Recent advances in the ventilatory strategies for ARDS

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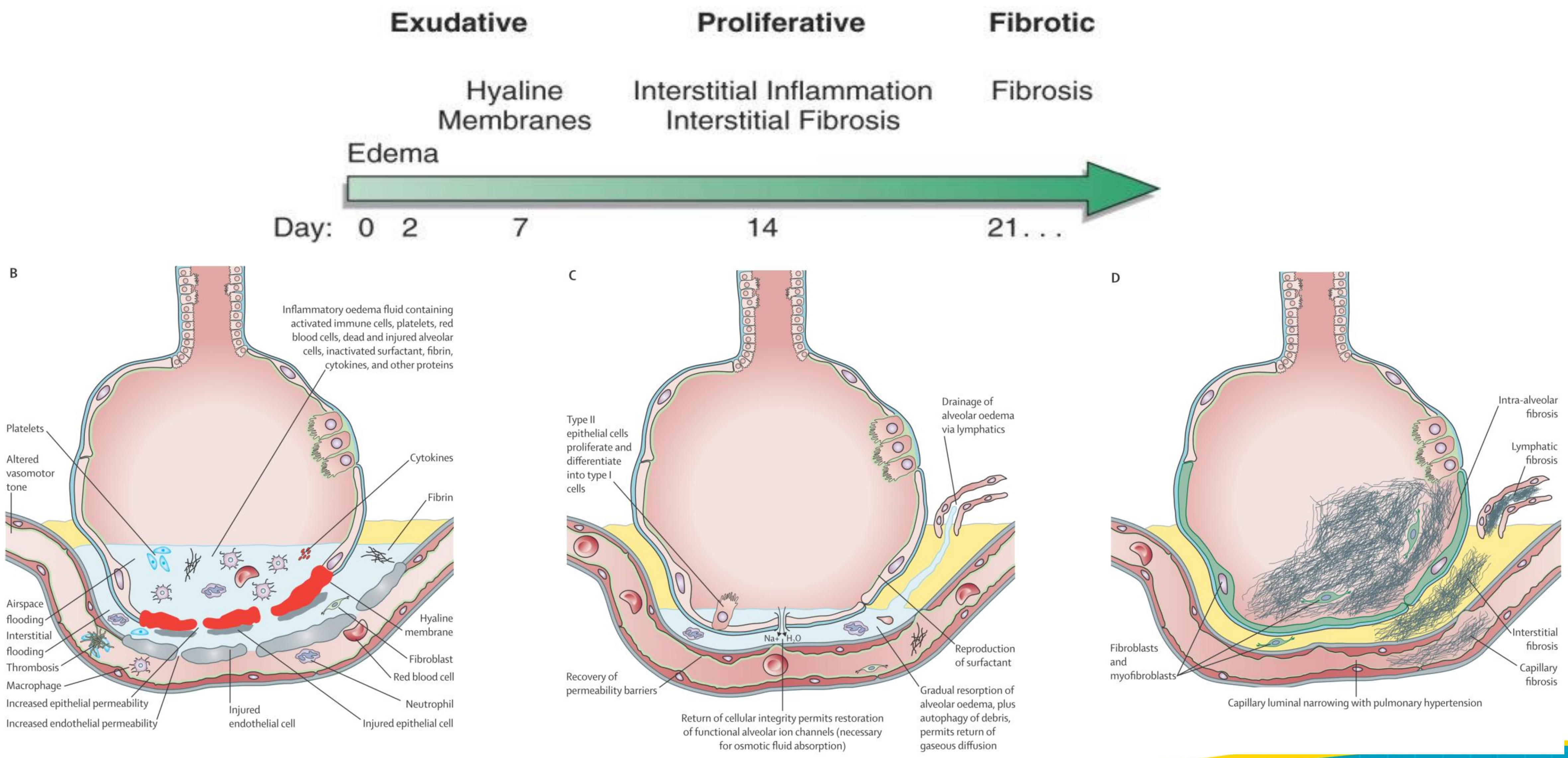
媽媽們，母親節快樂！

課程Outline

- ARDS ventilation 的核心問題
- ARDS 定義更新
- Lung-protective ventilation
- PEEP strategy
- Driving pressure and Optimal PEEP
- Recruitment maneuver and recruitability
- EIT-guided personalization
- APRV、HFOV、$ECCO_2$-R
- Take-home message

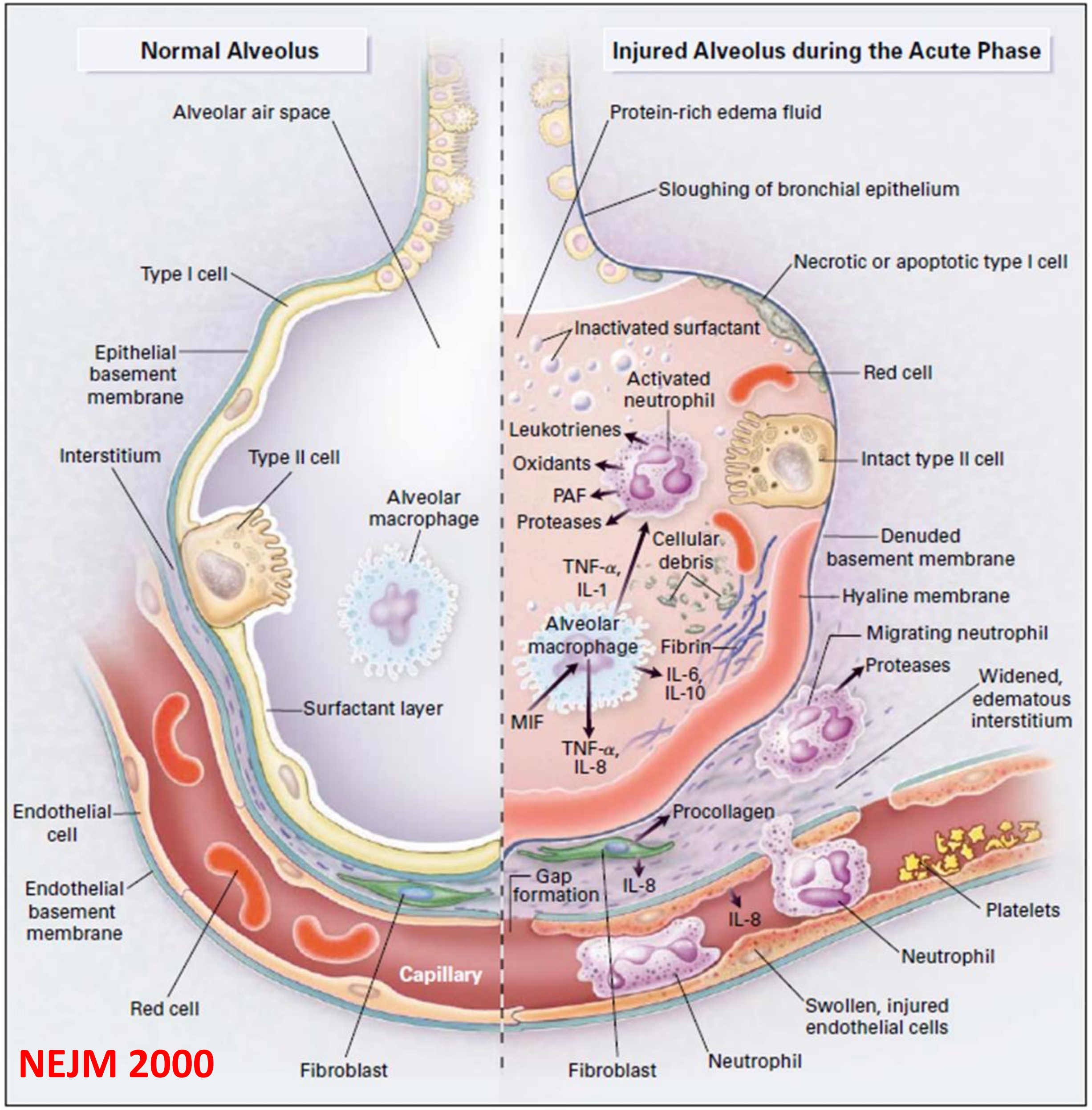
ARDS ventilation 的核心問題

ARDS的三個病程階段 (微觀層面)

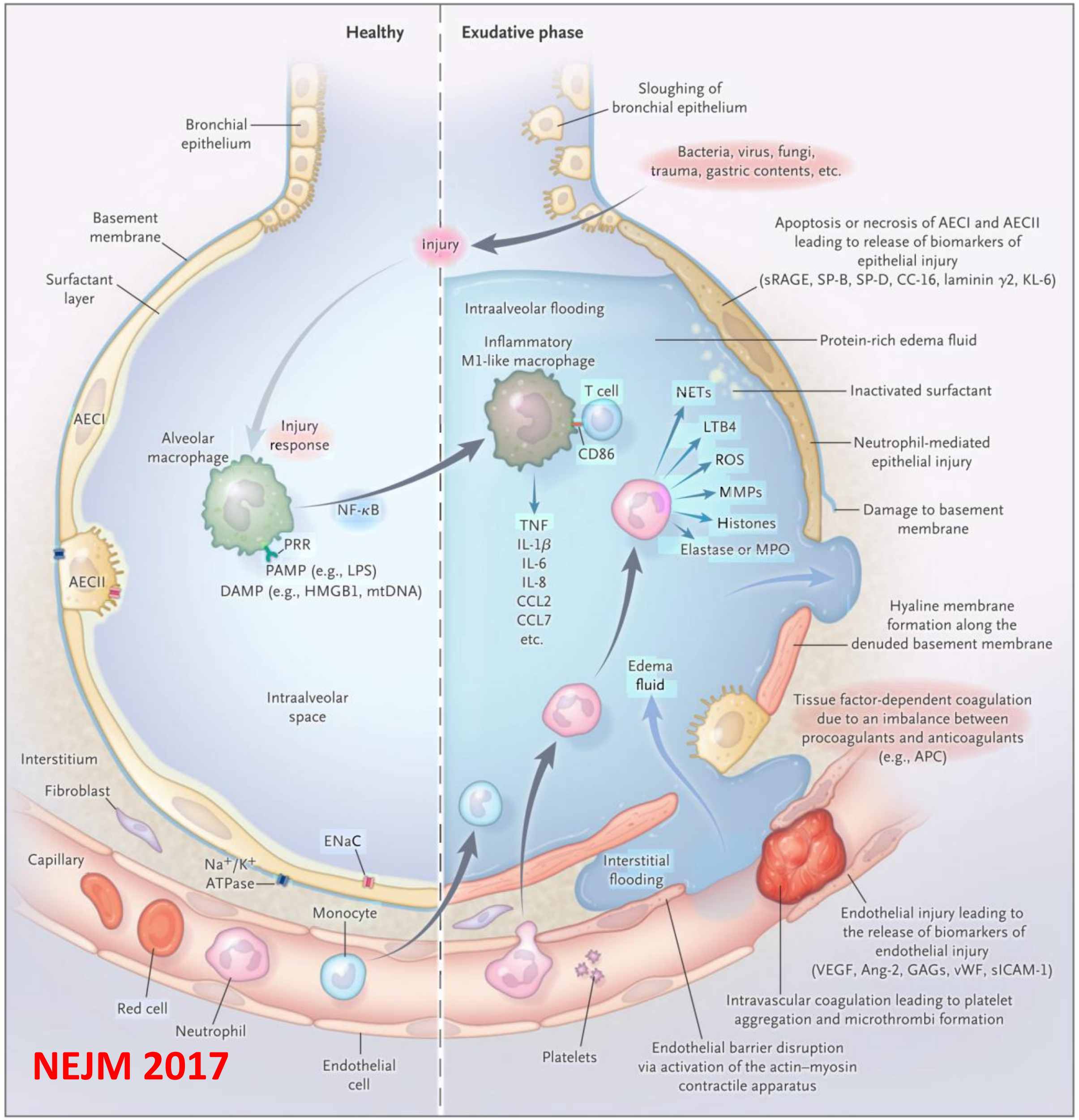


Lancet 2016; 388: 2416–30

Exudative phase in ARDS

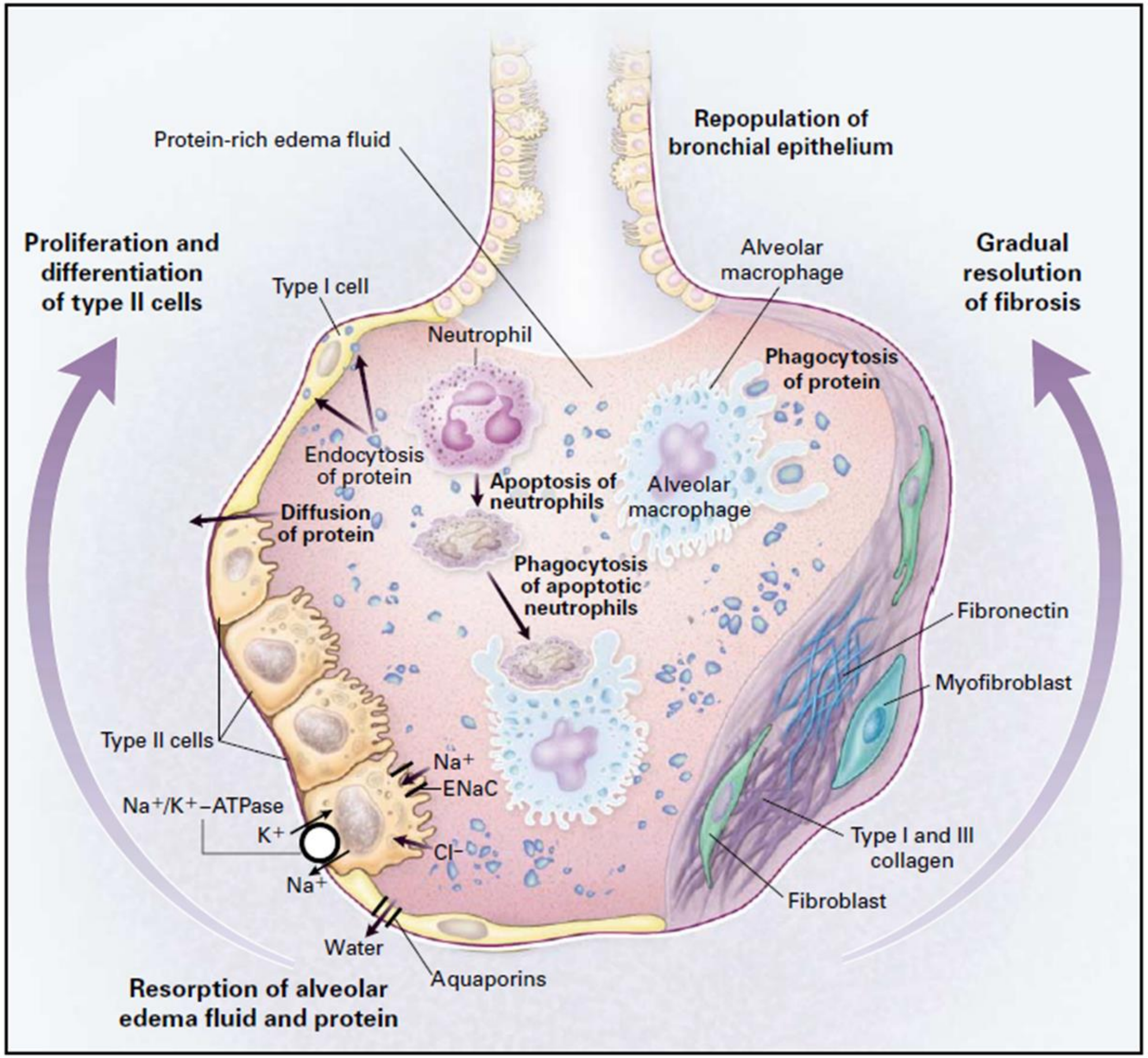


NEJM 2000

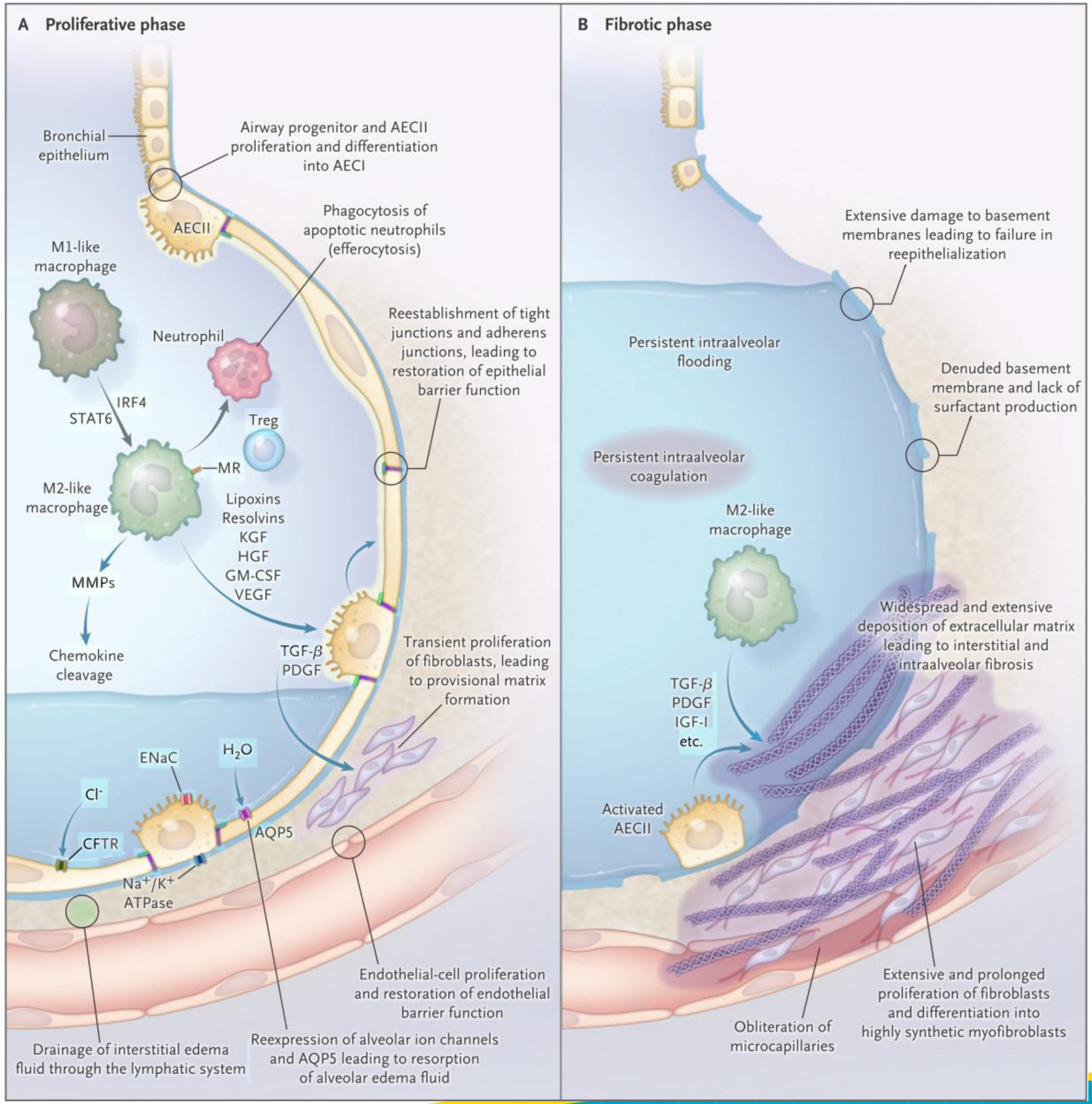


NEJM 2017

Proliferative and Fibrotic phase in ARDS



NEJM 2000



NEJM 2017

肺部狀態 (宏觀層面)

狀態

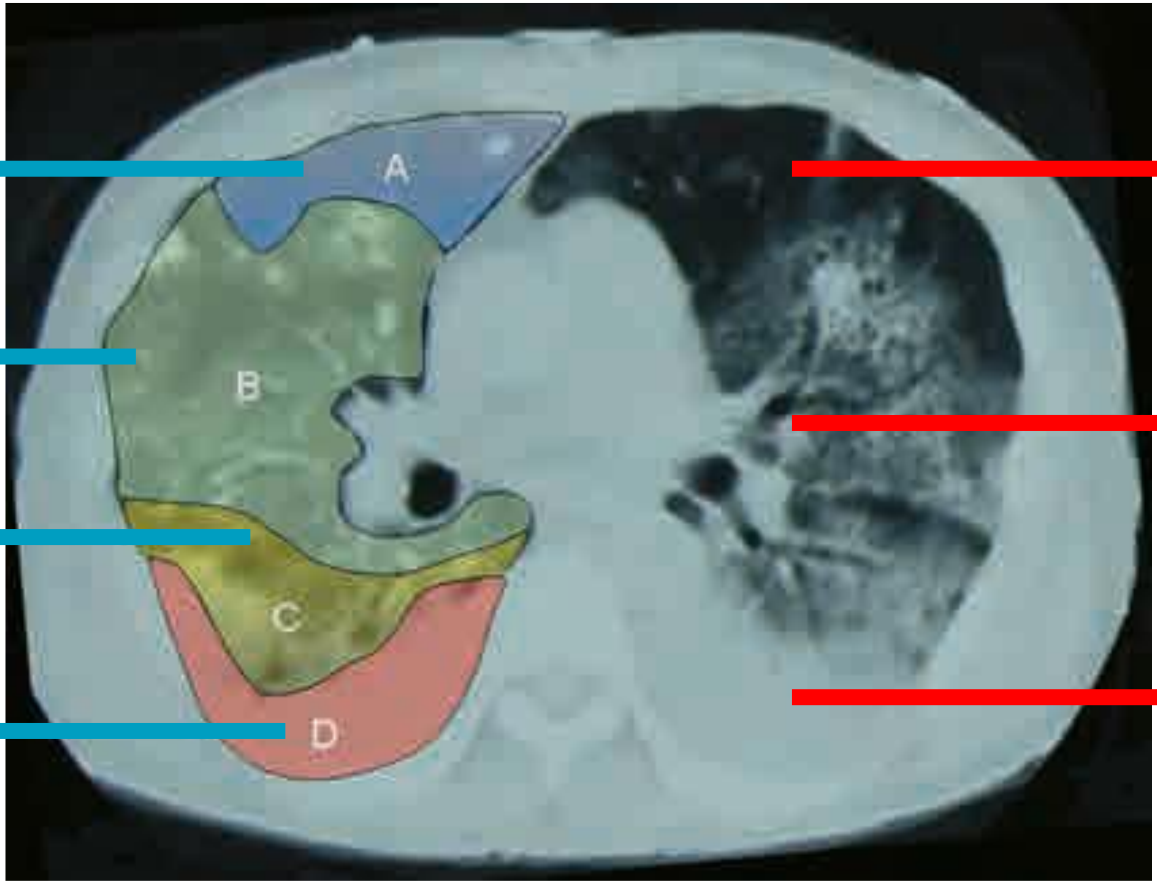
策略

Hyperinflation

Normal ventilation

Cyclical opening and closing

Collapse



Lung protection

Alveolar stabilization

Alveolar recruitment

“Open up the lung and keep the lung open”

— Lachmann, Intensive Care Medicine, 1992

“Open collapsed lung units and keep them opened”

— ART trial, JAMA, 2017

呼吸器治療ARDS的本質

- 不是設定一組漂亮參數
- 而是讓「輸入肺的機械能量」與「肺當下可承受的生物力學容量」相匹配
- ARDS ventilation is an energy-matching problem in a heterogeneous lung.

Mechanical power 機械功率

- Mechanical power : amount of energy per unit of time generated by the mechanical ventilation and released on the respiratory system, unifying the mechanical drivers of VILI, has been proposed as a determinant of the VILI pathogenesis.

$$MP(\text{J/min}) = 0.098 \times RR \times VT \times (P_{peak} - 0.5 \times \Delta P)$$

- 其中 0.098 為能量單位轉換係數。
- ΔP 代表驅動壓（Driving Pressure）。

Anesthesiology . 2016 May;124(5):1100-8.
Intensive Care Med 2016;42:1567-75.
Crit Care. 2020 May 24;24(1):246.

ARDS ventilation的終極理想目標

A. regional stress/strain distribution (病人端)先判斷肺是什麼樣的肺

- 重點不是只有 ARDS 嚴重度的P/F ratio
- 而是: baby lung 還剩多少
- recruitable lung 有多少
- 哪些區域在 cyclic opening-closing
- 哪些區域已經接近 overdistension
- 有沒有高 effort / pendelluft / RV strain

B. total energy load unit time （mechanical power）(治療端)再決定要灌進多少機械能量

- 所以不是先問「PEEP 要不要高一點？」
- 而是先問: 這個肺現在最怕的是 collapse，還是 overdistension？
- 現在最需要的是 recruitment，還是 unloading？
- 現在增加的每一分能量，是在打開肺，還是在傷害肺？

ARDS 定義更新

2012 Berlin Definition-柏林定義

表五：ARDS的柏林定義(Berlin definition)[20]

	急性呼吸窘迫症候群ARDS
發生時間	一周內發生的臨床事件或新的/惡化的呼吸症狀
胸部影像	無法完全以積液、肺塌陷或肺結節就可以解釋的雙側肺陰影(opacity)
肺水腫的來源	無法完全以心衰竭或積液過多解釋的呼吸衰竭 假如沒有ARDS危險因子的存在，就必須藉由其它的客觀方式，例如心臟超音波，來排除靜水性肺水腫(hydrostatic edema)
氧合能力	
輕度	200 mmHg < PaO_2/FiO_2 ≤ 300 mmHg + PEEP或CPAP ≧ 5 cm H_2O
中度	100 mmHg < PaO_2/FiO_2 ≤ 200 mmHg + PEEP ≧ 5 cm H_2O
重度	PaO_2/FiO_2 ≤ 100 mmHg + PEEP ≧ 5 cm H_2O

註：CPAP: Continuous Positive Airway Pressure 連續式正壓呼吸。

Berlin Definition of ARDS : 嚴重度高 死亡率高

Table 4. Predictive Validity of ARDS Definitions in the Clinical Database

	Modified AECC Definition[a]		Berlin Definition ARDS[a]		
	ALI Non-ARDS	ARDS	Mild	Moderate	Severe
No. (%) [95% CI] of patients	1001 (24) [23-25]	3187 (76) [75-77]	819 (22) [21-24]	1820 (50) [48-51]	1031 (28) [27-30]
Progression in 7 d from mild, No. (%) [95% CI]		336 (34) [31-37]		234 (29) [26-32]	33 (4) [3-6]
Progression in 7 d from moderate, No. (%) [95% CI]					230 (13) [11-14]
Mortality, No. (%) [95% CI][b]	263 (26) [23-29]	1173 (37) [35-38]	220 (27) [24-30]	575 (32) [29-34]	461 (45) [42-48]
Ventilator-free days, median (IQR)[b]	20 (2-25)	12 (0-22)	20 (1-25)	16 (0-23)	1 (0-20)
Duration of mechanical ventilation in survivors, median (IQR), d[b]	5 (2-10)	7 (4-14)	5 (2-11)	7 (4-14)	9 (5-17)

Abbreviations: AECC, American-European Consensus Conference; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; FIO_2, fraction of inspired oxygen; IQR, interquartile range; PaO_2, arterial partial pressure of oxygen; PEEP, positive end-expiratory pressure.

[a] The definitions are the following for ALI non-ARDS (200 mm Hg $< PaO_2/FIO_2 \leq$ 300 mm Hg, regardless of PEEP), ARDS ($PaO_2/FIO_2 \leq$ 200 mm Hg, regardless of PEEP), mild Berlin Definition (200 mm Hg $< PaO_2/FIO_2 \leq$ 300 mm Hg with PEEP $\geq$5 cm H_2O), moderate Berlin Definition (100 mm Hg $< PaO_2/FIO_2 \leq$ 200 mm Hg with PEEP $\geq$5 cm H_2O), and severe Berlin Definition ($PaO_2/FIO_2 \leq$ 100 mm Hg with PEEP $\geq$5 cm H_2O).

[b] Comparisons of mortality, ventilator-free days, and duration of mechanical ventilation in survivors across categories of modified AECC (ALI non-ARDS and ARDS) and across

ESICM vs. ATS guidelines in 2023

European Society of Intensive Care Medicine

American Thoracic Society

CONFERENCE REPORTS AND EXPERT PANEL

ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies

AMERICAN THORACIC SOCIETY DOCUMENTS

An Update on Management of Adult Patients with Acute Respiratory Distress Syndrome

An Official American Thoracic Society Clinical Practice Guideline

2024年新定義 - 情境更具體

A New Global Definition of Acute Respiratory Distress Syndrome

Several developments after Berlin definition in 2012:

- Use of high-flow nasal oxygenation (**HFNO**)
- Expansion use of pulse oximeter in place of ABG (**S/F ratio**)
- Use of **ultrasound** for chest image
- Need for applicability in **resources-limited settings**

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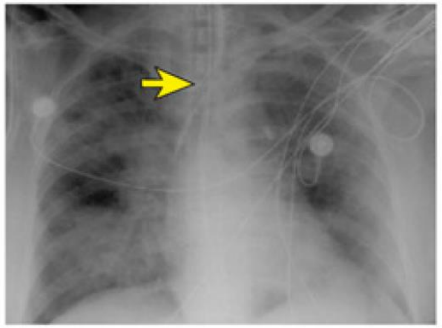
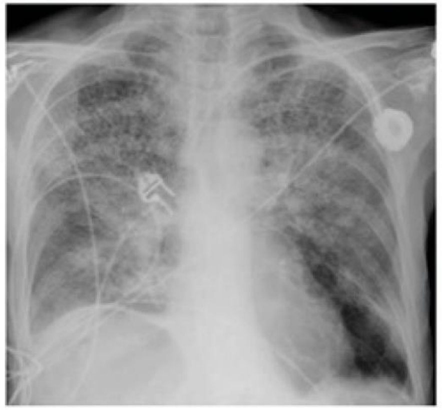
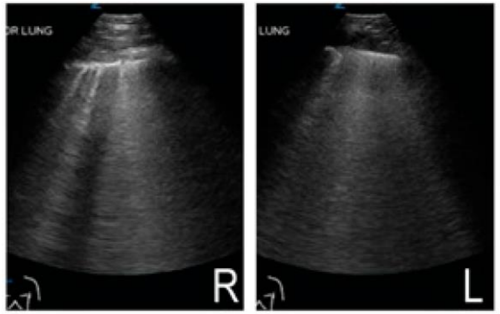
Patient Description	Imaging	Oxygenation	ARDS Categories
 68-year-old M with abdominal sepsis, septic shock, and acute hypoxemic respiratory failure		Mechanically ventilated Fi_{O_2} 0.5 Pa_{O_2} 75 P/F = 150 mm Hg	**Intubated ARDS** Severity: Moderate *Typical patient included in prior Berlin definition*
 54-year-old F with history of breast cancer, COVID-19 pneumonia, and worsening shortness of breath for the past 6 days		High-flow nasal oxygen HFNO 40L/min Fi_{O_2} 0.80 Sp_{O_2} 91% S/F = 114	**Nonintubated ARDS** *New category in Global definition*
 39-year-old F with abdominal sepsis and gram-negative bacteremia in a small under-resourced hospital without blood gases, radiography, or mechanical ventilation		Supplemental oxygen by face mask at 15L/min Fi_{O_2} 0.6 Sp_{O_2} 85% S/F = 142	**ARDS in resource-limited settings** *New category in global definition, consistent with the Kigali modification*

Criteria applicable to specific etiologies of ARDS

	Non-intubated ARDS	Intubated ARDS	Resource-limited settings
Oxygen and respiratory support requirement	P/F $\leq$ 300 or S/F $\leq$ 315	Mild: 200 < P/F $\leq$ 300 or 235 $\leq$ S/F $\leq$ 315	S/F $\leq$ 315
	HFNC $\geq$ 30L/min or	Moderate: 100 < P/F $\leq$ 200 or 148 < S/F $\leq$ 235	Neither NIV nor a minimum oxygen flow rate are required for diagnosis
	NIV (PEEP $\geq$ 5 cmH2O)	Severe: P/F $\leq$ 100 or S/F $\leq$ 148	

*apply S/F $\leq$ 97% in all non-intubated criteria
*estimated FiO2 = ambient FiO2 (e.g., 0.21) + 0.03 X O2 flow rate (L/min) for ***resource limited settings***
***Rice linear equation** to define cutoff values (*Comparison of the SpO2/FIO2 ratio and the PaO2/FIO2 ratio in patients with acute lung injury or ARDS. Chest 2007;132: 410 – 417.*)

S/F = 64 + 0.84 x (P/F)

ARDS的2023年最新指引又有哪些重點? (ESICM)

	2017	2023	CHANGE IN RECOMMENDATION	COMMENTS
Definition			★	No comparison available as the **2017** guidelines did not include a Definition domain.
Phenotypes			★	No comparison available as the **2017** guidelines did not include an ARDS Phenotype domain.
High flow nasal oxygen			★	No comparison available as the **2017** guidelines did not include recommendations on high flow nasal oxygen.
Non-invasive ventilation			★	No comparison available as the **2017** guideline did not include recommendations on non-invasive ventilation.
Tidal volume				In agreement with the use of low tidal volume strategies. **2023** guidelines extend this recommendation to patients with COVID-19.
Positive end-expiratory pressure				**2017:** suggest that adult patients with moderate or severe ARDS receive higher rather than lower levels of PEEP. **2023:** analysis of data does not allow to make a recommendation for or against higher PEEP strategy.
Recruitment maneuvers				**2017:** suggest that adult patients with ARDS receive RMs. **2023:** recommend against RMs due to increased mortality and risks.

Oscillatory ventilation	Available	Not available	Not considered	**2017:** recommend that HFOV not be used routinely in patients with moderate or severe ARDS. **2023:** not examined given the absence of studies since 2017 and the lack of use of HFVO in adults.
Prone position	Available	Available	No change	Agreement with the use of prone position in ARDS. Additions in **2023** are the use of awake proning and the use in COVID-19.
Neuromuscular blockade	Not available	Available	New recommendation/domain since 2017	No comparison available as the **2017** guidelines did not include recommendations on neuromuscular blockade.
Extracorporeal membrane oxygenation	Available	Available	Change in recommendation	**2017:** additional evidence is necessary to make a definitive recommendation. **2023:** recommend ECMO in patients with severe ARDS.
Extracorporeal CO_2 removal	Not available	Available	New recommendation/domain since 2017	No comparison available as the **2017** guidelines did not include recommendations on extracorporeal CO_2 removal. **2023** guidelines recommend against $ECCO_2R$ in ARDS.

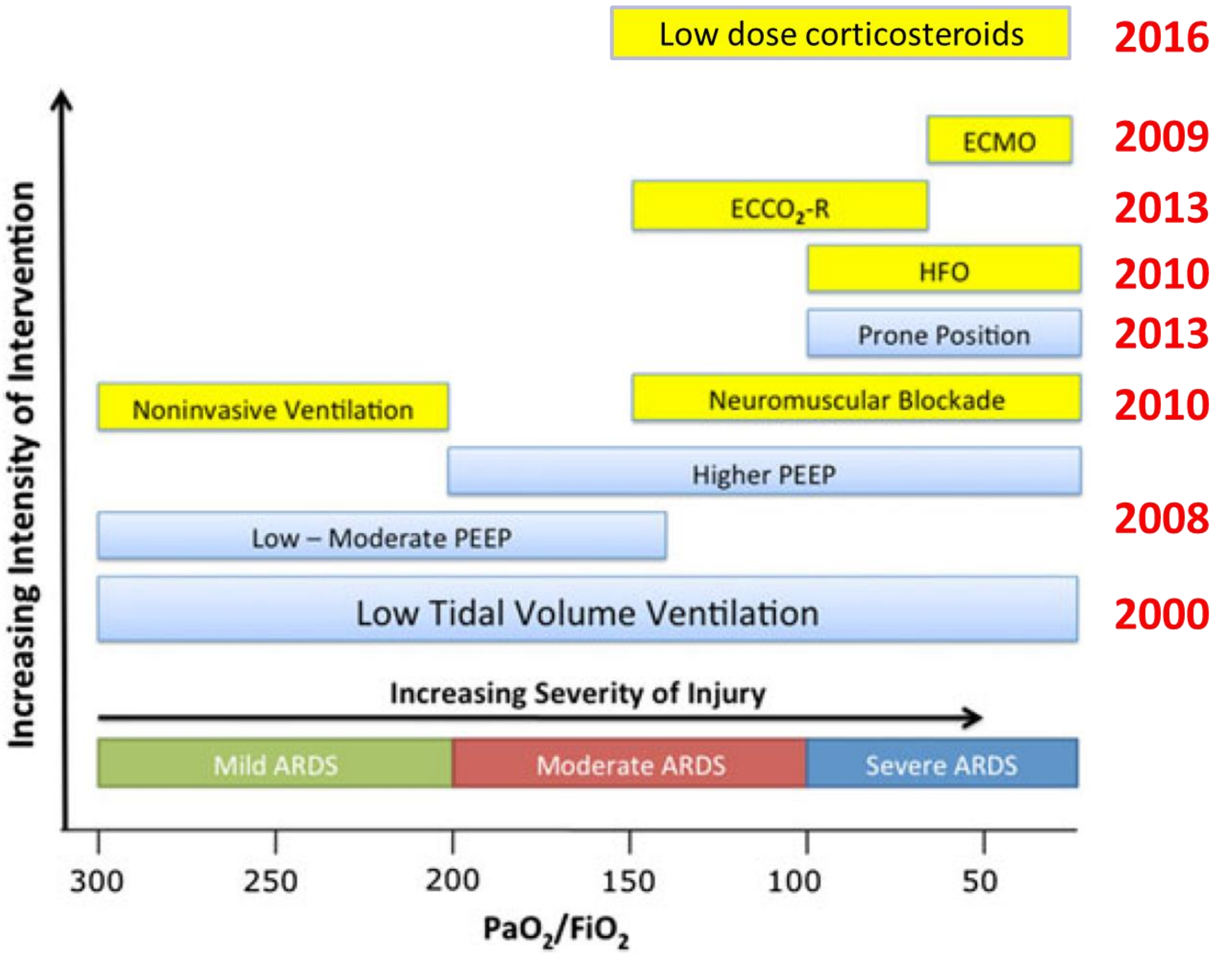
AVAILABLE — NOT AVAILABLE — NEW RECOMMENDATION /DOMAIN SINCE 2017 — CHANGE IN RECOMMENDATION — NO CHANGE — NOT CONSIDERED

ARDS: acute respiratory distress syndrome; **COVID-19:** coronavirus disease 2019; **$ECCO_2R$:** Extracorporeal CO_2 Removal; **ECMO:** extracorporeal membrane oxygenation; **HFOV:** High-frequency oscillatory ventilation; **PEEP:** positive end-expiratory pressure; **RM:** recruitment maneuver

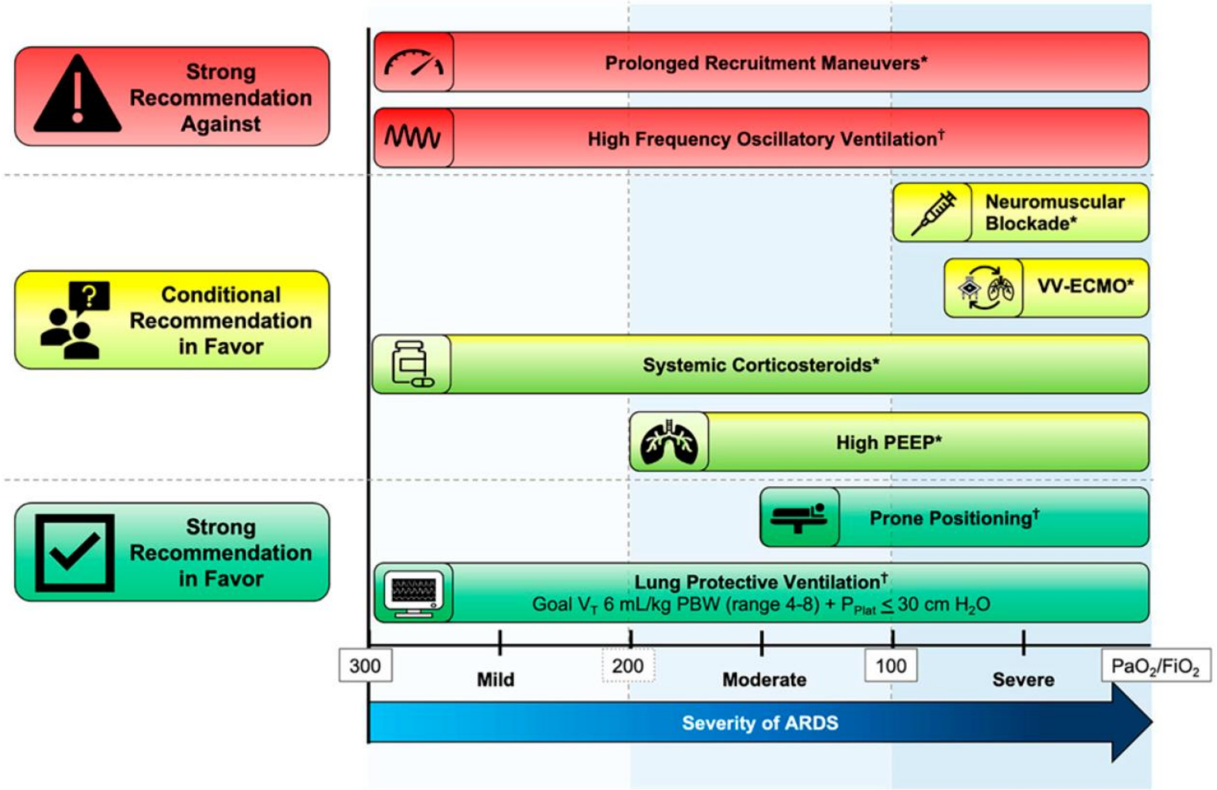
Phenotype, Sub-phenotype, and Endotype in ARDS (adapted from the ESICM 2023 ARDS guideline definitions) 可當作personalized treatment的參考

名稱	定義	重點	ARDS 例子
Phenotype	臨床上可觀察到的一組特徵，由基因與環境交互作用後呈現的外顯表現	看起來是什麼樣的病	ARDS 本身就是一種 phenotype：急性、瀰漫性、發炎性肺損傷，表現為低氧、雙側浸潤、肺順應性下降
Sub-phenotype	在同一 phenotype 內，可依一組可觀察、可測量、且可重現的特徵區分出的亞群	同一種 ARDS，其實不是同一種病人	Hyper-inflammatory vs hypo-inflammatory；focal vs diffuse morphology；recruitable vs non-recruitable lung
Endotype	具有不同功能性或病理生物機轉的 sub-phenotype，且理想上對特定治療有不同反應	不只長得不同，機轉也不同	例如 hyper-inflammatory ARDS 若被證實有特定發炎路徑活化，且對 PEEP、fluid strategy 或抗發炎治療反應不同，才更接近真正的 endotype

指引建議 ARDS treatment: 2012 vs. 2024



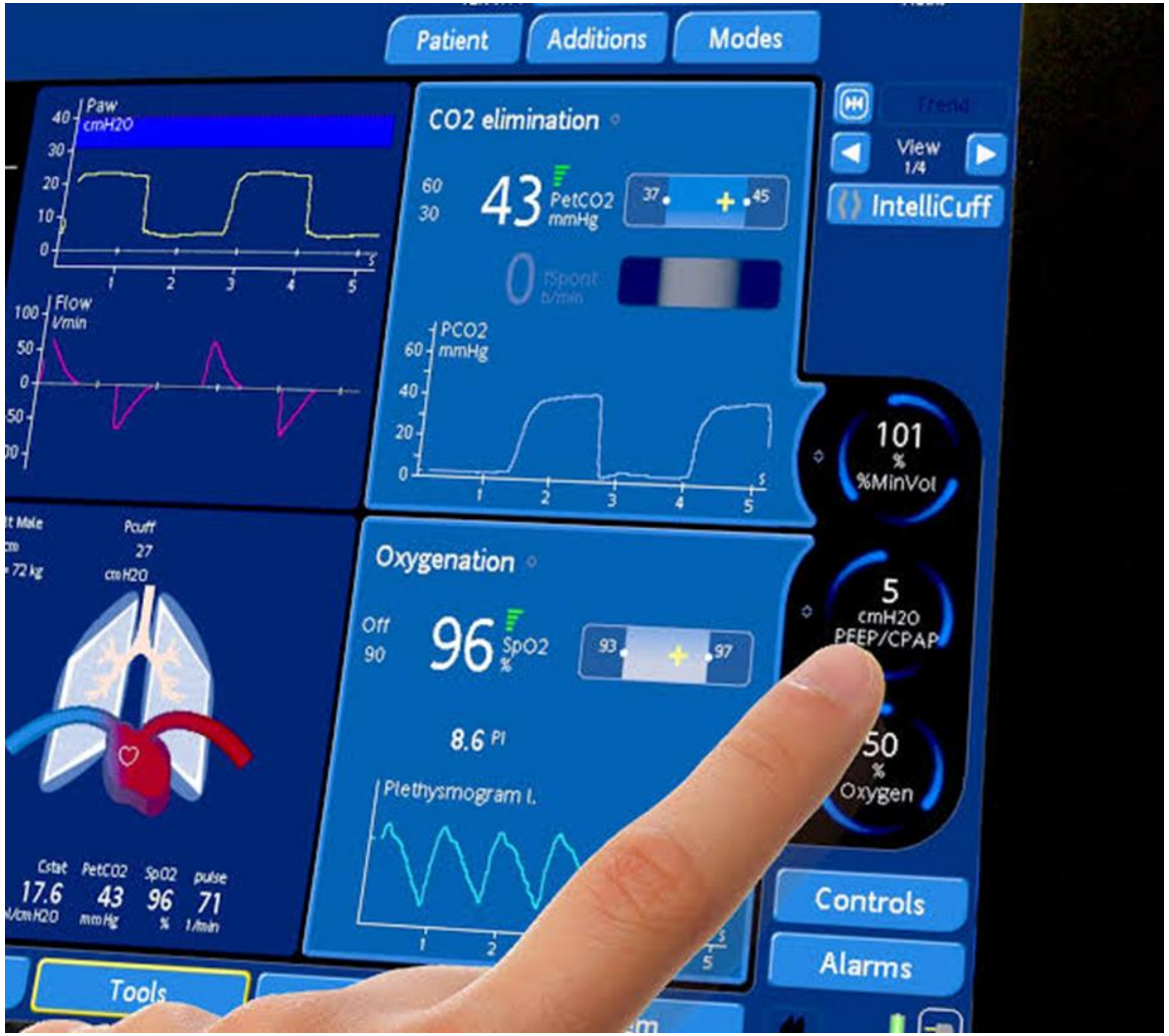
Intensive Care Med 2012; 38:1573-82



Am J Respir Crit Care Med Vol 209, Iss 1, pp 24–36, Jan 1, 2024

今天單純討論ARDS呼吸器治療策略

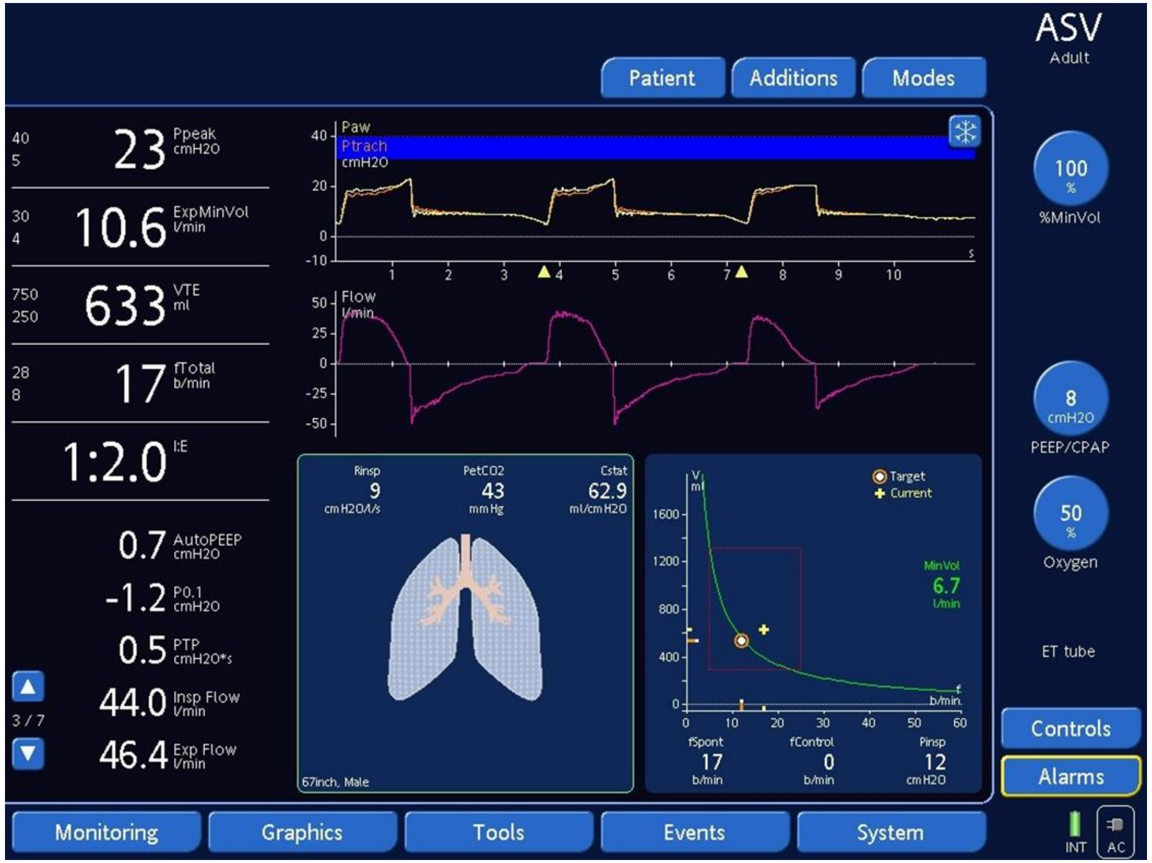
- Oxygenation
  - ✓FiO2
  - ✓PEEP
- Ventilation
  - ✓Tidal volume
  - ✓Respiratory rate
  - ✓Minute ventilation
- Monitoring and alarm system



Lung-protective ventilation

ARDS ventilatory strategy: 一般性目標

- Keep pH > 7.3
  - $PaCO_2$ < 50 mmHg
  - PaO_2 > 55 mmHg, SpO_2 > 88%
- To decrease work of breathing
- Lung protection
  - Keep plateau pressure < 30 cmH_2O
  - Keep driving pressure ≤ 14 cmH_2O



Better Survival in Lower Tidal Volume (6 vs 12 ml/kg)

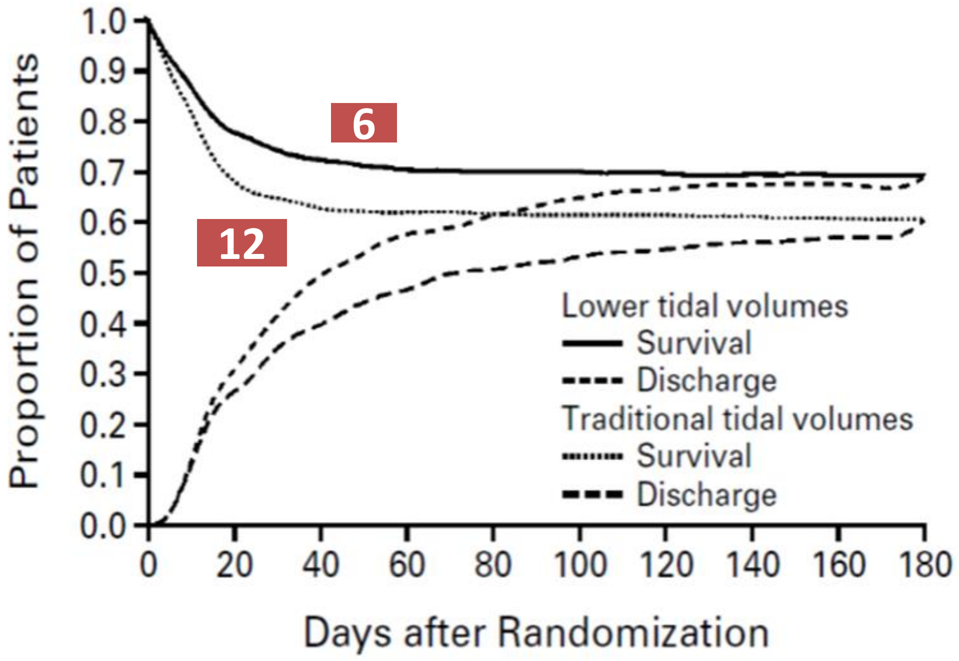


TABLE 4. MAIN OUTCOME VARIABLES.*

VARIABLE	6 GROUP RECEIVING LOWER TIDAL VOLUMES	12 GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	P VALUE
Death before discharge home and breathing without assistance (%)	31.0	39.8	0.007
Breathing without assistance by day 28 (%)	65.7	55.0	<0.001
No. of ventilator-free days, days 1 to 28	12±11	10±11	0.007
Barotrauma, days 1 to 28 (%)	10	11	0.43
No. of days without failure of nonpulmonary organs or systems, days 1 to 28	15±11	12±11	0.006

NEJM 2000; 342:1301-1308

LTV Mortality Meta-analysis in 2017 and 2019

Favors LTV

Study or Subgroup	Low tidal volume Events	Low tidal volume Total	No low tidal volume Events	No low tidal volume Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Open Lung							
Amato 1998	11	29	17	24	9.0%	0.54 [0.31, 0.91]	1998
Villar 2006	17	50	25	45	10.6%	0.61 [0.38, 0.98]	2006
Subtotal (95% CI)		**79**		**69**	**19.6%**	**0.58 [0.41, 0.82]**	
Total events	28		42				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.14$, df = 1 (P = 0.71); $I^2 = 0\%$							
Test for overall effect: Z = 3.07 (P = 0.002)							
No Open Lung							
Wu 1998	12	32	15	24	8.7%	0.60 [0.35, 1.03]	1998
Brochard 1998	27	58	22	58	11.7%	1.23 [0.80, 1.89]	1998
Brower 1999	13	26	12	26	8.3%	1.08 [0.62, 1.91]	1999
East 1999	36	103	32	97	13.0%	1.06 [0.72, 1.56]	1999
ARDSNet 2000	133	427	174	425	21.4%	0.76 [0.63, 0.91]	2000
Orme 2003	15	60	27	60	9.3%	0.56 [0.33, 0.93]	2003
Sun 2009	16	43	14	42	8.0%	1.12 [0.63, 1.99]	2009
Subtotal (95% CI)		**749**		**732**	**80.4%**	**0.87 [0.70, 1.08]**	
Total events	252		296				
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 11.12$, df = 6 (P = 0.08); $I^2 = 46\%$							
Test for overall effect: Z = 1.26 (P = 0.21)							
Total (95% CI)		**828**		**801**	**100.0%**	**0.80 [0.66, 0.98]**	
Total events	280		338				
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 14.93$, df = 8 (P = 0.06); $I^2 = 46\%$							
Test for overall effect: Z = 2.18 (P = 0.03)							
Test for subgroup differences: $Chi^2 = 3.82$, df = 1 (P = 0.05); $I^2 = 73.8\%$							

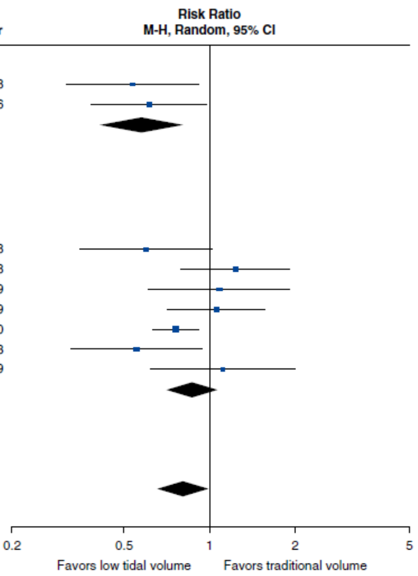


Figure 2. Analysis of mortality for low tidal volume or pressure-limited ventilation versus control strategy. Study details: Amato 1998 (20), 28-day mortality; ARDSNet 2000 (29), hospital mortality; Brochard 1998 (33), 60-day mortality; Brower 1999 (34), hospital mortality; East 1999 (35), hospital mortality; Orme 2003 (36), hospital mortality; Sun 2009 (38), 28-day mortality; Villar 2006 (21), hospital mortality; and Wu 1998 (37), hospital mortality. CI = confidence interval; df = degrees of freedom; Events = n with mortality outcome; I^2 = heterogeneity statistic; M-H = Mantel-Haenszel method; Total = total N in each study arm.

Favors LTV

Study or Subgroup	LTV Events	LTV Total	HTV Events	HTV Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 60 - day						
Brochard 1998	27	58	22	58	9.5%	1.23 [0.80, 1.89]
Subtotal (95% CI)		**58**		**58**	**9.5%**	**1.23 [0.80, 1.89]**
Total events	27		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.93 (P = 0.35)						
2.1.2 Hospital						
ARDS Network 2000	133	432	170	429	73.3%	0.78 [0.65, 0.93]
Brower 1999	13	26	12	26	5.2%	1.08 [0.62, 1.91]
Stewart 1998	30	60	28	60	12.0%	1.07 [0.74, 1.55]
Subtotal (95% CI)		**518**		**515**	**90.5%**	**0.83 [0.71, 0.98]**
Total events	176		210			
Heterogeneity: $Chi^2 = 3.15$, df = 2 (P = 0.21); $I^2 = 37\%$						
Test for overall effect: Z = 2.26 (P = 0.02)						
Total (95% CI)		**576**		**573**	**100.0%**	**0.87 [0.75, 1.01]**
Total events	203		232			
Heterogeneity: $Chi^2 = 5.71$, df = 3 (P = 0.13); $I^2 = 48\%$						
Test for overall effect: Z = 1.83 (P = 0.07)						
Test for subgroup differences: $Chi^2 = 2.74$, df = 1 (P = 0.10), $I^2 = 63.6\%$						

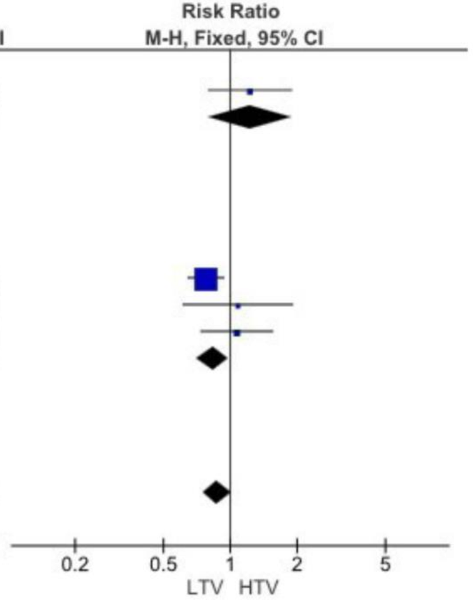


Figure 1 Sixty-day and hospital mortality comparing LTV and HTV mechanical ventilation in adult patients with ARDS. ARDS, acute respiratory distress syndrome; HTV, higher tidal volume; LTV, lower tidal volume.

Ann Am ThoracSoc. 2017 Oct;14(Supplement_4):S271-S279.

BMJ Open Resp Res 2019;6:e000420

ESICM 2023指引: LTV 死亡率證據統計上不顯著，但仍是保護性通氣基石

Table 1 Summary of studies comparing low vs high tidal volume ventilation

強建議使用LTV的理由不再是降低mortality，而是基於生理學上的高保護性

	Vt (ml/kg)		Paw Limit (cmH_2O)		Notes
	Interventional Arm	Control Arm	Interventional Arm	Control Arm	
ARDS Net [99]	4–8 PBW	12 PBW	Pplat ≤ 30	Pplat ≤ 50	PP allowed – Explicit weaning protocol
Orme et al. [100]	4–8 PBW	10–15 PBW	Pplat < 40	Pplat < 70	Explicit sedation and weaning protocol

Vt Tidal Volume, *Paw* Airway Pressure, *PBW* Predicted Body Weight, *ABW* Adjusted Body Weight, *PIP* Peak airway pressure, *Pplat* Plateu airway pressure, *ΔP* Driving Pressure, *RM* Recruitment Manouver, *PP* Prone Positioning

Recommendation 5.1

We **recommend** the use of low tidal volume ventilation strategies (i.e., 4–8 ml/kg PBW), compared to larger tidal volumes (traditionally used to normalize blood gases), to reduce mortality in patients with ARDS not due to COVID-19.
Strong recommendation based on expert opinion despite lack of statistical significance; high level of evidence.

This recommendation applies also to ARDS from COVID-19.
Strong recommendation; moderate level of evidence for indirectness.

ESICM ARDS guideline 2023

- Mortality: RR 0.96 95% CI 0.72-1.28
- Barotrauma: RR 0.8 95% CI 0.44-1.46
- Ventilator-free days: 2.25+ 95% CI -0.91-5.41

The primary analysis concerning mortality included three trials [95, 97, 99]

Ultra-low tidal volume ventilation for COVID-19-related ARDS

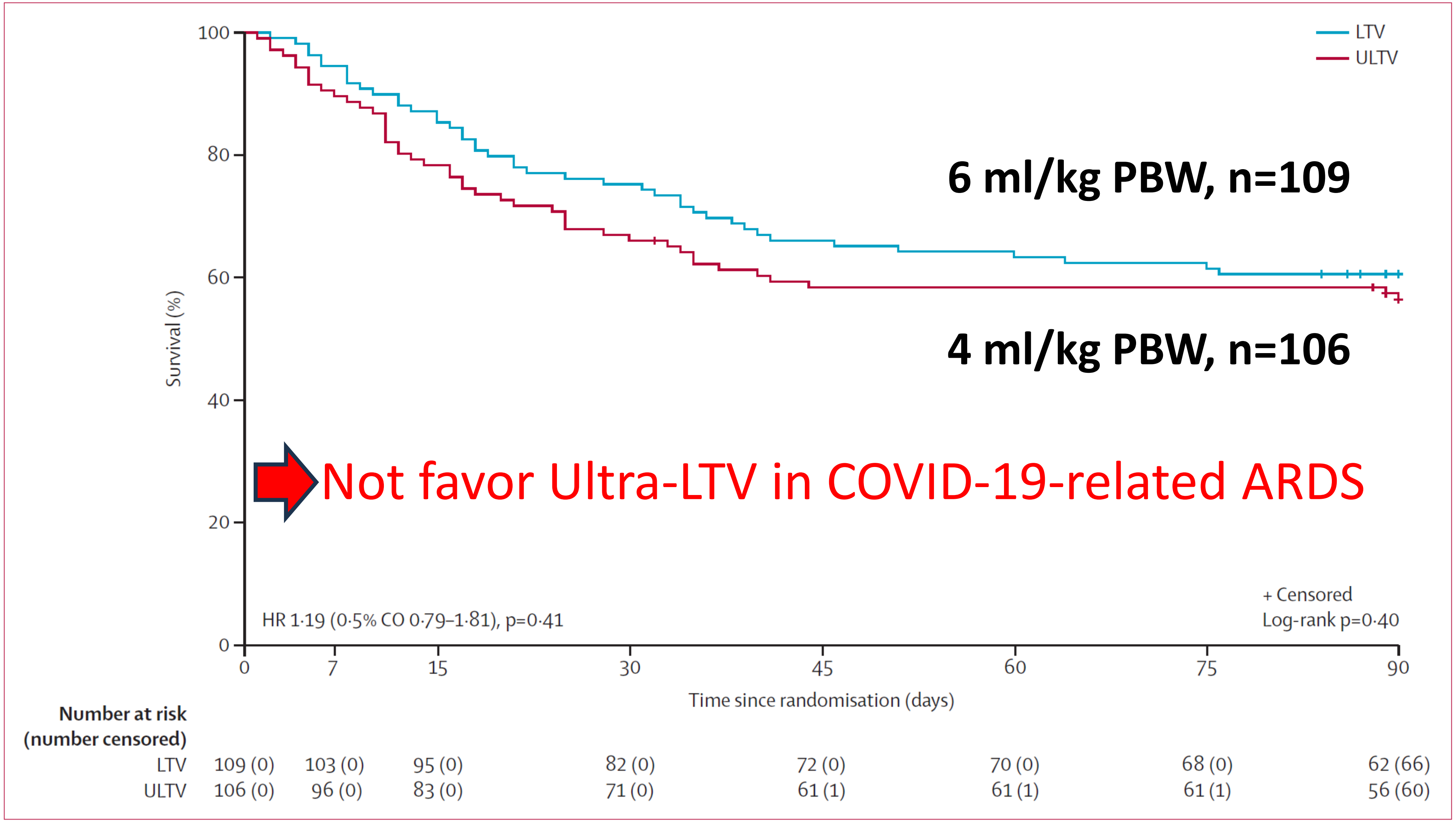


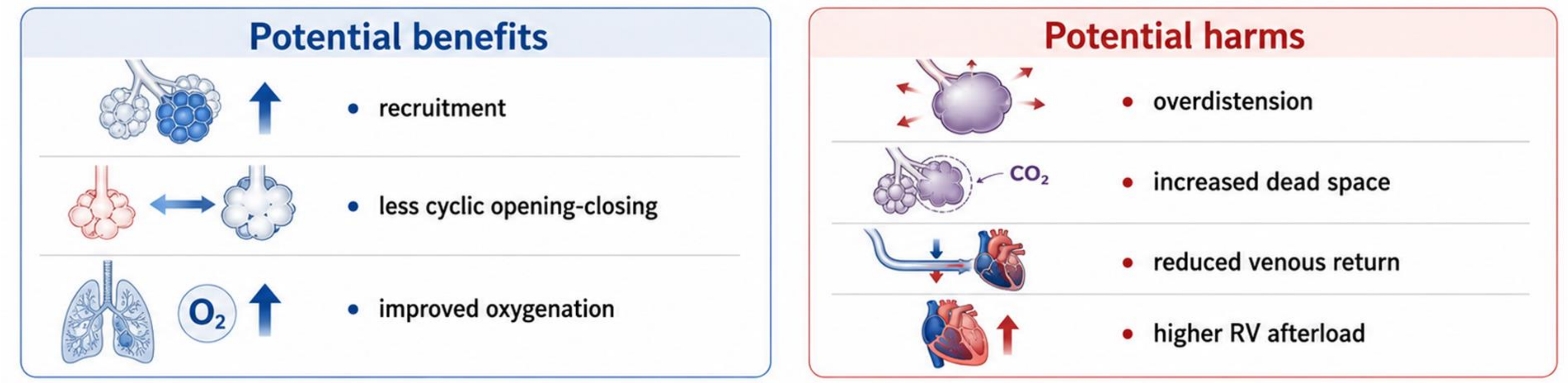
***Figure* 3: Kaplan-Meier survival analysis until day 90 in all participants who were randomly assigned**
Day 0 denotes study inclusion. LTV=low V_T ventilation. ULTV=ultra-low V_T ventilation. V_T=tidal volume.

Lancet Respir Med 2023;11: 991–1002

PEEP strategy:

1. Higher PEEP vs Lower PEEP
2. High PEEP + RM
3. PEEP titrated to Pplt 28-30

PEEP remains one of the hardest ARDS decisions



- The effect of the same PEEP level depends on recruitability, chest wall mechanics, and hemodynamic reserve
- The modern PEEP question is not 'how much oxygenation gain?', but 'at what mechanical and circulatory cost?'

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 22, 2004 VOL. 351 NO. 4

ALVEOLI trial, NEJM 2004 (1)

Higher versus Lower Positive End-Expiratory Pressures in Patients with the Acute Respiratory Distress Syndrome

Higher PEEP vs. Lower PEEP

First 80 patients at higher PEEP group, during the first four days after randomization

Recruitment maneuver CPAP 35-40 cmH_2O x 30 secs

The subsequent mean increase in arterial oxygenation was small and transient. Then D/C RM

Table 1. **Summary of Ventilator Procedures in the Lower- and Higher-PEEP Groups.***

Procedure	Value
Ventilator mode	Volume assist/control
Tidal-volume goal	6 ml/kg of predicted body weight
Plateau-pressure goal	≤30 cm of water
Ventilator rate and pH goal	6–35, adjusted to achieve arterial pH ≥7.30 if possible
Inspiration:expiration time	1:1–1:3
Oxygenation goal	
PaO_2	55–80 mm Hg
SpO_2	88–95%
Weaning	Weaning attempted by means of pressure support when level of arterial oxygenation acceptable with PEEP ≤8 cm of water and FiO_2 ≤0.40
Allowable combinations of PEEP and FiO_2†	

Lower-PEEP group														
FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18–24
Higher-PEEP group (before protocol changed to use higher levels of PEEP)														
FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0	
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22–24	
Higher-PEEP group (after protocol changed to use higher levels of PEEP)														
FiO_2	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0				
PEEP	12	14	14	16	16	18	20	22	22	22–24				

ALVEOLI trial, NEJM 2004 (2): Higher PEEP vs. Lower PEEP

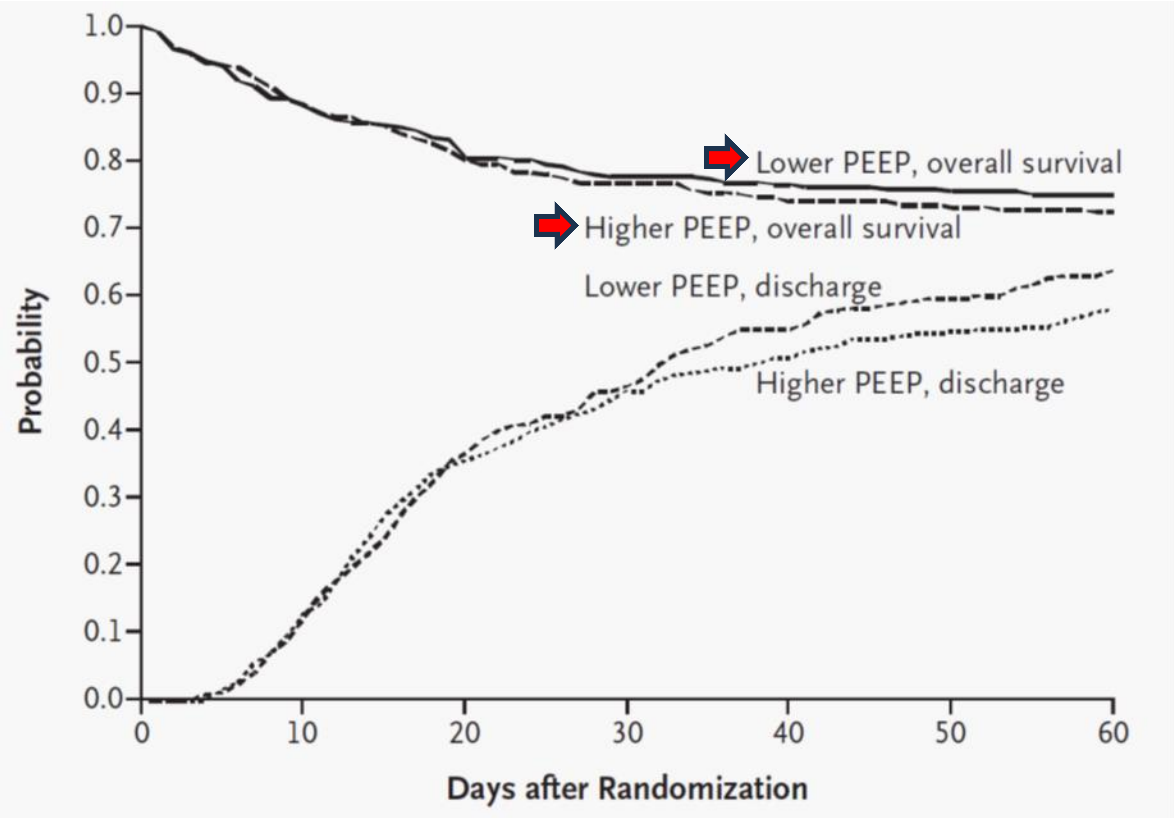


Table 4. Main Outcome Variables.*

Outcome	Lower-PEEP Group	Higher-PEEP Group	P Value
Death before discharge home (%)†			
Unadjusted	24.9	27.5	0.48
Adjusted for differences in baseline covariates	27.5	25.1	0.47
Breathing without assistance by day 28 (%)	72.8	72.3	0.89
No. of ventilator-free days from day 1 to day 28‡	14.5±10.4	13.8±10.6	0.50
No. of days not spent in intensive care unit from day 1 to day 28	12.2±10.4	12.3±10.3	0.83
Barotrauma (%)§	10	11	0.51
No. of days without failure of circulatory, coagulation, hepatic, and renal organs from day 1 to day 28	16±11	16±11	0.82

clinical outcomes are similar whether lower or higher PEEP levels are used

N EnglJ Med. 2004 Jul 22;351(4):327-36.

LOVS trial, JAMA 2008 (1) : High PEEP + RM

Ventilation Strategy Using Low Tidal Volumes, Recruitment Maneuvers, and High Positive End-Expiratory Pressure for Acute Lung Injury and Acute Respiratory Distress Syndrome
A Randomized Controlled Trial

RM CPAP 40 cmH_2O x 40 secs
QID until FiO2≤ 40%

把肺打開、再用高PEEP維持、允許Pplt到40cmH2O

Table 1. Protocol Components

Component Variables	Control Ventilation Strategy	Lung Open Ventilation Strategy
Ventilator mode	Volume-assist control	Pressure control
Tidal volume target, mL/kg predicted body weight	6	6
Tidal volume range, mL/kg predicted body weight	4-8	4-8
Plateau airway pressure, cm H_2O	≤30	≤40
Positive end-expiratory pressure, cm H_2O	See Table 2	See Table 2
Partial pressure of oxygen, arterial, mm Hg	55-80	55-80
Oxygen saturation as measured by pulse oximetry, %	88-93	88-93
pH	≥7.30	≥7.30
Ventilator rate, breaths/min	≤35	≤35
Inspiration:expiration time	1:1-1:3	1:1-1:3
Recruitment maneuvers	Not permitted	After ventilator disconnects

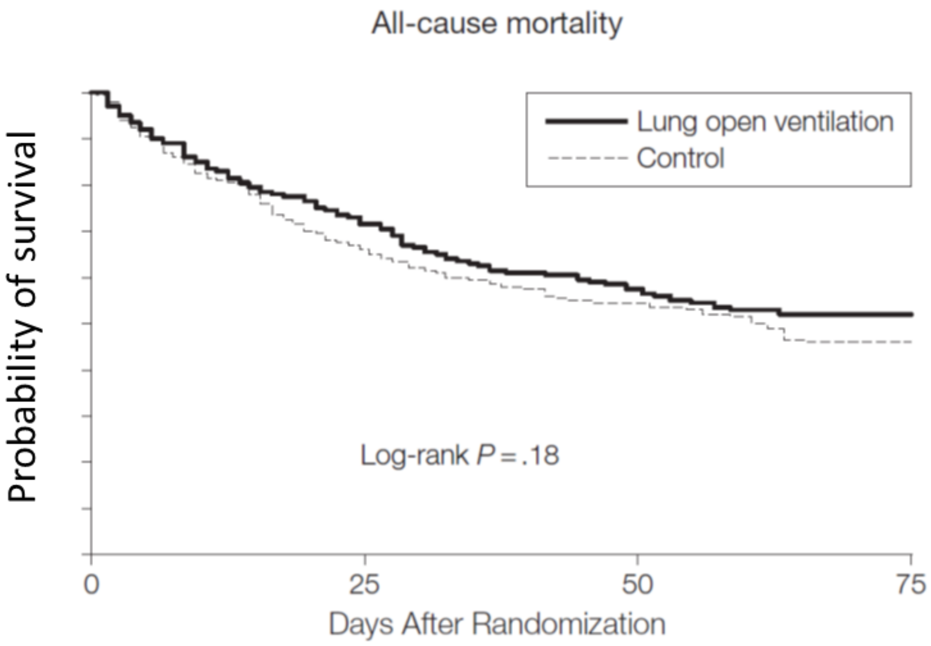
Table 2. Allowable PEEP Ranges at Specified Levels of FIO_2[a]

	Fraction of Inspired Oxygen (FIO_2)							
	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
Control PEEP ranges, cm H_2O	5	5-8	8-10	10	10-14	14	14-18	18-24
Lung open ventilation PEEP ranges, cm H_2O								
Before protocol change	5-10	10-14	14-20	20	20	20	20	20-24
After protocol change	5-10	10-18	18-20	20	20	20-22	22	22-24

LOVS trial, JAMA 2008 (2)

Table 6. Outcomes[a]

Outcomes	No. (%) Lung Open Ventilation (n = 475)	No. (%) Control Ventilation (n = 508)	Relative Risk (95% Confidence Interval)	*P* Value
Death in hospital	173 (36.4)	205 (40.4)	0.90 (0.77-1.05)	.19
Death in intensive care unit	145 (30.5)	178 (35.0)	0.87 (0.73-1.04)	.13
Death during mechanical ventilation	136 (28.6)	168 (33.1)	0.87 (0.72-1.04)	.13
Death during first 28 d	135 (28.4)	164 (32.3)	0.88 (0.73-1.07)	.20
Barotrauma[b]	53 (11.2)	47 (9.1)	1.21 (0.83-1.75)	.33
Refractory hypoxemia	22 (4.6)	52 (10.2)	0.54 (0.34-0.86)	.01
Death with refractory hypoxemia	20 (4.2)	45 (8.9)	0.56 (0.34-0.93)	.03
Refractory acidosis	29 (6.1)	42 (8.3)	0.81 (0.51-1.31)	.39
Death with refractory acidosis	27 (5.7)	38 (7.5)	0.85 (0.51-1.40)	.52
Refractory barotrauma	14 (3.0)	12 (2.4)	1.10 (0.54-2.26)	.80
Death with refractory barotrauma	8 (1.7)	8 (1.6)	1.00 (0.41-2.40)	.99
Eligible use of rescue therapies[c]	24 (5.1)	47 (9.3)	0.61 (0.38-0.99)	.045
Total use of rescue therapies[c]	37 (7.8)	61 (12.0)	0.68 (0.46-1.00)	.05
Days of mechanical ventilation[d]	10 (6-17)	10 (6-16)		.92
Days of intensive care[d]	13 (8-23)	13 (9-23)		.98
Days of hospitalization[d]	28 (17-48)	29 (16-51)		.96



no significant difference in all-cause hospital mortality or barotrauma compared with an established low-tidal-volume protocolized ventilation strategy.

JAMA. 2008 Feb 13;299(6):637-45.

EXPRESS trial, JAMA 2008: PEEP titrated to Pplt 28-30

Positive End-Expiratory Pressure Setting in Adults With Acute Lung Injury and Acute Respiratory Distress Syndrome
A Randomized Controlled Trial

PEEP as high as possible without increasing the maximum inspiratory plateau pressure > 28-30 cm H2O

在限制Pplt下盡量提高 PEEP

Table 1. Ventilation Characteristics in the Minimal Distension and Increased Recruitment Groups

Ventilator Mode	Volume-Assist Control
Tidal volume goal	6 mL/kg of predicted body weight[a]
Plateau pressure limit	≤30 cm H_2O
Ventilation rate and pH goals	≤35; adjusted for a pH between 7.30 and 7.45
Oxygenation goals	
PaO_2	55-80 mm Hg
SpO_2	88%-95%
PEEP[b]	
Minimal distension group[c]	Total PEEP between 5 and 9 cm H_2O
Increased recruitment group[d]	Plateau pressure between 28 and 30 cm H_2O
Recruitment maneuvers	Allowed but not recommended
Adjunctive therapies (prone position or inhaled nitric oxide or almitrine bismesylate)	Allowed when the oxygenation goal was not met despite FIO_2 ≥0.8
PEEP weaning test	
In patients with PaO_2:FIO_2 >150 mm Hg with FIO_2 ≤0.6 daily from day 4 onward; FIO_2 of 0.5 and PEEP of 5 cm H_2O for 20-30 min	Successful if PaO_2 ≥100 mm Hg; subsequent ventilation with PEEP of 5 cm H_2O, tidal volume <10 mL/kg predicted body weight, and plateau pressure <30 cm H_2O

JAMA. 2008 Feb 13;299(6):646-55.

EXPRESS trial, JAMA 2008

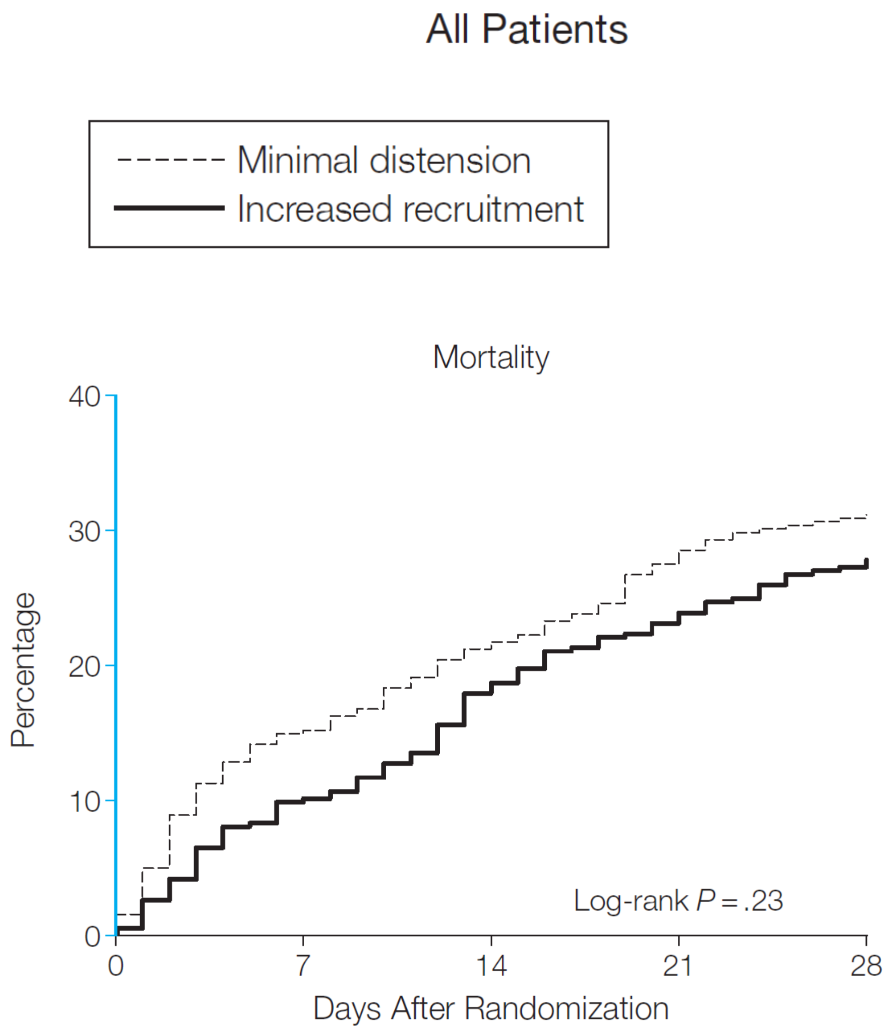


Table 4. Main Outcome Variables

Outcome	Minimal Distension (n = 382)	Increased Recruitment (n = 385)	*P* Value
	No. (%)		
Death in the first 28 d[a]	119 (31.2)	107 (27.8)	.31
Death before hospital discharge	149 (39.0)	136 (35.4)	.30
Death in the first 60 d	151 (39.5)	138 (35.9)	.31
Pneumothorax between day 1 and day 28[b]	22 (5.8)	26 (6.8)	.57
	Median (IQR)		
No. of days between day 1 and day 28			
Ventilator-free[c]	3 (0-17)	7 (0-19)	.04
Organ failure–free[d]	2 (0-16)	6 (0-18)	.04
Cardiovascular failure–free[d]	21 (4-26)	23 (10-26)	.09
Renal failure–free[d]	27.5 (8.0-28.0)	28.0 (11.0-28.0)	.23

A strategy for setting PEEP aimed at increasing alveolar recruitment while limiting hyperinflation did not significantly reduce mortality.

JAMA. 2008 Feb 13;299(6):646-55.

LOVS vs. EXPRESS

面向	LOVS	EXPRESS
RM	intervention 的一部分	allowed but not recommended
PEEP 調整	PEEP/FiO2 table	plateau pressure-guided
High PEEP 哲學	open lung + prevent collapse	raise PEEP until Pplat 28–30
Plateau pressure 上限	experimental arm 可到 40	目標 28–30，超過 32 要處理
Control group	ARDSNet-like low VT + conventional PEEP	minimal distension：total PEEP 5–9
	把肺打開、再用高PEEP維持、允許Pplt到40cmH2O	**在限制Pplt下盡量提高 PEEP**

JAMA 2010: Systematic Review and Meta-analysis

Table 1. Characteristics of Included Trials

Characteristic	Trial: ALVEOLI,[8] 2004	LOVS,[9] 2008	EXPRESS,[10] 2008
Inclusion criteria	Acute lung injury with $PaO_2:FIO_2 \leq 300$[a]	Acute lung injury with $PaO_2:FIO_2 \leq 250$[a]	Acute lung injury with $PaO_2:FIO_2 \leq 300$[a]
Recruitment period	1999-2002	2000-2006	2002-2005
Recruiting hospitals (country)	23 (United States)	30 (Canada, Australia, Saudi Arabia)	37 (France)
Patients randomized to higher vs lower PEEP	276 vs 273	476 vs 509[b]	385 vs 383[c]
Validity			
Concealed allocation	Yes	Yes	Yes
Follow-up for primary outcome, %	100	100	100
Blinded data analysis	Yes	Yes	Yes
Stopped early	Stopped for perceived futility	No	Stopped for perceived futility
Experimental intervention	Higher PEEP according to FIO_2 chart, recruitment maneuvers for first 80 patients	Higher PEEP according to FIO_2 chart, required plateau pressures ≤ 40 cm H_2O, recruitment maneuvers	PEEP as high as possible without increasing the maximum inspiratory plateau pressure >28-30 cm H_2O
Control intervention	Conventional PEEP according to FIO_2 chart, required plateau pressures ≤ 30 cm H_2O, no recruitment maneuvers	Conventional PEEP according to FIO_2 chart, required plateau pressures ≤ 30 cm H_2O, no recruitment maneuvers	Conventional PEEP (5-9 cm H_2O) to meet oxygenation goals
Ventilator procedures	Target tidal volumes of 6 mL/kg of predicted body weight; plateau pressures ≤ 30 cm H_2O (with exception as above); respiratory rate ≤ 35/min, adjusted to achieve arterial pH 7.30-7.45; ventilator mode: volume-assist control (except higher PEEP group in LOVS required pressure control); oxygenation goals: PaO_2 55-80 mm Hg and SPO_2 88%-95%; standardized weaning)		

Abbreviations: ALVEOLI, Assessment of Low Tidal Volume and Elevated End-Expiratory Pressure to Obviate Lung Injury; EXPRESS, Expiratory Pressure Study; FIO_2, fraction of inspired oxygen; LOVS, Lung Open Ventilation to Decrease Mortality in the Acute Respiratory Distress Syndrome; PEEP, positive end-expiratory pressure; SPO_2, oxygen saturation.

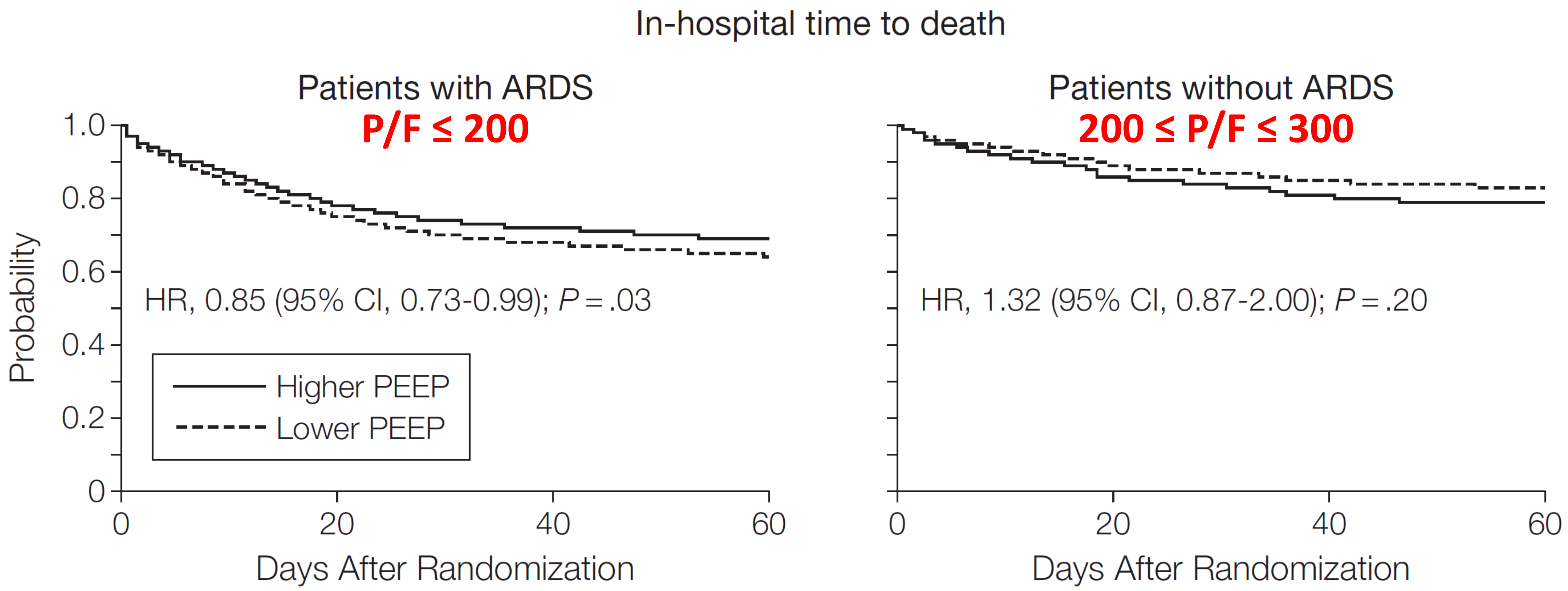
[a] Acute lung injury defined according to the American-European Consensus Conference.[12]

[b] Includes 2 patients for whom consent was withdrawn prior to protocol initiation, without patient, family, and caregivers being aware of group assignment (ie, 983 patients analyzed).

[c] Includes 1 patient for whom consent was withdrawn prior to protocol initiation, without patient, family, and caregiver awareness of assignment (ie, 767 patients included in the analysis).

JAMA. 2010 Mar 3;303(9):865-73.

AECC: ARDS P/F ≤ 200、 ALI P/F ≤ 300



Treatment with higher vs lower levels of PEEP was not associated with improved hospital survival. However, higher levels were associated with improved survival among the subgroup of patients with ARDS.

JAMA. 2010 Mar 3;303(9):865-73.

關於PEEP，兩份指引略有不同

Recommendation 6.1

We are **unable to make a recommendation** for or against routine PEEP titration with a higher PEEP/FiO_2 strategy versus a lower PEEP/FiO_2 strategy to reduce mortality in patients with ARDS.
No recommendation; high level of evidence of no effect.

This statement applies also to ARDS from COVID-19.
No recommendation; moderate level of evidence of no effect for indirectness.

Recommendation 6.3

We **recommend against** use of prolonged high-pressure recruitment maneuvers (defined as airway pressure maintained ≥ 35 cmH_2O for at least one minute) to reduce mortality of patients with ARDS.
Strong recommendation; moderate level of evidence against.

This recommendation applies also to ARDS from COVID-19.
Strong recommendation; low level of evidence against for indirectness.

Question 4: Should Patients with ARDS Receive Higher Compared with Lower PEEP, with or without LRMs?

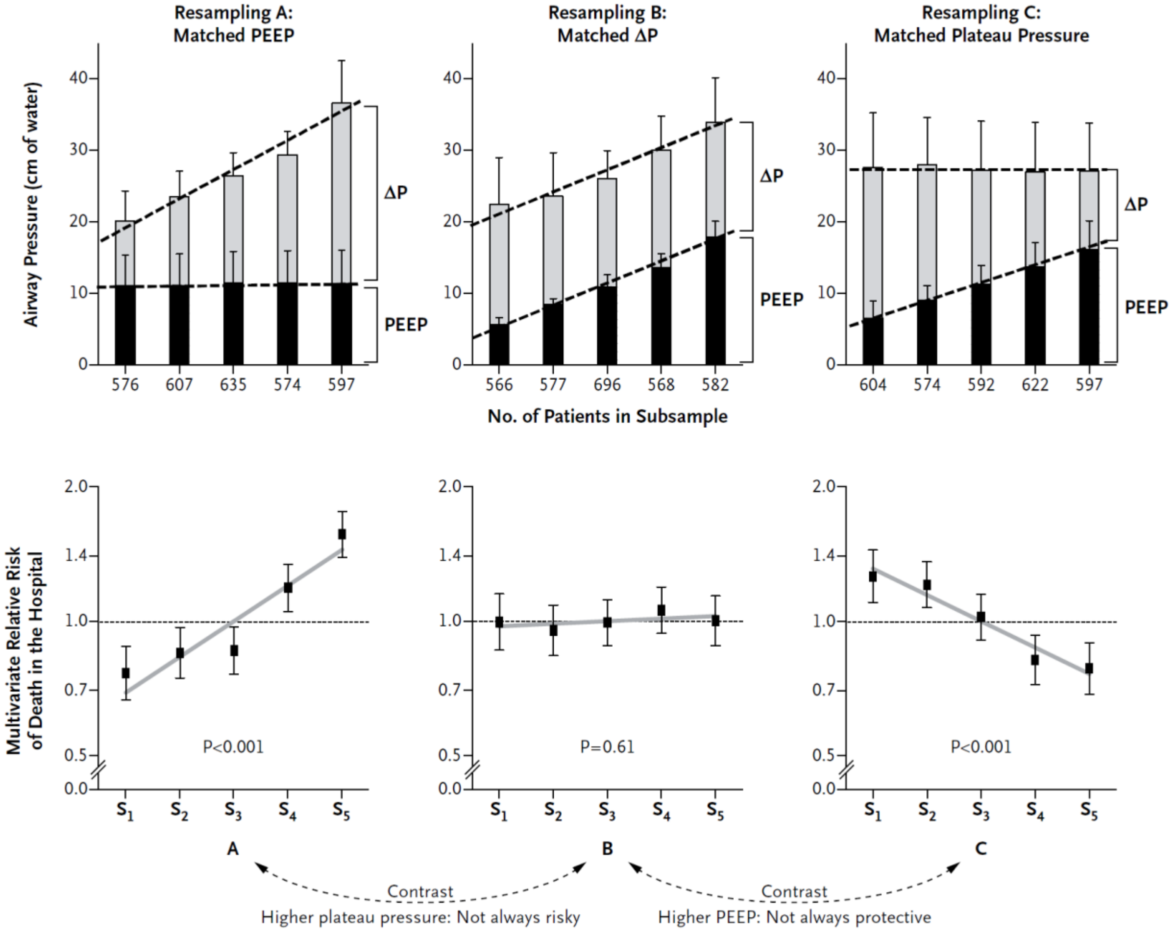
Recommendation. We suggest using higher PEEP without LRMs rather than lower PEEP in patients with moderate to severe ARDS (conditional recommendation, low-moderate certainty). We recommend against using prolonged (PEEP ⩾35 cm H_2O for >60 s) LRMs in patients with moderate to severe ARDS (strong recommendation, moderate certainty).

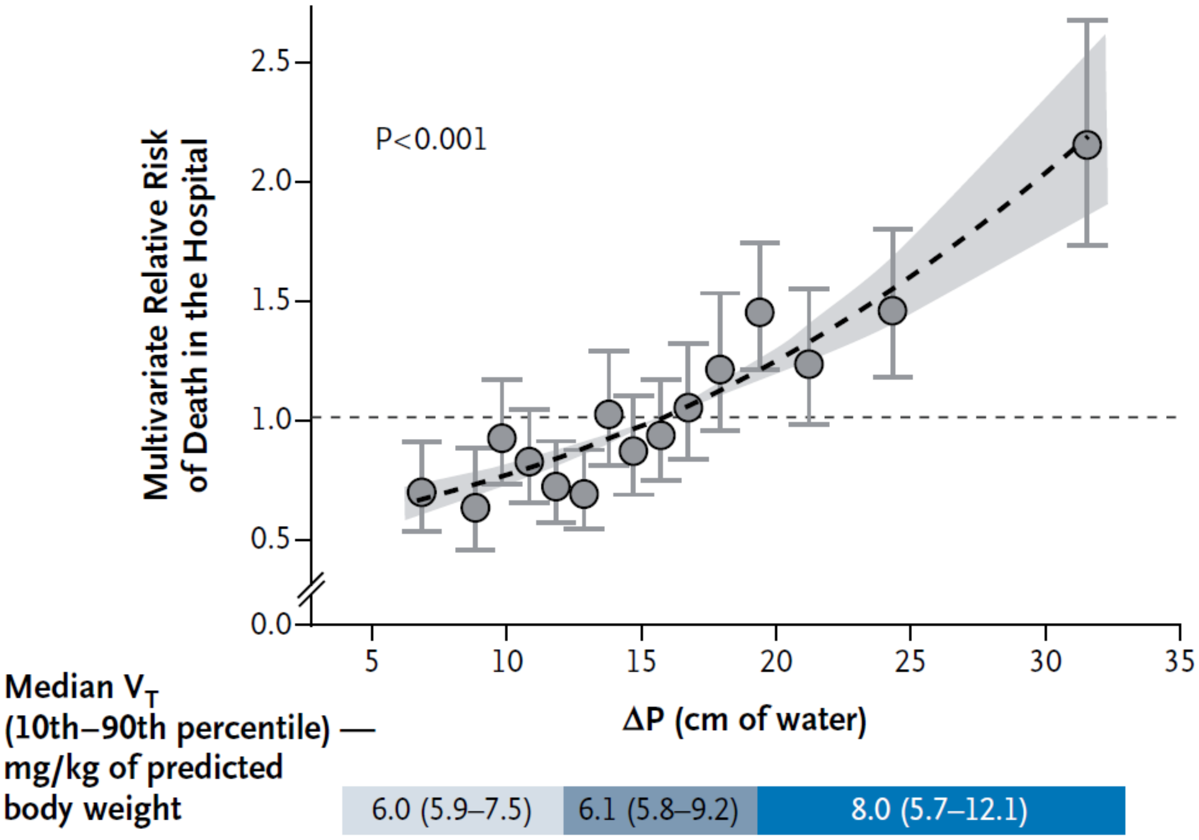
Driving pressure and Optimal PEEP

Driving Pressure and Survival, NEJM 2015

Driving pressure 應被視為「可操作的監測指標」而不是單純治療目標

3562 ARDS patients In 9 RCTs



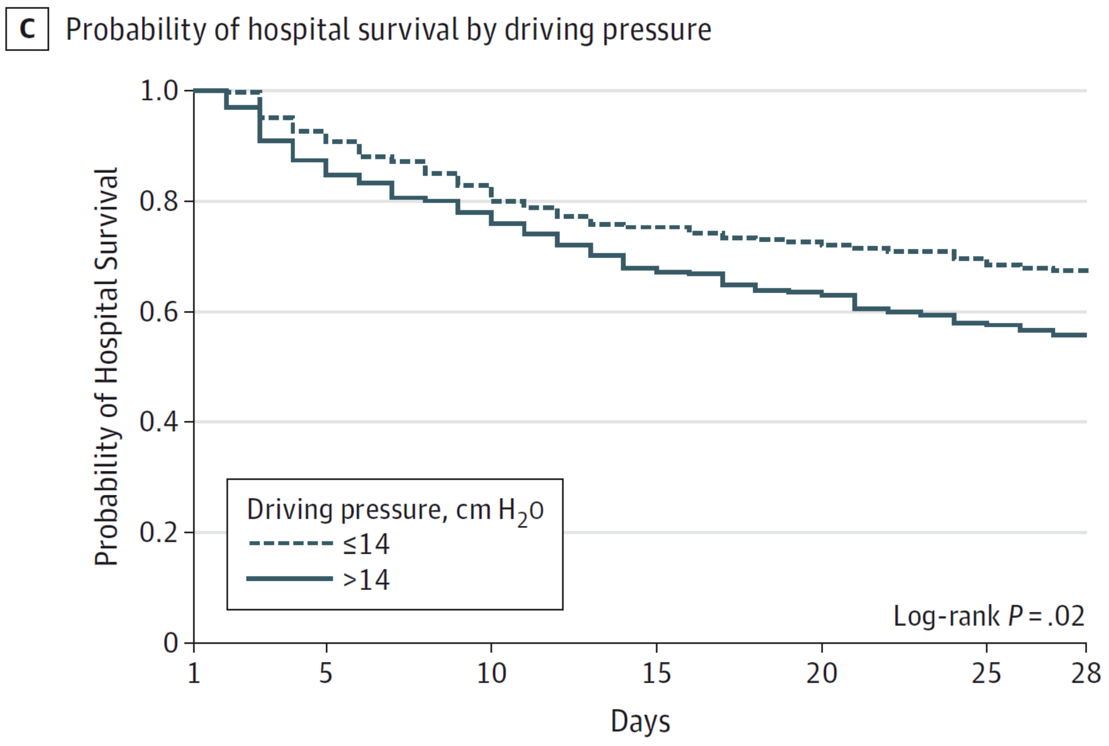


NEJM 2015;372:747-55.

Driving pressure ≤ 14cm H_2O的由來

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries



Patients with a driving pressure of greater than 14 cm H_2O on day 1 of ARDS criteria had a higher mortality.

JAMA. 2016;315(8):788-800.

Individualized PEEP Setting in ARDS, Pintado et al. in 2013

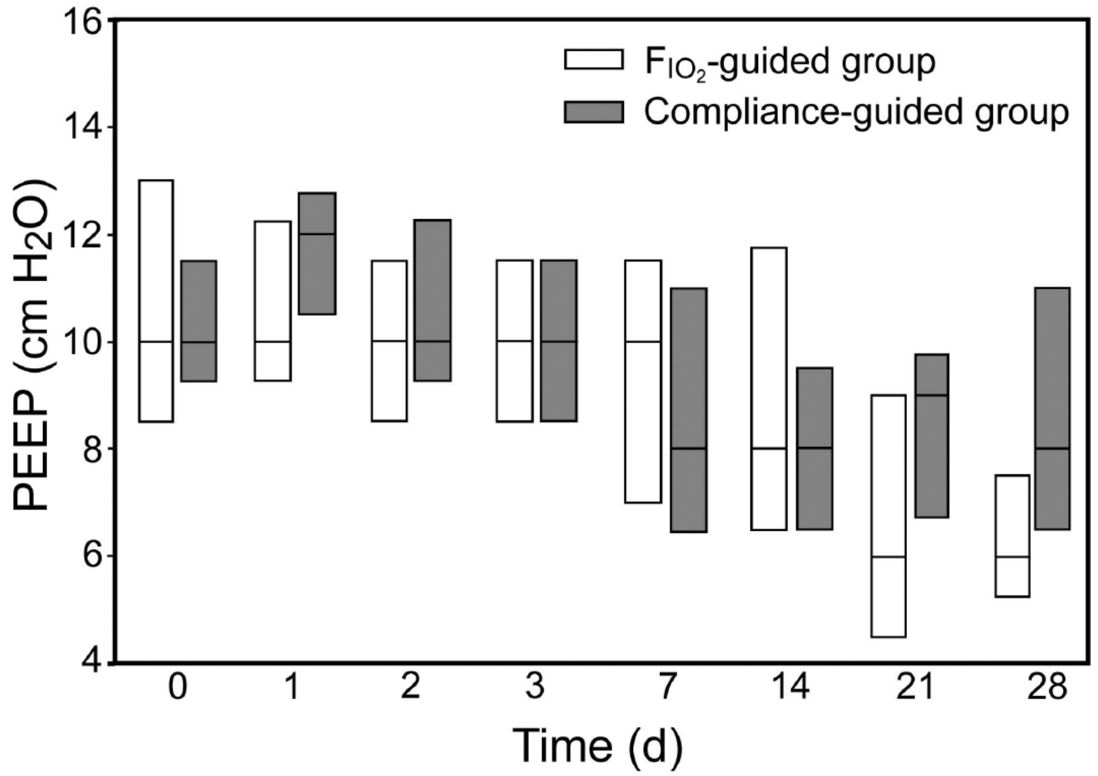


Fig. 2. PEEP in the first 28 days.

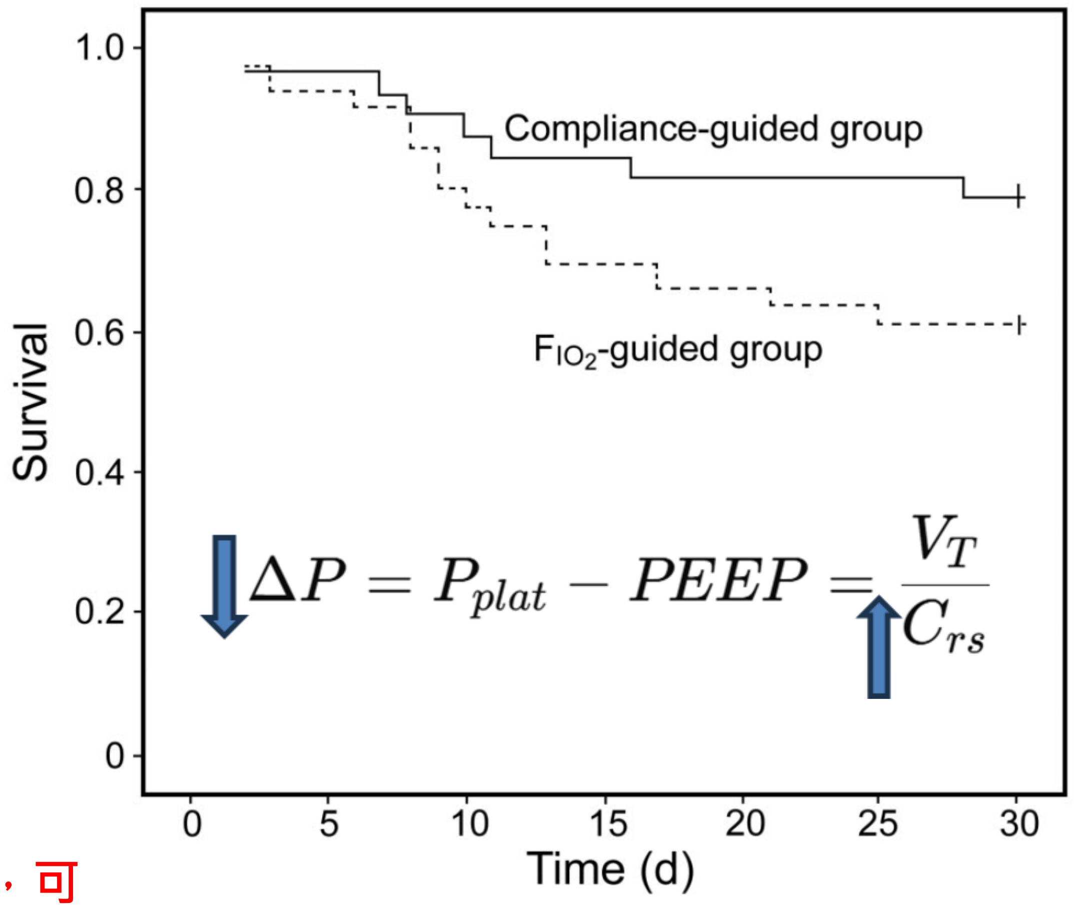


Fig. 4. Kaplan-Meier curves for survival.

- 單中心
- 樣本數只有 70 人
- pilot study 性質
- 不足以證明 mortality benefit

- compliance 是全肺平均值，可能掩蓋區域性 overdistension 與 dependent lung recruitment 的差異

Respir Care. 2013 Sep;58(9):1416-23.

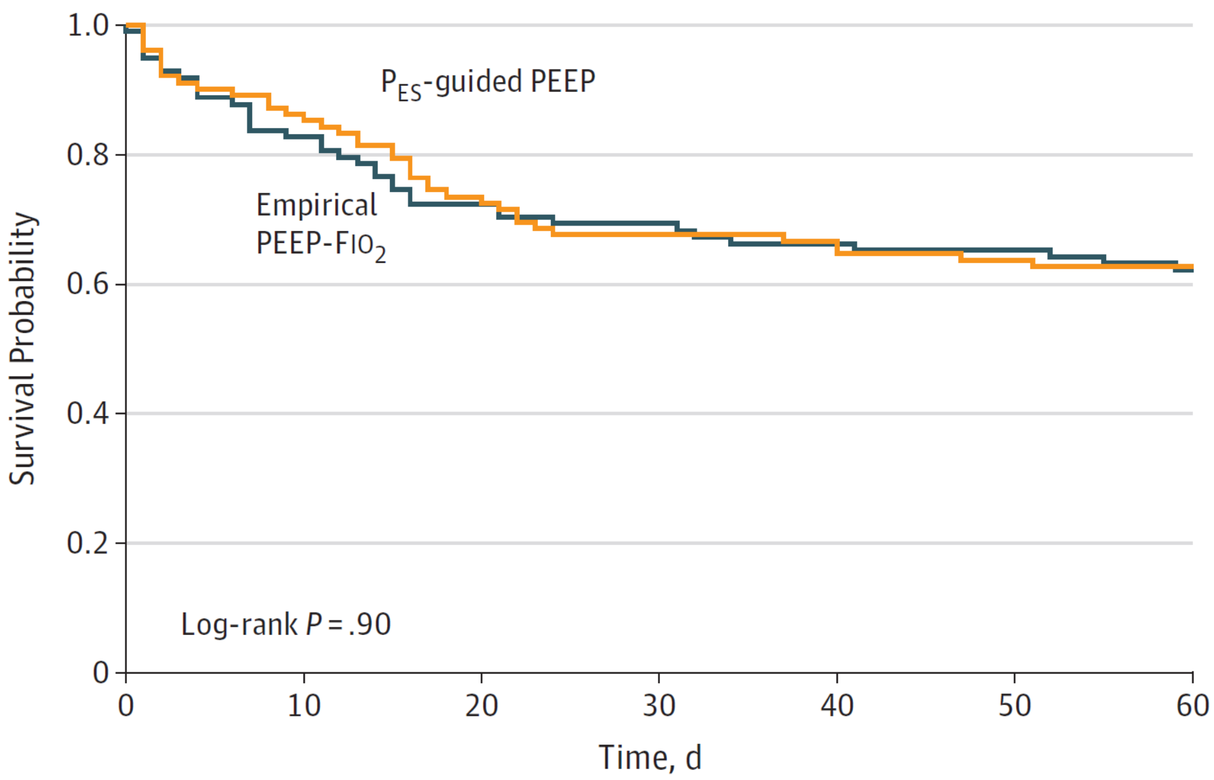
Transpulmonary pressure-guided PEEP

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Titrating Positive End-Expiratory Pressure (PEEP) With an Esophageal Pressure–Guided Strategy vs an Empirical High PEEP-FIO_2 Strategy on Death and Days Free From Mechanical Ventilation Among Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

Figure 3. Kaplan-Meier Survival Analysis Through Day 60



Among patients with moderate to severe ARDS,PES-guided PEEP, compared with empirical highPEEP-FIO2, resulted in no significant difference in death and days free from mechanical ventilation.

JAMA. 2019;321(9):846-857.

Recruitment maneuver and recruitability

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

ART trial, JAMA 2017

Multicenter, 120 ICUs, 9 countries, 1013 pts, P/F 117-119, 66% septic shock

先用力打開肺

Steps for Maximum Alveolar Recruitment Maneuver:

Step 1

- Start with PEEP of 25cmH_2O
- Delta pressure above PEEP of 15cmH_2O

Peak pressure of 40cmH_2O

Keep it for 1 minute (15 respiratory cycles)

Step 2

- Increase PEEP to 30cmH_2O
- Delta pressure above PEEP of 15cmH_2O

Peak pressure of 45cmH_2O

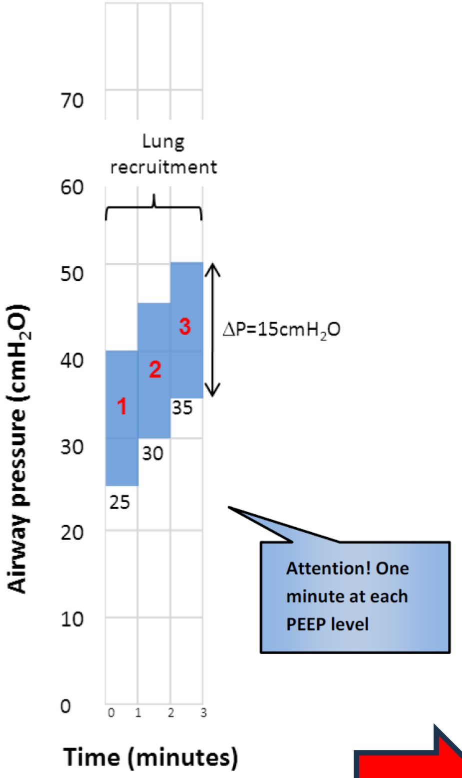
Keep it for 1 minute (15 respiratory cycles)

Step 3

- Increase PEEP to 35cmH_2O
- Delta pressure above PEEP of 15cmH_2O

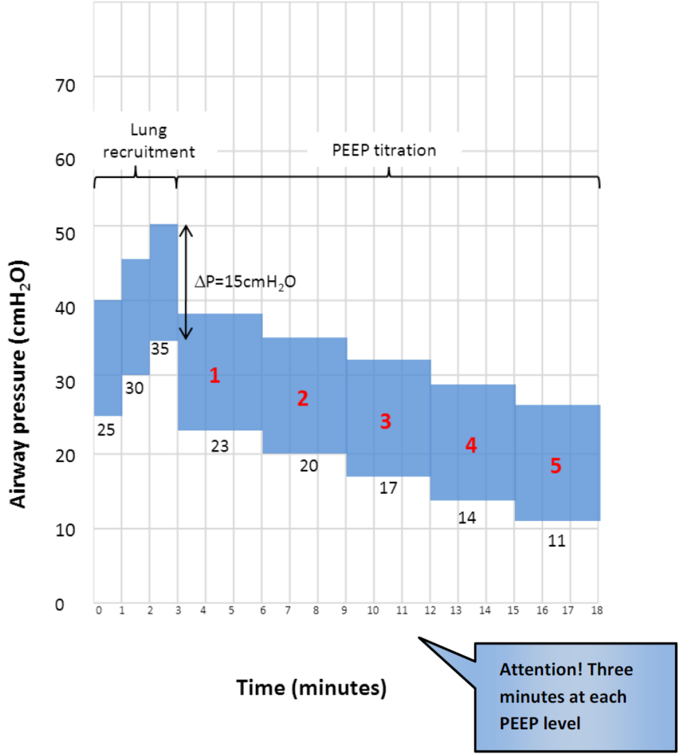
Peak pressure of 50cmH_2O

Keep it for 1 minute (15 respiratory cycles)



找出最大compliance

Steps for PEEP Titration:



Step 1: PEEP of 23 cmH_2O (keeping other parameters)
After 3 minutes, calculate compliance

Step 2: PEEP of 20 cmH_2O (keeping other parameters)
After 3 minutes, calculate compliance

Step 3: PEEP of 17 cmH_2O (keeping other parameters)
After 3 minutes, calculate compliance

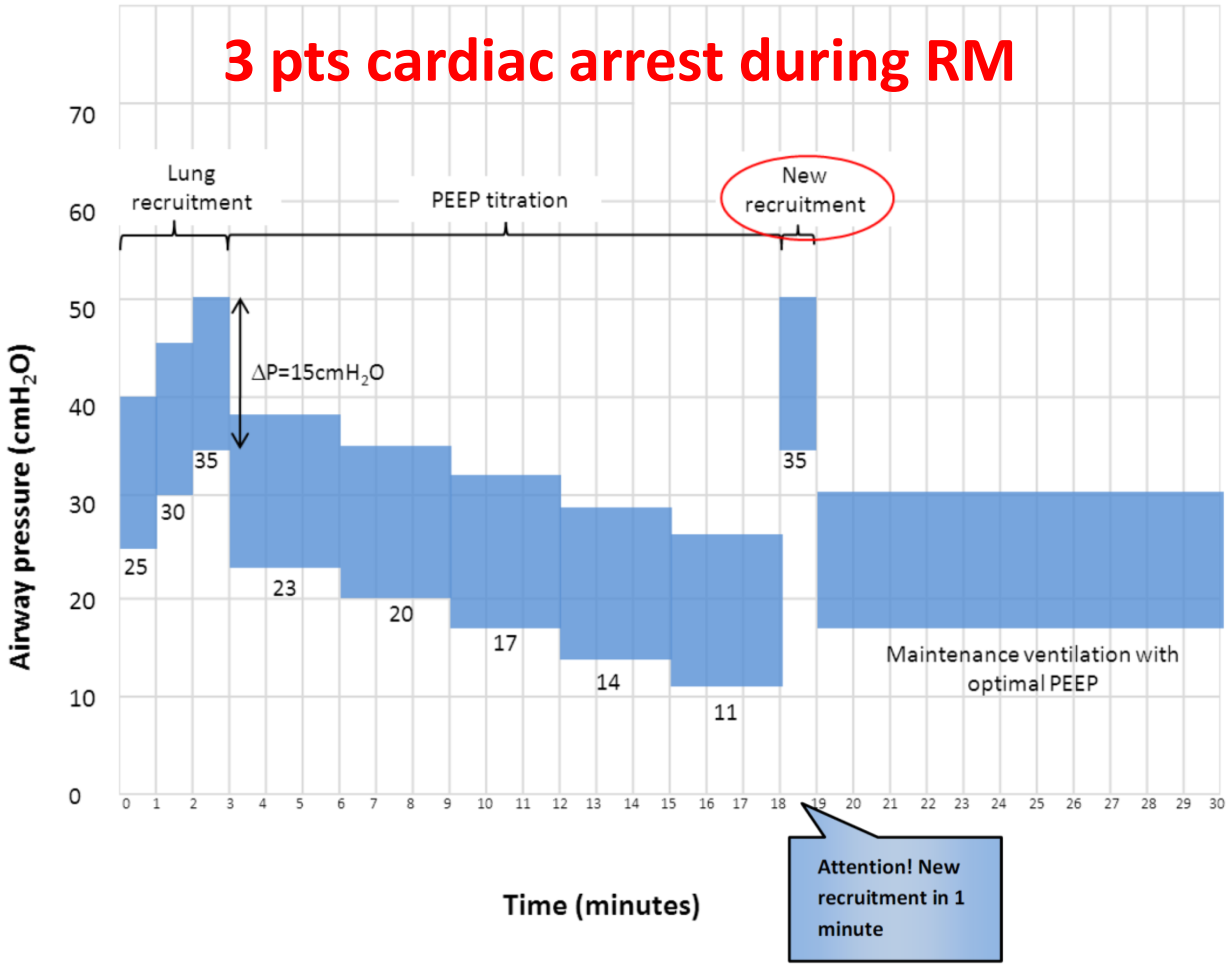
Step 4: PEEP of 14 cmH_2O (keeping other parameters)
After 3 minutes, calculate compliance

Step 5: PEEP of 11 cmH_2O (keeping other parameters)
After 3 minutes, calculate compliance

Optimal PEEP = PEEP value at maximum compliance plus 2 cmH_2O

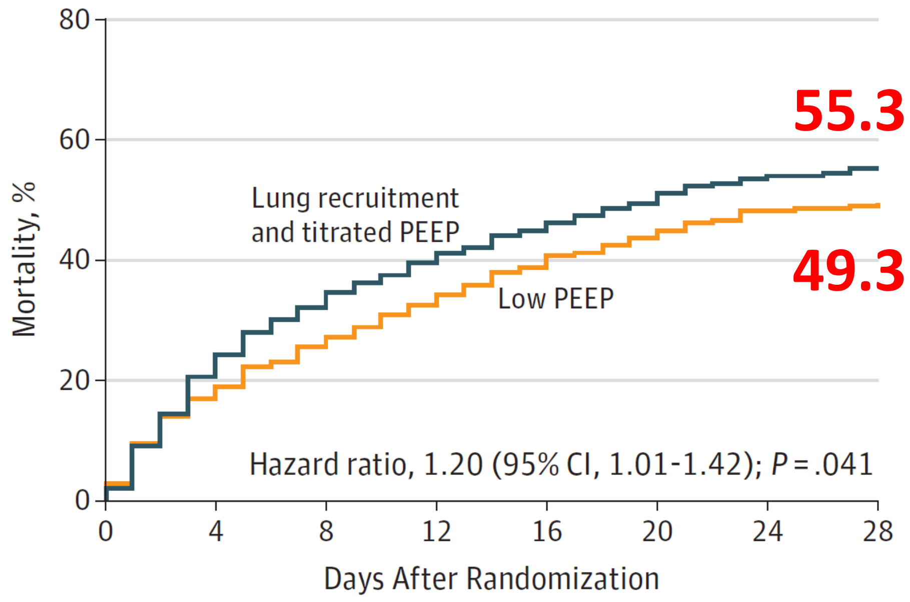
JAMA. 2017 Oct 10;318(14):1335-1345.

ART trial, JAMA 2017



After performing a new alveolar recruitment, follow the steps in the section:
"ART STRATEGY - MAINTENANCE VENTILATION – INITIAL PARAMETERS"

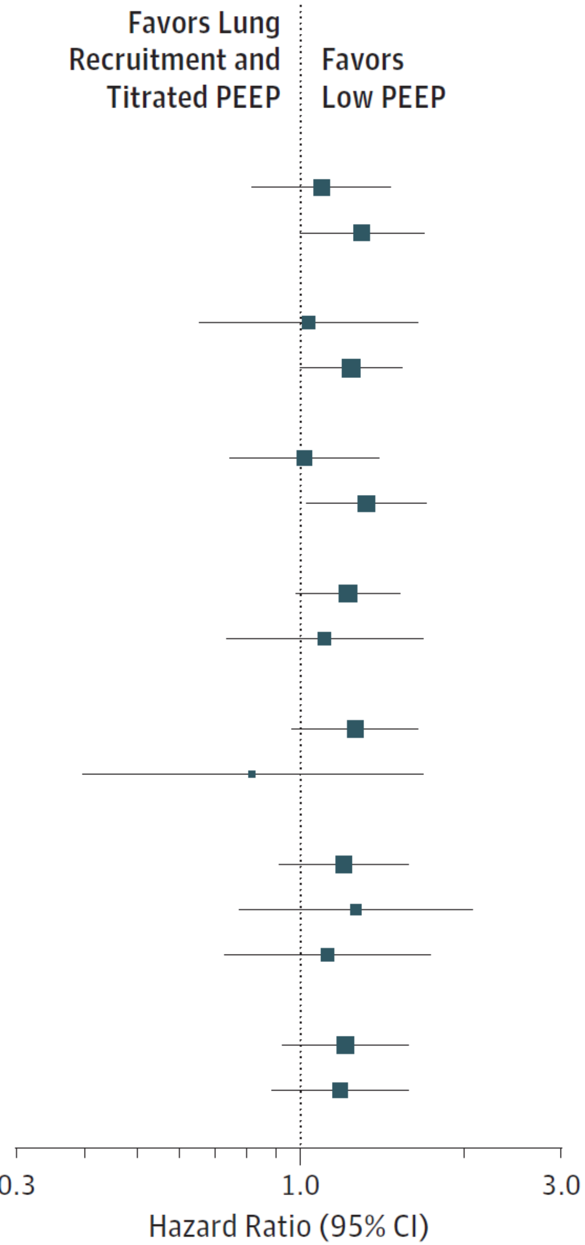
Figure 2. 28-Day Mortality in the Lung Recruitment Maneuver With Titrated PEEP Group vs the Low-PEEP Group



- **Not support routine use of lung recruitment maneuver and PEEP titration in moderate to severe ARDS.**

Figure 3. Effects of the Lung Recruitment Maneuver With Titrated PEEP vs the Low-PEEP Group on Mortality According to Subgroups

Subgroup	No. of Deaths/Total No. (%) Lung Recruitment and Titrated PEEP (n = 501)	Low PEEP (n = 509)	Hazard Ratio (95% CI)	P Value for Interaction
PaO_2: FIO_2				
≤100 mm Hg	117/197 (59.4)	120/214 (56.1)	1.09 (0.82-1.46)	.33
>100 mm Hg	160/304 (52.6)	131/295 (44.4)	1.30 (1.00-1.69)	
Simplified Acute Physiology Score 3				
<50	47/117 (40.2)	48/119 (40.3)	1.03 (0.65-1.64)	.42
≥50	230/384 (59.9)	203/390 (52.1)	1.24 (1.00 -1.54)	
Type of ARDS				
Extrapulmonary	98/188 (52.1)	102/196 (52)	1.02 (0.74-1.40)	.15
Pulmonary	179/313 (57.2)	149/313 (47.6)	1.32 (1.03-1.69)	
Duration of ARDS at randomization, h				
≤36	214/388 (55.2)	196/405 (48.4)	1.22 (0.98-1.52)	.63
>36 to <72	63/113 (55.8)	55/104 (52.9)	1.11 (0.73-1.67)	
Position 1 h after randomization				
Supine (dorsal decubitus) or lateral decubitus	153/274 (55.8)	132/273 (48.4)	1.26 (0.96-1.64)	.21
Prone	19/31 (61.3)	20/30 (66.7)	0.82 (0.40-1.67)	
Duration of mechanical ventilation before randomization, d				
0-2	160/297 (53.9)	152/320 (47.5)	1.20 (0.92-1.56)	.91
3-4	54/88 (61.4)	41/77 (53.2)	1.26 (0.77-2.07)	
≥5	63/116 (54.3)	58/112 (51.8)	1.12 (0.73-1.71)	
Protocol modification				
Before	151/273 (55.3)	138/280 (49.3)	1.21 (0.93-1.57)	.89
After	126/228 (55.3)	113/229 (49.3)	1.18 (0.88-1.58)	



對於ART trial的反思

- **1. PaO2:FiO2 ≤100：氧合很差，不等於一定 recruitable**
  – 低氧合可能來自不同機制：recruitable collapse、flooding / edema、consolidation、shunt、vascular dysregulation、overdistension 造成 dead space
- **2. SAPS 3 ≥50：全身病情嚴重，對胸腔內高壓更脆弱**
  – 66%受試者有 septic shock，平均 nonpulmonary organ failure 超過 2 個
- **3. Pulmonary ARDS：不是所有肺都能被 recruit**
  – 若不可 recruit 的區域多，高壓 recruitment 與高 PEEP 反而造成baby lung overdistension，

如何判斷病人有recruitability呢?

- 2024 ATS guideline 提到lung recruitability assessment，包括

✓ oxygenation response
✓ driving pressure change
✓ recruitment/inflation ratio
✓ stress index
✓ electrical impedance tomography, EIT

這些可能幫助 individualized PEEP titration。

Recruiting

Careful Ventilation in Acute Respiratory Distress Syndrome (CAVIARDS)

ClinicalTrials.gov ID NCT03963622

Sponsor Unity Health Toronto

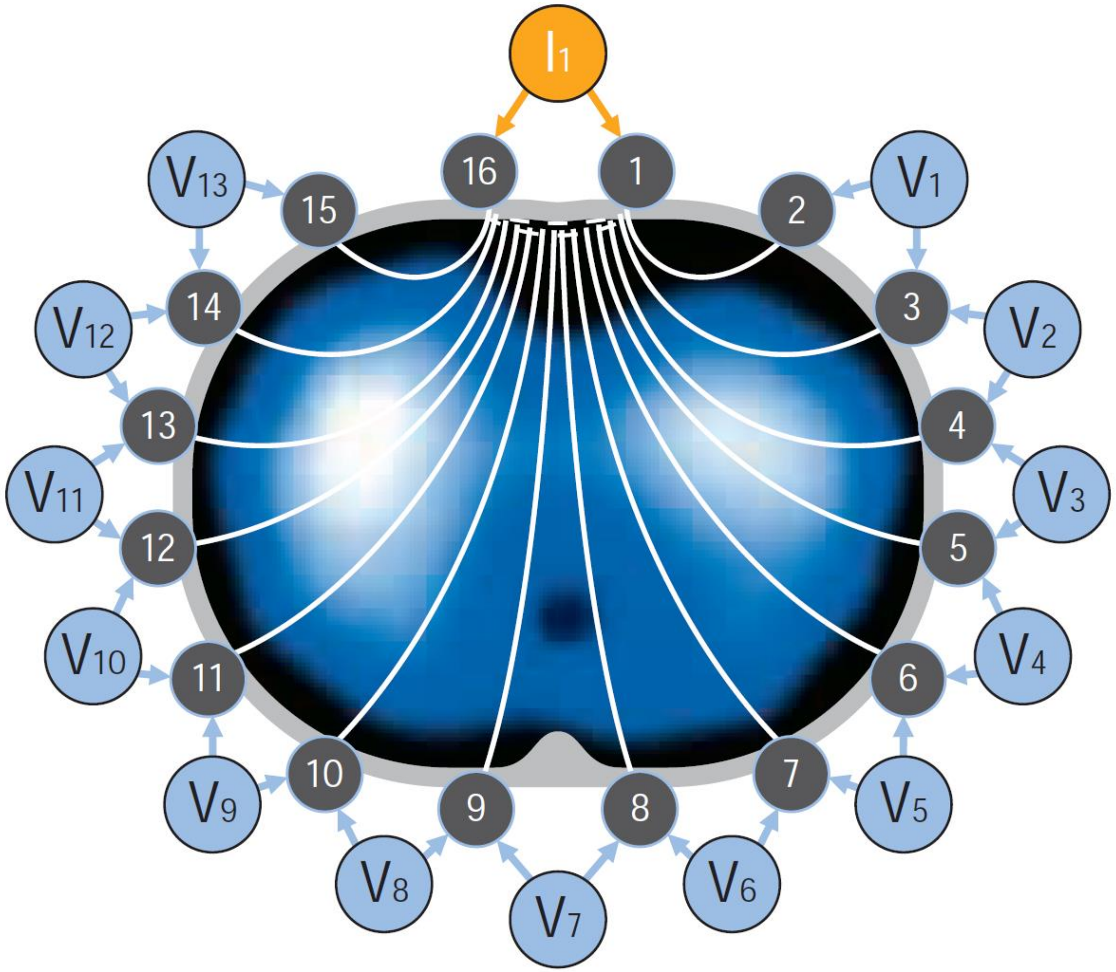
Information provided by Unity Health Toronto (Responsible Party)

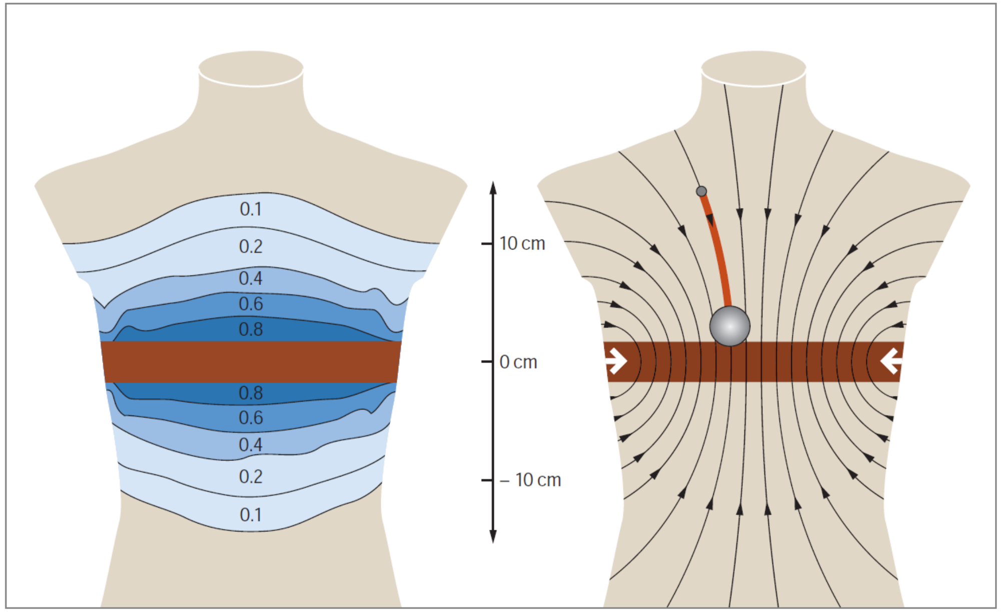
Last Update Posted 2026-01-16

A large multicenter trial evaluating setting PEEP based on respiratory mechanics (recruitability and effort) is ongoing.

EIT-guided personalization

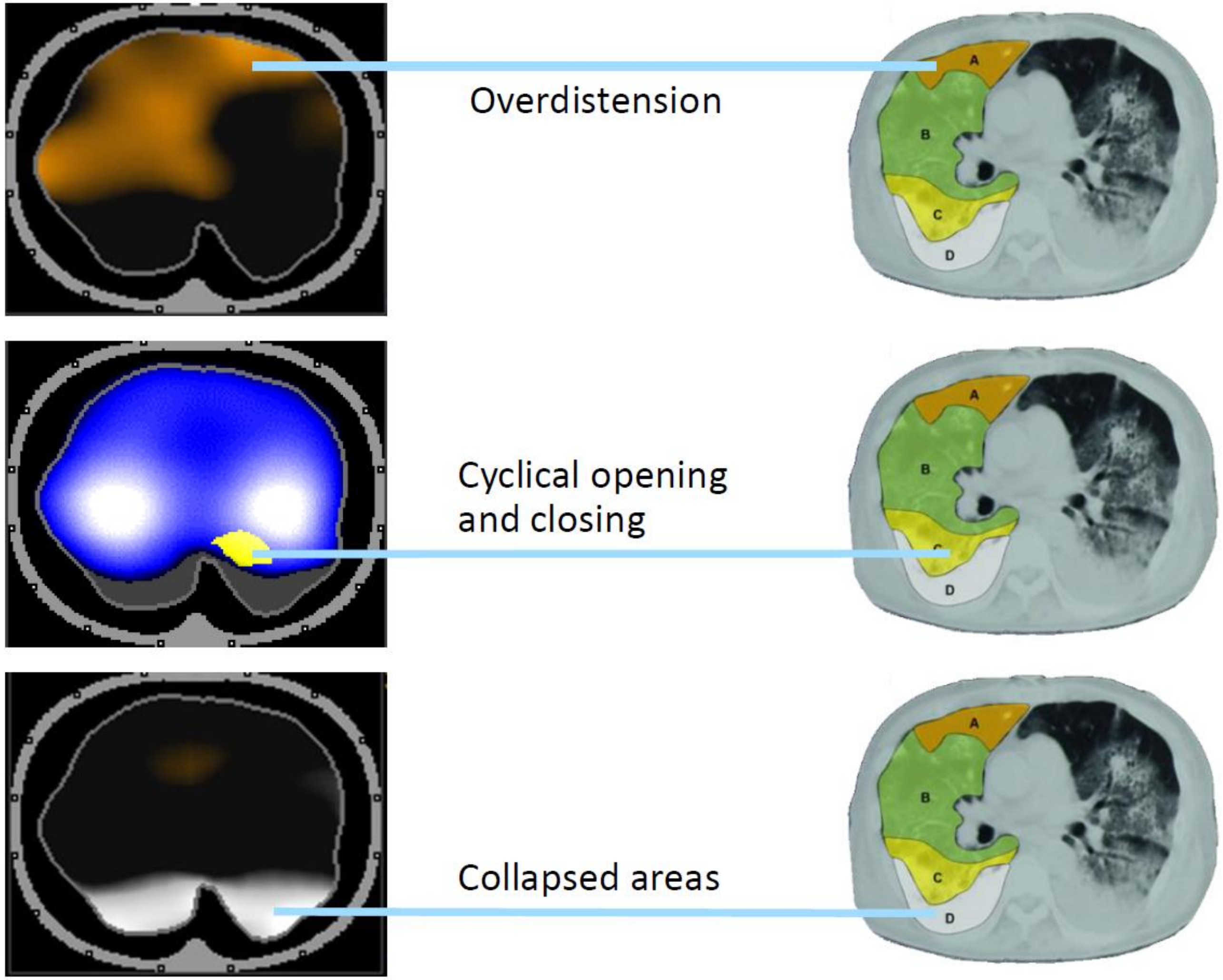
Electrical Impedance Tomography (EIT) 電阻抗斷層影像





[1] Costa et al. Intensive Care Med 2009;3
[2] Murders et al. Critical Care Med 2012;

Display of harmful lung conditions



Decrease of compliance towards higher PEEP levels.

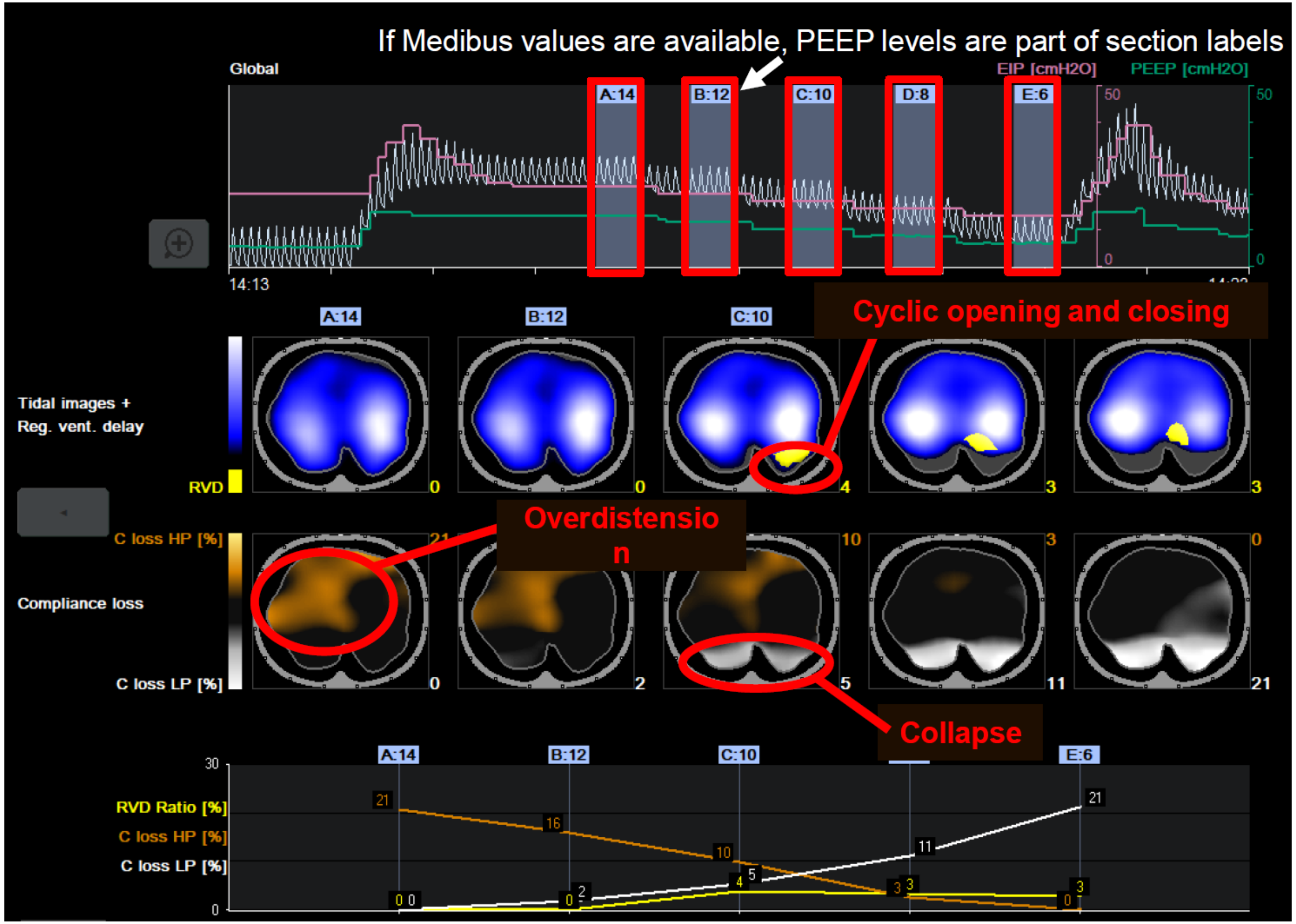
This typically occurs in ventral regions at high PEEP levels and may be interpreted as overdistension.[1]

The parameter RVD defines the extent of the temporal delay of the regional inspiration compared to the global inspiration and may indicate cyclical opening and closing.[2]

Decrease of compliance towards lower PEEP levels.

This typically occurs in dorsal regions at low PEEP levels and may be interpreted as collapse or derecruitment.[1]

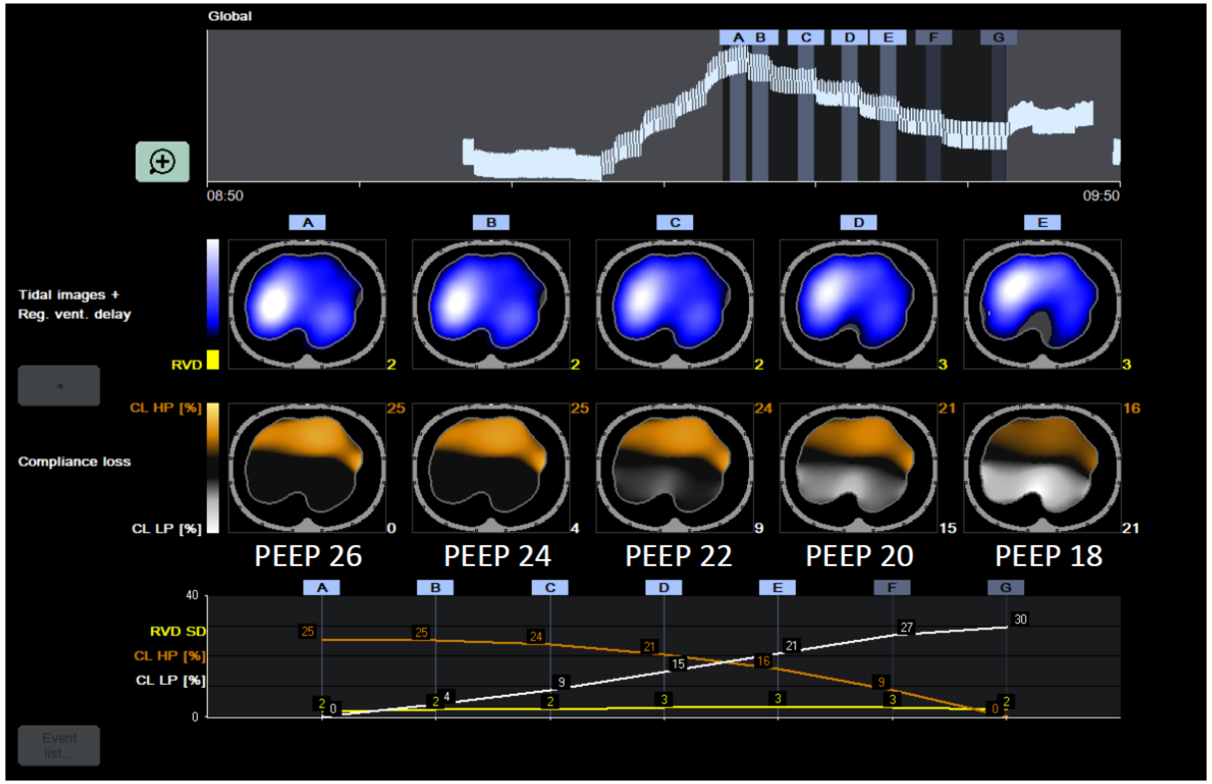
EIT-guided PEEP (1)

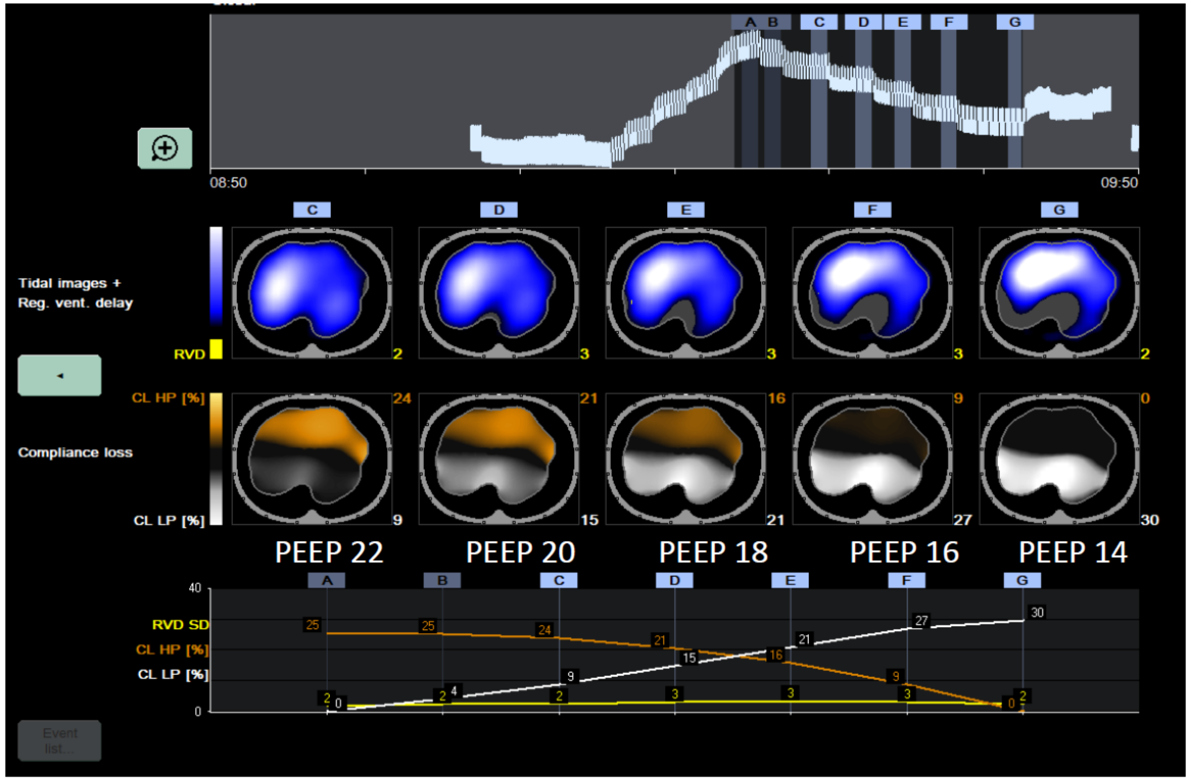


EIT-guided PEEP (2)

RM was done with max PEEP 26, followed by 2 cmH_2O stepwise decremental trail to 14

Optimal PEEP was 19, based on minimal collapse / over-distension theory proposed by Prof. Amato





EIT facilitates real-time, individualized PEEP adjustments, improving respiratory system mechanics.

Study or Subgroup	EIT Mean	EIT SD	EIT Total	Conventional Mean	Conventional SD	Conventional Total	Weight	Mean difference IV, Random, 95% CI
5.1.1 NRS								
Becher 2021	37.9	11.4	20	38.2	8.8	20	4.8%	-0.30 [-6.61 , 6.01]
Di Pierro 2022	27.67	14.7	31	23.96	9.64	31	5.0%	3.71 [-2.48 , 9.90]
Eronia 2017	49.5	12	14	44.6	11	14	2.6%	4.90 [-3.63 , 13.43]
Gibot 2021	39	8.15	17	35.11	11.49	51	7.7%	3.89 [-1.11 , 8.89]
Heines 2019	49	24	39	45	23	39	1.8%	4.00 [-6.43 , 14.43]
Jonkman 2023	34.46	10.84	108	28.2	9.19	108	26.7%	6.26 [3.58 , 8.94]
Liu 2022	42.61	13.77	14	38.39	13.86	14	1.8%	4.22 [-6.01 , 14.45]
Somhorst 2022	49.33	21.48	75	45.67	19.26	75	4.5%	3.66 [-2.87 , 10.19]
Zhao 2019	25.9	5.9	24	20.4	5.3	31	21.2%	5.50 [2.49 , 8.51]
Subtotal (95% CI)			**342**			**383**	**76.0%**	**4.92 [3.34 , 6.51]**
Heterogeneity: Tau² = 0.00; Chi² = 4.23, df = 8 (P = 0.84); I² = 0%								
Test for overall effect: Z = 6.08 (P < 0.00001)								
5.1.2 RCT								
He 2021	33.67	13.33	61	30.33	9.63	56	10.9%	3.34 [-0.85 , 7.53]
Hsu 2021	33.7	7.6	42	32.5	11.6	45	11.4%	1.20 [-2.90 , 5.30]
Jimenez 2023	39.56	10.91	6	34.62	7.68	6	1.7%	4.94 [-5.74 , 15.62]
Subtotal (95% CI)			**109**			**107**	**24.0%**	**2.43 [-0.39 , 5.26]**
Heterogeneity: Tau² = 0.00; Chi² = 0.74, df = 2 (P = 0.69); I² = 0%								
Test for overall effect: Z = 1.69 (P = 0.09)								
Total (95% CI)			**451**			**490**	**100.0%**	**4.33 [2.94 , 5.71]**
Heterogeneity: Tau² = 0.00; Chi² = 7.24, df = 11 (P = 0.78); I² = 0%								
Test for overall effect: Z = 6.13 (P < 0.00001)								

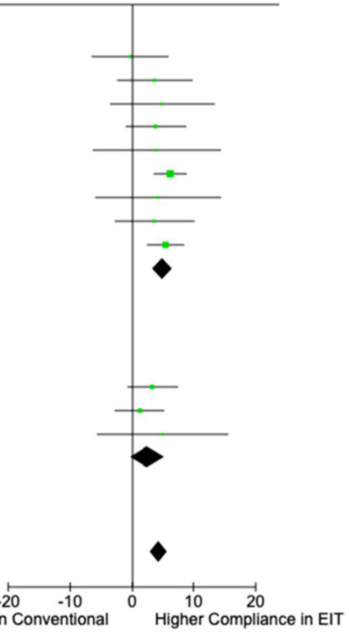


Fig. 2 Comparison of lung compliance between EIT-guided and conventional PEEP titration. *CI* confidence interval, *df* degrees of freedom, I^2 heterogeneity statistic, *IV* inverse variance method

Compliance ↑

Study or Subgroup	EIT Mean	EIT SD	EIT Total	Conventional Mean	Conventional SD	Conventional Total	Weight	Mean difference IV, Random, 95% CI
Gibot 2021	28.27	5.63	17	32.1	10.78	51	14.5%	-3.83 [-7.82 , 0.16]
Jimenez 2023	21.77	6.53	6	23.52	4.5	6	5.7%	-1.75 [-8.10 , 4.60]
Liu 2022	13.92	2.18	14	15.87	2.53	14	75.5%	-1.95 [-3.70 , -0.20]
Scaramuzzo 2020	22.37	13.78	20	19.17	9.7	20	4.2%	3.20 [-4.19 , 10.59]
Total (95% CI)			**57**			**91**	**100.0%**	**-1.99 [-3.51 , -0.47]**

Heterogeneity: Tau² = 0.00; Chi² = 2.72, df = 3 (P = 0.44); I² = 0%
Test for overall effect: Z = 2.57 (P = 0.01)
Test for subgroup differences: Not applicable

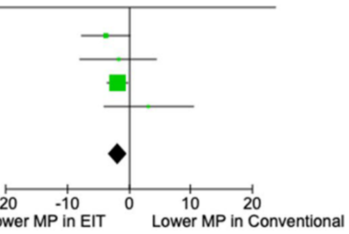


Fig. 3 Comparison of mechanical power between EIT-guided and conventional PEEP titration. *MP* mechanical power, *CI* confidence interval, *df* degrees of freedom, I^2 heterogeneity statistic, *IV* inverse variance method

Mechanical power ↓

Study or Subgroup	EIT Mean	EIT SD	EIT Total	Conventional Mean	Conventional SD	Conventional Total	Weight	Mean difference IV, Random, 95% CI
Becher 2021	10.4	2	20	10.4	2.2	20	8.7%	0.00 [-1.30 , 1.30]
Di Pierro 2022	9.21	1.63	31	9.33	1.92	31	9.3%	-0.12 [-1.01 , 0.77]
Eronia 2017	9.3	1.9	14	10.2	1.9	14	8.6%	-0.90 [-2.31 , 0.51]
Gibot 2021	12	1.48	17	13.33	3.83	51	8.8%	-1.33 [-2.59 , -0.07]
He 2021	13	2.96	61	13	1.48	56	9.4%	0.00 [-0.84 , 0.84]
Hsu 2021	10.9	2.5	42	12.4	3.6	45	8.7%	-1.50 [-2.80 , -0.20]
Jimenez 2023	10.6	1.82	6	11.91	1.57	6	7.7%	-1.31 [-3.23 , 0.61]
Jonkman 2023	8.62	2.25	108	13.33	3.7	108	9.4%	-4.71 [-5.53 , -3.89]
Liu 2022	10	3.51	14	10.57	4.6	14	5.8%	-0.57 [-3.60 , 2.46]
Scaramuzzo 2020	11.33	3.56	20	10.4	3.41	20	7.2%	0.93 [-1.23 , 3.09]
Somhorst 2022	10.17	4.07	75	10.67	4.44	75	8.6%	-0.50 [-1.86 , 0.86]
Zhao 2019	15.1	3.1	24	19.1	3.7	31	7.9%	-4.00 [-5.80 , -2.20]
Total (95% CI)			**432**			**471**	**100.0%**	**-1.20 [-2.33 , -0.07]**

Heterogeneity: Tau² = 3.37; Chi² = 101.25, df = 11 (P < 0.00001); I² = 89%
Test for overall effect: Z = 2.09 (P = 0.04)
Test for subgroup differences: Not applicable

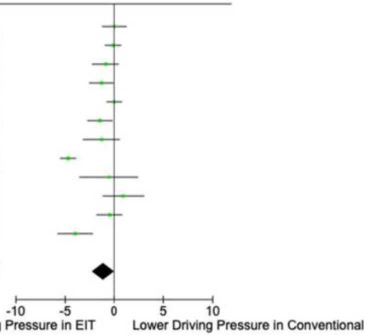
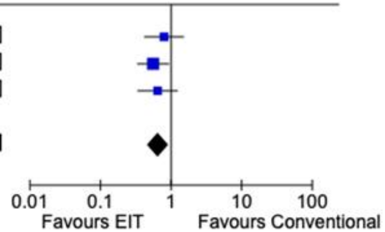


Fig. 4 Comparison of driving pressure between EIT-guided and conventional PEEP titration. *CI* confidence interval, *df* degrees of freedom, I^2 heterogeneity statistic, *IV* inverse variance method

Driving pressure ↓

Study or Subgroup	EIT Events	EIT Total	Conventional Events	Conventional Total	Weight	Risk ratio IV, Random, 95% CI
He 2021	13	61	15	56	28.5%	0.80 [0.42 , 1.52]
Hsu 2021	13	42	25	45	44.0%	0.56 [0.33 , 0.94]
Zhao 2019	8	24	16	31	27.5%	0.65 [0.33 , 1.25]
Total (95% CI)		**127**		**132**	**100.0%**	**0.64 [0.45 , 0.91]**
Total events:	34		56			

Heterogeneity: Tau² = 0.00; Chi² = 0.70, df = 2 (P = 0.70); I² = 0%
Test for overall effect: Z = 2.51 (P = 0.01)
Test for subgroup differences: Not applicable



Mortality RR 0.64
來自少數研究

Intensive Care Med (2024) 50:617–631

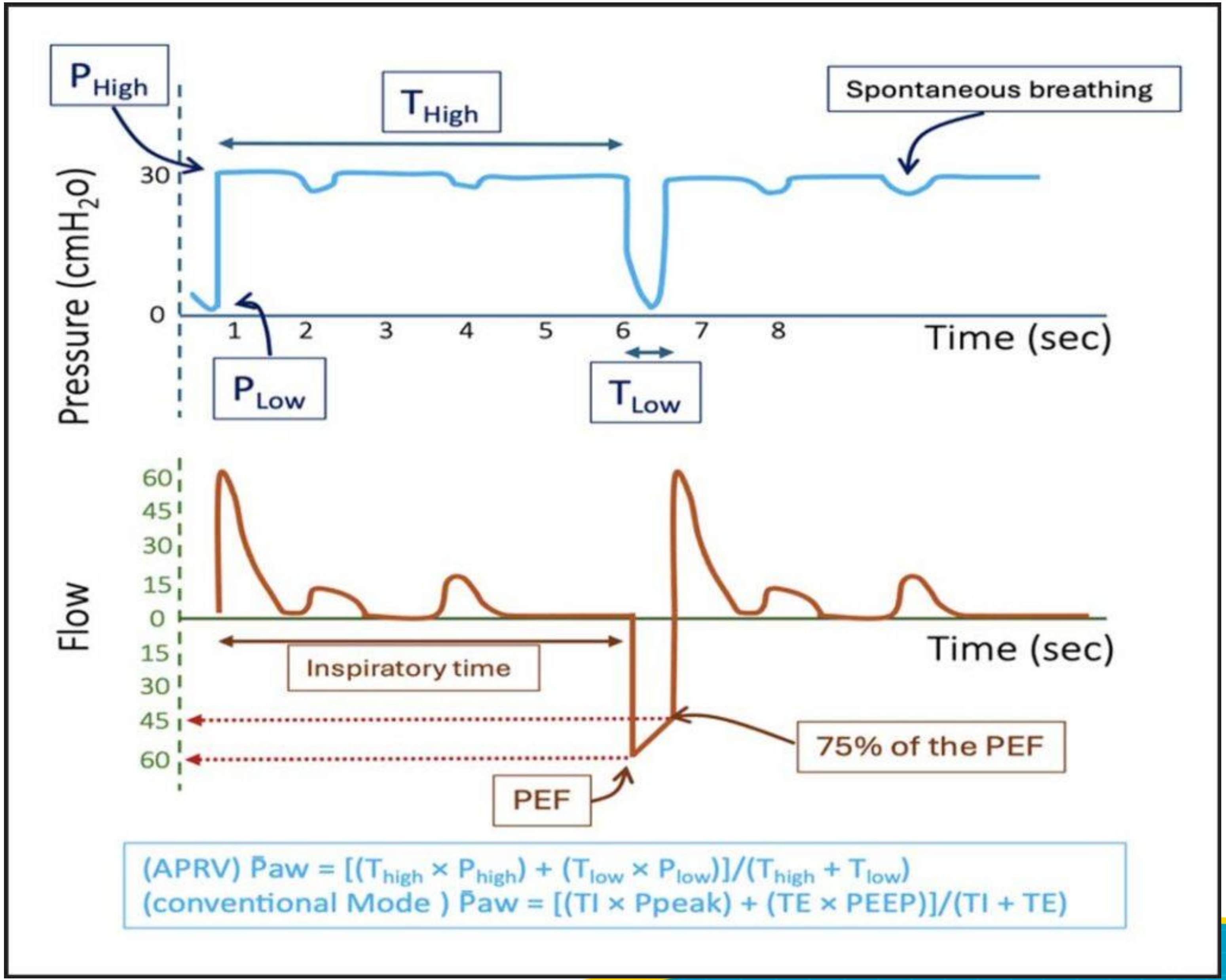
APRV、HFOV、$ECCO_2$-R

APRV: airway pressure release ventilation

APRV generates a higher mean airway pressure ($\bar{P}aw$) compared with conventional ventilation.

APRV can support for spontaneous breathing throughout the ventilation cycle

maintain diaphragm activity, improving patient comfort and synchrony (?)



Efficacy of airway pressure release ventilation for ARDS

-6 個 RCT、共 360 位 ARDS 病人

-所有研究都有unclear risk of bias

-APRV 的設定高度不一致

-對 PaO2/FiO2 的結果並沒有顯著改善

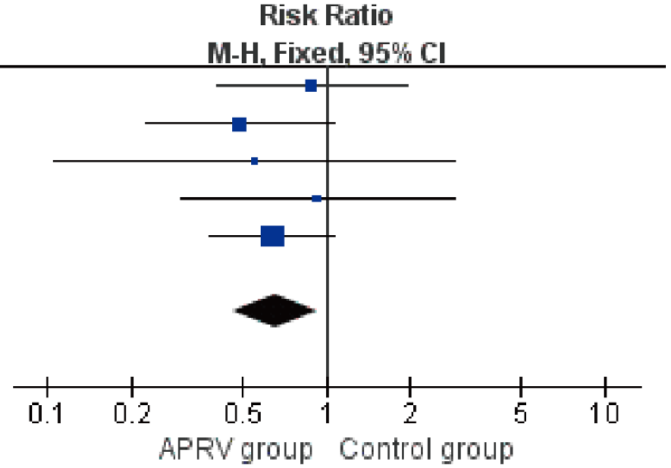
Table 1 The basic information of the studies

Studies included	Intervention measures	Sample size	Male and female ratios	Age: APRV group	Age: Control group	Country	Outcomes
Zhou Y 2017	APRV + LTV	138	91/47	51.5±15.0	52.0±15.1	China	PaO_2/FiO_2, 28-day mortality, MAP, Ppeak
Li JQ 2016	APRV + SIMV	52	NA	54.3±8.4	53.6±9.5	China	PaO_2/FiO_2, 28-day mortality, MAP, Ppeak
Varpula T 2004	APRV + SIMV	58	39/19	50.0 (38.5–60.5)	44.0 (35.5–53.0)	Finland	PaO_2/FiO_2, 28-day mortality, MAP
Varpula T 2003	APRV + SIMV-PC/PS	33	25/8	50.0 (37.0–60.0)	46.5 (37.2–55.3)	Finland	28-day mortality
Ota K 2009	APRV + SIMV	57	NA	NA	NA	USA	PaO_2/FiO_2, 28-day mortality
Song S 2016	APRV + SIMV	22	13/9	63 [40, 73]	73 [53, 80]	China	PaO_2/FiO_2, MAP, Ppeak

28-day mortality

Study or Subgroup	APRV group Events	APRV group Total	Control group Events	Control group Total	Weight	Risk Ratio M-H, Fixed, 95% CI
J.-Q.LI 2016	8	26	9	26	15.7%	0.89 [0.41, 1.94]
Ota, K 2009	5	17	24	40	24.9%	0.49 [0.23, 1.07]
T.VARPULA 2003	2	18	3	15	5.7%	0.56 [0.11, 2.90]
T.VARPULA 2004	5	30	5	28	9.0%	0.93 [0.30, 2.88]
Zhou Y 2017	17	71	25	67	44.7%	0.64 [0.38, 1.08]
Total (95% CI)		**162**		**176**	**100.0%**	**0.66 [0.47, 0.94]**
Total events	37		66			

Heterogeneity: Chi² = 1.53, df = 4 (P = 0.82); I² = 0%
Test for overall effect: Z = 2.30 (P = 0.02)



Ann Palliat Med. 2021 Oct;10(10):10349-10359.

Chest 2025搭配EIT: APRV可改善生理數值

CRITICAL CARE

In Patients With ARDS, Does Airway Pressure Release Ventilation Have Benefits Compared With Low Tidal Volume Ventilation?

CHEST

STUDY DESIGN

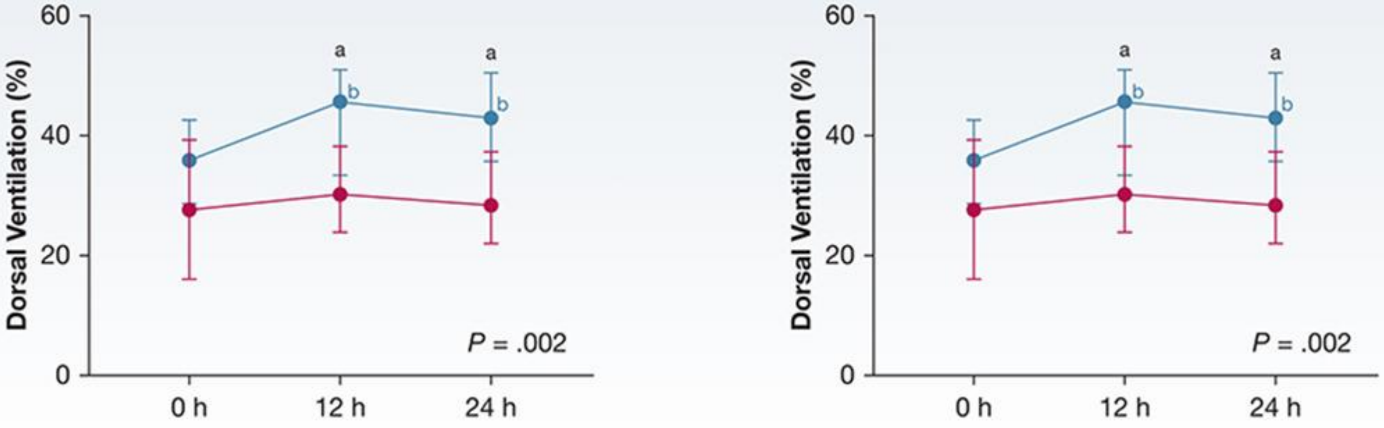
Single-center randomized controlled trial of 40 patients with moderate-to-severe ARDS

Compared lung ventilation and ventilation/perfusion ($\dot{V}/\dot{Q}$) homogeneity at 0, 12, and 24 hours via electrical impedance tomography

RESULTS

Patients with airway pressure release ventilation had:

Increased dorsal ventilation	Decreased dorsal shunt
Increased dorsal $\dot{V}/\dot{Q}$ matching	Lower ventilation distribution heterogeneity
Higher PaO_2/FiO_2 ratio	Higher respiratory system compliance
Lower CO_2	



Dorsal V/Q at 0, 12, and 24 hours for low tidal volume (LTV) and airway pressure release ventilation (APRV)

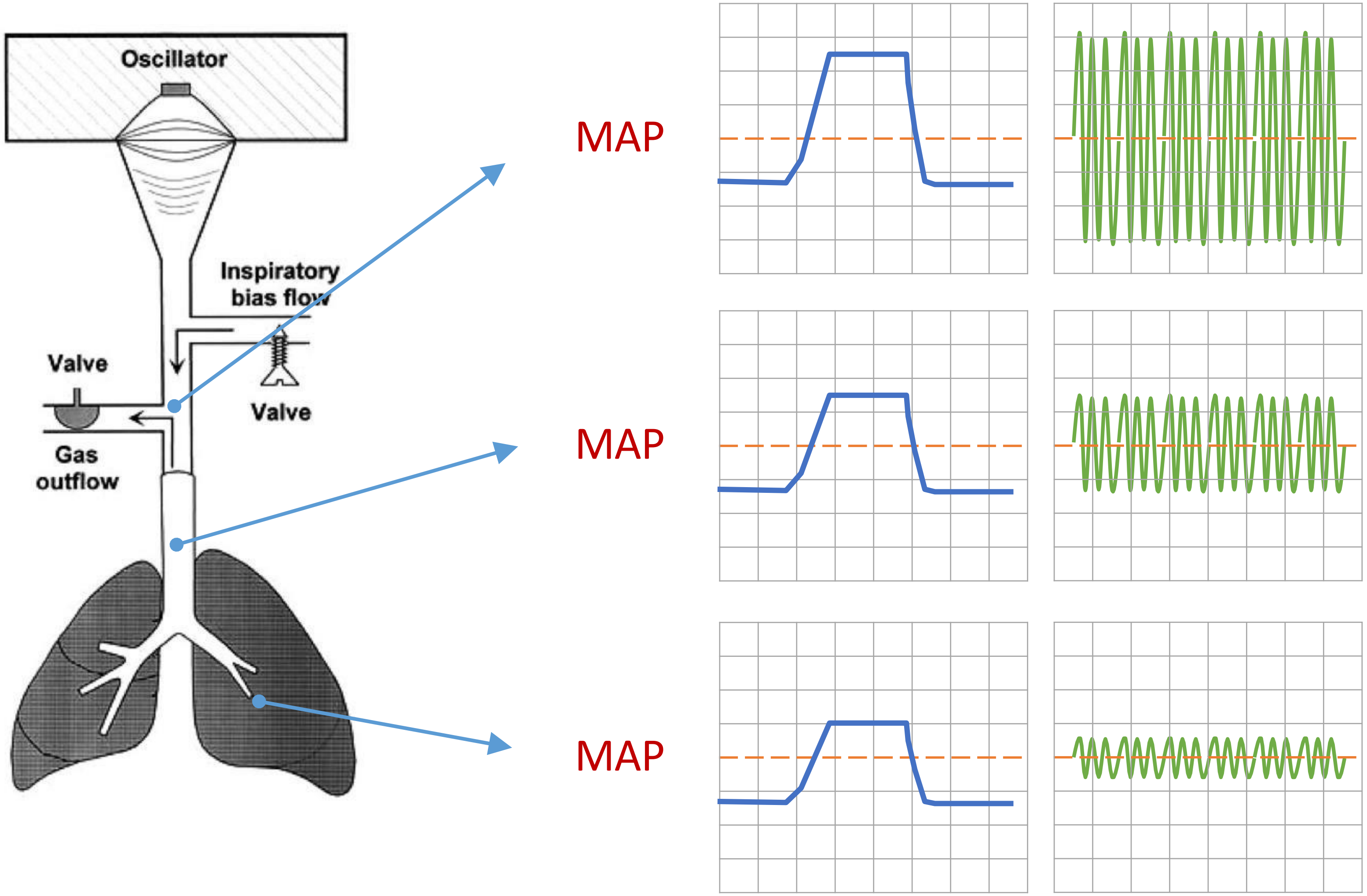
In ventilated patients with ARDS, compared with low tidal volume, airway pressure release ventilation recruited dorsal lung, decreased dorsal shunt, and improved dorsal $\dot{V}/\dot{Q}$ matching, which may contribute to higher blood oxygenation and compliance.

Yang L, et al. *CHEST* February 2025 | @journal_CHEST | https://doi.org/10.1016/j.chest.2024.08.050

High-Frequency Oscillation Ventilation 高頻震盪通氣

Paw: 25-35 cm H2O
Frequency: 3-6 Hz
ΔP: 60-90 cm H2O

Tidal volume: 1-3 mL/kg



Chan. Chest 2007

HFOV高頻震盪通氣的理論基礎

- High mean Paw
- Very small tidal volume (1-3 mL/kg)

- Potential benefits
- ↑ Lung recruitment
- ↓ Stress/strain (VILI)

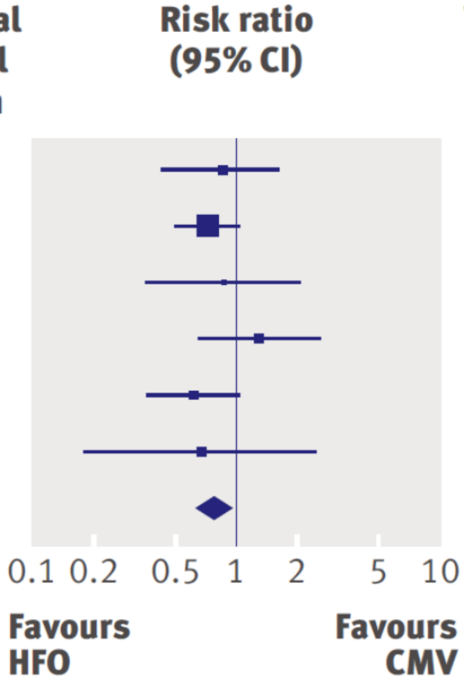
BMJ

RESEARCH

High frequency oscillation in patients with acute lung injury and acute respiratory distress syndrome (ARDS): systematic review and meta-analysis

Sachin Sud, fellow,[1] Maneesh Sud, medical student,[2] Jan O Friedrich, assistant professor,[3] Maureen O Meade, associate professor,[4] Niall D Ferguson, assistant professor,[5] Hannah Wunsch, assistant professor,[6] Neill K J Adhikari, lecturer[7]

	High frequency oscillation	Conventional mechanical ventilation	Weight (%)	Risk ratio (95% CI)
Arnold 1994	10/29	12/29	13.0	0.83 (0.43 to 1.62)
Derdak 2002	28/75	38/73	42.6	0.72 (0.50 to 1.03)
Shah 2004	6/15	6/13	7.9	0.87 (0.37 to 20.4)
Bollen 2005	16/37	8/24	12.5	1.30 (0.66 to 2.55)
Mentzelopoulus 2007	11/27	18/27	20.6	0.61 (0.36 to 1.04)
Samransamruajkit 2005	2/6	5/10	3.4	0.67 (0.18 to 2.42)
Total (95% CI)	73/189	87/176	100.0	0.77 (0.61 to 0.98)



Test for heterogeneity: $\tau^2=0.00$, $\chi^2=3.36$, df=5, P=0.64, $I^2=0\%$

Test for overall effect: z=2.12, P=0.03

Fig 2 | Hospital or 30 day mortality in patients with acute lung injury/acute respiratory distress syndrome allocated to high frequency oscillation or conventional mechanical ventilation

BMJ 2010;340:c2327

OSCILLATE Trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 28, 2013 VOL. 368 NO. 9

High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome

Niall D. Ferguson, M.D., Deborah J. Cook, M.D., Gordon H. Guyatt, M.D., Sangeeta Mehta, M.D., Lori Hand, R.R.T., Peggy Austin, C.C.R.A., Qi Zhou, Ph.D., Andrea Matte, R.R.T., Stephen D. Walter, Ph.D., Francois Lamontagne, M.D., John T. Granton, M.D., Yaseen M. Arabi, M.D., Alejandro C. Arroliga, M.D., Thomas E. Stewart, M.D., Arthur S. Slutsky, M.D., and Maureen O. Meade, M.D., for the OSCILLATE Trial Investigators and the Canadian Critical Care Trials Group*

N Engl J Med 2013;368:795-805

OSCAR Trial

ORIGINAL ARTICLE

High-Frequency Oscillation for Acute Respiratory Distress Syndrome

Duncan Young, D.M., Sarah E. Lamb, D.Phil., Sanjoy Shah, M.D., Iain MacKenzie, M.D., William Tunnicliffe, M.Sc., Ranjit Lall, Ph.D., Kathy Rowan, D.Phil., and Brian H. Cuthbertson, M.D., for the OSCAR Study Group*

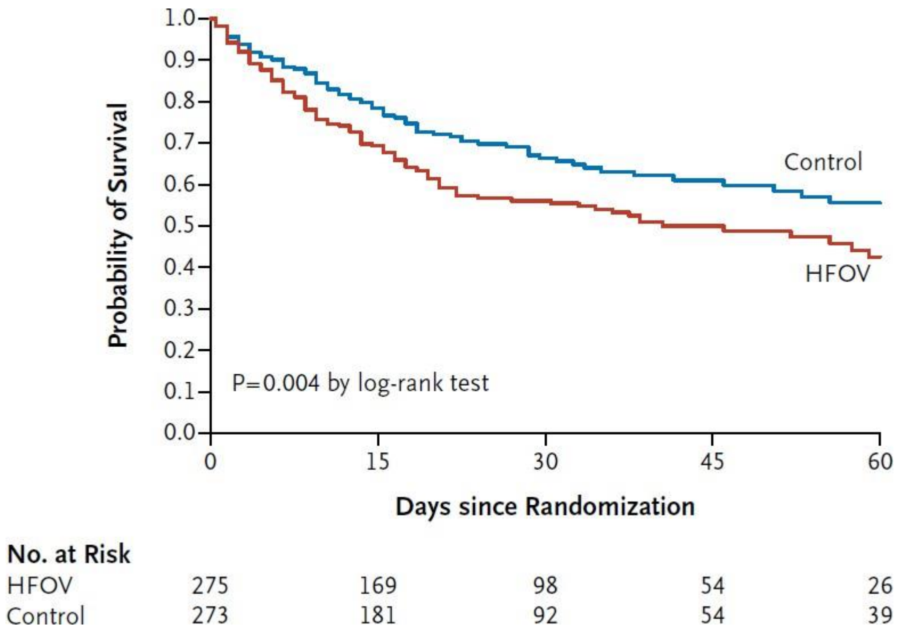
N Engl J Med 2013;368:806-813

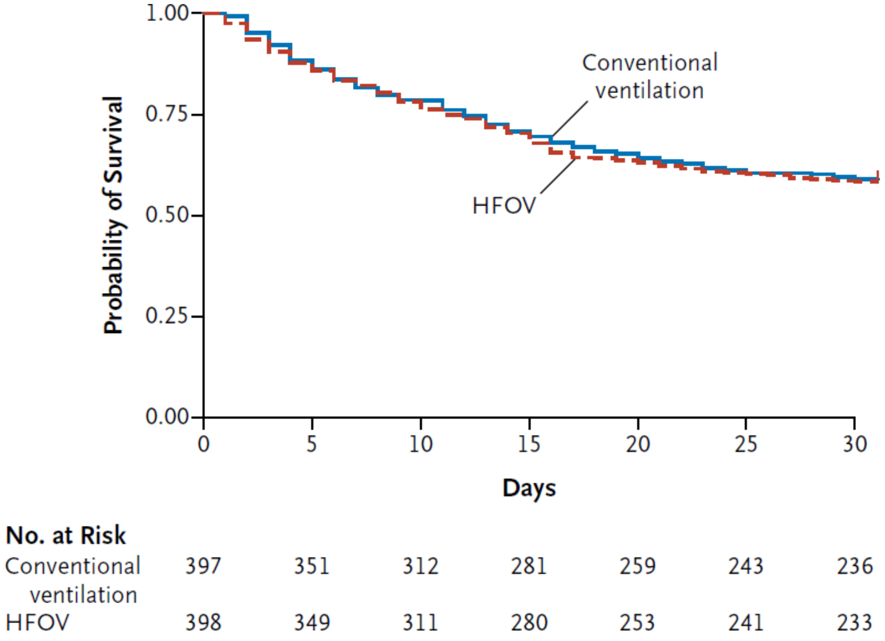
	OSCILLATE	OSCAR
PaO2:FiO2	117 mmHg	113 mmHg
Mean airway pressure (D1)	30 cm H_2O	26.9 cm H_2O
Frequency	5.5	7.8
Recruitment maneuvers	Prior to HFOV	Nil

-HFOV 雖降低 tidal stretch，但可能增加 static stress

-HFOV較高的mean airway pressure可能影響右心功能

-需要深度鎮靜與肌鬆





ECCO$_2$ removal + low tidal volume, JAMA 2021

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Lower Tidal Volume Ventilation Facilitated by Extracorporeal Carbon Dioxide Removal vs Standard Care Ventilation on 90-Day Mortality in Patients With Acute Hypoxemic Respiratory Failure

The REST Randomized Clinical Trial

以目前證據，沒有證明EECO$_2$-R能改善死亡率且adverse event發生率較高

JAMA. 2021;326(11):1013-1023.

Figure 2. Kaplan-Meier Curve of the Time to Death by Treatment Group in a Study of Lower Tidal Volume Facilitated by Extracorporeal Carbon Dioxide Removal in Patients With Acute Hypoxemic Respiratory Failure

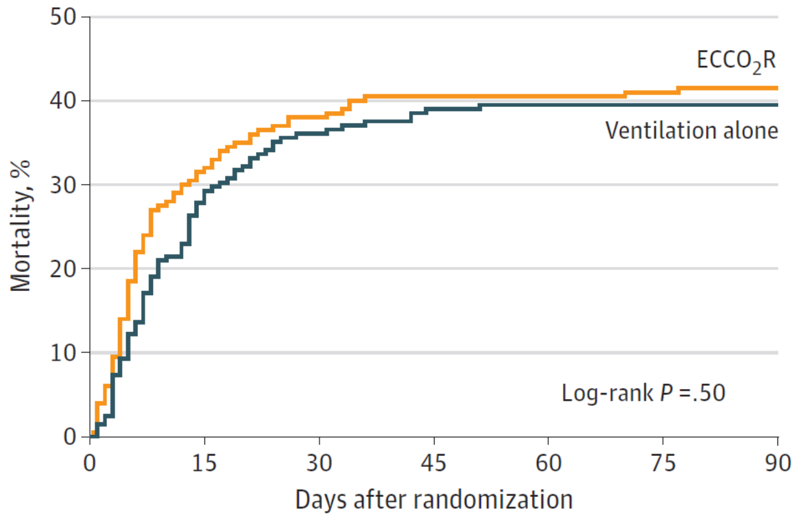
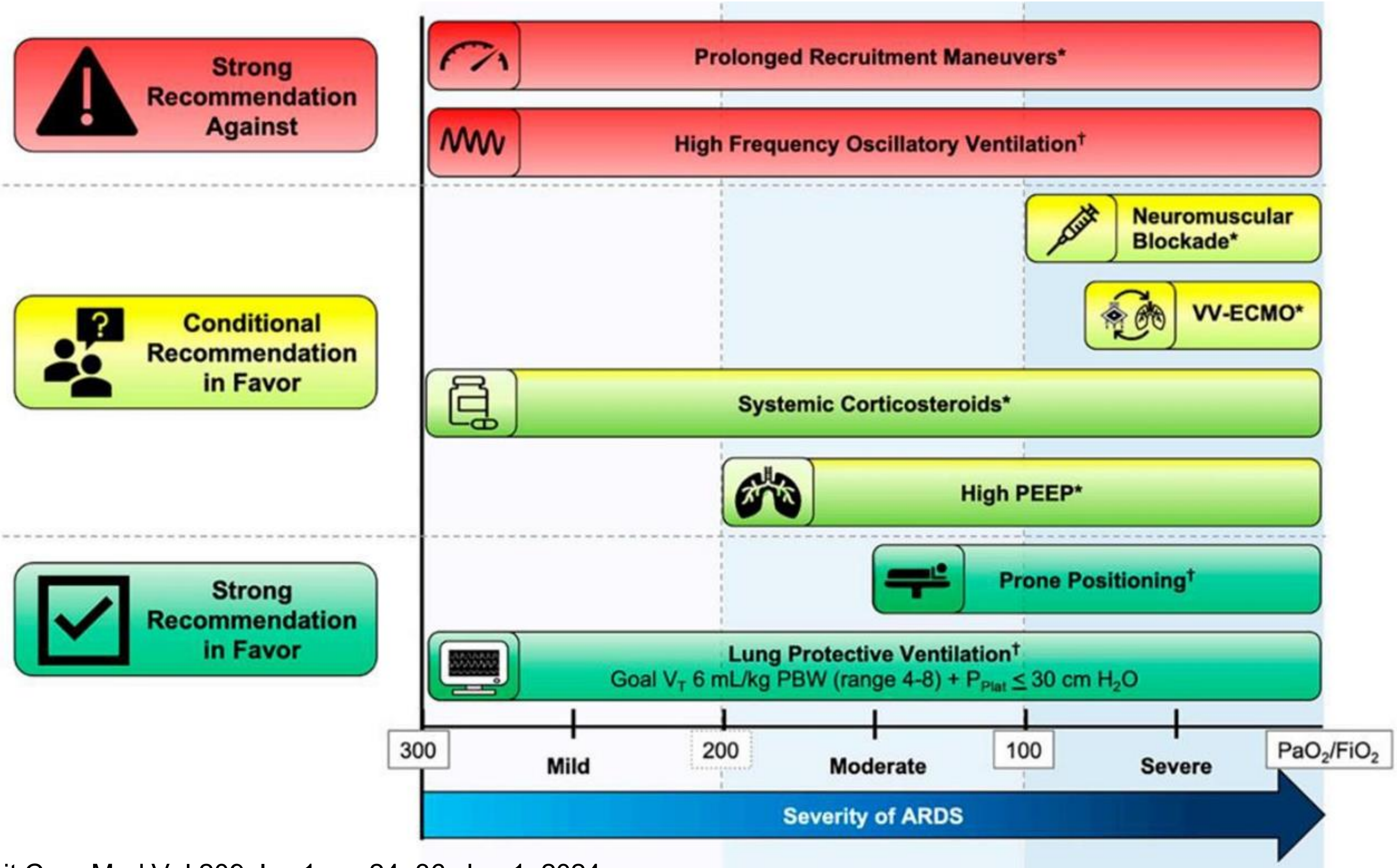


Table 3. Adverse Events in a Study of Lower Tidal Volume Facilitated by Extracorporeal Carbon Dioxide Removal in Patients With Acute Hypoxemic Respiratory Failure

	ECCO$_2$R (n = 202)		Ventilation alone (n = 210)	
Adverse event	No. of events	No. (%) of patients	No. of events	No. (%) of patients
Adverse events[a]	168	106 (52.5)	61	48 (22.9)
Related to study intervention[a,b]	65	51 (25.3)	0	0
Serious adverse events[c,d]	70	62 (30.7)	20	18 (8.6)
Related to study intervention[b]	22	21 (10.4)	0	0

ARDS的2023年最新指引 (ATS)



Am J Respir Crit Care Med Vol 209, Iss 1, pp 24–36, Jan 1, 2024

Take Home Messages

1. ARDS ventilation is not oxygenation chasing.
   -Same P/F ratio ≠ same lung.
2. Lung protection remains the foundation.
   -Low VT、Pplat limitation、lower driving pressure.
3. PEEP is a double-edged tool.
   -High PEEP is not always better; individualized PEEP is the goal.
4. Recruitment requires proof, not belief.
   -Severe hypoxemia does not necessarily mean recruitable lung.
5. The future is bedside personalization.
   -EIT is promising for real-time regional assessment, but outcome evidence is still evolving.

Before every ventilator adjustment, ask:

"Am I opening the lung or injuring it?"