ARDS: which rescue firstly in ARDS, prone positioning vs ECMO?

- Prone Positioning

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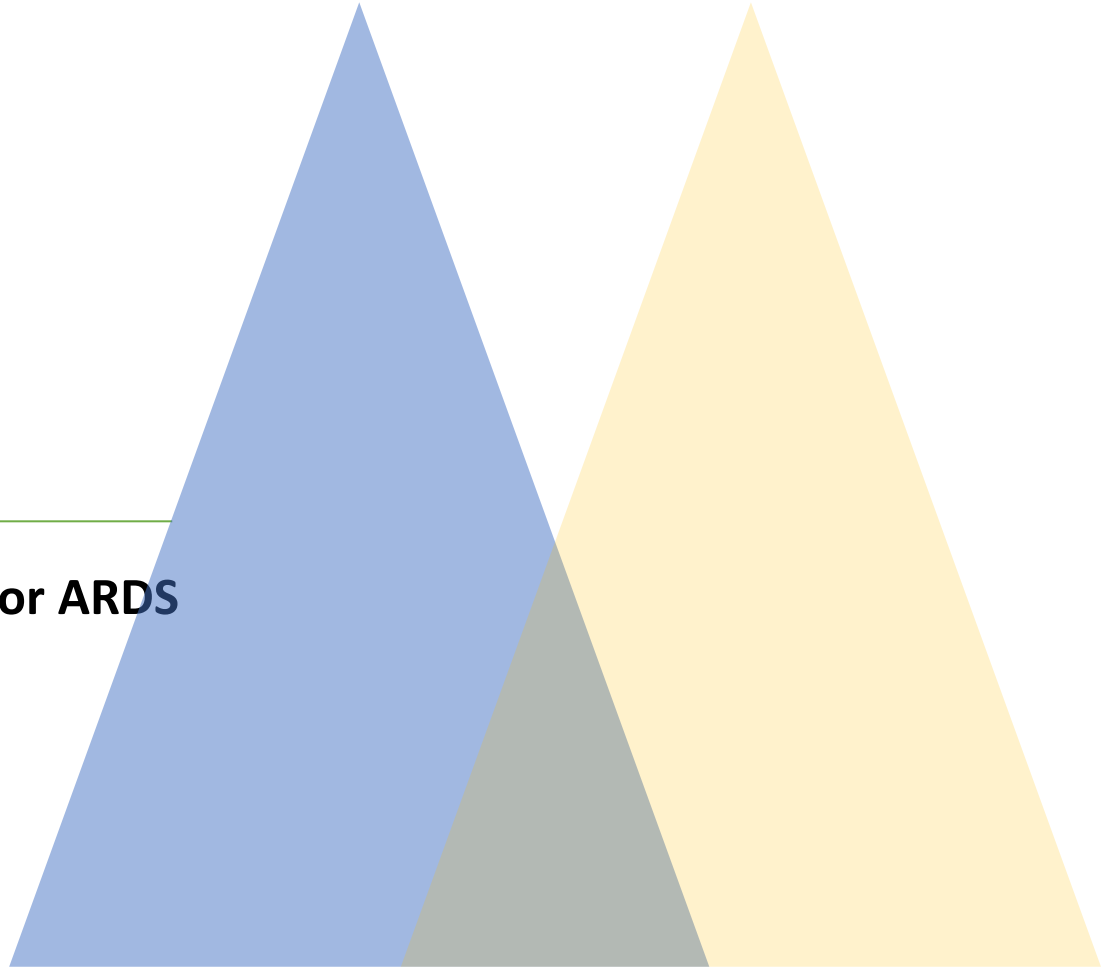
In acute respiratory distress syndrome…

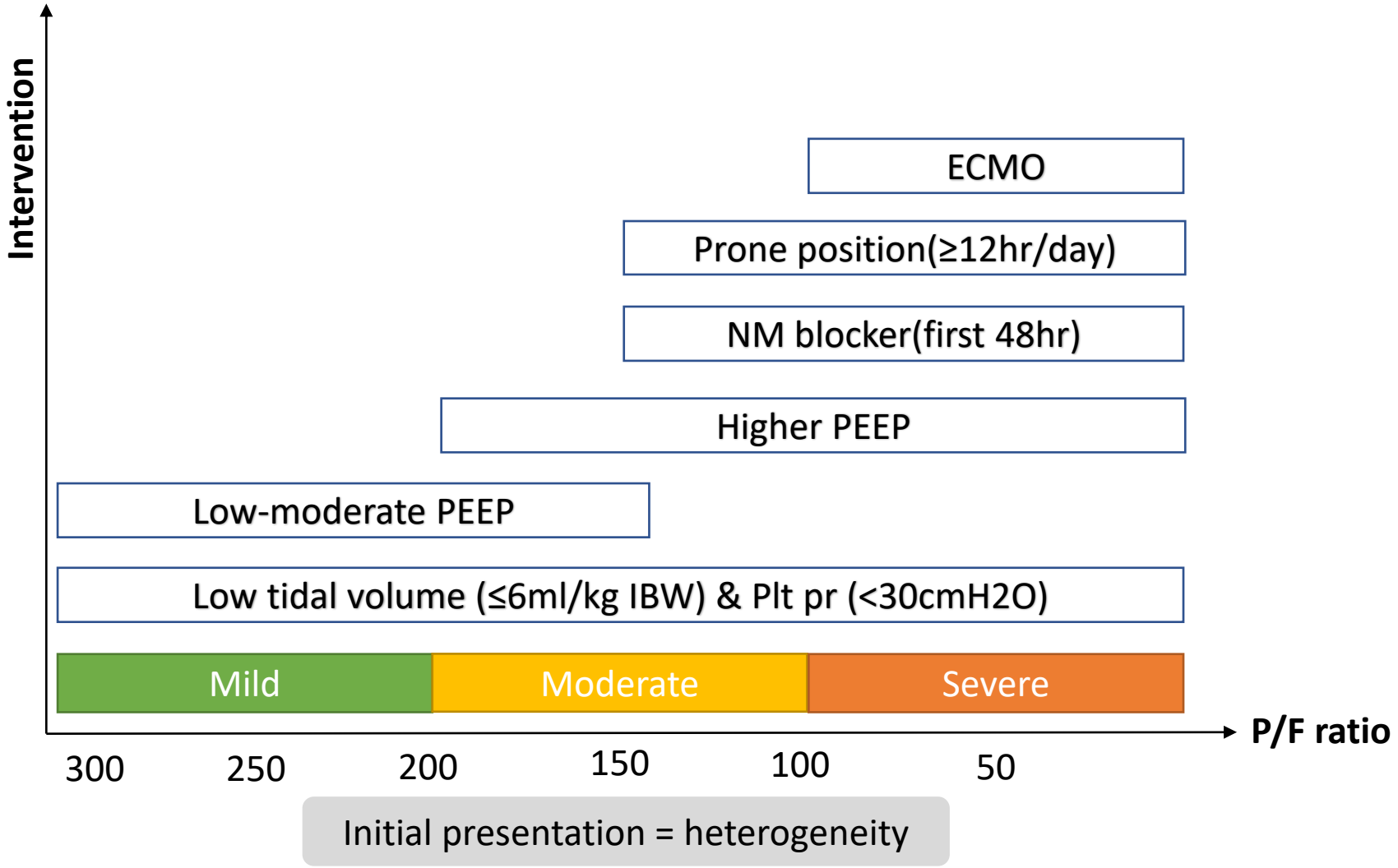
- Current evidence & recommendation for prone position for ARDS
- Scientific evidences of prone position
- Suggestion?

001

Current evidence & recommendation for prone position for ARDS



Treatment Paradigm according to severity by Berlin (2012) definition



BMJ Open Resp Res 2019;6:(2000420

ATS/ESICM/ SCCM guideline MV in ARDS (2017)

Intervention	ARDS Severity	Quality of Evidence (GRADE)	Strength of Recommendation	Comments
Mechanical ventilation with low tidal volumes and inspiratory pressures[a]	All ARDS • LTV 4-8 mL/kg PBW • Pplat < 30cmH_2O	Moderate[61]	Strong	Initial tidal volume should be set at 6 mL/kg predicted body weight and can be increased up to 8 mL/kg predicted body weight if the patient is double triggering or if inspiratory pressure decreases below PEEP
Prone positioning <12 h/d	Severe	Moderate-high[62]	Strong	Lack of consensus for recommendation in moderate ARDS
High-frequency oscillatory ventilation	Moderate or severe	Moderate-high[63]	Strong	Strong recommendation against the routine use of high-frequency oscillatory ventilation in patients with moderate or severe ARDS, although may be considered in patients with refractory hypoxemia (ie, Pao_2/Fio_2 <64 mm Hg)
Higher PEEP	Moderate or severe	Moderate[64]	Conditional	Can implement a higher PEEP strategy that was used in the large randomized clinical trials included in the evidence synthesis
Recruitment maneuvers	Moderate or severe	Low-moderate[65]	Conditional	Caution in patients with preexisting hypovolemia or shock
Venovenous extracorporeal membrane oxygenation	Severe	Not applicable[66]	Not applicable	No recommendation for or against use due to insufficient evidence

JAMA. 2018;319(7):698-710. doi:10.1001/jama.2017.21907
Am J Respir Crit Care Med Vol 195, Iss 9, pp 1253–1263, May 1, 2017

Studies for prone position

1970s

2001 | 2004 | 2006 | 2009 | 2013

PROSEVA trial

Gattinoni et al.	Guerin et al.	Mancebo et al.	Taccone et al.	Guerin et al.
(n=304)	(n=802)	(n=142)	(n=344)	(n=466)
Average P/F = 127, PEEP = 10	Average P/F = 152, PEEP = 8	Average P/F = 105, PEEP = 7	Average P/F = 113, PEEP = 10	Average P/F = 100, PEEP = 10
Duration of PP = 7h x 5d	Duration of PP = 9h x 4d	Duration of PP = 9h x 4d	Duration of PP = 18h x 8d	Duration of PP = 17h x 4d
Protective ventilation (no)	Protective ventilation (no)	Protective ventilation (<10ml/kg)	Protective ventilation (<10ml/kg)	Protective ventilation (6ml/kg)
f/u = 6mo	f/u = 90d	f/u hospital discharge	f/u 6mo	f/u 90d
Mortality : SP (58.3%) vs PP (62.2%)	Mortality : SP (42.2%) vs PP (43.3%)	Mortality : SP (60%) vs PP (50%)	Mortality : SP (52.9%) vs PP (47.6%)	Mortality : SP (41%) vs PP (23.6%)
P=0.5	P=0.74	P=0.22	P=0.33	P=0.001

2016 | 2019 | 2022

Meta-analysis
For
Prone position

2016 급성호흡곤란증후군 (ARDS) 임상진료지침 (12개 임상 질문)

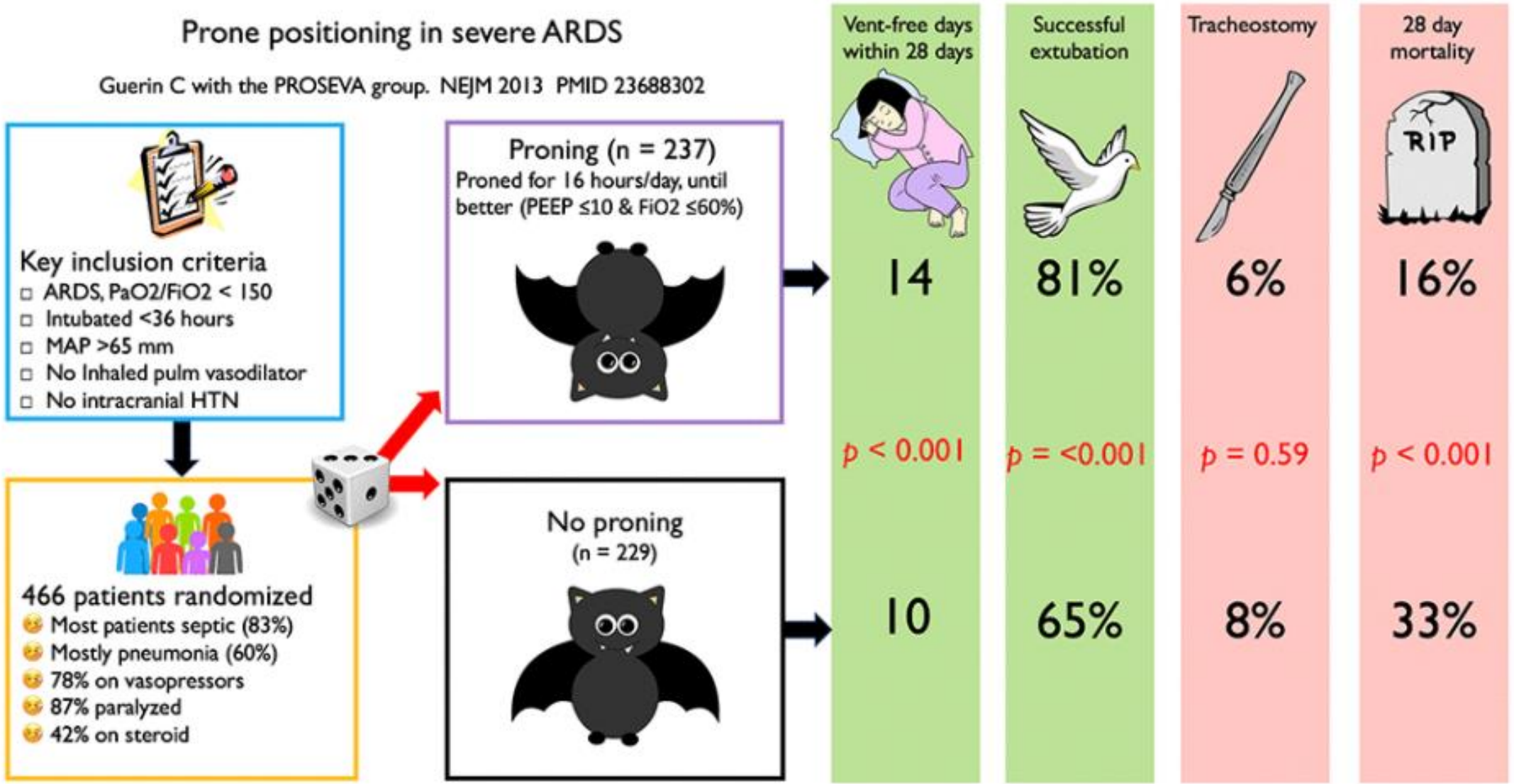
3. 기계 환기를 시행하는 성인 급성호흡곤란증후군 환자에서 복와위 (prone position)가 앙아위 (supine position)와 비교해서 사망률을 낮출 수 있는가?

- **중등도 이상** 급성호흡곤란증후군에서 금기가 아니면 복와위 적용을 권고한다 (1B)
- 기계환기를 시행해도 산소화 호전이 없는 급성호흡곤란증후군 환자에서 **조기에 적용**할 것을 권장한다
- 복복와위는 **최소 10시간 이상** 시행할 것을 권장한다
- **폐 보호 환기를 적용**할 것을 권장한다

COVID-19

2022 급성호흡곤란증후군 (ARDS) 임상진료지침 (개정 중)

Prone position in severe ARDS (PROSEVA trial)



N Engl J Med 368;23 nejm.org june 6, 2013

Prone positioning compared with standard care for ARDS

Outcomes	Illustrative comparative risk (95% CI)		Relative Effect (95% CI)	No. of Participants (studies)	Quality of evidence	Comments
	Control risk	Intervention risk				
	Standard Care	Prone positioning				
Mortality (pooled)	467 per 1000	421 per 1000 (383 to 458)	RR 0.90 (0.82 to 0.98)	2141 (eight studies)	+--- Very low d/t serious risk of bias, very serious inconsistency and serious indirectness	Failure to blind outcome allocation concealment outcome data Includes sub-groups receiving additional interventions known to demonstrate a potential mortality benefit
Subgroup analysis **PP with LPV**	447 per 1000	326 per 1000 (227 to 384)	**RR 0.73 (0.62 to 0.86)**	910 (five studies)	+++- Moderate d/t serious risk of bias	Failure to blind outcome, failure of allocation concealment, and incomplete outcome data
Subgroup analysis PP without LPV	483 per 1000	488 per 1000 (435 to 546)	RR 1.01 (0.9 to 1.13)	1231 (three studies)	+++- Moderate d/t serious risk of bias	See above
Subgroup analysis **PP≥12hrs**	479 per 1000	359 per 1000 (311 to 416)	**RR 0.75 (0.65 to 0.87)**	1006 (five studies)	+++- Moderate d/t serious risk of bias	See above
Subgroup analysis PP<12hrs	457 per 1000	471 per 1000 (416 to 535)	RR 1.03 (0.91 to 1.17)	1135 (three studies)	+++- Moderate d/t serious risk of bias	See above

BMJ Open Resp Res 2019;6:2000420

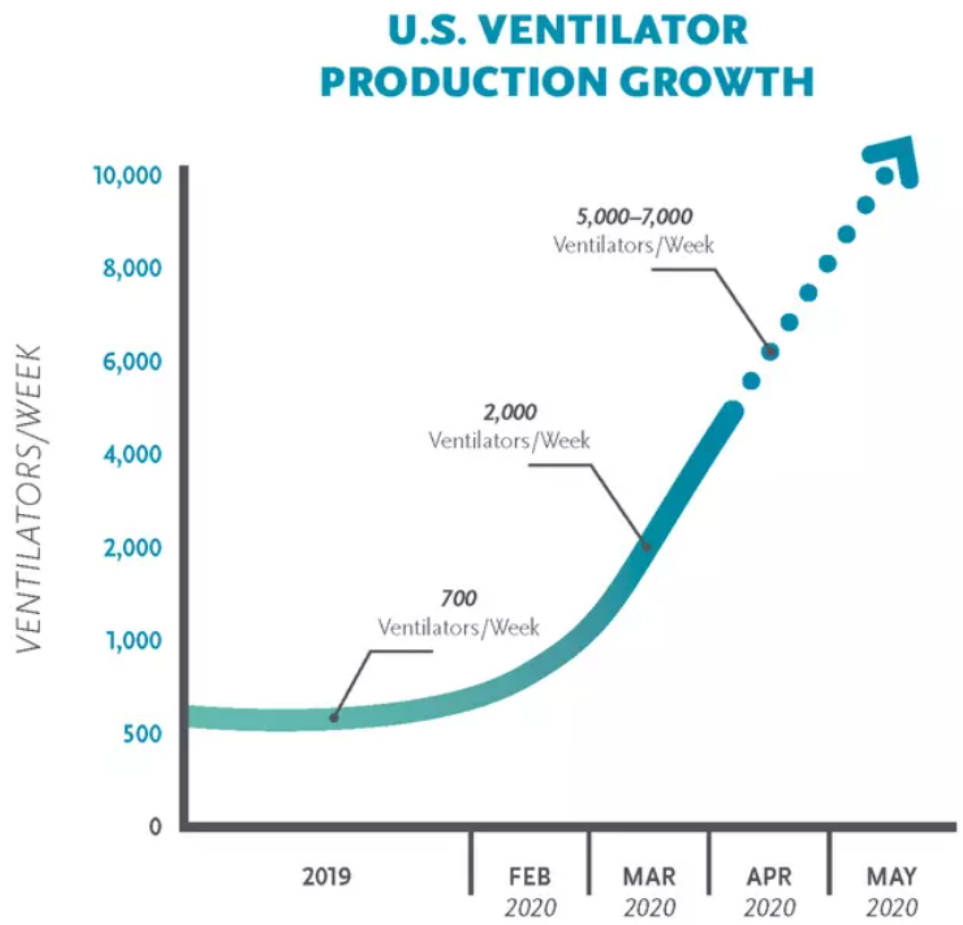
Prone positioning compared with standard care for ARDS

Outcomes	Illustrative comparative risk (95% CI)		Relative Effect (95% CI)	No. of Participants (studies)	Quality of evidence	Comments
	Control risk	Intervention risk				
	Standard Care	Prone positioning				
Adverse events (pooled)	188 per 1000	207 per 1000 (190 to 226)	RR 1.10 (1.01 to 1.2)	7377 (seven studies)	+--- Very low d/t serious risk of bias, very serious inconsistency	Failure to blind outcome, failure of allocation concealment, and incomplete outcome data
Adverse events **Cardiac event**	278 per 1000	281 per 1000 (242 to 325)	RR 1.01 (0.87 to 1.17)	1599 (three studies)	+--- Very low d/t serious risk of bias	Failure to blind outcome allocation concealment outcome data
Adverse events **Endotracheal tube displacement**	101 per 1000	134 per 1000 (103 to 176)	RR 1.33 (1.02 to 1.74)	1597 (five studies)	++-- Low d/t serious risk of bias and serious imprecision	See above
Adverse events **VAP**	248 per 1000	218 per 1000 (176 to 270)	RR 0.88 (0.71 to 1.09)	1007 (four studies)	++-- Low d/t serious risk of bias and serious imprecision	See above
Adverse events **Pressure sore**	372 per 1000	462 per 1000 (402 to 529)	RR 1.23 (1.07 to 1.41)	1095 (two studies)	++-- Low d/t serious risk of bias and serious imprecision	See above

BMJ Open Resp Res 2019;6:2000420

COVID-19 pandemic

COVID-19 RESPONSE



COVID-19 awake proning for self care

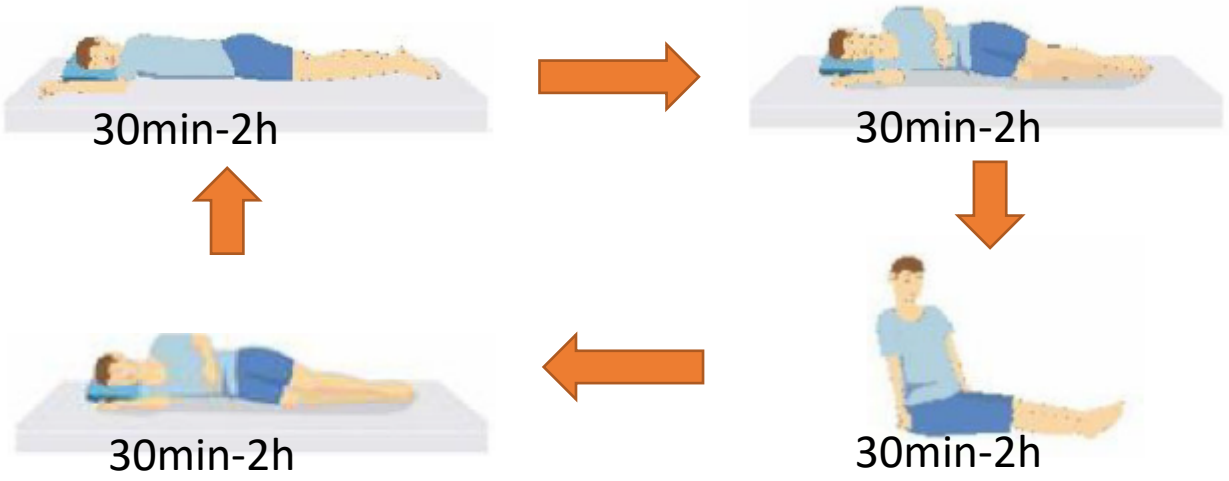
- Who? → FiO2 ≥ 28% to maintain SpO2 92-96% (88-92% in hypercapnic resp failure) despite basic respiratory support
- Avoid proning for an hour after meals
- Avoid proning

- Pregnancy (case report?) / DVT (treated <48hr) / major cardiac conditions / unstable spine, fevor or pelvic fracture

Rodin's thinker

Dolphin Position

Reverse Trendelenburg



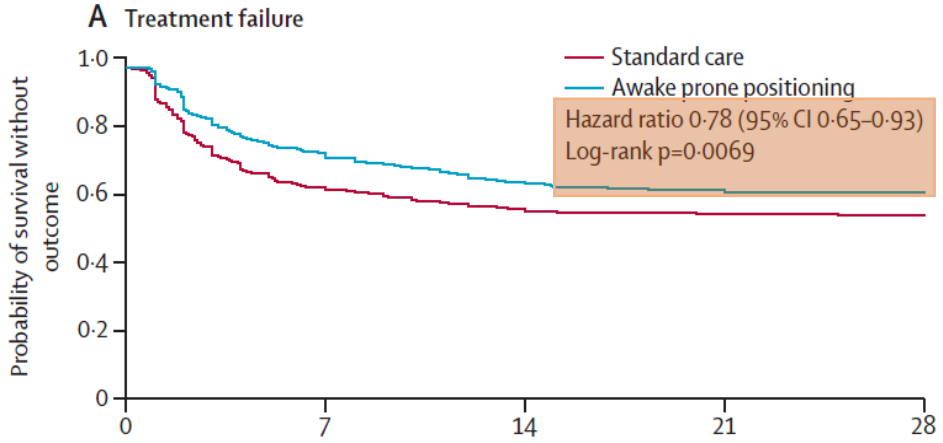
The Application of Awake-Prone Positioning Among Non-intubated Patients with COVID-19-Related ARDS: A Narrative Review, Front. Med. 9:817689

Awake prone position for non-intubated patients with COVID-19

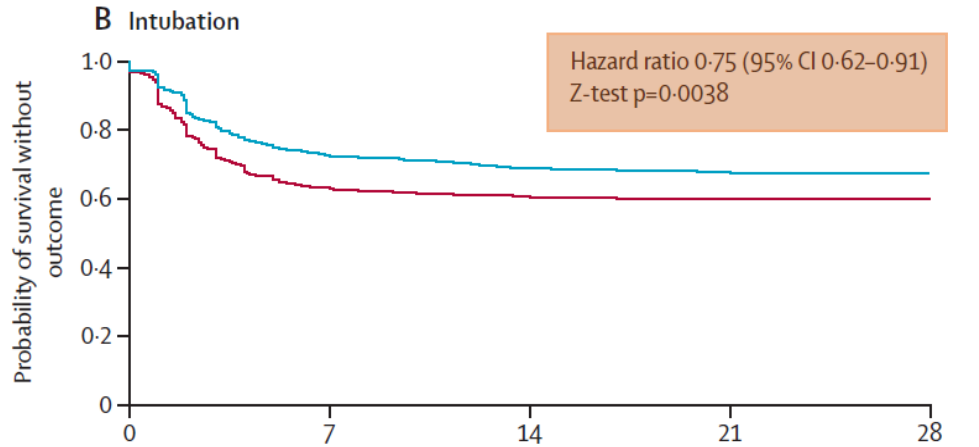
Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial

Stephan Ehrmann, Jie Li*, Miguel Ibarra-Estrada*, Yonatan Perez*, Ivan Pavlov*, Bairbre McNicholas*, Oriol Roca*, Sara Mirza, David Vines, Roxana Garcia-Salcido, Guadalupe Aguirre-Avalos, Matthew W Trump, Mai-Anh Nay, Jean Dellamonica, Saad Nseir, Idrees Mogri, David Cosgrave, Dev Jayaraman, Joan R Masclans, John G Laffey, Elsa Tavernier, for the Awake Prone Positioning Meta-Trial Group†*

intubation or death



Number at risk (number censored)					
Standard care	557 (0)	345 (0)	310 (0)	299 (0)	298 (298)
Awake prone positioning	564 (0)	405 (0)	358 (0)	344 (0)	341 (341)



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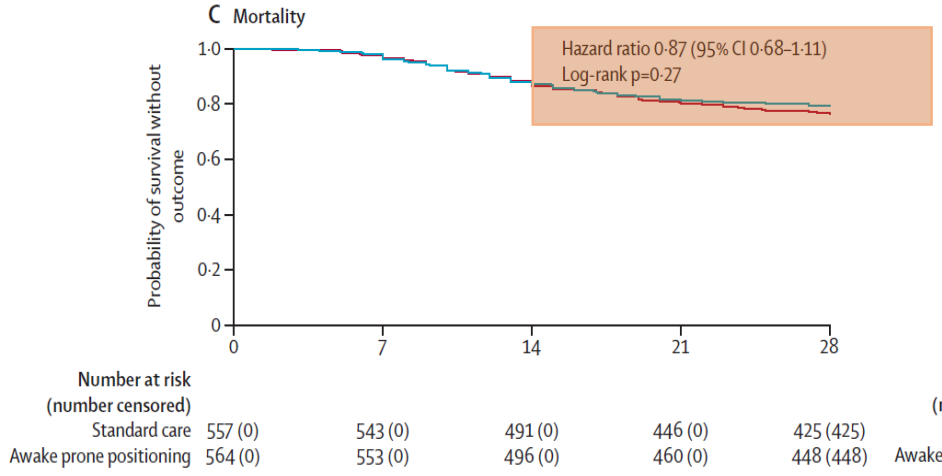
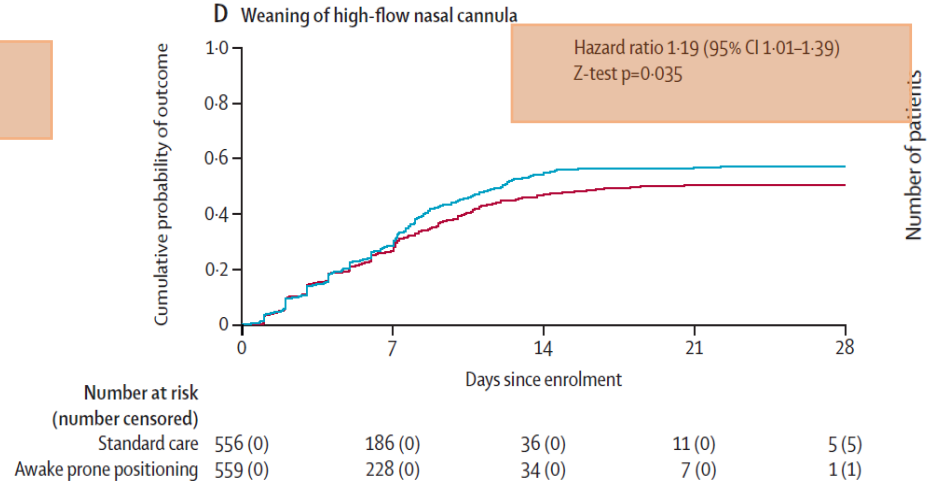
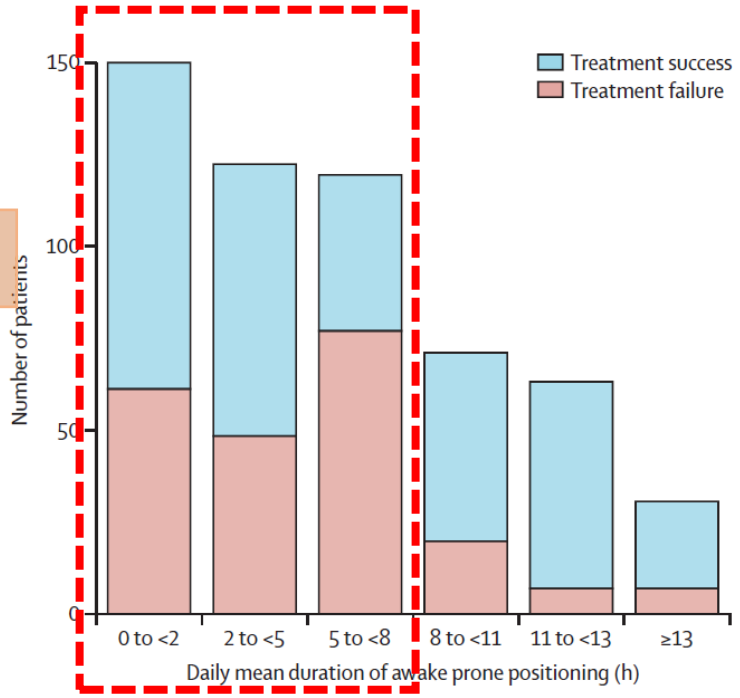
Cf) Postgrad Med J 2021;0:1-5

1) Transient increase of SpO2/FiO2
2) Unable to tolerate more than two APP episodes







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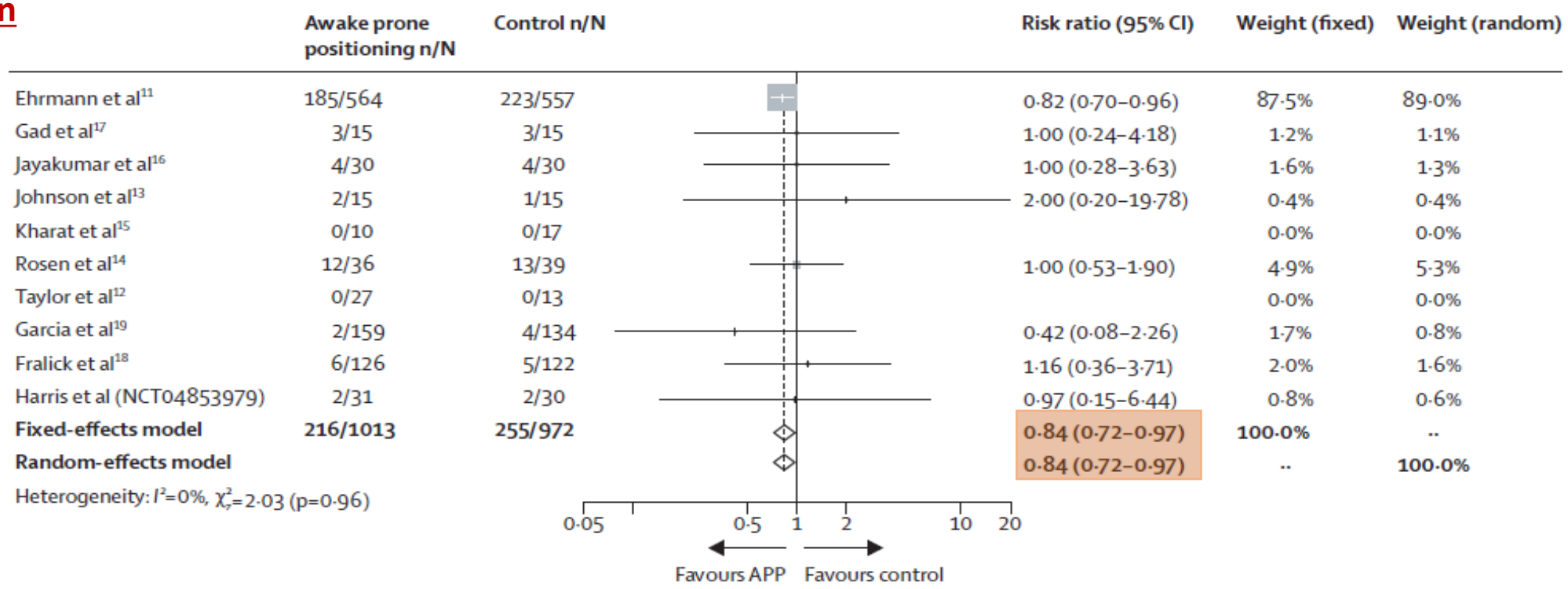
Intubation



Lancet Respir Med 2022 Mar 16;S2213-2600(22)00043-1

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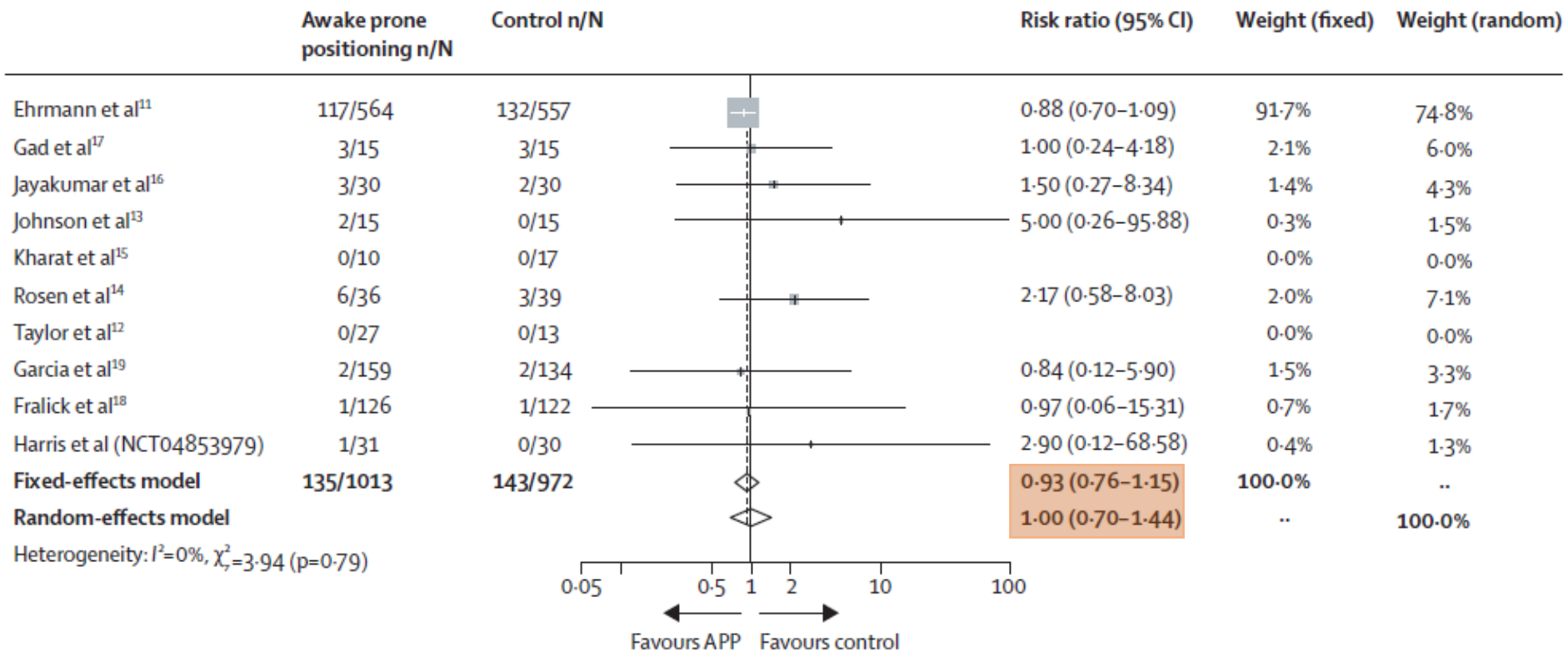
Mortality



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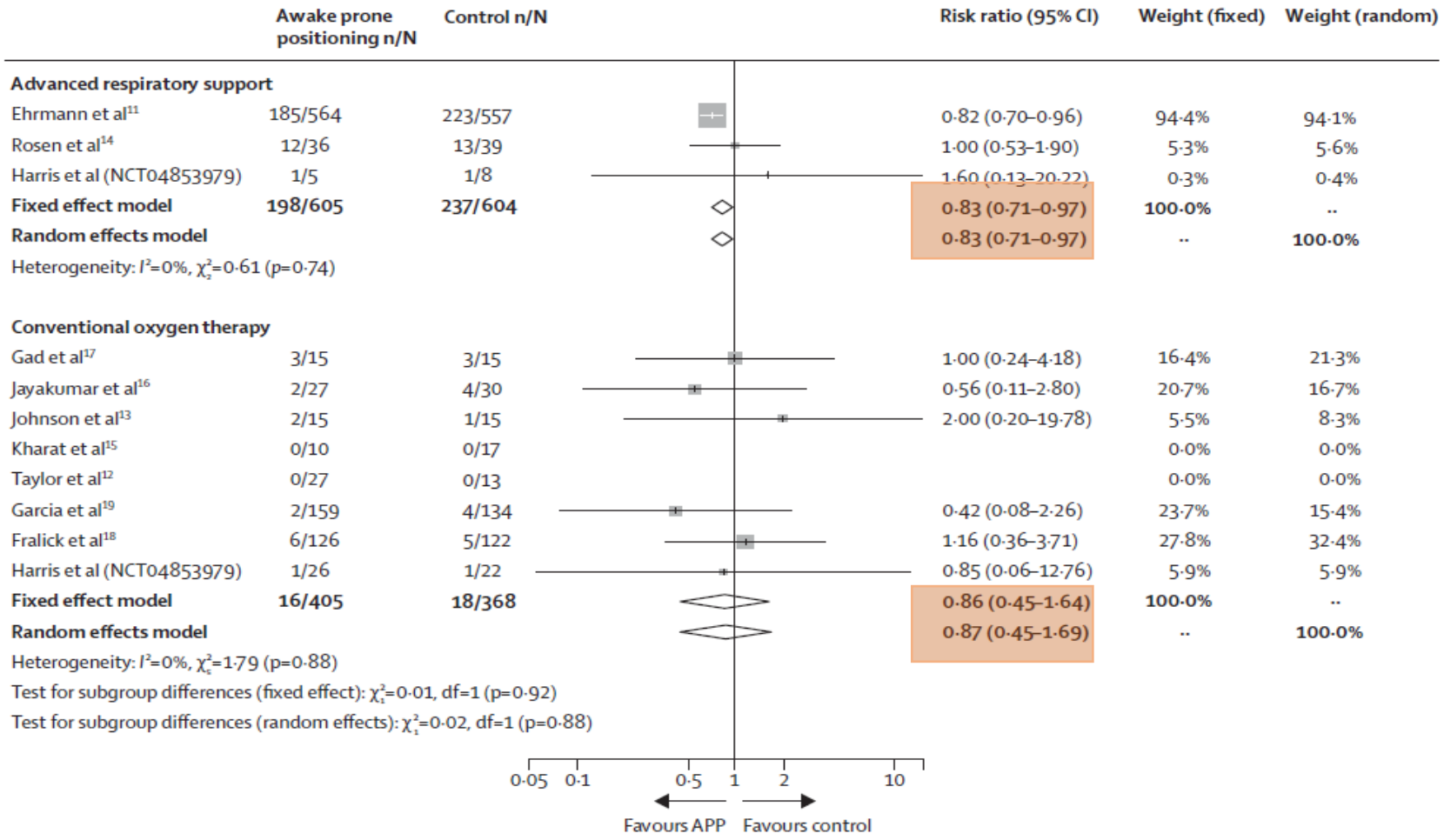
Advanced vs. conventional respiratory support



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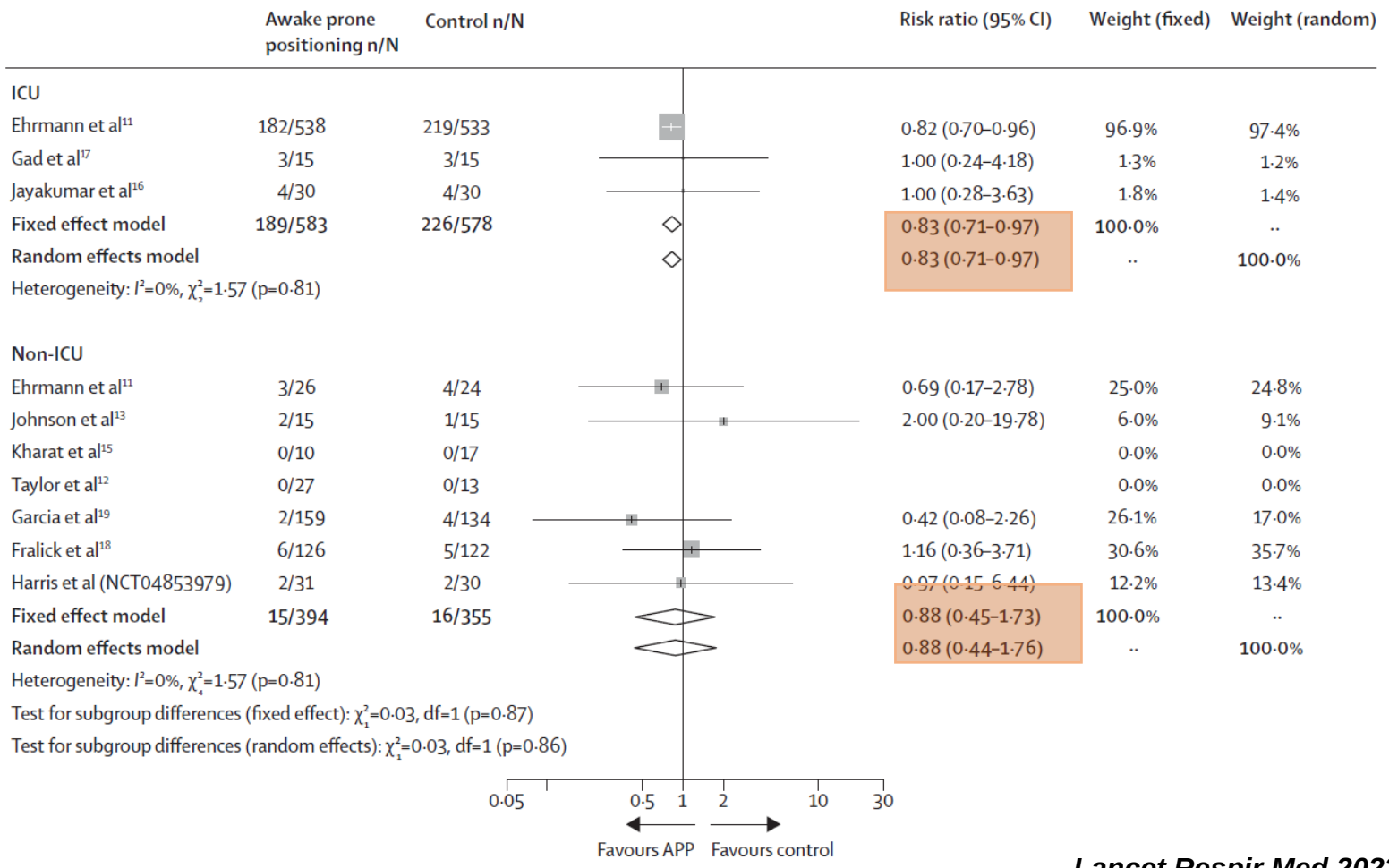
ICU vs. Non-ICU



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Awake prone; Early or Late ?

RESEARCH Open Access

Early versus late awake prone positioning in non-intubated patients with COVID-19

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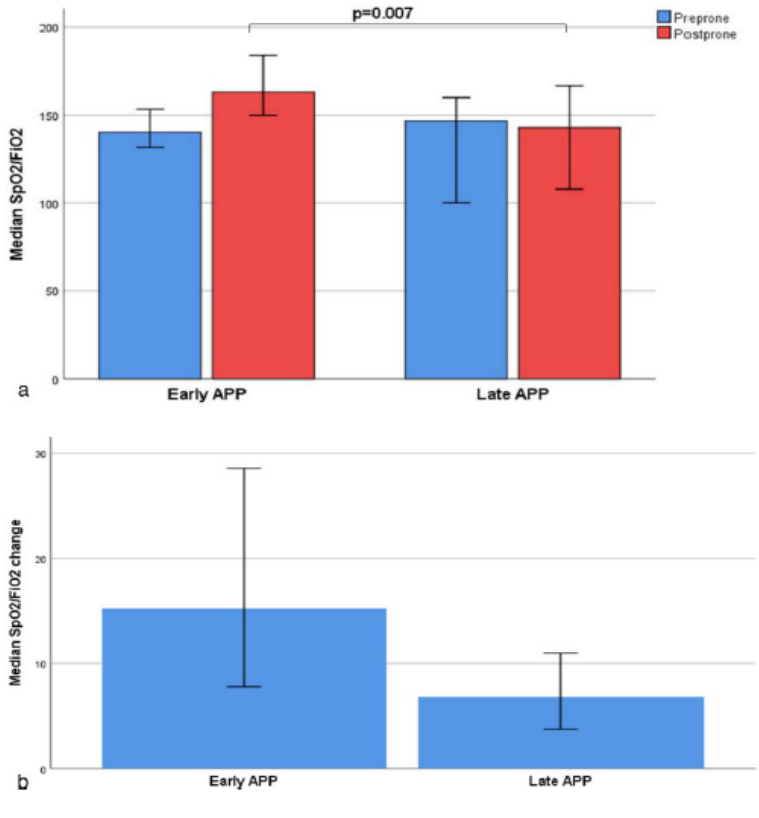
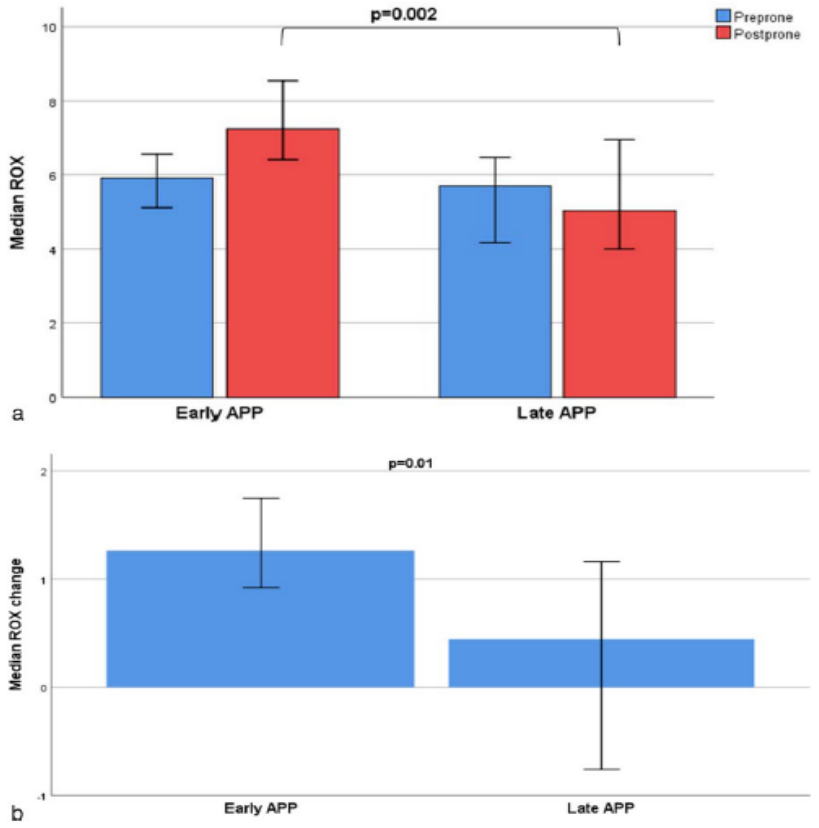
- Post-hoc analysis
- Enrollment : SpO2/FiO2 < 240
- HFNC FiO2 target : 50L/min 90~95% SpO2
- HFNC wean-off : 0.4 and flow 40L/min

PP	HFNC to PP (h)	Duration PP (h/day)
Early (<24h of HFNC start) (n=92)	2.25 (0.8-12.82)	5.07 (2.0-9.05)
Early (≥24h of HFNC start) (n=33)	36.35 (30.2-75.23)	3.0 (1.09-5.64)





Kaur et al. Crit Care (2021) 25:340

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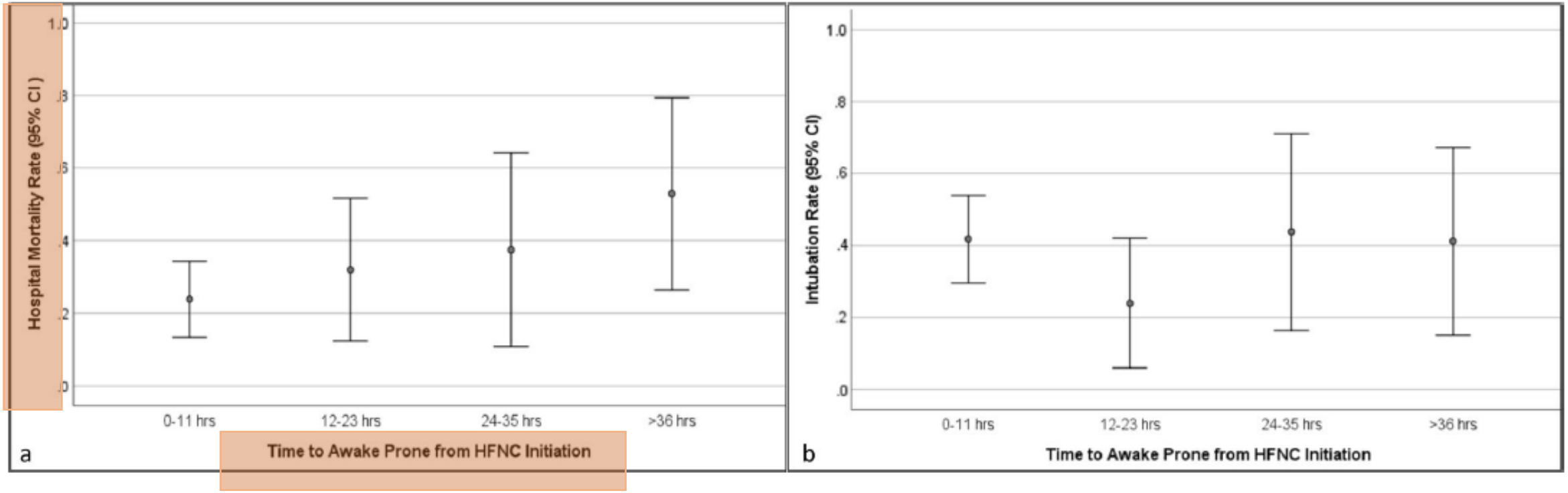
Risk for delayed intubation???



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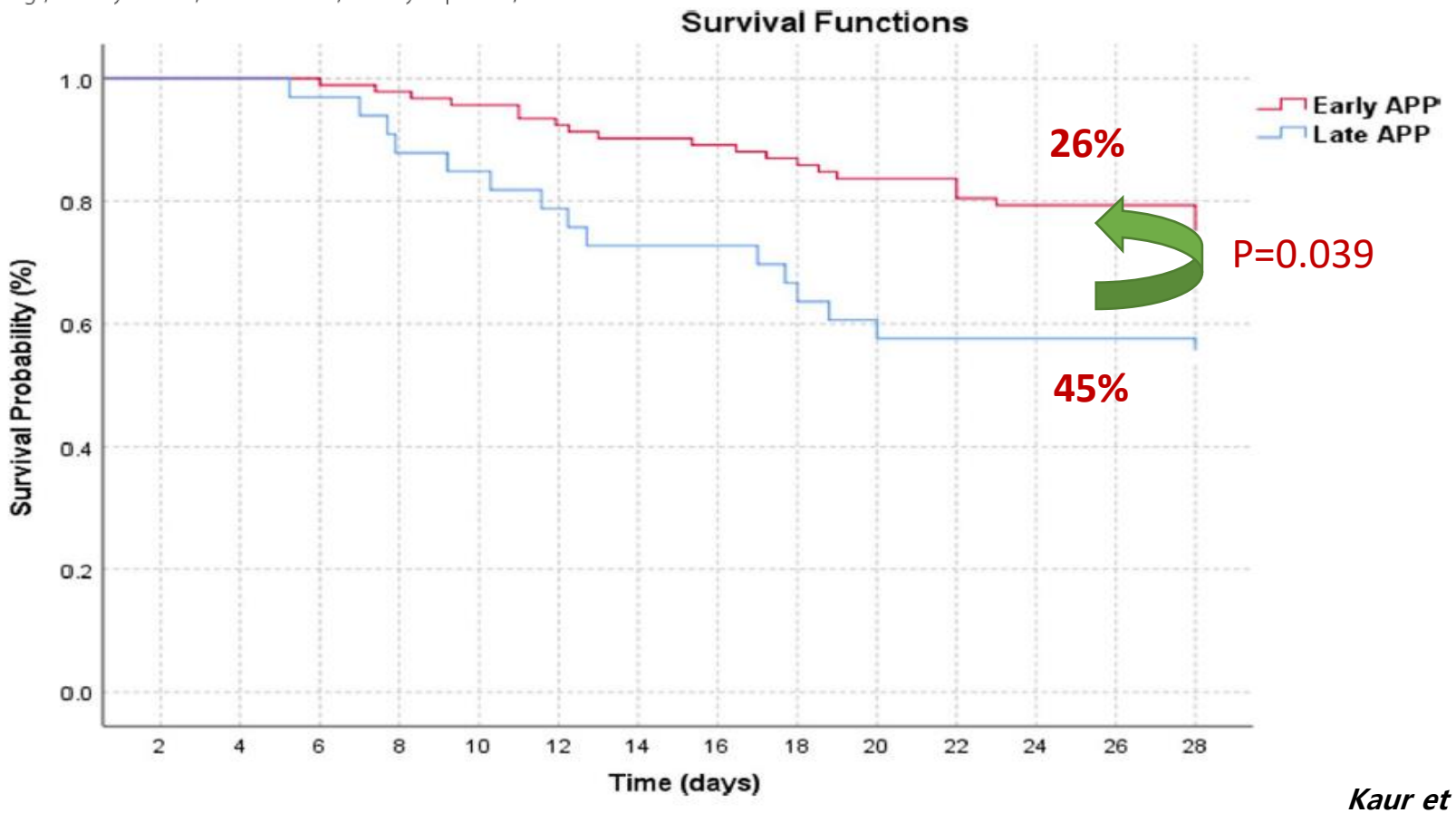

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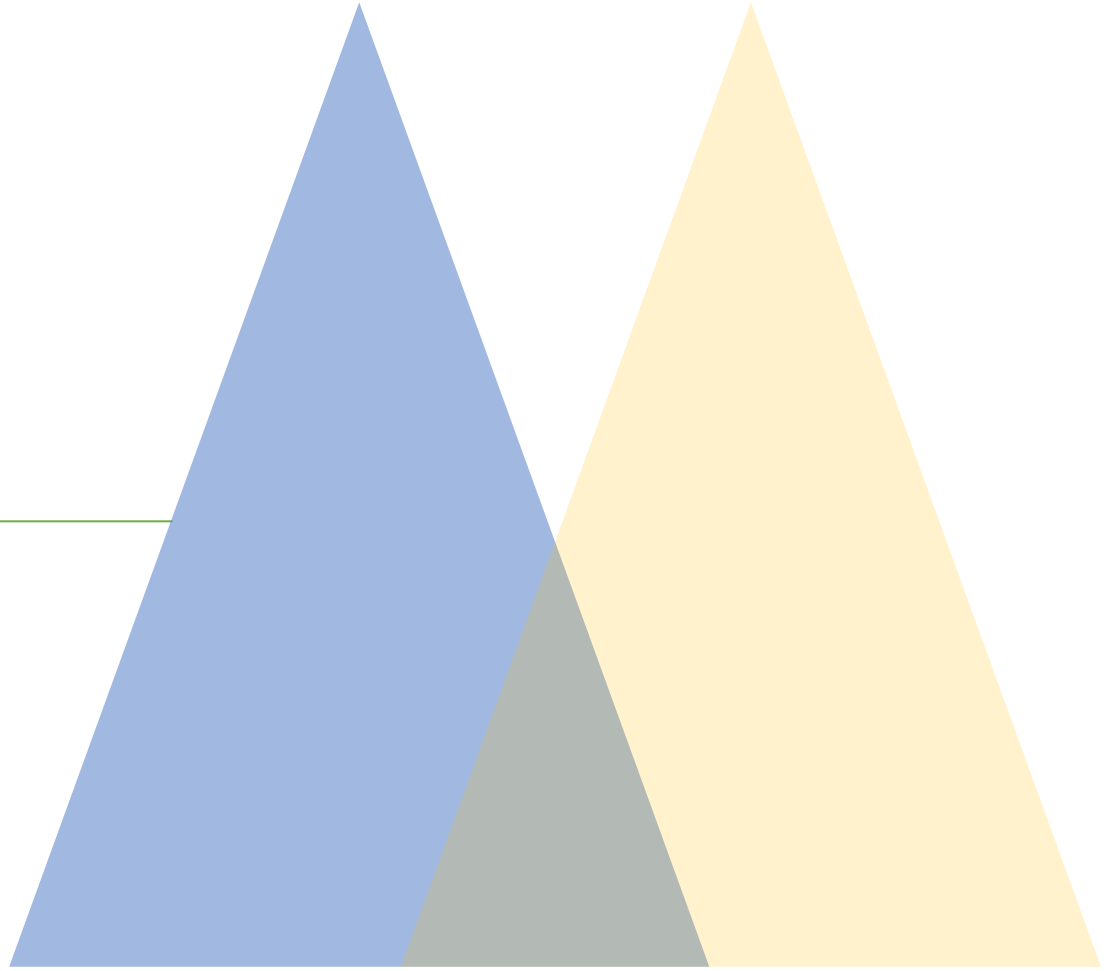
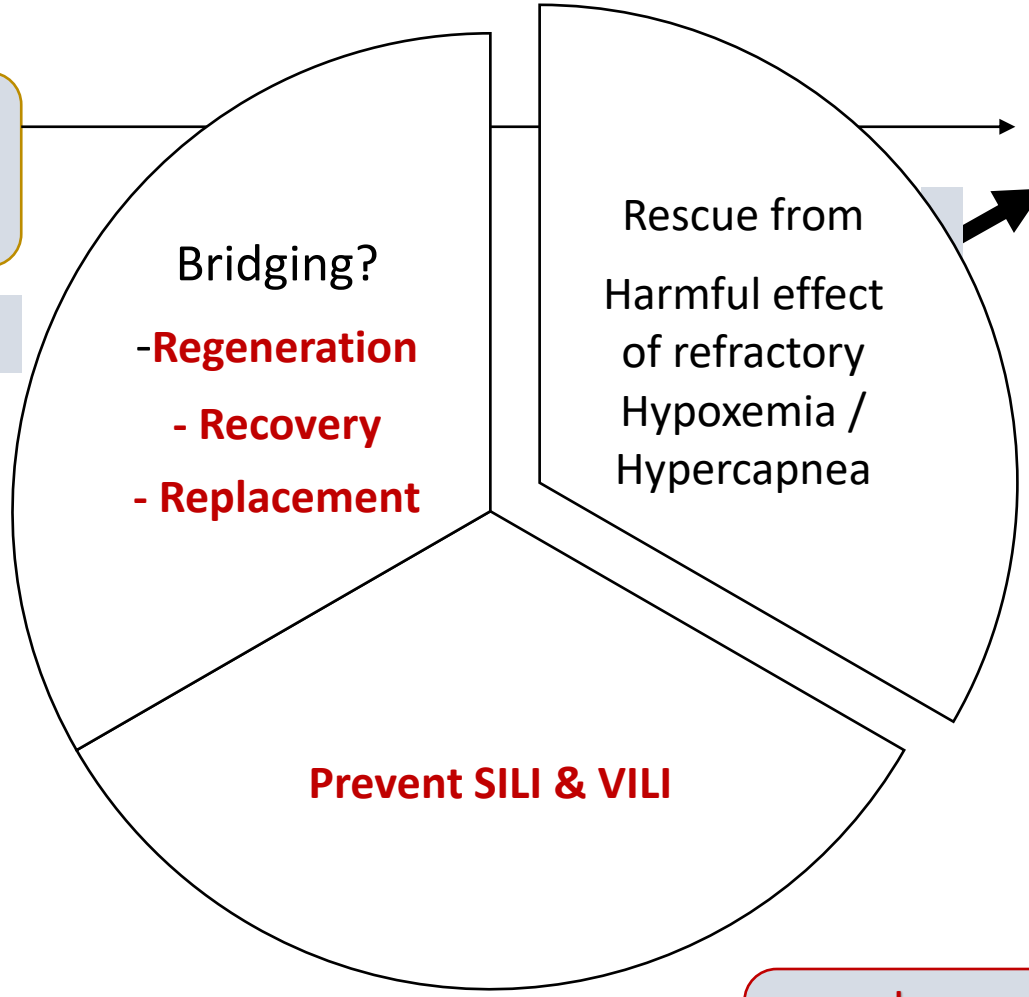
Scientific evidences of prone position



What is the final goal for ARDS in the era of COVID-19?

- Lung transplant
- Stem cell therapy
- ????

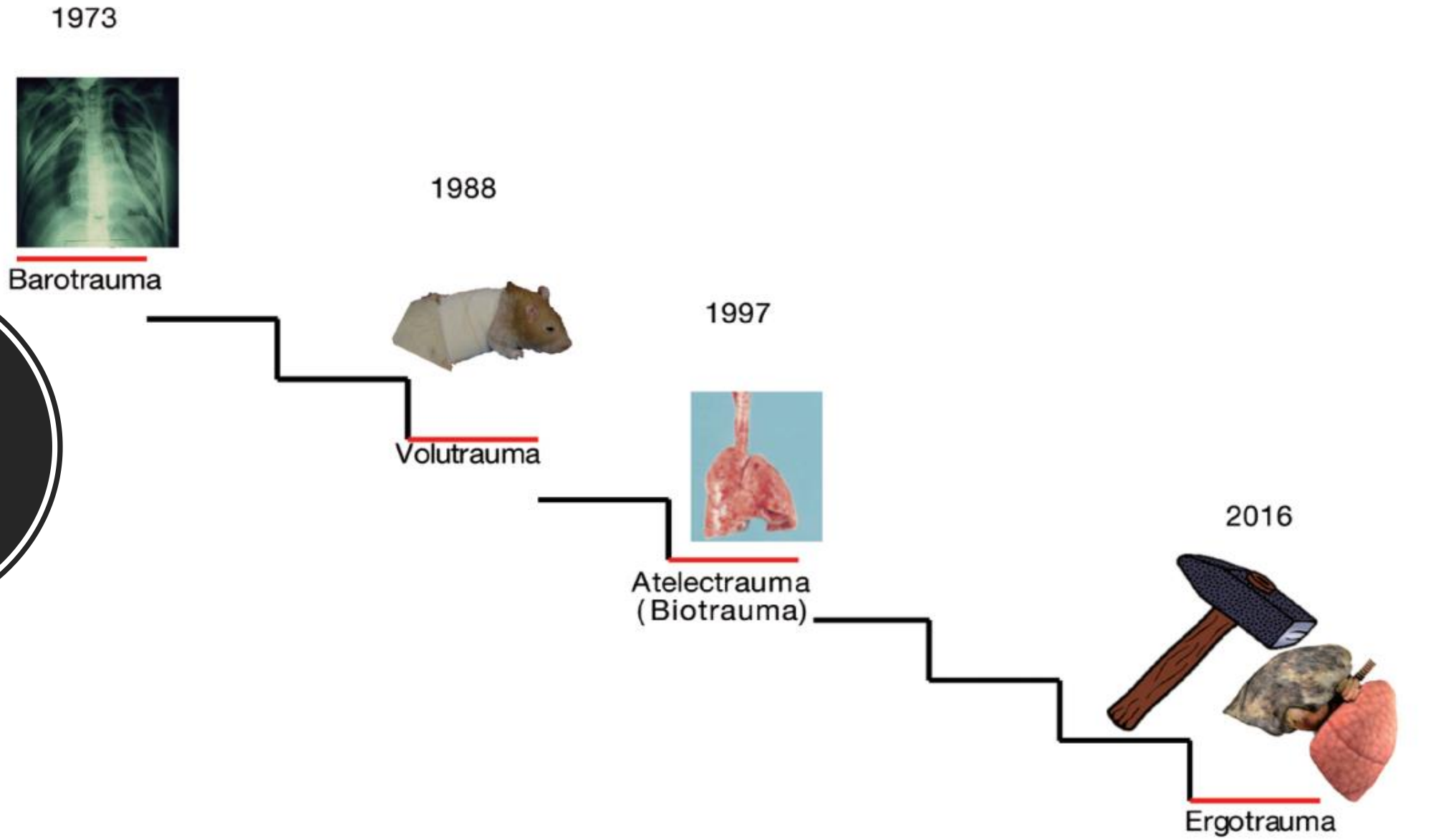
Definite treatment for ARDS?



Extracorporeal Life Support

- Lung protective ventilator strategy
- **Prone Position**
- NM Blocker

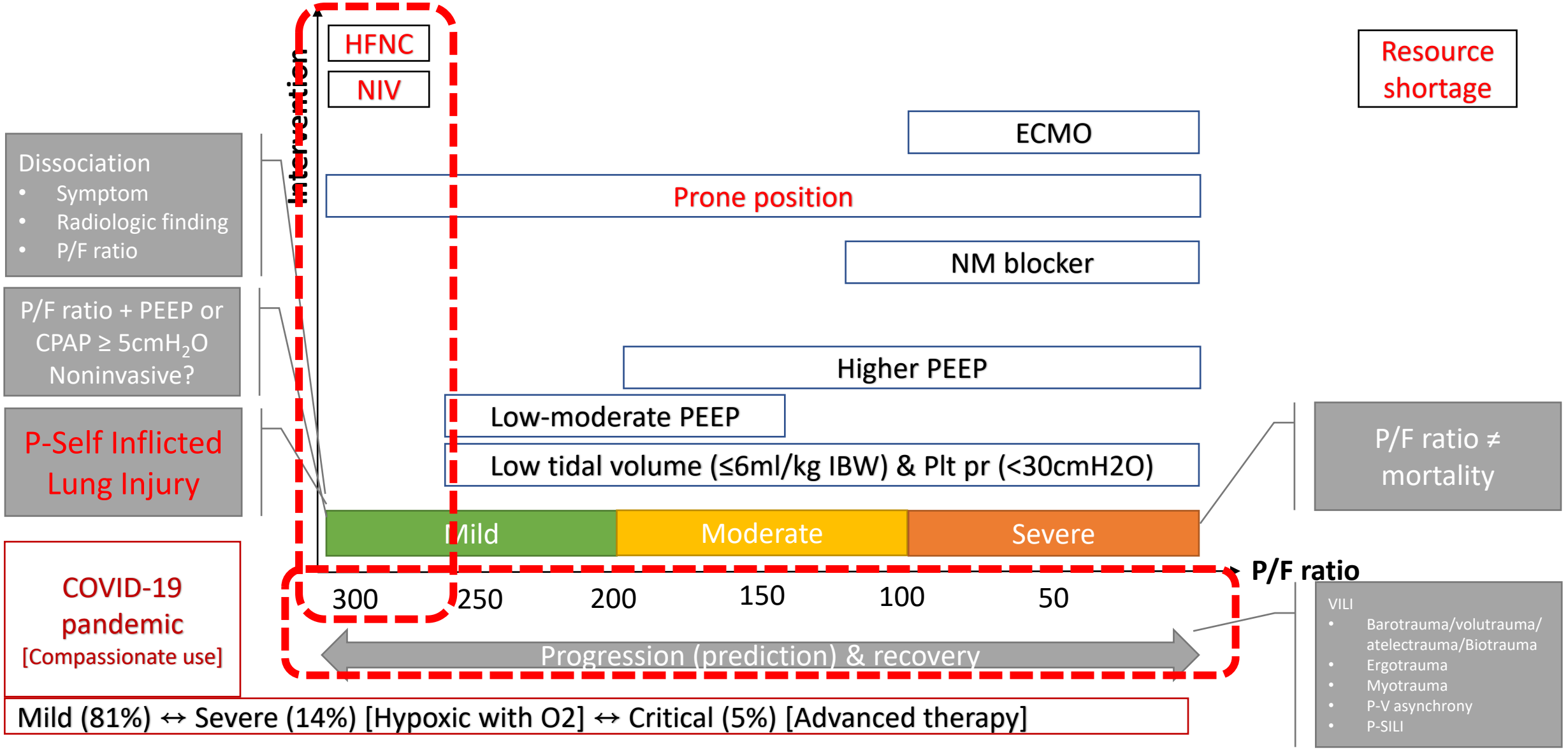
ARDS advances in diagnosis and treatment (JAMA 2018)



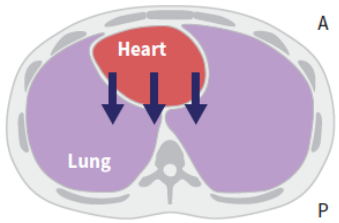
*Mechanical Power = 0.098 * tidal volume * respiratory rate * Ppeak -1/2*ΔP*

JAMA. 2018;319(7):698-710. doi:10.1001/jama.2017.21907
Ann Transl Med 2017;5(14):286

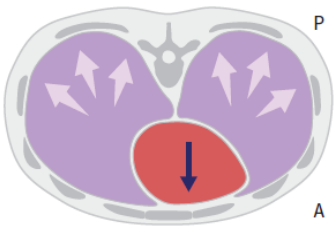
Treatment Paradigm according to pathophysiology & mortality?



Physiology for PP

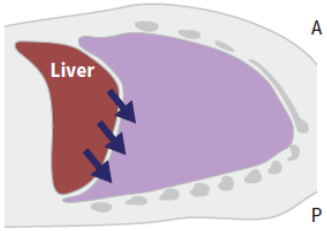


Gravitational pressure of heart and mediastinum on the lungs.

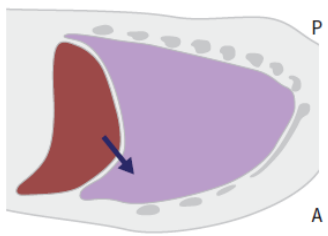


Decreased gravitational pressure of heart and mediastinum on the lungs.

FRC↑

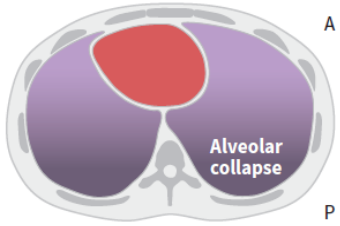


Compressive effects of the abdominal organs on the lungs.

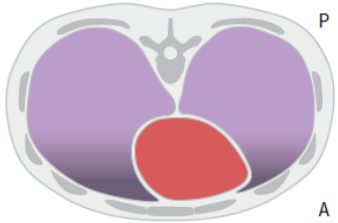


Decreased compressive effects of the abdominal organs on the lungs.

Chest wall/abdomen compliance ↑



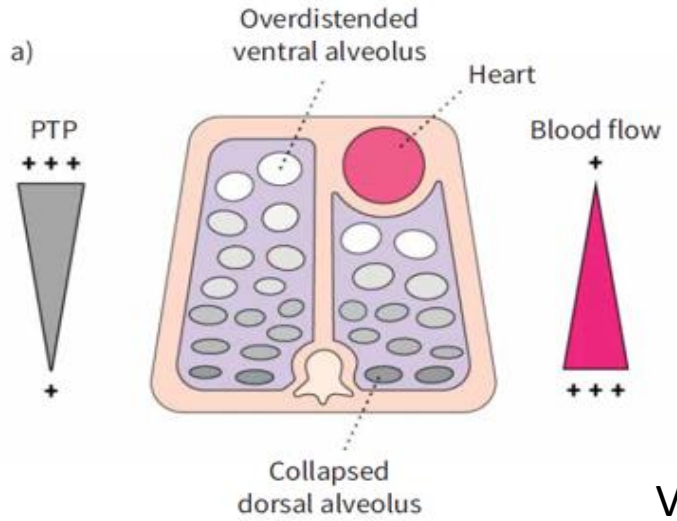
Expansion of the chest wall and overall less homogeneous chest wall compliance.



More homogeneous chest wall compliance due to restriction of anterior chest wall movement.

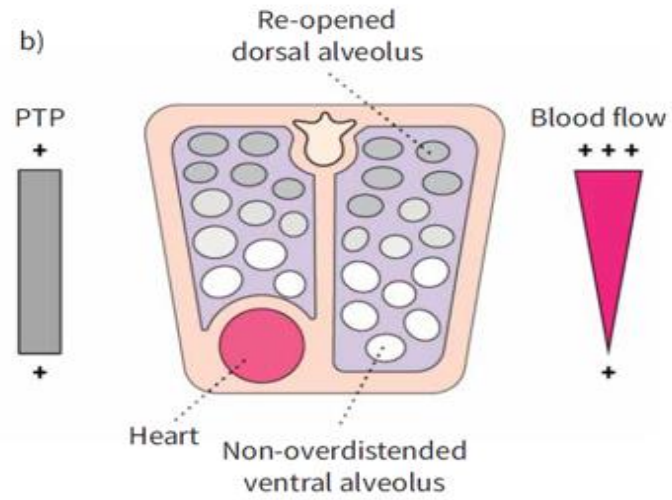
Homogeneity↑

Lung stress ↓ =SILI ? ↓



V/Q mismatch ↓

= P/F ratio ↑

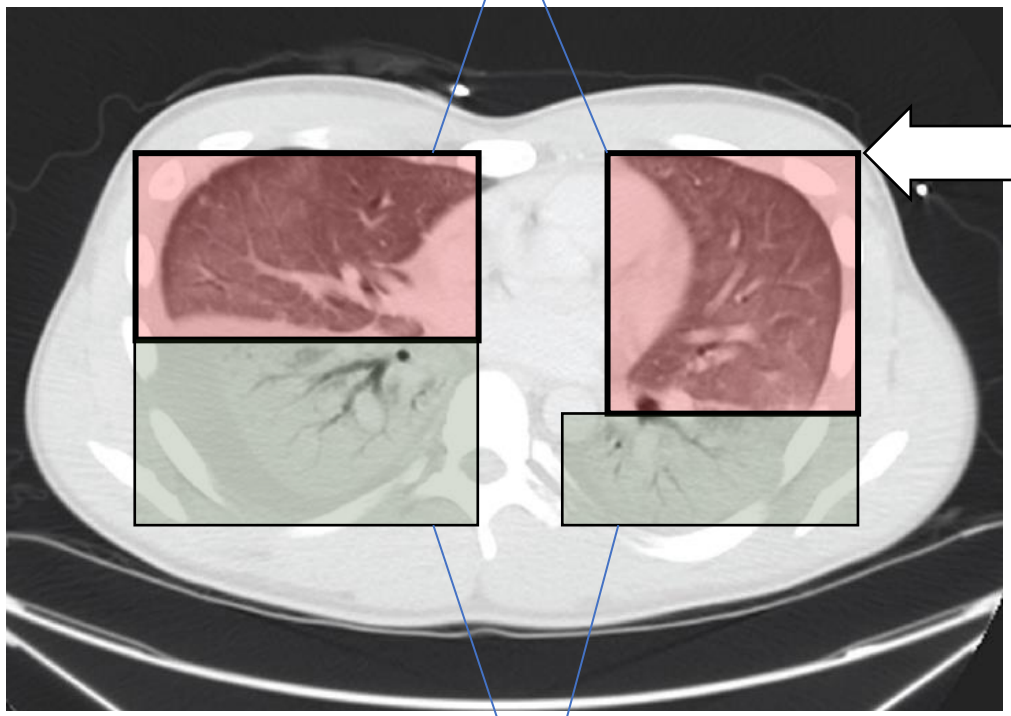


CMAJ 2020 November 23;192:E1532-7
Eur Respir Rev 2021;30:210022

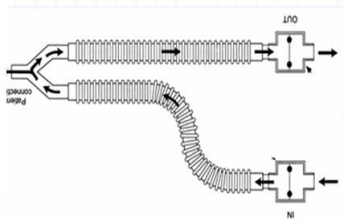
Typical ARDS

"**Baby lung**" : the problem is not that it is stiff, but rather, that it is small (size)

$$\triangle P = \text{Pplat} - \text{PEEP} = \frac{Tidal\ Volume}{Compliance}$$



Ventilator-delivered volume



The degree of dependent consolidation correlates with

- Shunt fraction
- Degree of hypoxemia
- Pulmonary hypertension

Stress & strain

$Stress = K \times strain$ (K= specific elastance, 12cmH2O in human, unchanged in severe ARDS)

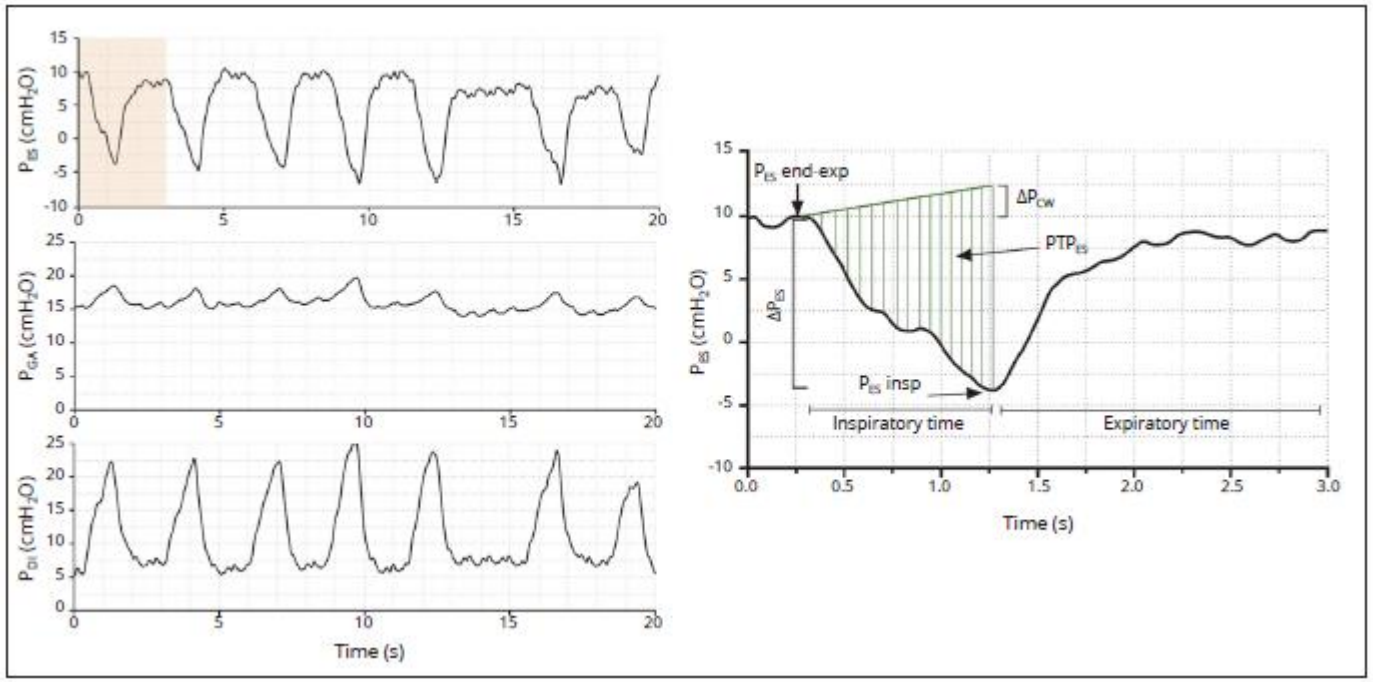
Lung stress; transpulmonary pressure (Ptp)

injurious stress = 'barotrauma' injurious strain = 'volutrau

$airway\ pressure - pleural\ pressure = K \cdot \frac{tidal\ volume}{FRC}$

plateau pressure (usually unknown) estimated by Peso

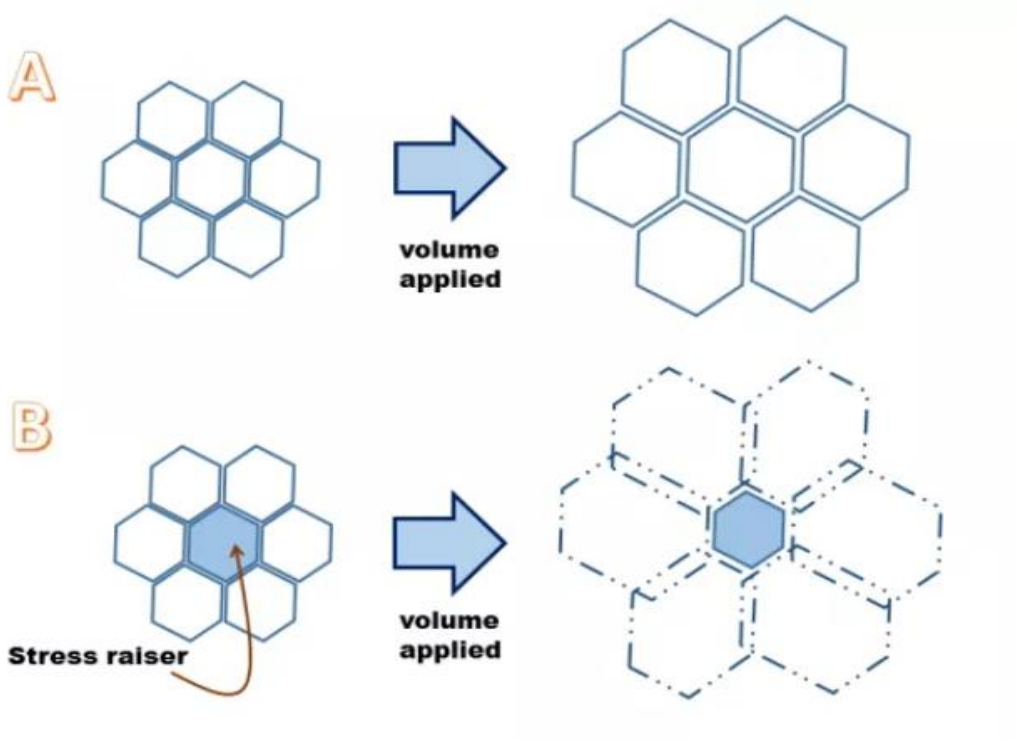
Rec) Transpulmonary driving pressure < 12cmH2O



Am J Respir Crit Care Med. **2019 May 30**

Stress & strain – SILI (inspiratory effort) & VILI (mechanical power)

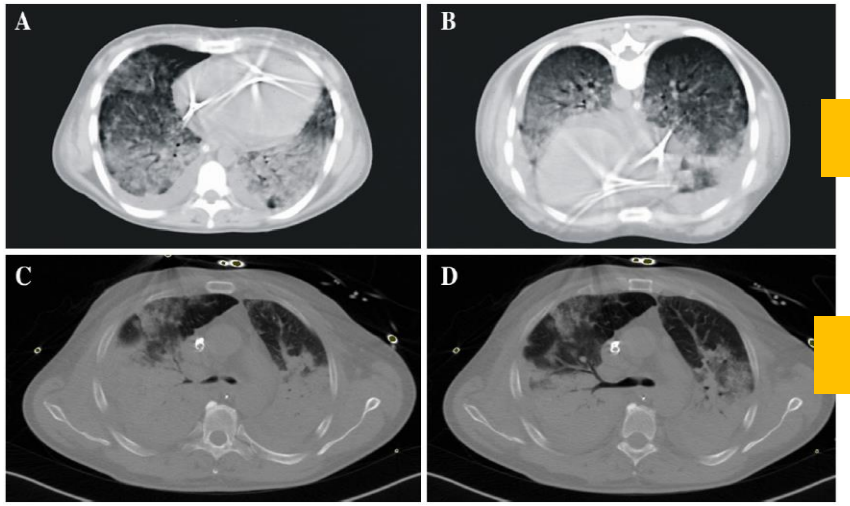
Stress	• Forced applied to an area in lung-represented by transpulmonary pressures • the fiber tension within the lung skeleton
Strain	• Physical deformation or change in shape of an alveolus, caused by stress • not simply the absolute volume administered by the ventilator, but rather it is the volume applied by the ventilator relative to the volume within the lung available for gas exchange



Stress raiser :

atelectasis, age-related anatomical changes, scar, edema, secretions, consolidation etc.

Any area of two, adjacent materials of differing elasticity



: Prone

: PEEP

Lung inhomogeneities and time course of ventilator-induced mechanical injuries. The Journal of the American Society of Anesthesiologists, 2015. 123(3): p. 618-627.

Phenotype for COVID-19 ARDS (?) : Gattinoni H/L hyp

Happy hypoxemia?

JAMA Insights | CLINICAL UPDATE

Management of COVID-19 Respiratory Dis

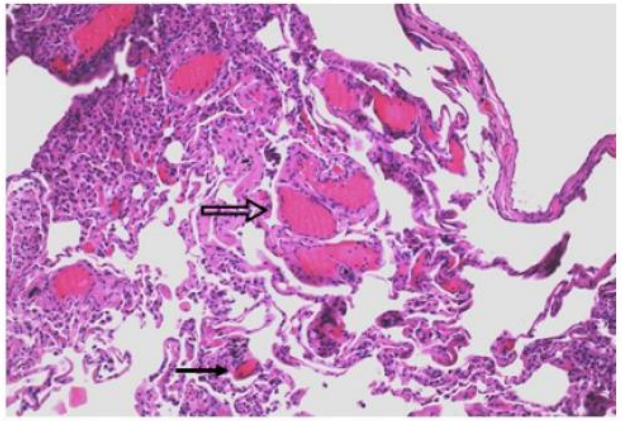
John J. Marini, MD; Luciano Gattinoni, MD

Phenotype	Symptom	Oxygenation	Chest CT	elastance	compliance	Response to PEEP (recruitability)	V/Q
Type-L (1)	Little (MV ↑)	Very poor	Limited GGO	low	high	Low	[illegible]ia)
Type-H (2)	severe	poor	extensive	high	low	High	[illegible]unt

Transition?

(P-SILI?)

Pathophysiology – COVID-19→ATII / Vascular endothelium / Widespread micro- and macro- thrombosis / V-Q mismatch



- Autopsy study

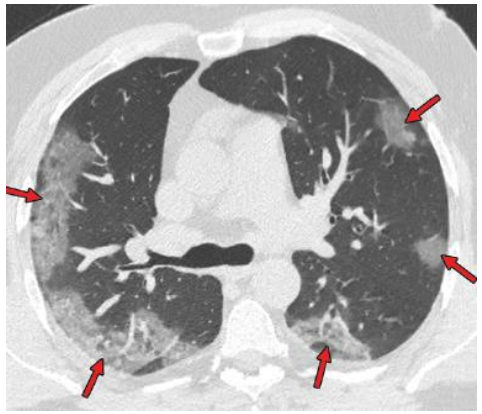
DAD

Thrombosis (micro-thrombi)

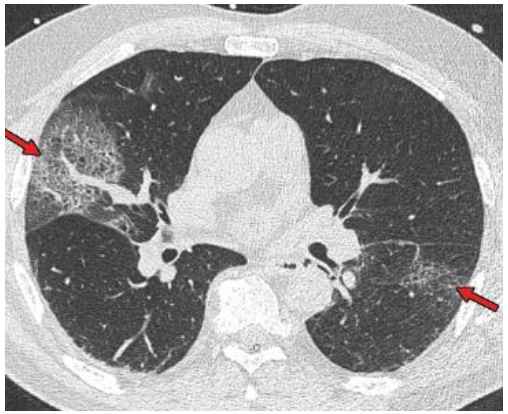
Lung fibrosis

JAMA June 9, 2020 Volume 323, Number 22
Intensive Care Med (2020) 46:1099-1102
Curr Opin Pulm Med 2021, 26:000–000

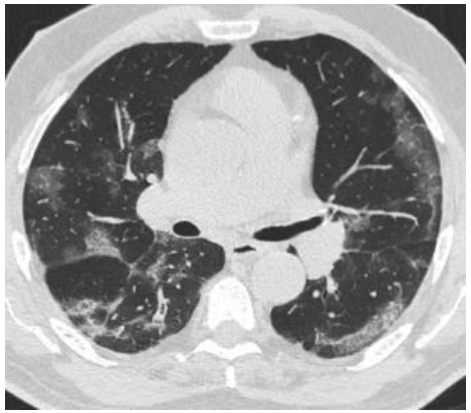
Stress raiser? = COVID-19 pneumonia in Chest CT



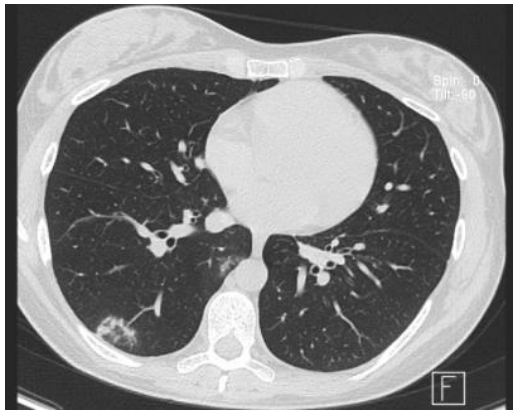
ground-glass opacities (arrows) in a peripheral distribution



ground-glass opacities, with superimposed septal thickening (arrows) in the middle lobe and left lower lobe.

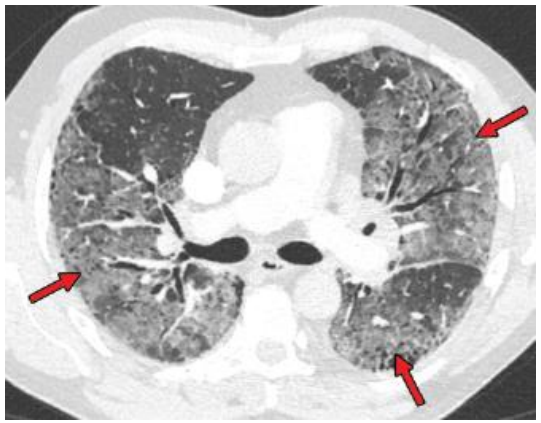


"crazy-paving" pattern



Reverse halo sign

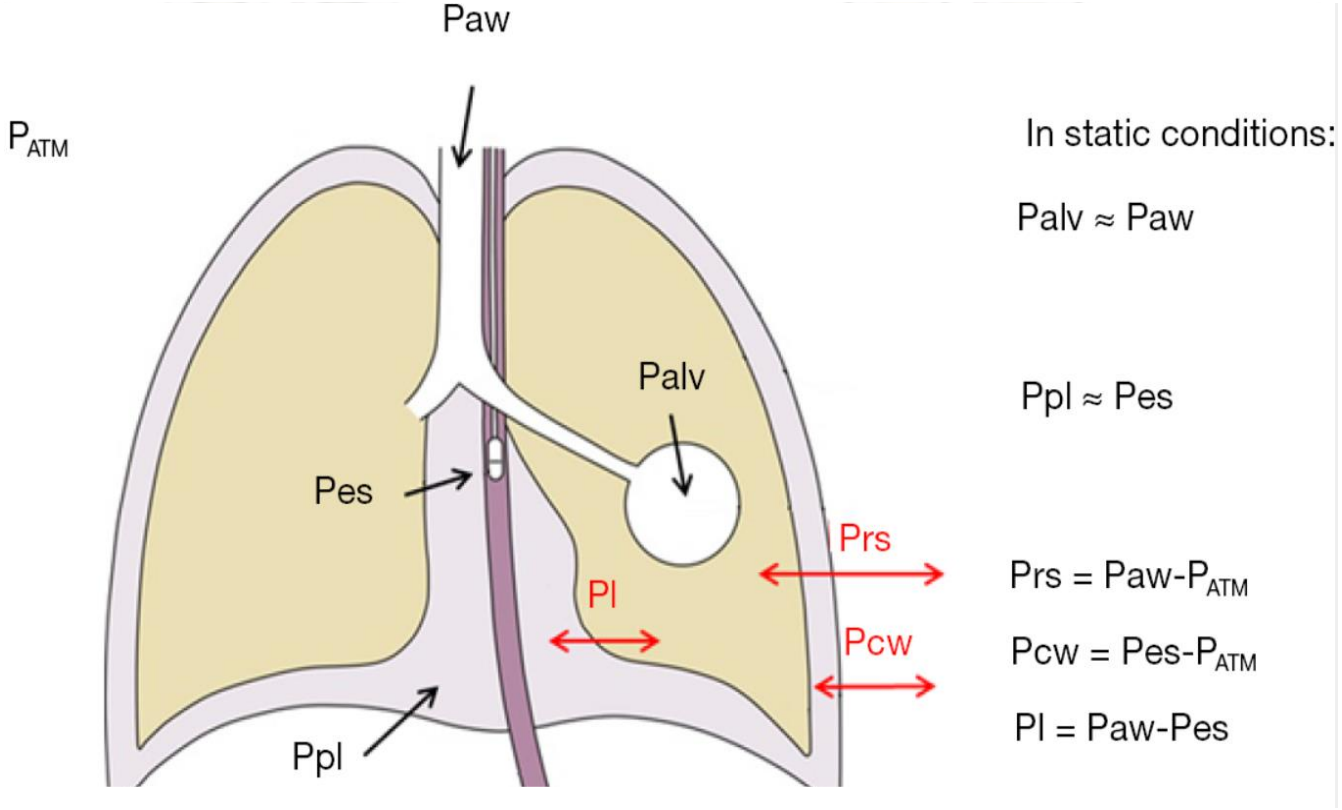
L type → H type



ARDS progression

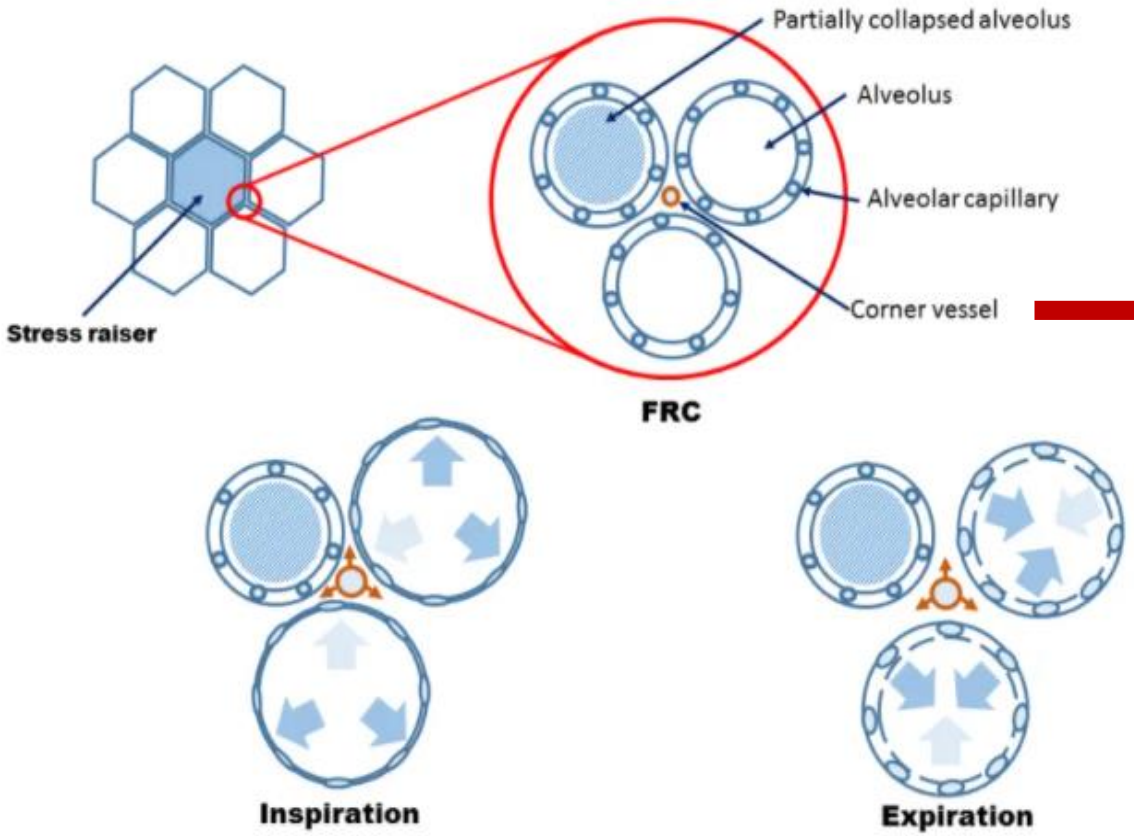
Increased inspiratory effort & trans-pulmonary pressure

[tachypnea (RR ↑) ≠ hyperpnea (dyspnea) (Tidal ventilation↑)]



Interpretation of the transpulmonary pressure in the critically ill patient, Ann Trans Med 2018;6(19):383

"Vascular injury" – SILI (inspiratory effort) & VILI (mechanical power)



- Particularly susceptible to injury
- Siphoning of blood towards areas of high stress

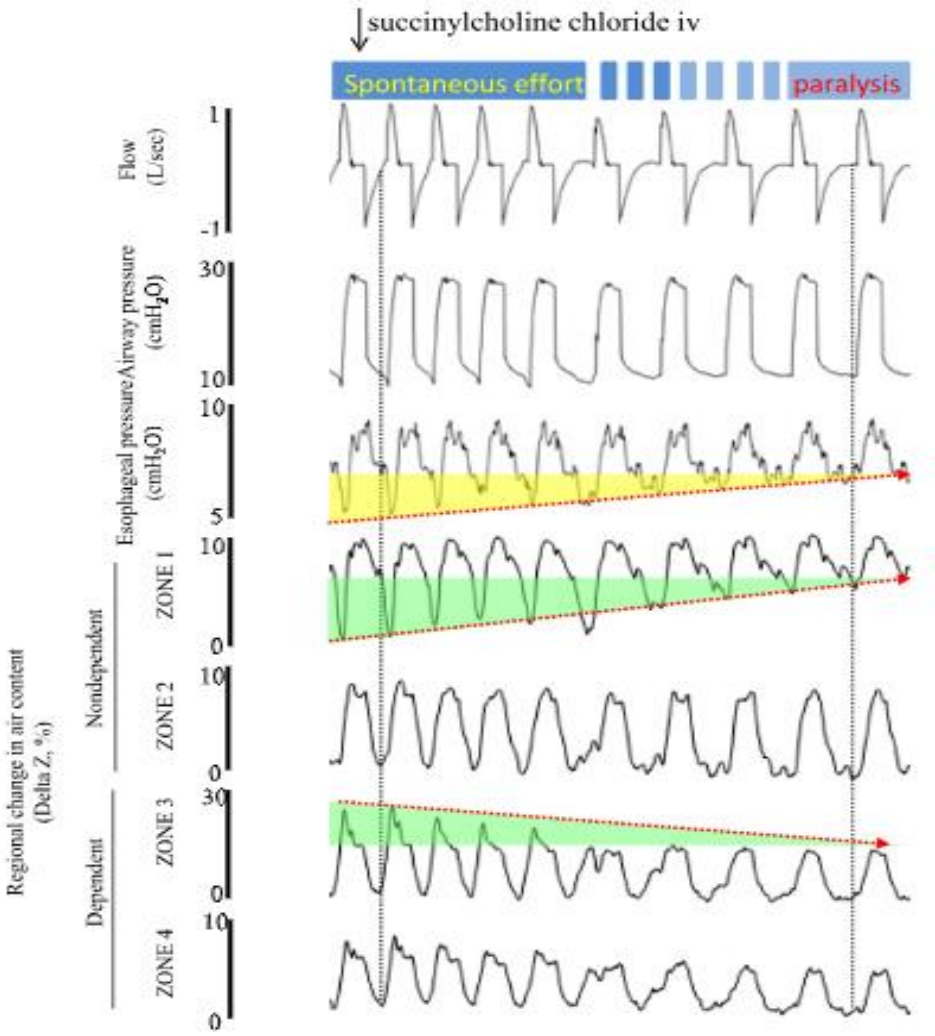
Vasoplegia

The persistence of high pulmonary blood flow to non-aerated lung alveoli appears to be caused by the relative failure of the hypoxic pulmonary vasoconstriction mechanism

→ **V/Q mismatch ↑**

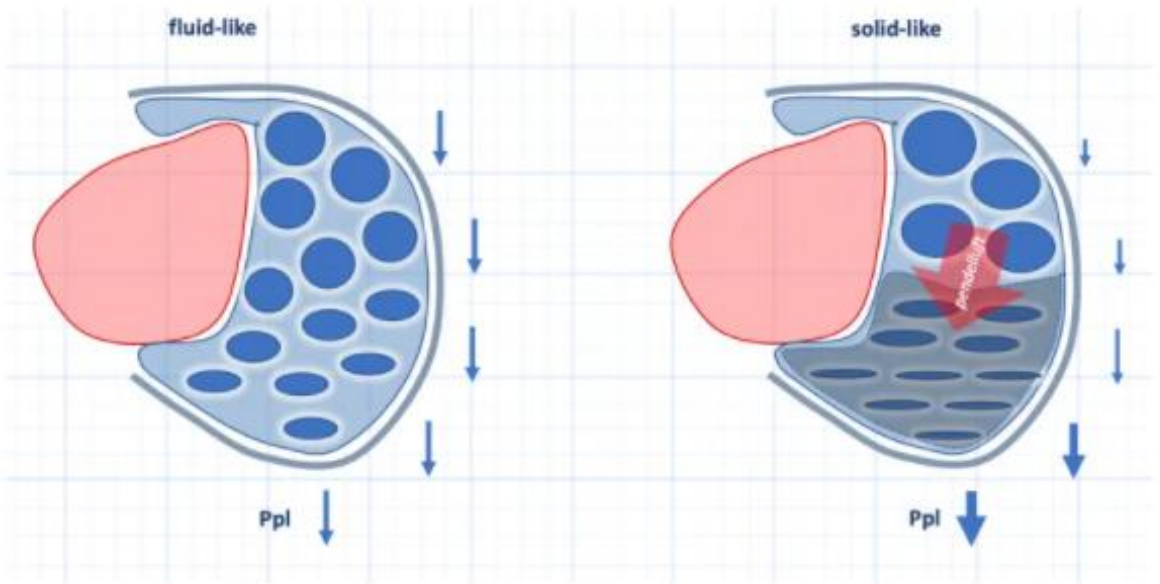
Marini JJ, Hotchkiss JR, Broccard AF: Bench-to-bedside review: microvascular and airspace linkage in ventilator-induced lung injury. Critical Care 2003, 7(6):435.

“Pendelluft effect” – SILI (inspiratory effort) & VILI (mechanical power)



“Pendelluft effect”
Movement of air within the lung
from nondependent to dependent regions
without change in tidal volume

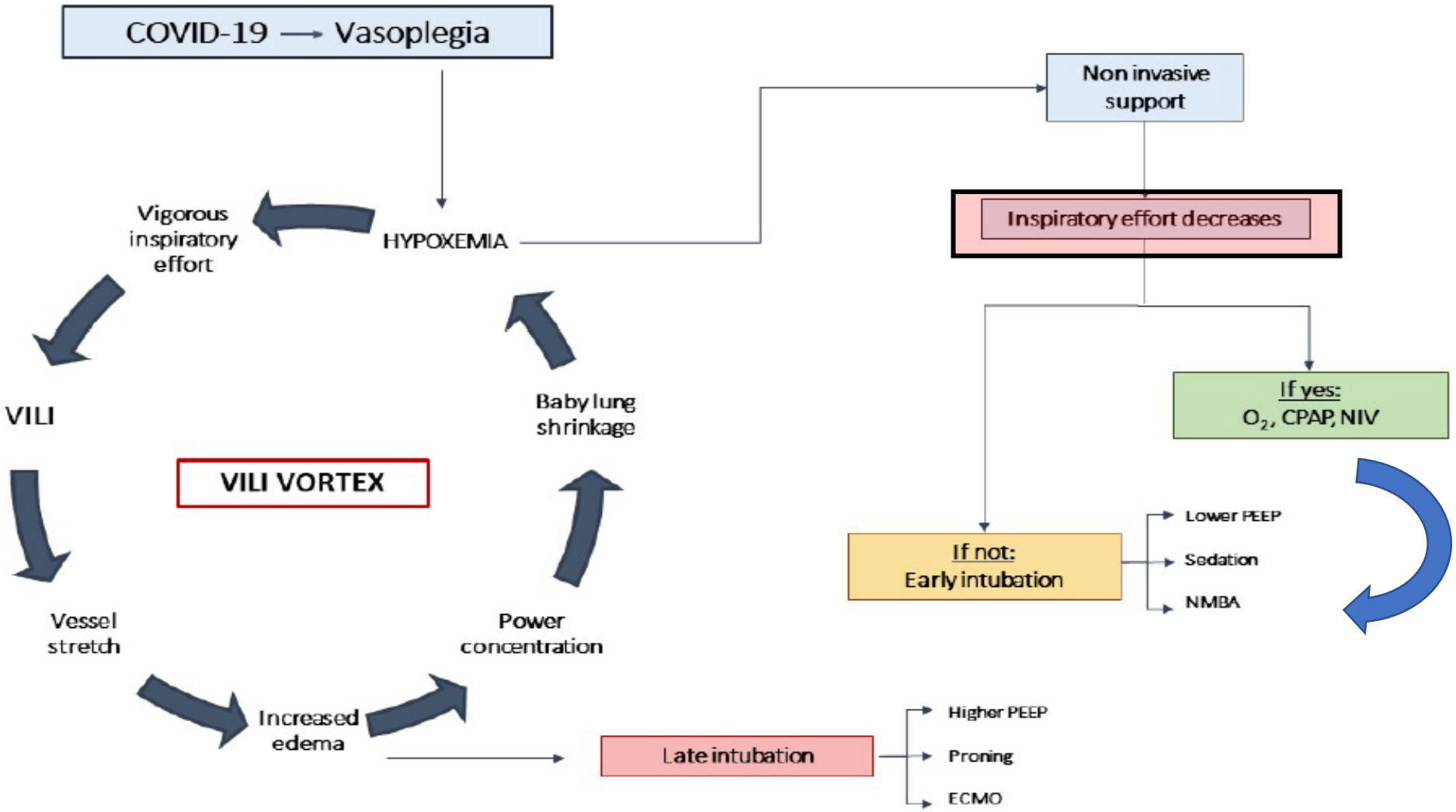
Overstretch in dependent lung



Mechanical ventilation to minimize progression of lung injury in acute respiratory failure. Am J Respir Crit Care Med. 2017;195(4):438-442
Am J Respir Crit Care Med Vol 188, Iss. 12, pp 1420–1427, Dec 15, 201

Pathophysiology for COVID-19 ARDS

By Luciano Gattinoni



JAMA June 9, 2020 Volume 323, Number 22

Treatment approach for COVID-19 ARDS

Table. Time Course and Treatment Approach to Ventilation Support for Patients With CARDS

Time period	Objective	Respiratory support options	Rationale
Before intubation	Adequate gas exchange Avoid P-SILI	Supplemental oxygen, CPAP, NIV, HFNC Awake prone positioning, Target nonvigorous breathing	Powerful respiratory effort can cause reinforcing lung and vascular stress, resulting in injury
During mechanical ventilation	Avoid pulmonary deterioration and VILI vortex	Minimize PEEP, frequency and tidal volume Adjust to acceptable gas exchange Maintain fluid balance Reduce O_2 demand Consider ECMO	Minimize transpulmonary and vascular stresses
After intubation	Minimize pulmonary stress Optimize O_2 Avoid VILI vortex	Type L[a]: use lower PEEP (<10 cm H_2O) Use more liberal tidal volume (7-9 mL/kg) as needed Reduce O_2 demand Consider prone positioning	Lower tidal volumes are unnecessary Higher PEEP is ineffective, creates dead space, and adversely redirects blood flow
	Reduce and evenly distribute lung and vascular stresses Optimize O_2 Avoid VILI vortex	Type H[a]: use higher PEEP (<15 cm H_2O) Lower tidal volume (5-7 mL/kg) Reduce O_2 demand Implement prone positioning	More closely behaves and responds like typical ARDS
Weaning phase	Avoid reversion to previously worsened pulmonary state by causing VILI and worsening edema	Make transitions cautiously Avoid abrupt changes Spontaneous trials only at the very end of the weaning process	Strong spontaneous efforts raise O_2 demand, increase edema, and promote P-SILI

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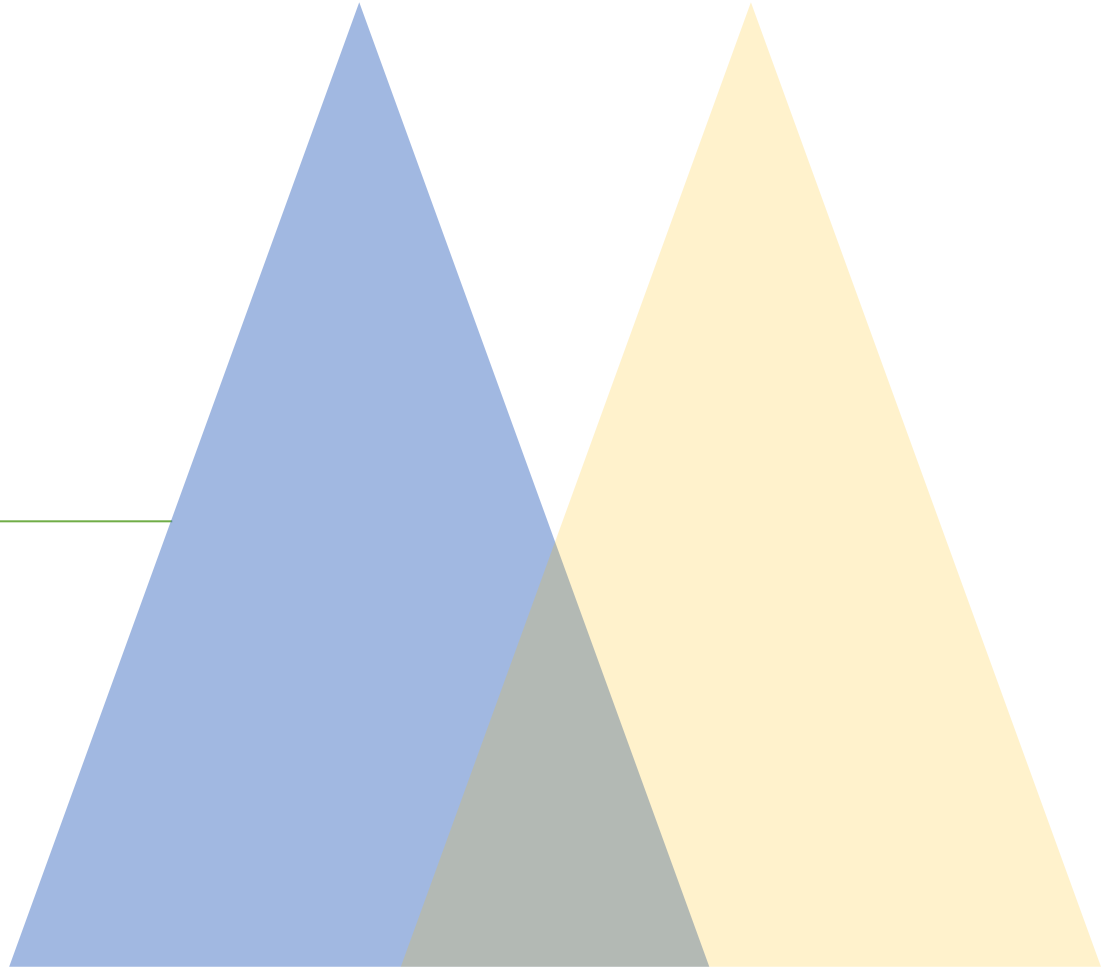
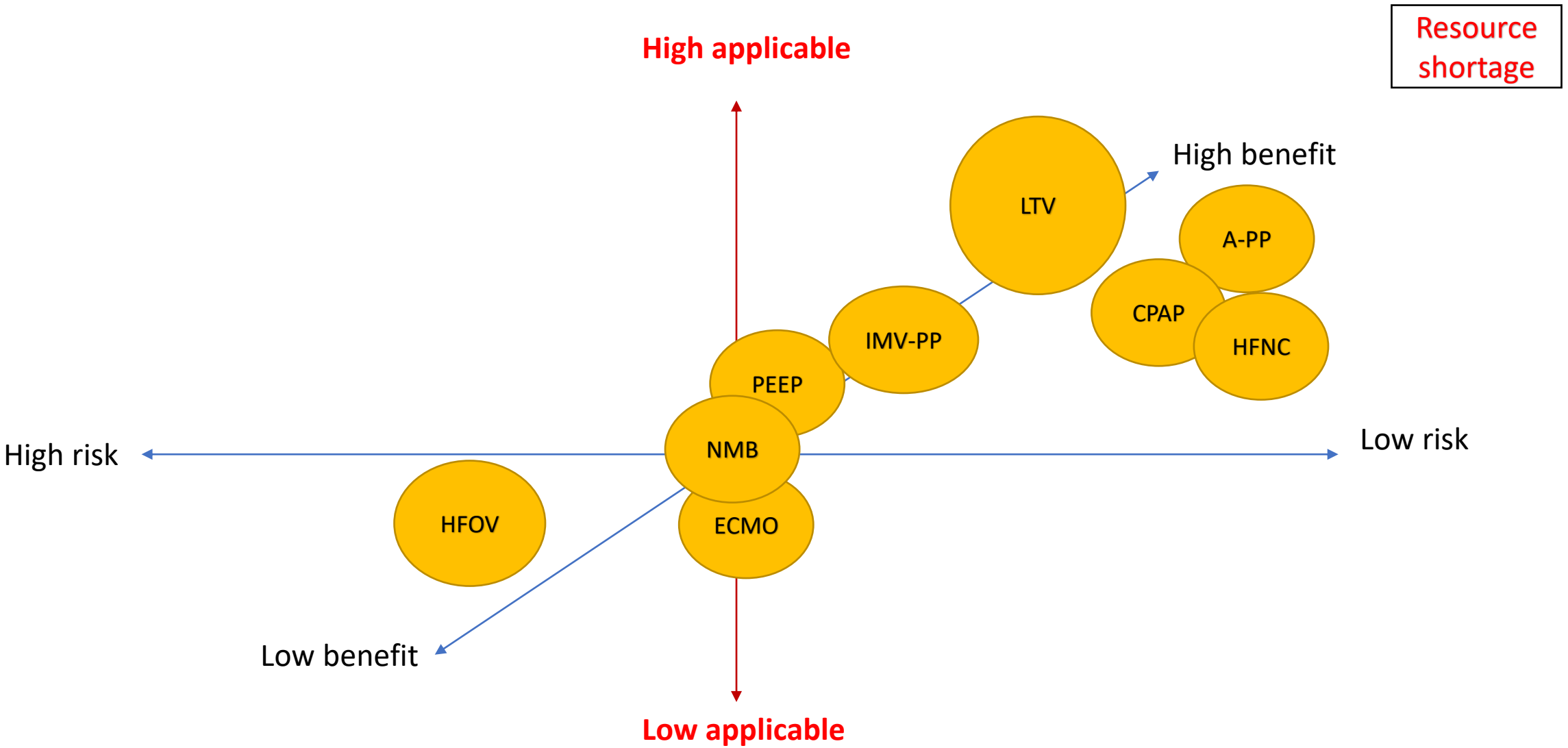
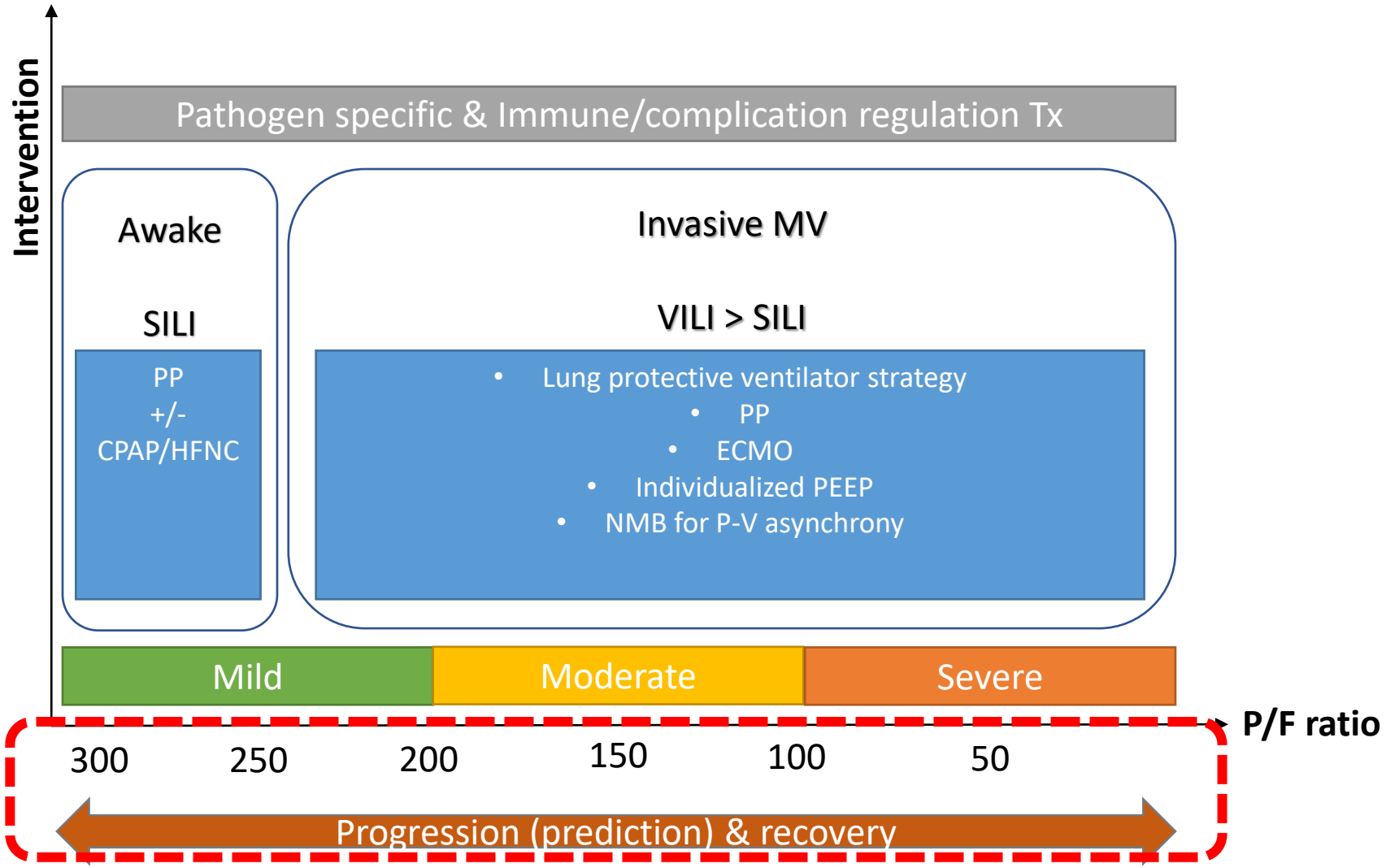
Suggestion?



Guideline considering multifaceted factors?



VILI (SILI) preventive ARDS treatment strategy (before and After IMV)



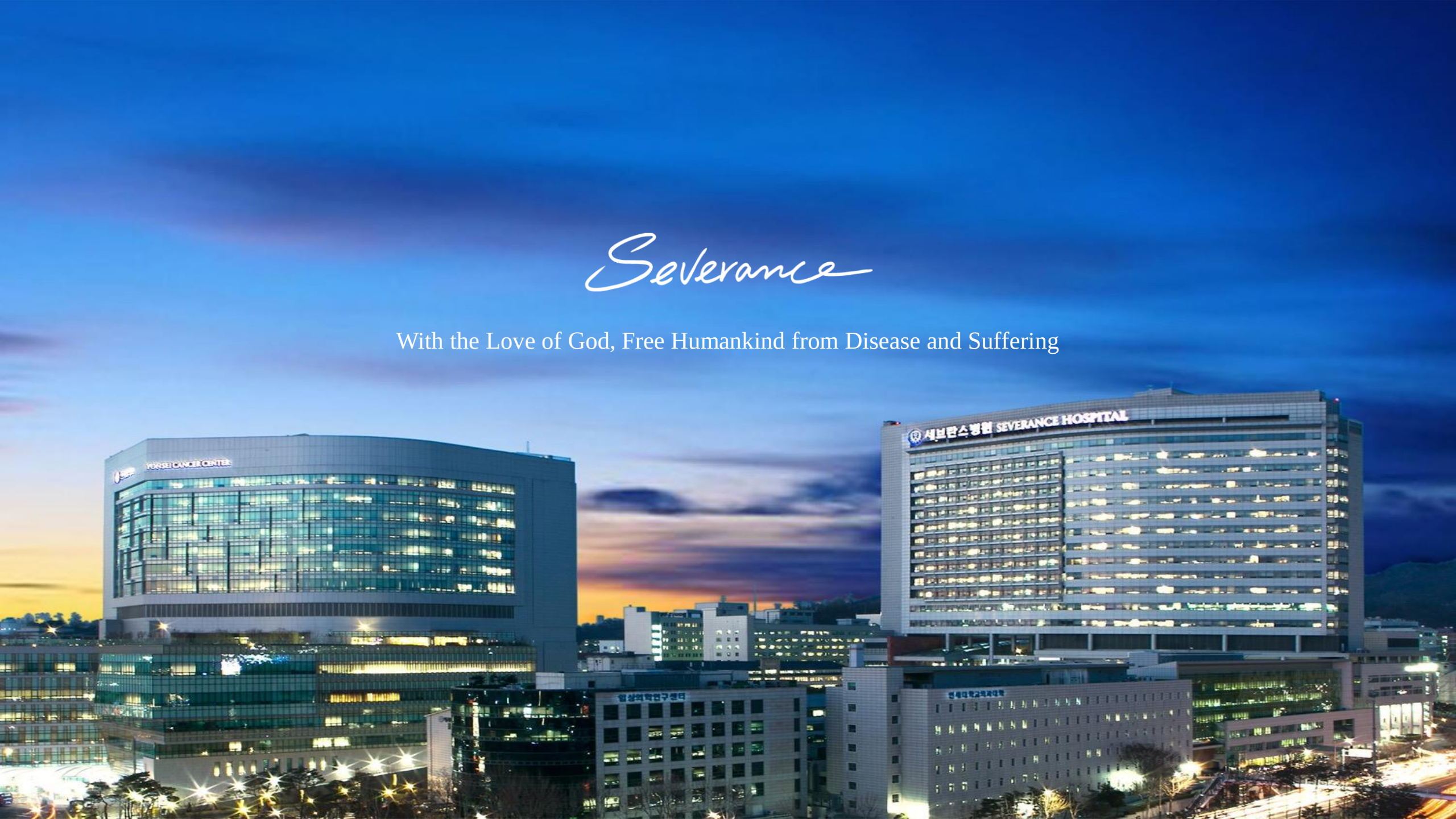
In acute respiratory distress syndrome…

The prone position should be considered at the beginning of ARDS

However, side effects d/t delayed intubation should be prevented

Physiologically, proper protocol for awake prone and IMV prone should be established. (SILI & VILI)

ARDS Guideline must take into account multifaceted factors including resource shortage


Severance
With the Love of God, Free Humankind from Disease and Suffering
YONSEI CANCER CENTER
SEVERANCE HOSPITAL