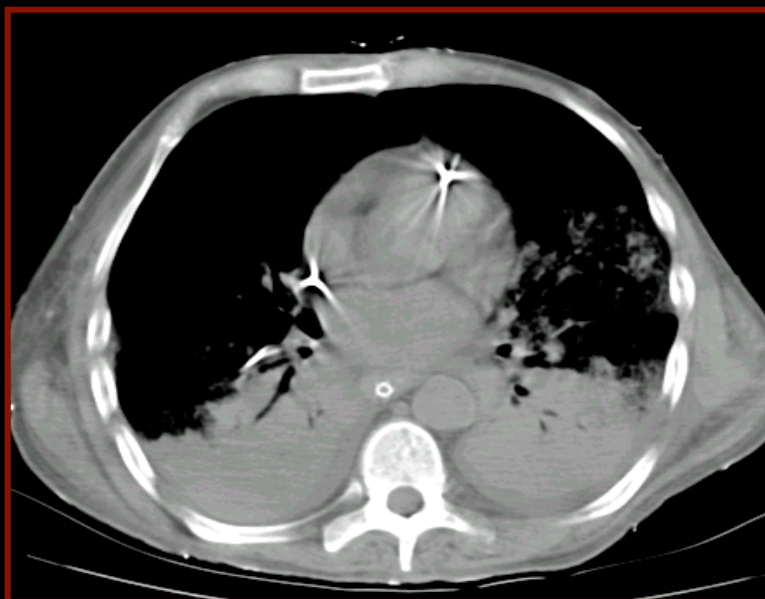


Mean duration of Prone sessions 48h

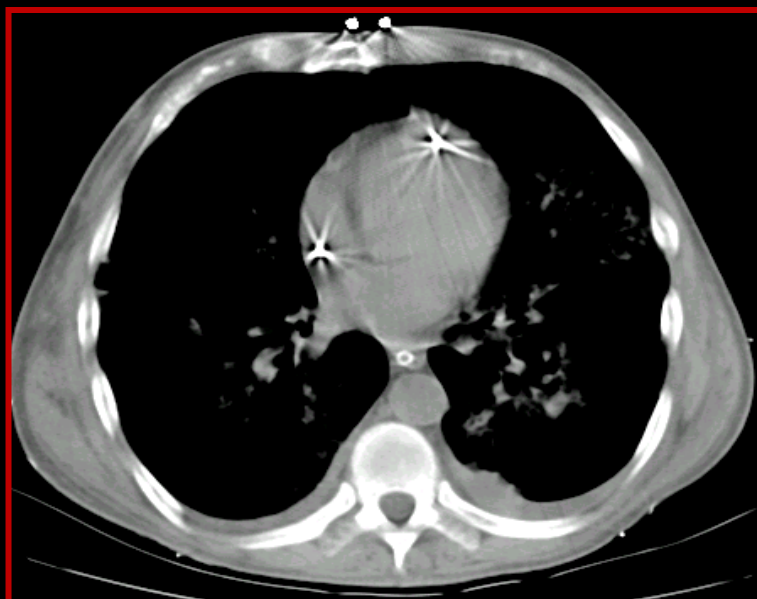
# Lung Recruitment and individualized PEEP

When lung collapse is an important pathophysiological component...

Baseline

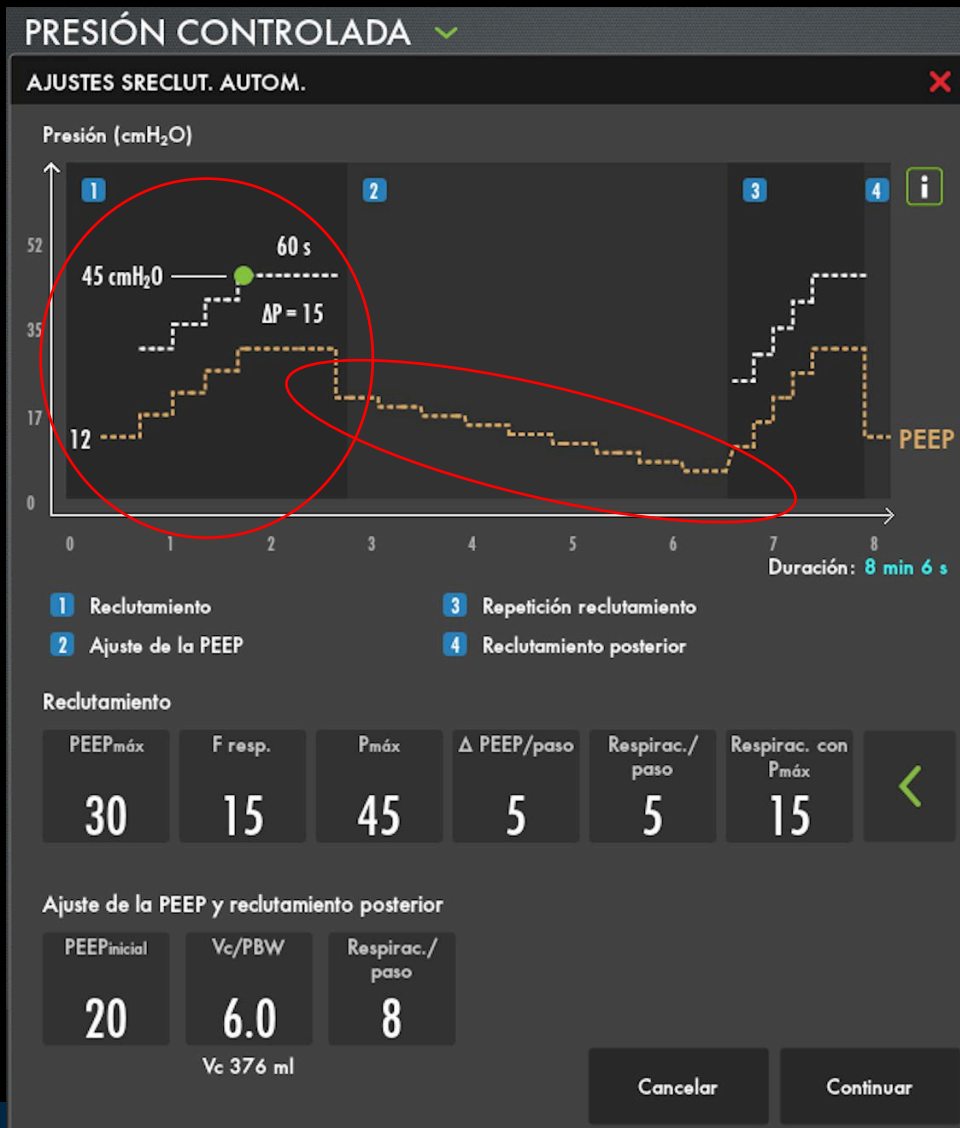


Post-Recruitment + PEEP



Less heterogeneity  
Increased functional size  
Increased compliance  
Larger EELV

# Automated Open Lung Procedure



## Recruitment Phase

Cycling Pressure Controlled Ventilation  
Incremental PEEP steps with fixed  $\Delta P$

## PEEP titration

Volume Controlled Ventilation

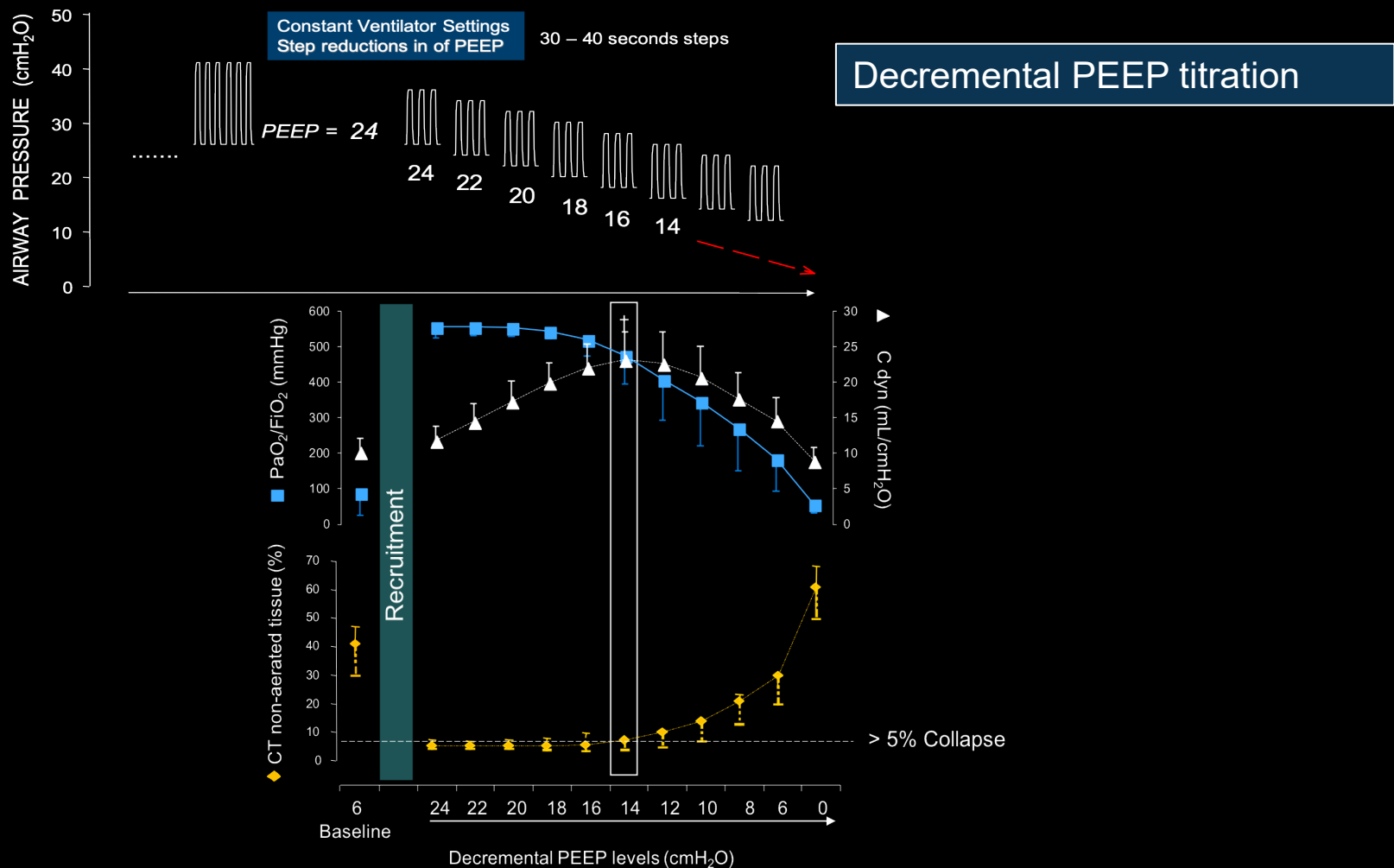
2 cmH<sub>2</sub>O PEEP steps

Automatic detection of optimal PEEP

Based on maximal C<sub>dyn</sub>

# Individualized PEEP

PEEP that minimizes lung collapse and overdistension



# Automatic PEEP detection



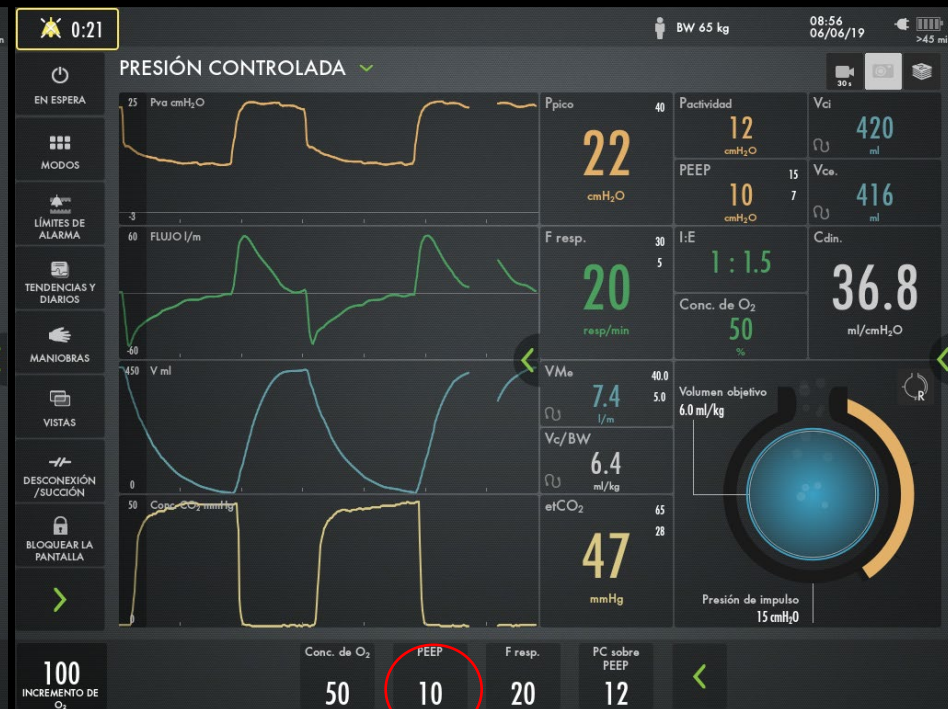
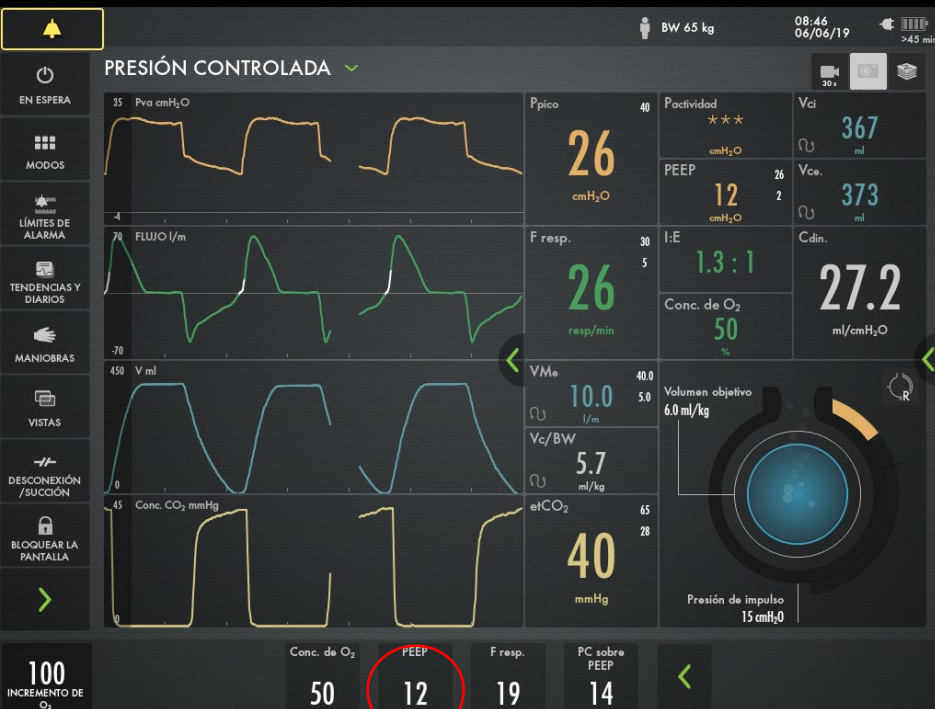
Automatic PEEP detection at 10 cmH<sub>2</sub>O

PaO<sub>2</sub>/FIO<sub>2</sub> 161 mmHg  
 PaCO<sub>2</sub> 49 mmHg  
 Cdyn 37 mL/cmH<sub>2</sub>O



Before

After..... (10 min later)



PaO<sub>2</sub>/FIO<sub>2</sub> 136 mmHg  
 PaCO<sub>2</sub> 47 mmHg  
 Cdyn 33 mL/cmH<sub>2</sub>O

PaO<sub>2</sub>/FIO<sub>2</sub> 161 mmHg  
 PaCO<sub>2</sub> 49 mmHg  
 Cdyn 37 mL/cmH<sub>2</sub>O



# Assessment of recruitability

SRECLUT. AUTOM. (PC) → PRESIÓN CONTROLADA

## Maniobra detenida

No se pudo establecer el cierre de PEEP.

Aumento constante de Cdin

Posibles motivos:

- Paciente no dependiente de PEEP
- Comprobar posible fuga

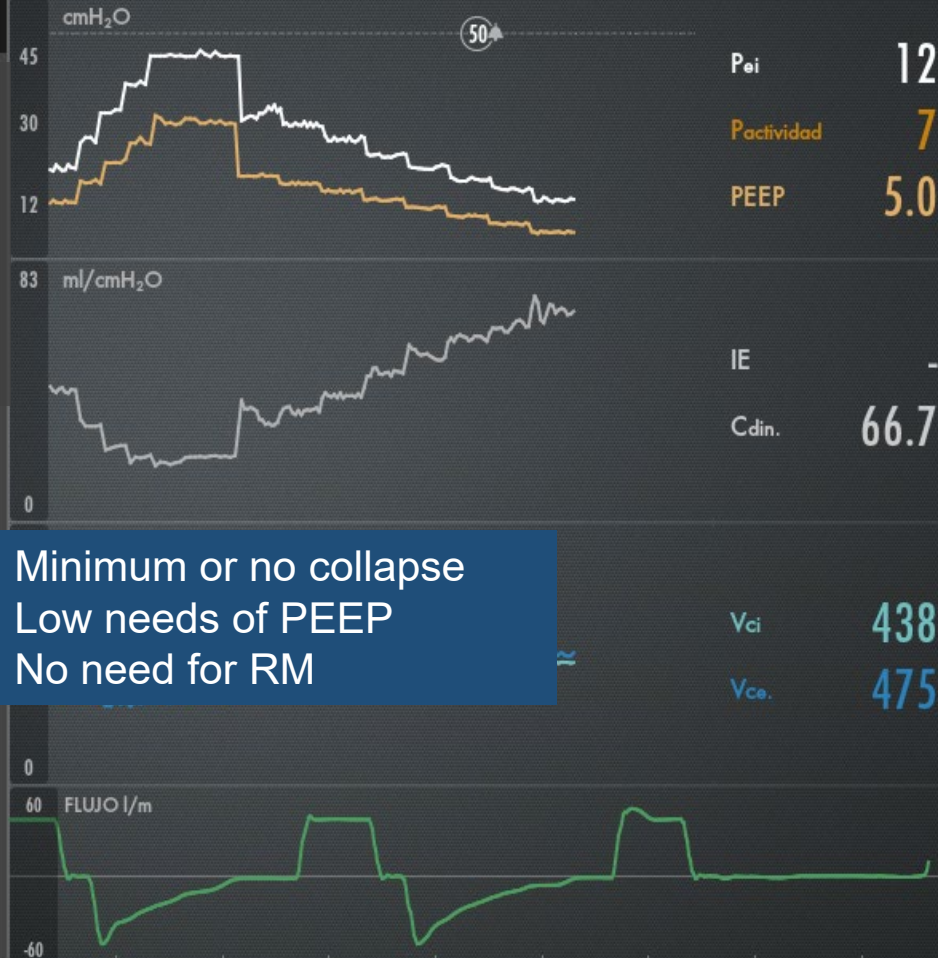
Closing Pressure could not be detected

Constant Increase in Cdyn

Possible reasons:

- Patient not depending on PEEP
- Check for leaks

Cerrar

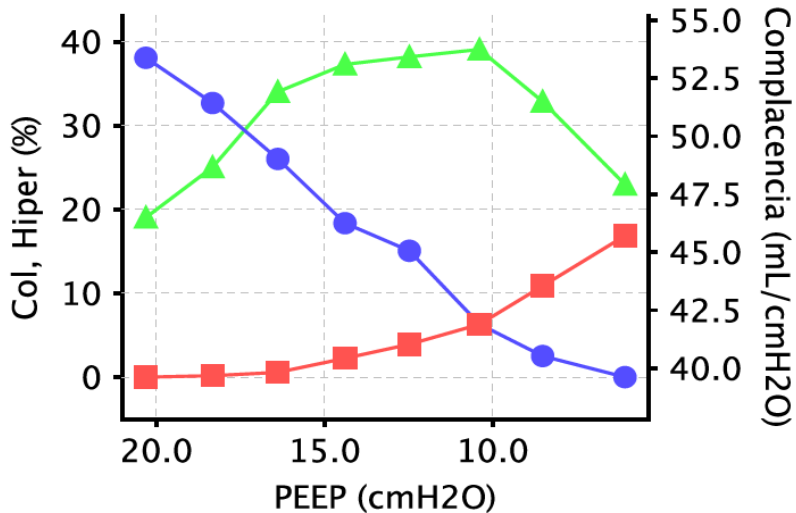


Minimum or no collapse  
Low needs of PEEP  
No need for RM

# COVID-ARDS PEEP tritration examples



# Decremental PEEP titration



■ Colapso ● Hiperdistensión ▲ Complacencia

PEEP (cmH <sub>2</sub> O)	Compl (mL/c)
20.3	
18.3	
16.4	
14.4	
12.5	
10.4	
8.5	
6.1	

Paso de la PEEP: 1

Hiperdistensión      Colapso Acumulado

PEEP: 20.3 cmH<sub>2</sub>O  
Hiperdistensión: 38.1%  
Colapso: 0.0%  
Complacencia: 46.5 mL/cmH<sub>2</sub>O

Paso de la PEEP: 2

Hiperdistensión      Colapso Acumulado

PEEP: 18.3 cmH<sub>2</sub>O  
Hiperdistensión: 32.7%  
Colapso: 0.2%  
Complacencia: 48.7 mL/cmH<sub>2</sub>O

Paso de la PEEP: 3

Hiperdistensión      Colapso Acumulado

PEEP: 16.4 cmH<sub>2</sub>O  
Hiperdistensión: 26.0%  
Colapso: 0.6%  
Complacencia: 51.9 mL/cmH<sub>2</sub>O

Paso de la PEEP: 4

Hiperdistensión      Colapso Acumulado

PEEP: 14.4 cmH<sub>2</sub>O  
Hiperdistensión: 18.4%  
Colapso: 2.2%  
Complacencia: 53.1 mL/cmH<sub>2</sub>O

Paso de la PEEP: 5

Hiperdistensión      Colapso Acumulado

PEEP: 12.5 cmH<sub>2</sub>O  
Hiperdistensión: 15.1%  
Colapso: 3.9%  
Complacencia: 53.4 mL/cmH<sub>2</sub>O

Paso de la PEEP: 6

Hiperdistensión      Colapso Acumulado

PEEP: 10.4 cmH<sub>2</sub>O  
Hiperdistensión: 6.3%  
Colapso: 6.3%  
Complacencia: 53.7 mL/cmH<sub>2</sub>O

Paso de la PEEP: 7

Hiperdistensión      Colapso Acumulado

PEEP: 8.5 cmH<sub>2</sub>O  
Hiperdistensión: 2.5%  
Colapso: 10.9%  
Complacencia: 51.5 mL/cmH<sub>2</sub>O

Paso de la PEEP: 8

Hiperdistensión      Colapso Acumulado

PEEP: 6.1 cmH<sub>2</sub>O  
Hiperdistensión: 0.0%  
Colapso: 16.9%  
Complacencia: 47.9 mL/cmH<sub>2</sub>O

Colapso Acumulado

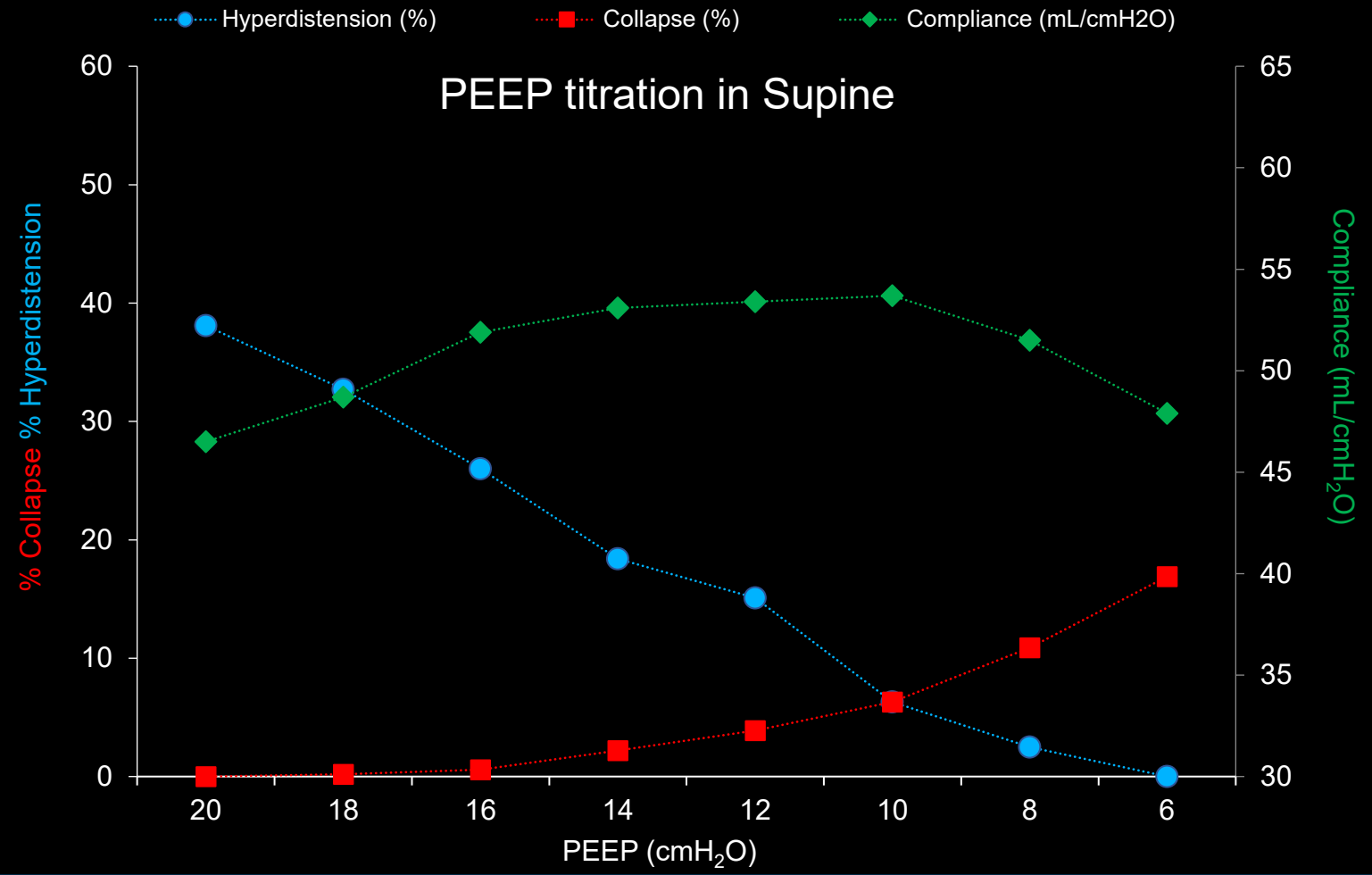
■ Colapso ● Hiperdistensión ▲ Complacencia

Calidad Señal



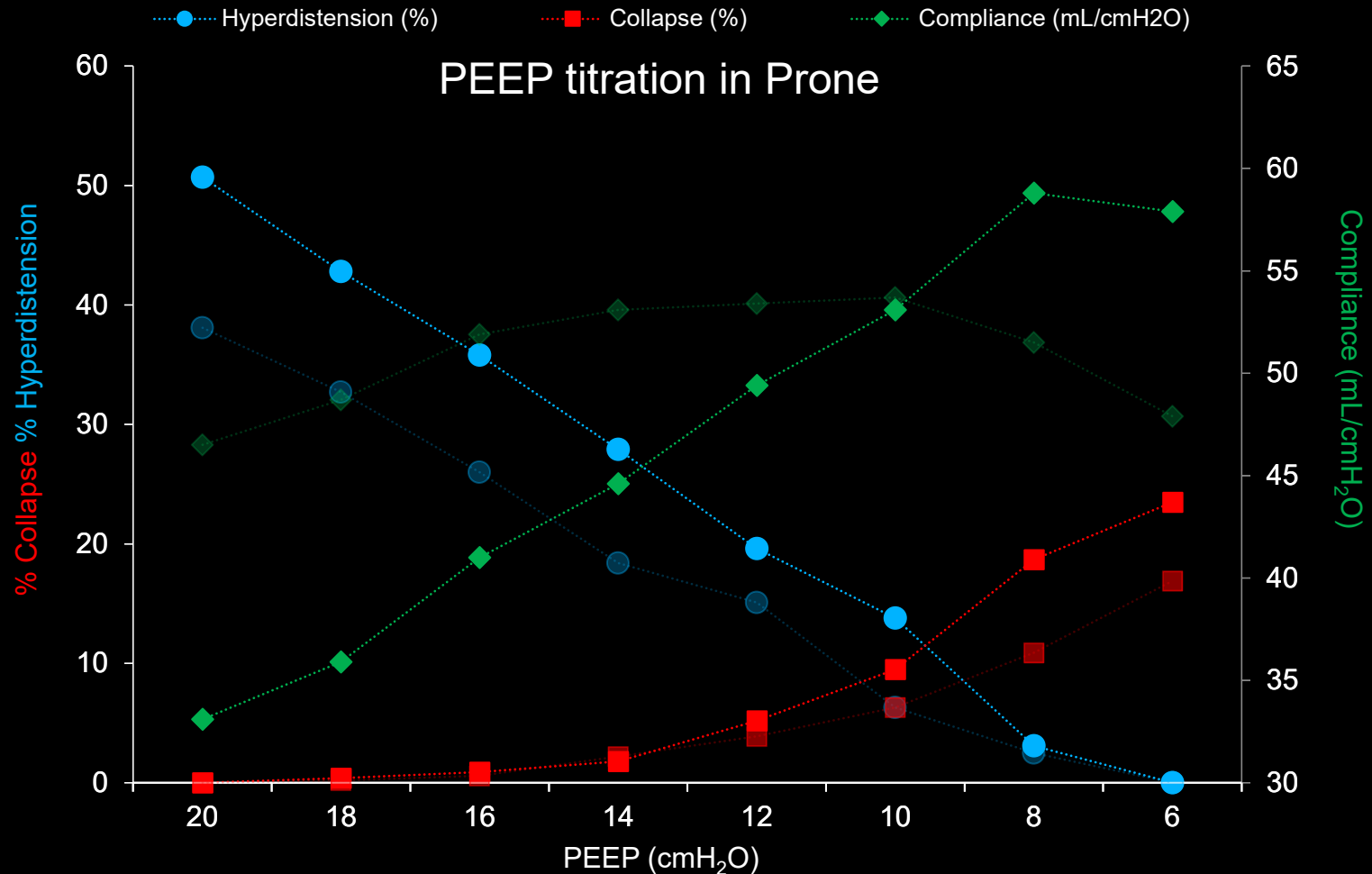
# Individualizing the PEEP level

C-ARDS patient



# Individualizing the PEEP level

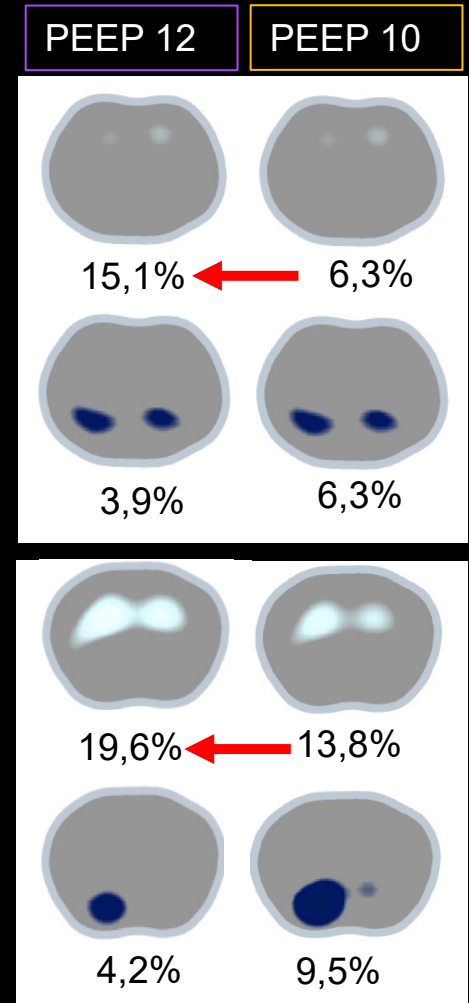
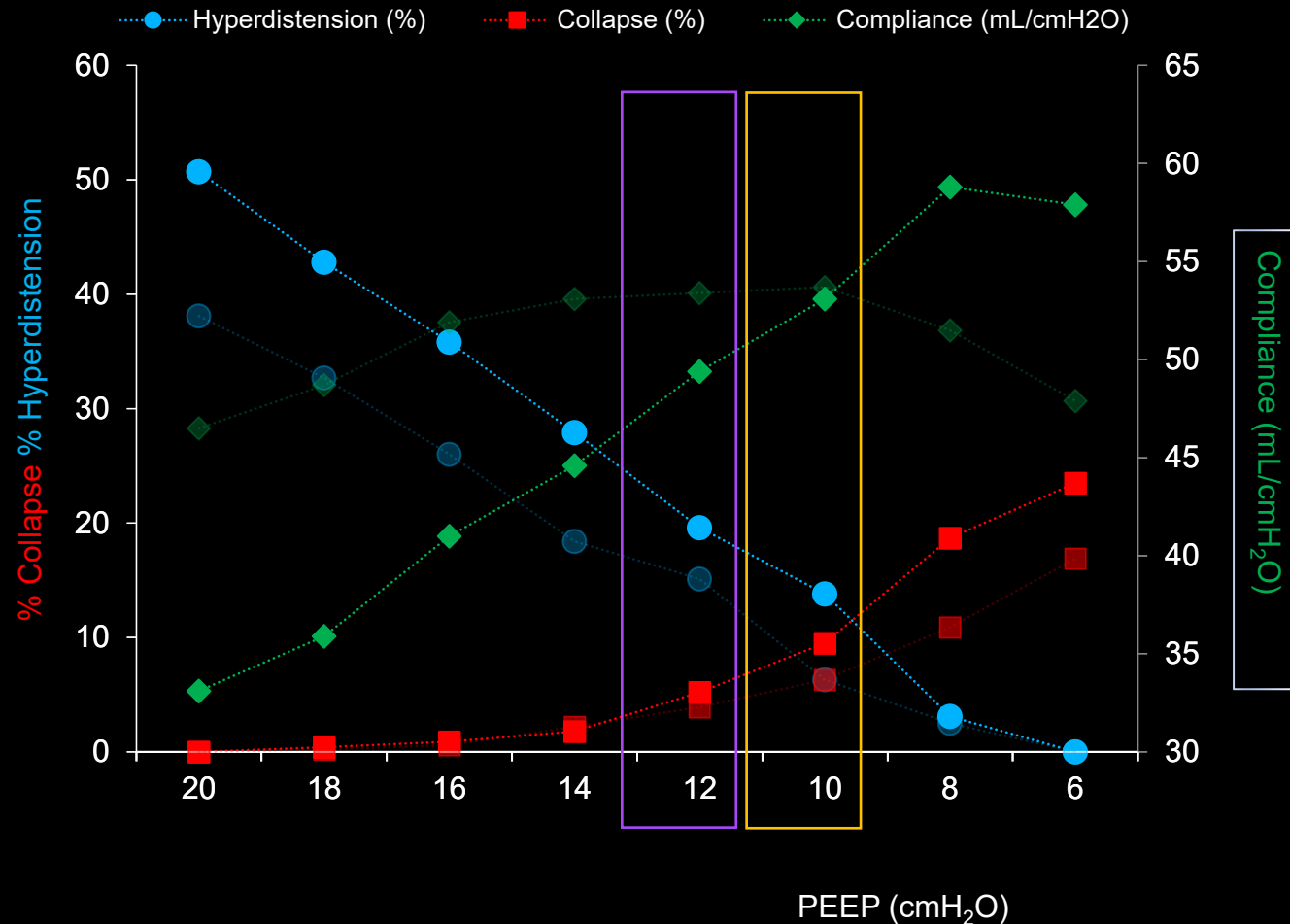
C-ARDS patient





# Careful when selecting your PEEP!

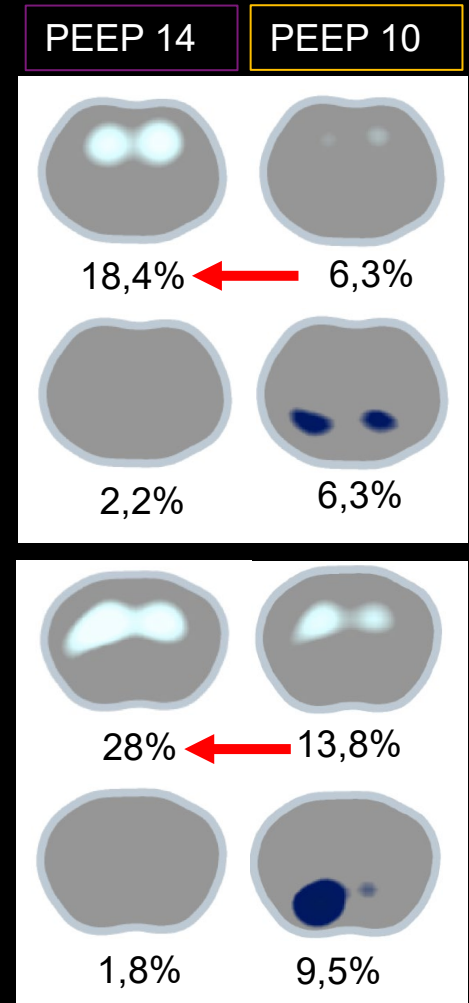
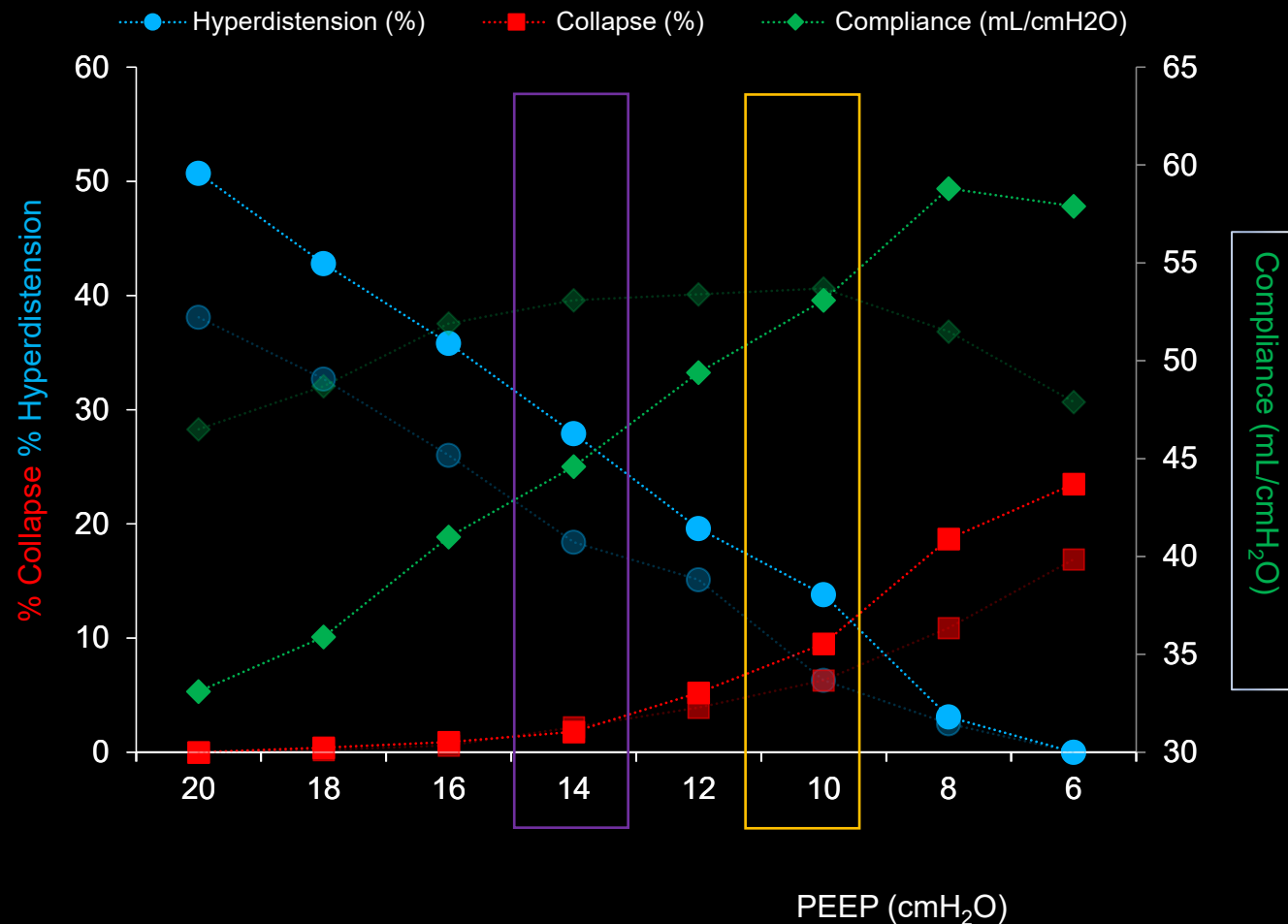
## C-ARDS patient





# Careful when selecting your PEEP!

## C-ARDS patient



## 90 Fully recored Decremental PEEP titrations (60 in supine 30 in prone)

$PEEP_{Clin} \ 11.3 \pm 3.6$

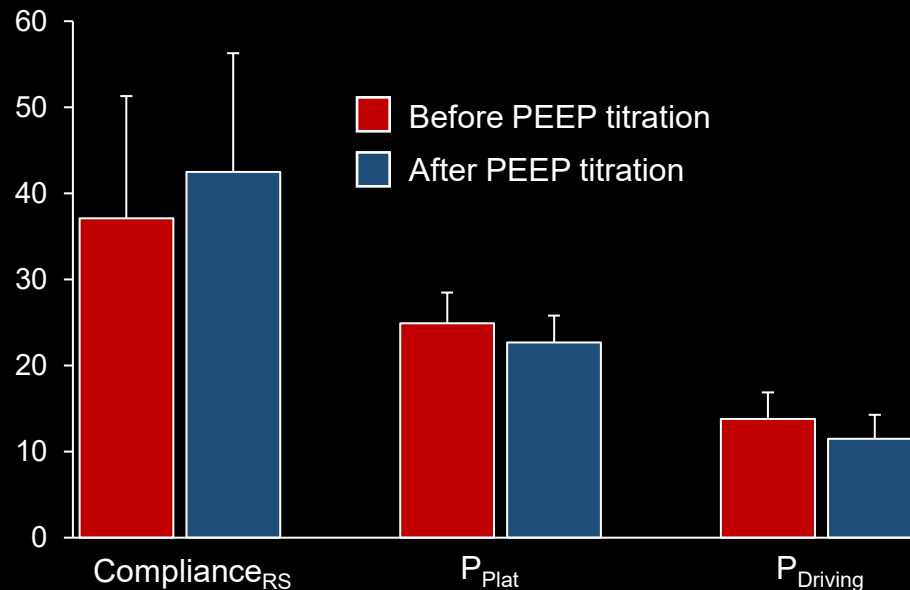
$PEEP_{Cdyn} \ 10.5 \pm 3.1$

$PEEP_{Cdyn} < PEEP_{CLIN} \ 62\% \ (2.6 \pm 2 \text{ cmH}_2\text{O})$

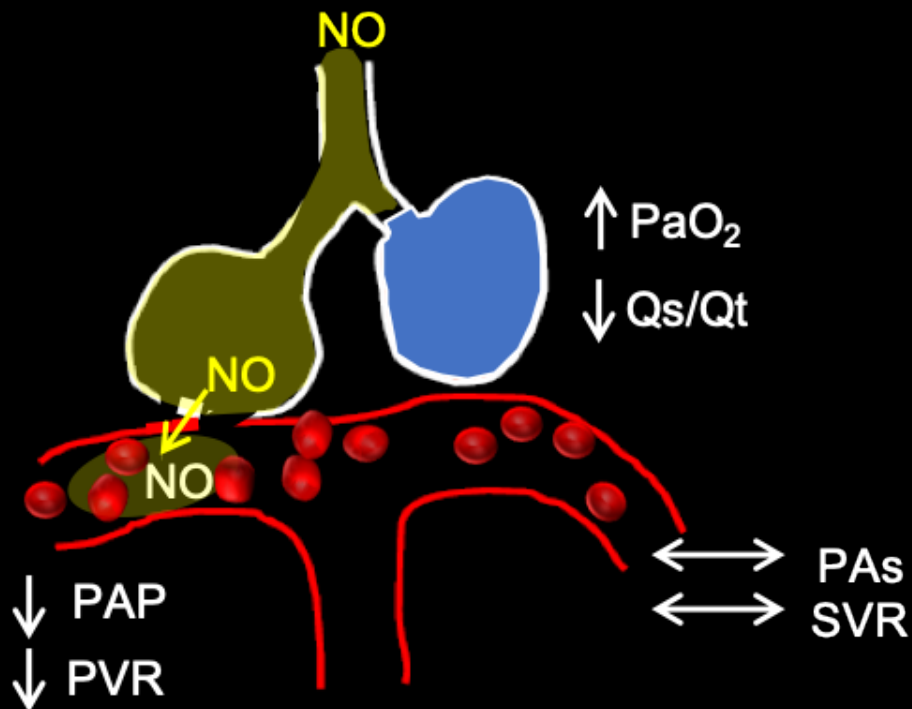
$PEEP_{Cdyn} > PEEP_{CLIN} \ 28\% \ (3.1 \pm 1.7 \text{ cmH}_2\text{O})$

$PEEP_{Cdyn} = PEEP_{CLIN} \ 10\%$

### Overall improvement in lung mechanics

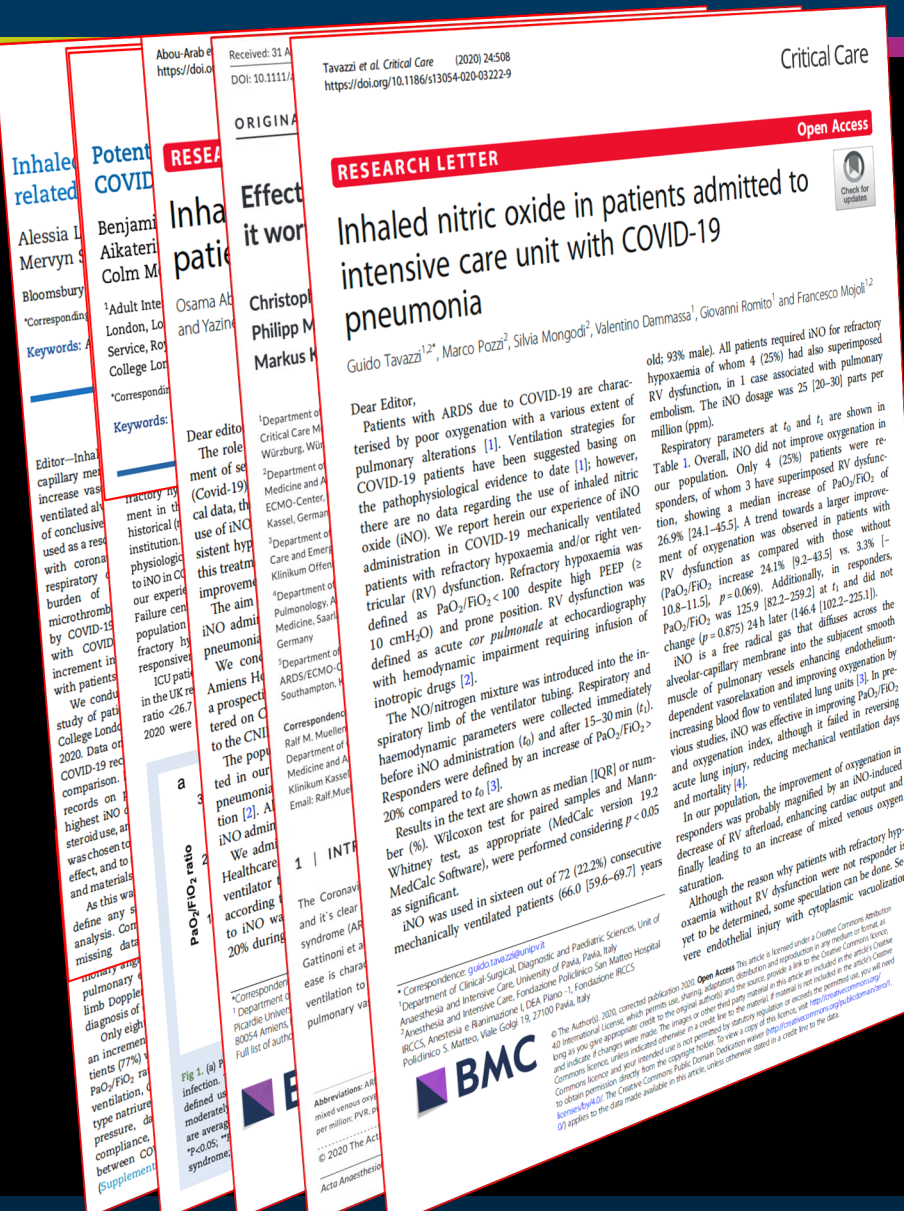


# Physiological effects of iNO



- Selective Pulmonary Vasodilator
- Improved VQ  
Blood Flow redistribution to better aerated regions  
Dosis ≤10 ppm
- Improved Pulmonary Hemodynamics  
↓PVR and PAP  
Dosis ≥15-20 ppm

# Nitric Oxide in C-ARDS



iNO improves oxygenation in a majority of C-ARDS patients

Causes for lack of response are not known

There may be benefits beyond oxygenation (not thoroughly studied)

## RESEARCH LETTER

### Inhaled nitric oxide in patients admitted to intensive care unit with COVID-19 pneumonia

Guido Tavazzi<sup>1,2\*</sup>, Marco Pozzi<sup>2</sup>, Silvia Mongodi<sup>2</sup>, Valentino Dammasa<sup>1</sup>, Giovanni Romito<sup>1</sup> and Francesco Mojoli<sup>1,2</sup>

Dear Editor,  
Patients with ARDS due to COVID-19 are characterised by poor oxygenation with a various extent of pulmonary alterations [1]. Ventilation strategies for COVID-19 patients have been suggested basing on the pathophysiological evidence to use of inhaled nitric oxide (iNO). We report herein our experience of iNO administration in COVID-19 mechanically ventilated patients with refractory hypoxaemia and/or right ventricular (RV) dysfunction. Refractory hypoxaemia was defined as PaO<sub>2</sub>/FIO<sub>2</sub> < 100 despite high PEEP (≥ 10 cmH<sub>2</sub>O) and prone position. RV dysfunction was defined as acute cor pulmonale at echocardiography with hemodynamic impairment requiring infusion of inotropic drugs [2].  
The NO/nitrogen mixture was introduced into the inspiratory limb of the ventilator tubing. Respiratory and haemodynamic parameters were collected immediately before iNO administration (t<sub>0</sub>) and after 15–30 min (t<sub>1</sub>). Responders were defined by an increase of PaO<sub>2</sub>/FIO<sub>2</sub> > 20% compared to t<sub>0</sub> [3].  
Results in the text are shown as median [IQR] or number (%). Wilcoxon test for paired samples and Mann-Whitney test, as appropriate (MedCalc version 19.2 MedCalc Software), were performed considering p < 0.05 as significant.  
iNO was used in sixteen out of 72 (22.2%) consecutive mechanically ventilated patients (66.0 [59.6–69.7] years

old; 93% male). All patients required iNO for refractory hypoxaemia of whom 4 (25%) had also superimposed RV dysfunction, in 1 case associated with pulmonary embolism. The iNO dosage was 25 [20–30] parts per million (ppm).  
Respiratory parameters at t<sub>0</sub> and t<sub>1</sub> are shown in Table 1. Overall, iNO did not improve oxygenation in our population. Only 4 (25%) patients were responders, of whom 3 have superimposed RV dysfunction, showing a median increase of PaO<sub>2</sub>/FIO<sub>2</sub> of 26.9% [24.1–45.5]. A trend towards a larger improvement of oxygenation was observed in patients without RV dysfunction as compared with those with RV dysfunction increase 24.1% [9.2–43.5] vs 3.3% [0.8–11.5], p = 0.069. Additionally, in responders, PaO<sub>2</sub>/FIO<sub>2</sub> was 125.9 [82.2–259.2] at t<sub>1</sub> and did not change (p = 0.875) 24 h later (146.4 [102.2–225.1]). iNO is a free radical gas that diffuses across the alveolar-capillary membrane into the subjacent smooth muscle of pulmonary vessels enhancing oxygenation by dependent vasorelaxation and improving oxygenation by increasing blood flow to ventilated lung units [3]. In previous studies, iNO was effective in improving PaO<sub>2</sub>/FIO<sub>2</sub> and oxygenation index, although it failed in reversing acute lung injury, reducing mechanical ventilation days and mortality [4].  
In our population, the improvement of oxygenation was probably magnified by an iNO-induced decrease of RV afterload, enhancing cardiac output and finally leading to an increase of mixed venous oxygen saturation.  
Although the reason why patients with refractory hypoxaemia without RV dysfunction were not responder yet to be determined, some speculation can be done. Severe endothelial injury with cytoplasmic vacuolization

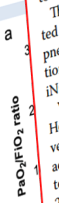


Fig. 1. (a) PaO<sub>2</sub>/FIO<sub>2</sub> ratio over time.





Check for updates

# Inhaled nitric oxide in patients admitted to intensive care unit with COVID-19 pneumonia

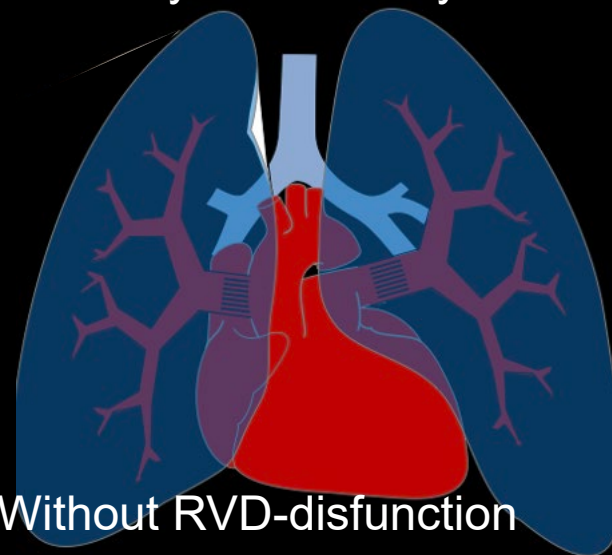
Tavazzi et al. *Critical Care* (2020) 24:508  
<https://doi.org/10.1186/s13054-020-03222-9>

Guido Tavazzi<sup>1,2\*</sup>, Marco Pozzi<sup>2</sup>, Silvia Mongodi<sup>2</sup>, Valentino Dammasa<sup>1</sup>, Giovanni Romito<sup>1</sup> and Francesco Mojoli<sup>1,2</sup>

## Conclusion

Overall, iNO did not improve oxygenation in COVID-19 patients with refractory hypoxaemia, when administered as a rescue treatment after prone position. A subgroup of patients with RV dysfunction was better iNO responders probably due to the haemodynamic improvement associated with RV unloading.

## Pulmonary Vascular Dysfunction



iNO 20 - 30 ppm

With RV disfunction

Without RVD-disfunction

PaO<sub>2</sub>/FIO<sub>2</sub> improvement

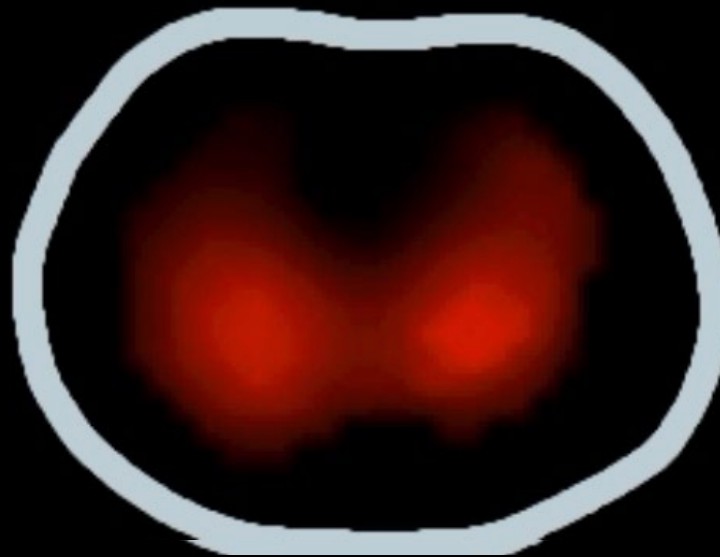
24.1% [9.2–43.5]

3.3% [-10.8 –11.5]

p = 0.069

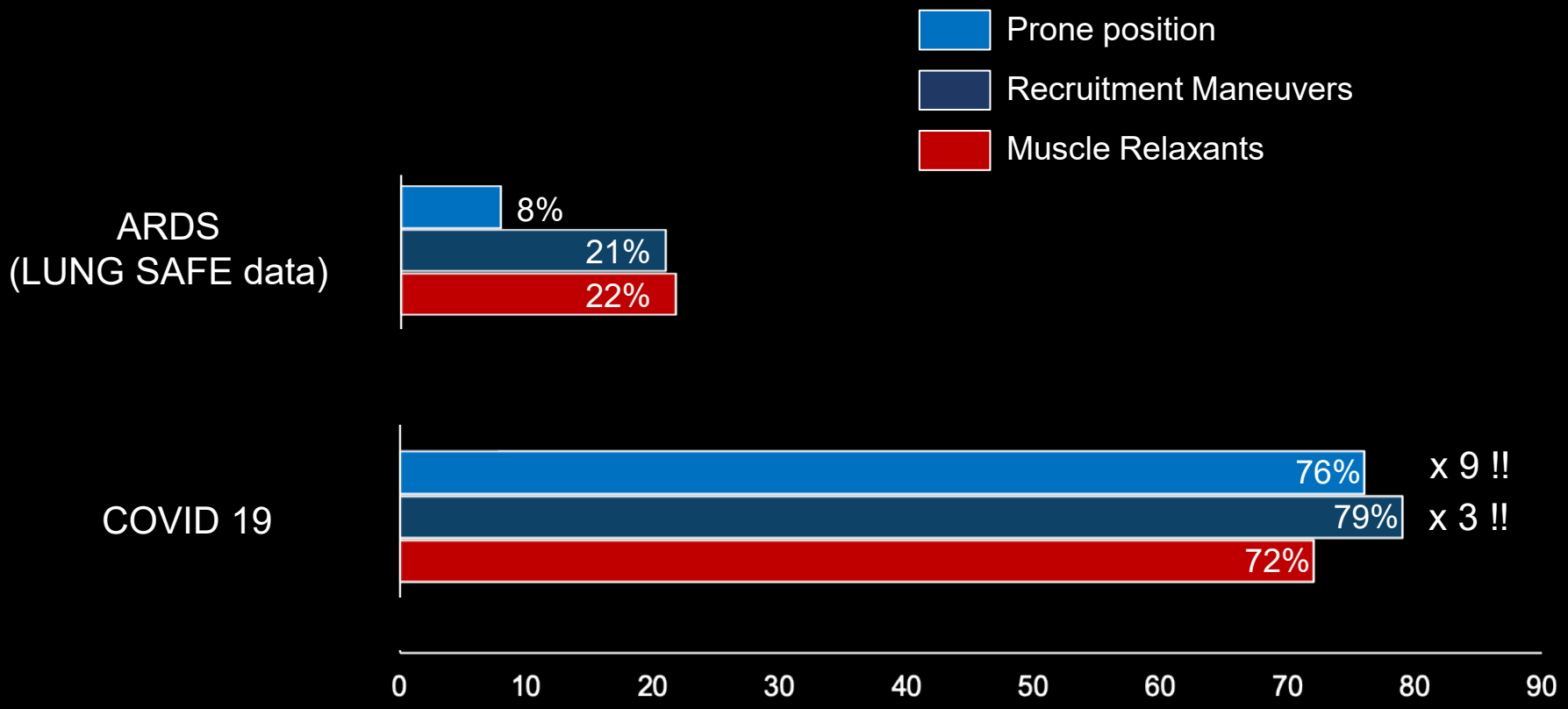


- Variable response N= 8
- Shift of perfusion measured by EIT
- Dorsal shift --- decrease in oxygenation and efficiency
- Ventral shift – Increase in oxygenation PaO<sub>2</sub>/FiO<sub>2</sub> by 30± 28%
- Decrease in PaCO<sub>2</sub> by 2.3%
- Best response evident between 5 and 15 ppm of iNO



iNO 20 ppm

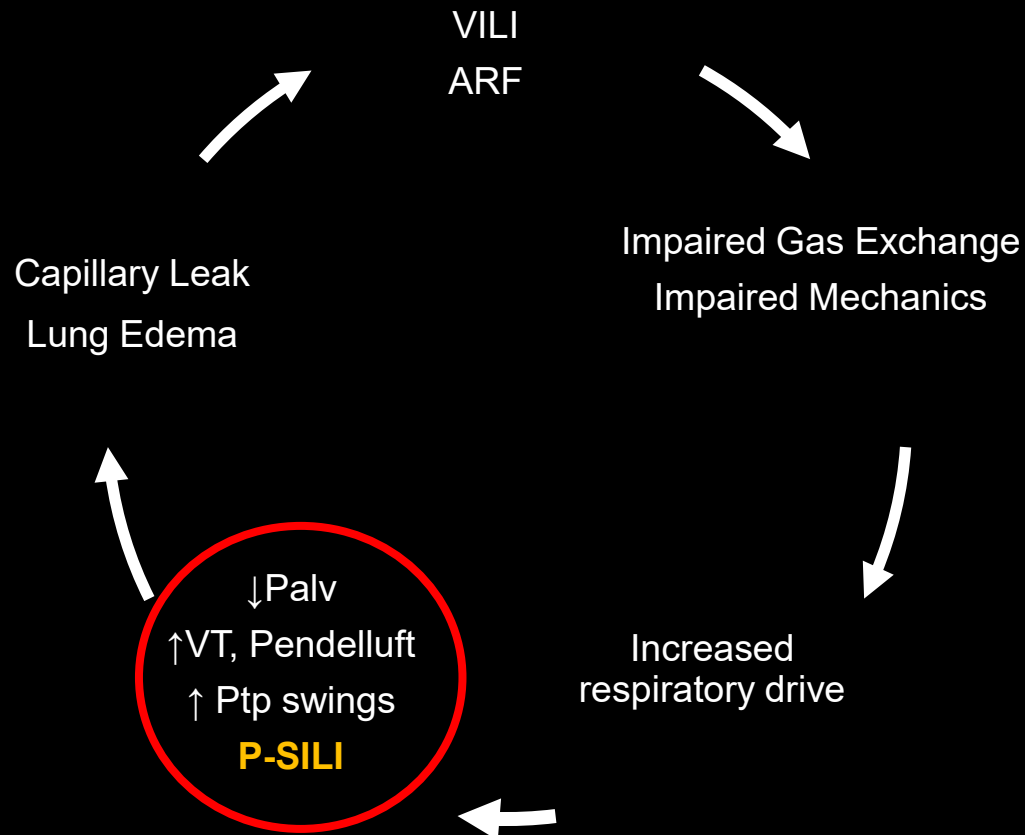
# Adjunctive measures during C-ARDS



Ferrando C, Suarez-Sipmann F *et al. Intens Care Med* **46**, 2200–2211 (2020).

# The transition to spontaneous breathing

## P-SILI Patient Self Inflicted Lung Injury

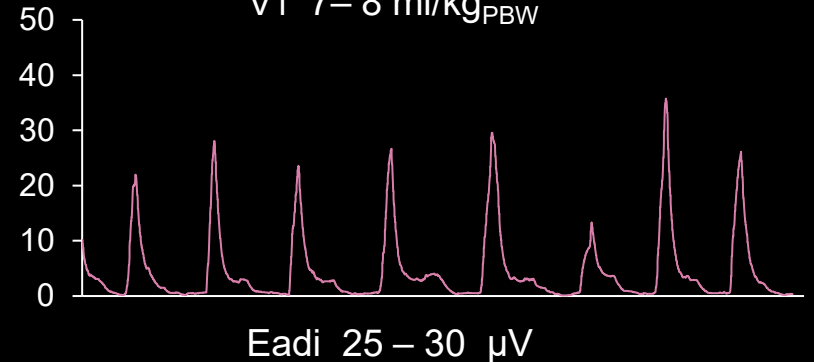
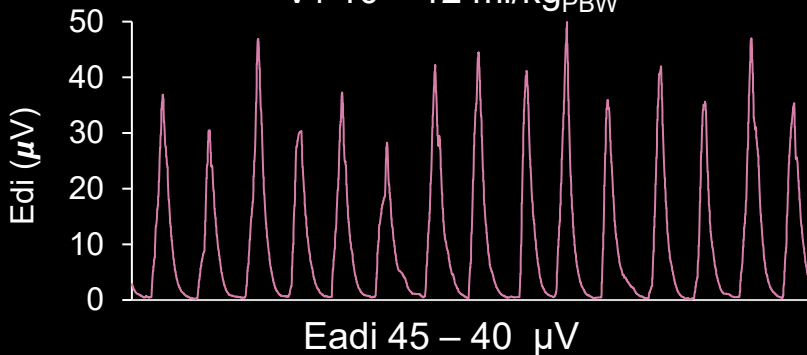
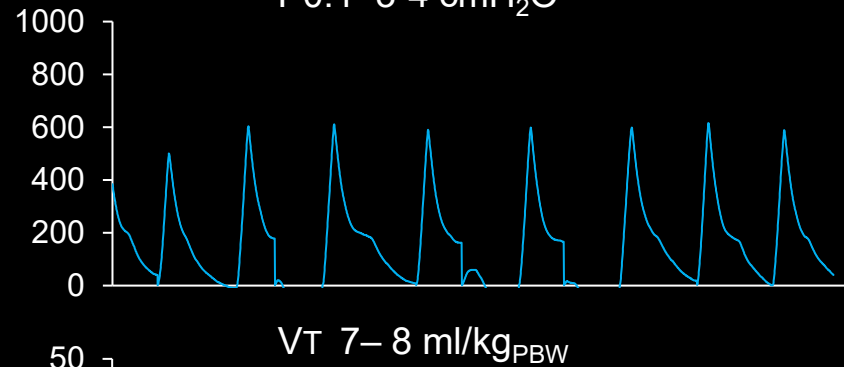
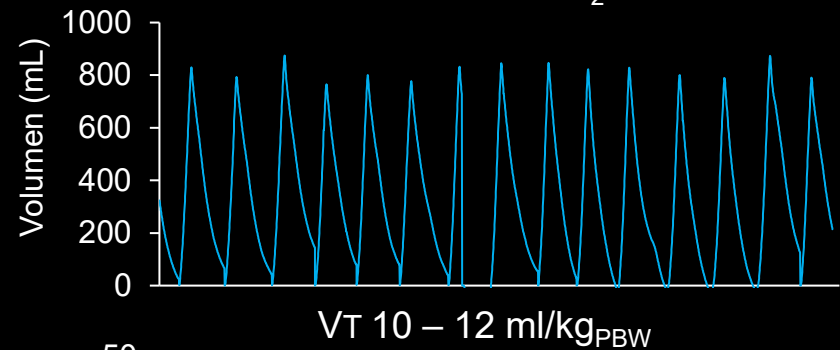
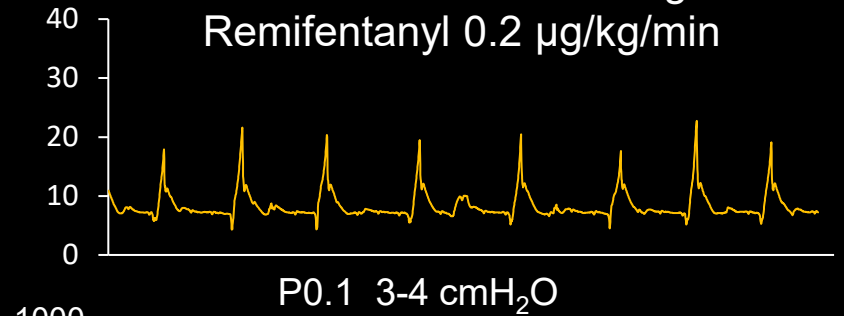
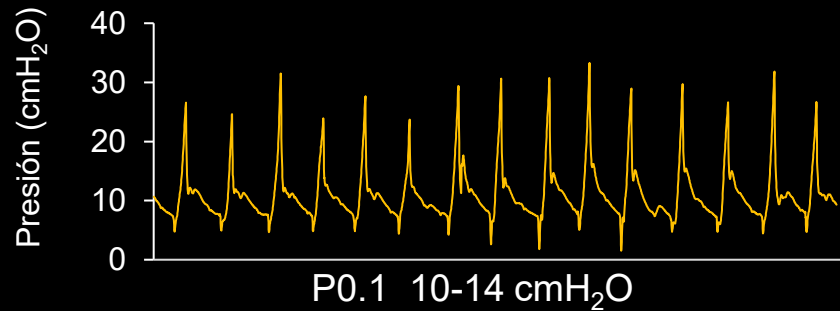


Modified from Brochard et al AJRRCM 2017;195, 438–442

# High respiratory drive

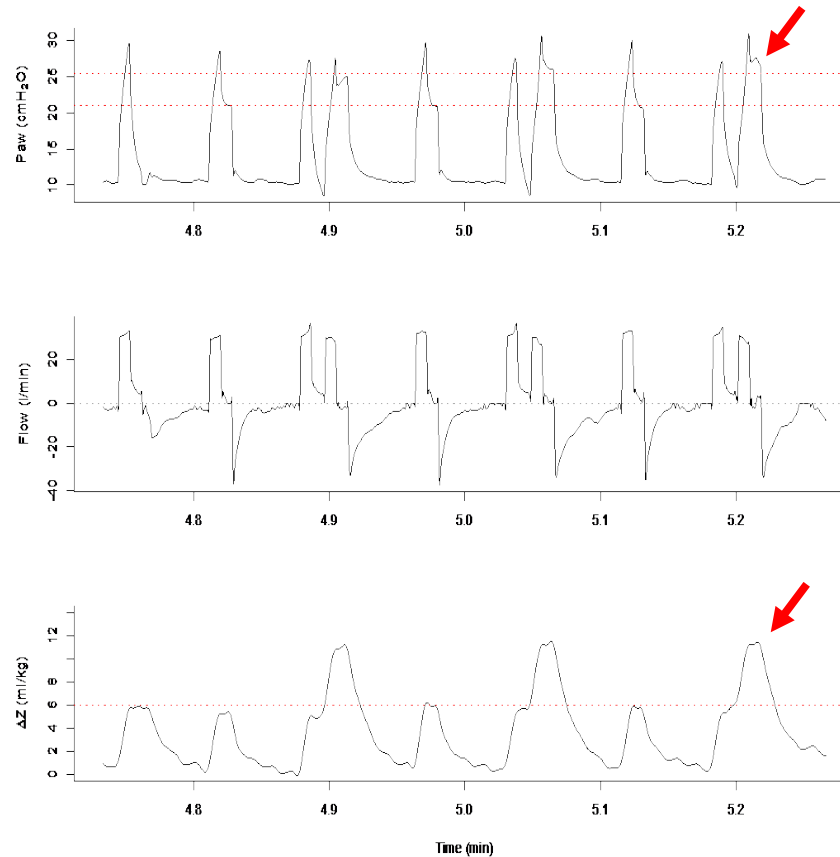
NAVA level 0.4

After 16h Rocuronium 5 – 6 mg/h  
Remifentanyl 0.2  $\mu\text{g}/\text{kg}/\text{min}$



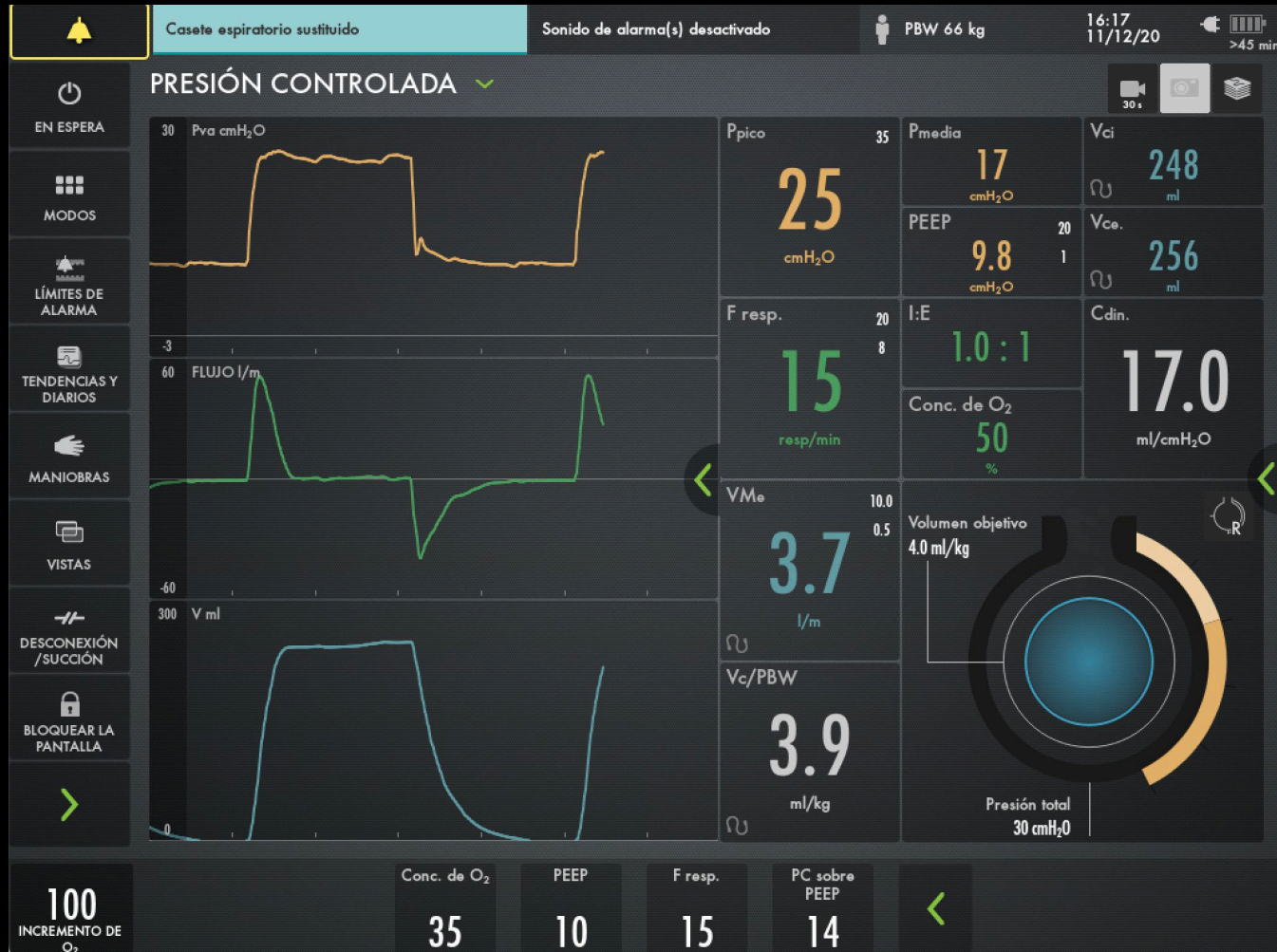
# Double Triggering and breath stacking

Patient ventilated with set  $V_T = 6 \text{ mL/kg}$  –  
 Sacked breaths :  $V_T = 12 \text{ mL/kg}$  and  $P_{\text{PLAT}} = 28 \text{ cmH}_2\text{O}$

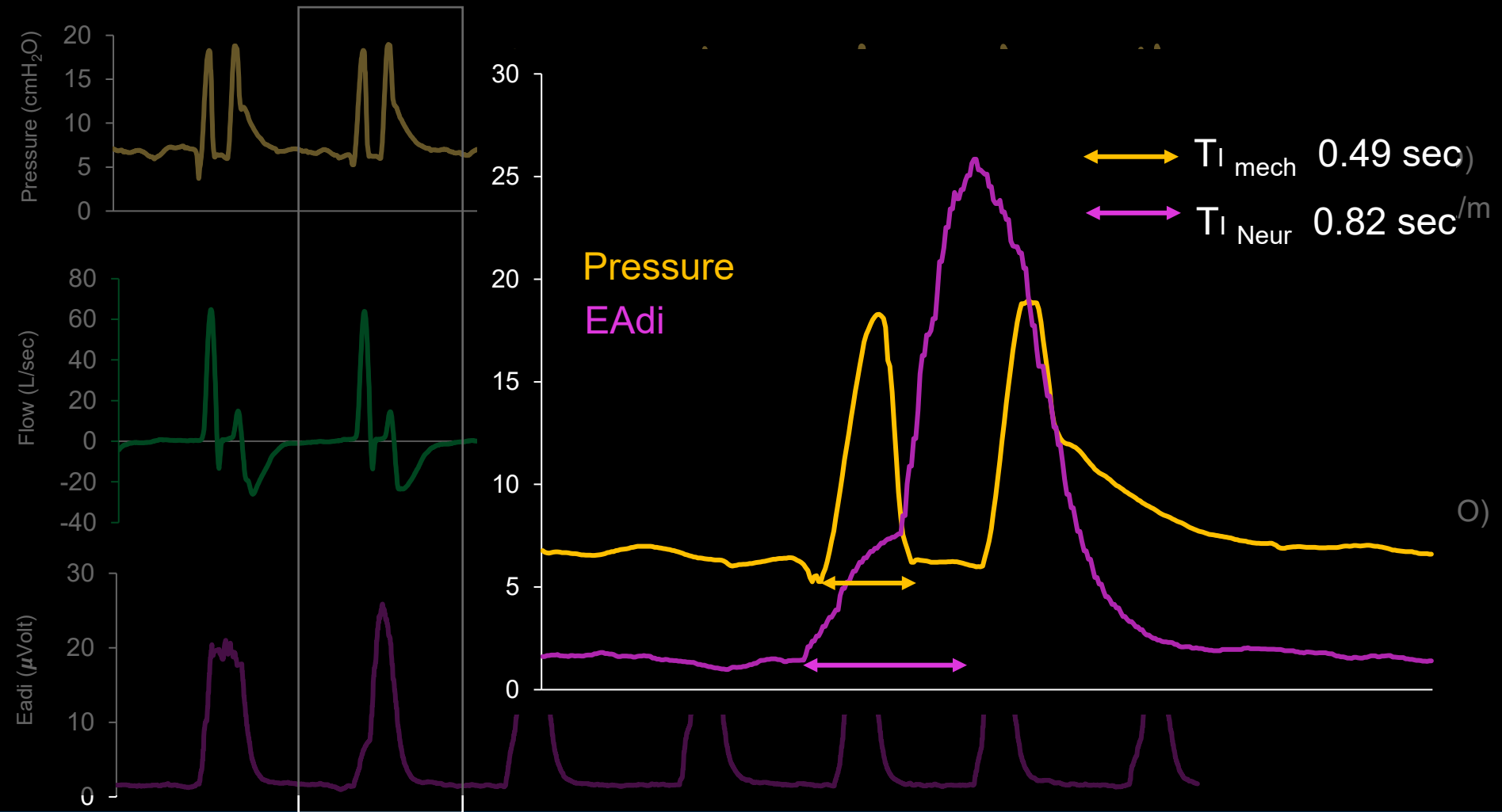




# Do you recognize this...?



# C-ARDS after 3 weeks of evolution





# And so... the Paella is ready





# Děkuji mnohokrát!! / Muchas Gracias!!



Hospital Universitario  
de La Princesa

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Dept. Intensive Care Medicine  
Hospital Universitario La Princesa  
Universidad Autonoma de Madrid  
Spain

Hedenstierna Laboratory



Dept. Surgical Sciences  
Hedenstierna Laboratory  
Uppsala University  
Sweden  
[Fsuarez.sipmann@surgsci.uu.se](mailto:Fsuarez.sipmann@surgsci.uu.se)