ARDS

Πρεκατές Αθανάσιος
Πνευμονολόγος
Τζάνειο Νοσοκομείο, Β' ΥΠΕ

2Οο Πανελλήνιο Συνέδριο Νοσημάτων
Θώρακος 25 Νοε 2011 ώρα 16.00

ARDS - Οξεία διάχυτη κυψελιδική βλάβη

- **A.** Βαριά ανθεκτική υποO2 (πρώϊμη διασωλήνωση)
- **B.** Πνευμονικό οίδημα με Αυξημένη διαπερατότητα
- **C.** Μειωμένη διατασιμότητα
- **D.** Υψηλή Θνητότητα (40%)

Ορισμός ARDS

i. Προδιαθεσικός παράγοντας
ii. Οξεία έναρξη
iii. Αμφοτερόπλευρα διηθήματα στην Ro θώρακος
iv. PCWP < 18mmHg
v. PaO_2/FiO_2 < 200mmHg ή SpO_2/FiO_2 < 235

1994: American-European consensus conference

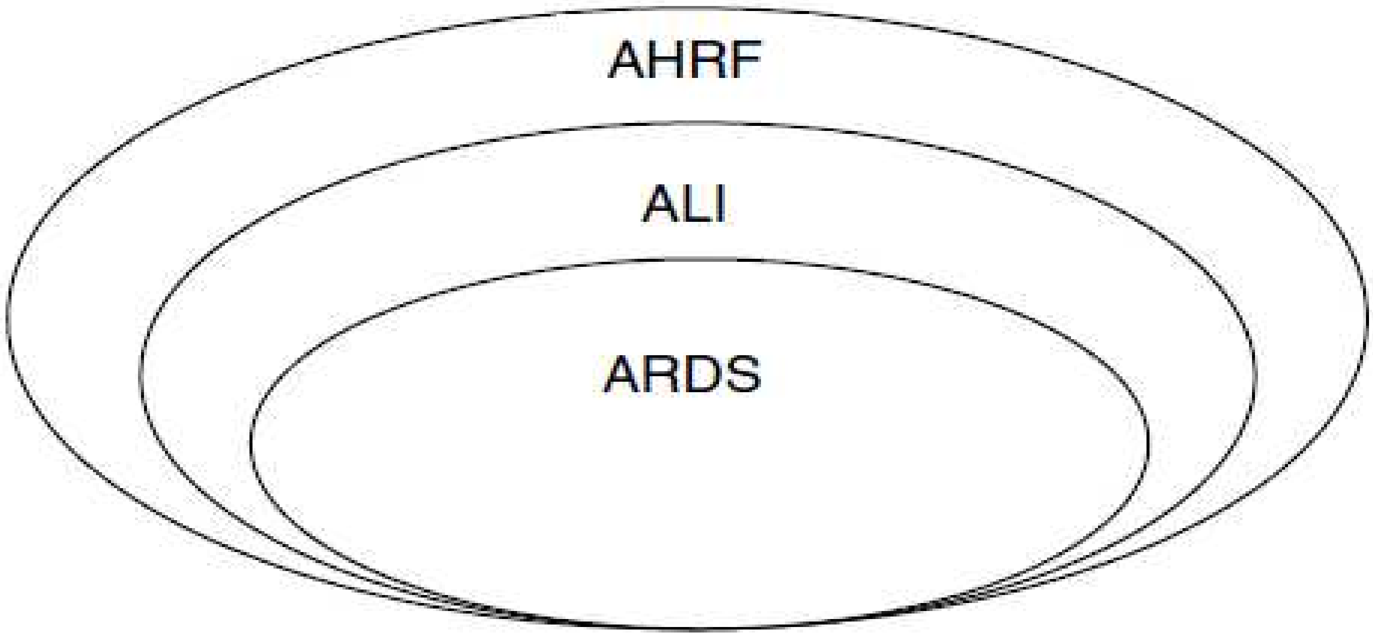


FIGURE 38-2 Schematic representation of the relationships among acute hypoxemic respiratory failure (AHRF), acute lung injury (ALI) and the acute respiratory distress syndrome (ARDS). Note that ALI is a more severe subgroup of AHRF and that ARDS is a more severe form of ALI.

Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

ΑΙΤΙΟΛΟΓΙΑ ARDS (1)
ΑΜΕΣΗ ΠΝΕΥΜΟΝΙΚΗ ΒΛΑΒΗ

- **Η βλάβη είναι στο επιθήλιο του πνεύμονα**

- Πνευμονία (46%)
- Εισρόφηση γαστρικού περιεχομένου (29%)
- Πνευμονική θλάση (34%)
- Λιπώδης εμβολή
- Παρ’ολίγον πνιγμός
- Εισπνοή τοξικών ουσιών
- Βλάβη από επαναιμάτωση

Bersten AD. AJRCCM 2002; 165:476, Pelosi P. ICM 2001; 27:457

ΑΙΤΙΟΛΟΓΙΑ ARDS (2)
ΕΜΕΣΗ - ΕΞΩΠΝΕΥΜΟΝΙΚΗ ΒΛΑΒΗ

- **Η βλάβη στο <u>ενδοθήλιο αγγείων</u>**

- Σήψη (25-46%)
- Πολλαπλούν Τραύμα (41%)
- Αορτοστεφανιαία παράκαμψη
- Τοξική δόση φαρμάκων
- Οξεία παγκρεατίτιδα (25%)
- Μαζική ή Μεταγγίσεις παραγώγων αίματος (TRALI)

Bersten AD. AJRCCM 2002; 165:476, Pelosi P. ICM 2001; 27:457

<u>Παράγοντες Κινδύνου για την ανάπτυξη του ARDS</u>

- Χρόνιος Αλκοολισμός
- Ηλικία και φύλο
- APACHE II, Υπολευκωματιναιμία
- Υπερμεταγγίσεις παραγόντων αίματος
- **<u>Γενετικοί παράγοντες</u>** (δεσμοί μεταλλάξεων στο γονίδιο της surfactant protein B (SP-B) και στο γονίδιο της ACE

Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

- **ARDS – ΠΑΘΟΓΕΝΕΙΑ**

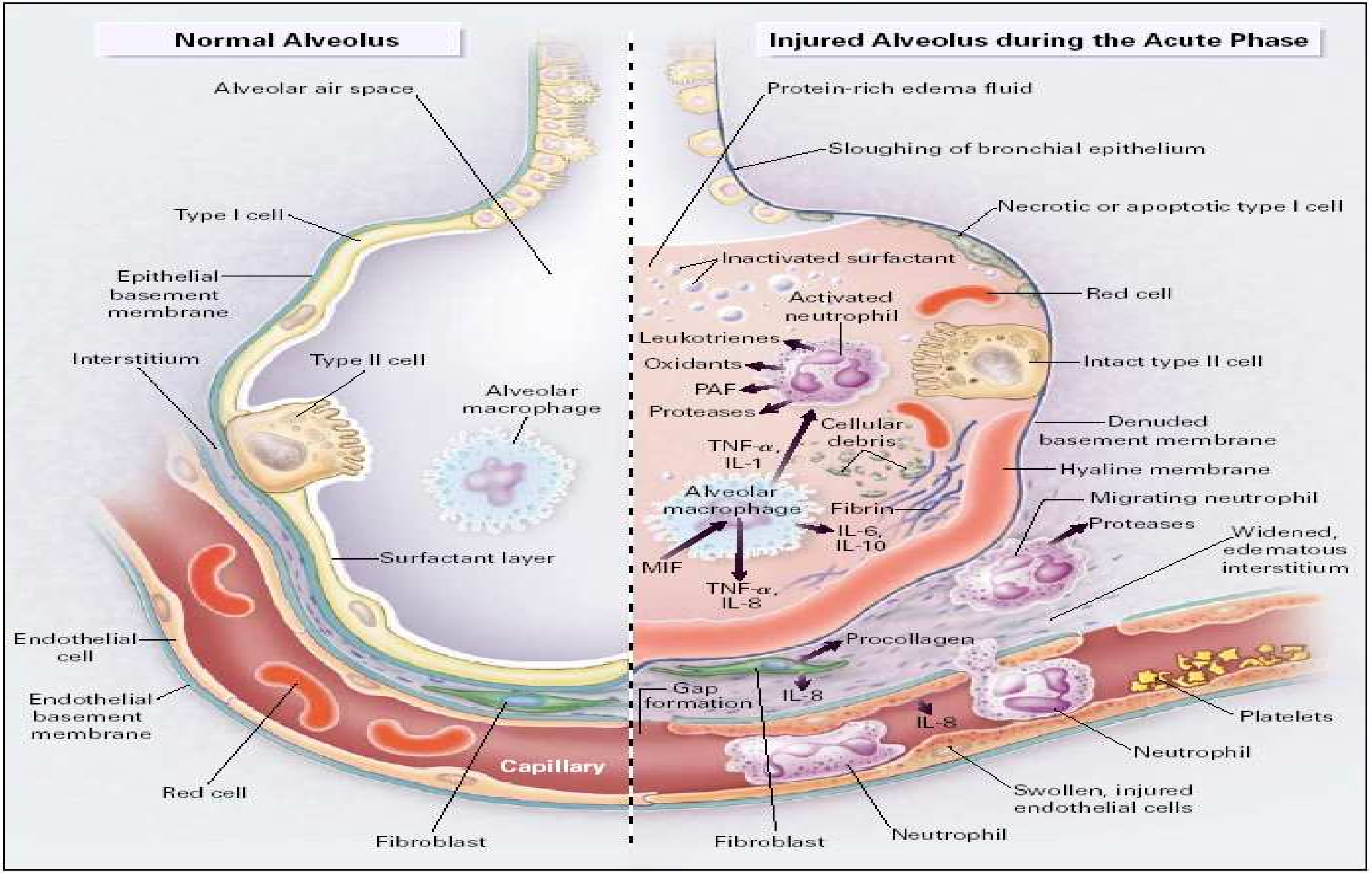


Figure 3. The Normal Alveolus (Left-Hand Side) and the Injured Alveolus in the Acute Phase of Acute Lung Injury and the Acute Respiratory Distress Syndrome (Right-Hand Side).

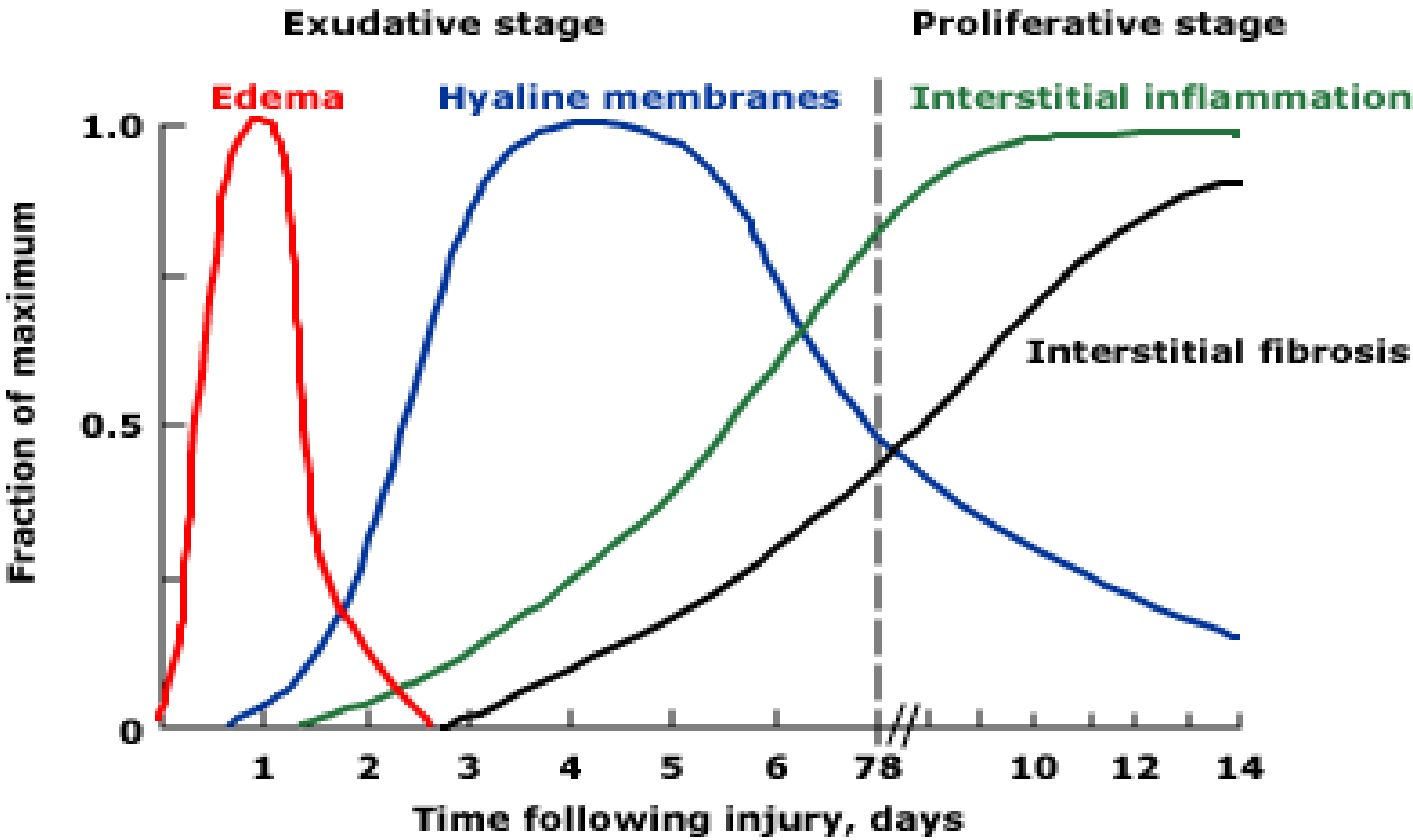
Ware LB, Matthay MA. NEJM 2000; 342:1334

ΧΑΡΑΚΤΗΡΙΣΤΙΚΑ ARDS

	ΠΡΩΪΜΑ	ΟΨΙΜΑ
– Δίκτυο Κολλαγόνου	άθικτο	βλάβη
– Οίδημα	επικρατεί	μέτριο
– Ατελεκτασία	επικρατεί	μειωμένη
– Ινωση	μικρή	επικρατεί

Marini J, 2010 The Essentilas, pp: 430-54, Doyle RL. AJRCCM 1995; 152:1818, Rubenfeld GD. NEJM 2005; 353:1685

Η ΧΡΟΝΙΚΗ ΠΟΡΕΙΑ ΤΟΥ ARDS



Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

- **ARDS - ΠΑΘΟΦΥΣΙΟΛΟΓΙΑ**

Table 29.3 Pathophysiology of acute lung injury (ALI) and adult respiratory distress syndrome (ARDS)

Feature	Cause(s)
Hypoxaemia	True shunt (perfusion of non-ventilated airspaces) Impaired hypoxic pulmonary vasoconstriction *V/Q* mismatch is a minor component
↑ Dependent densities (CT)	Surfactant dysfunction alveolar instability
(Collapse/consolidation)	Exaggeration of normal compression of dependent lung due to ↑ weight (↑ lung water, inflammation)
↑ Elastance (↓ compliance)	Surfactant dysfunction (↑ specific elastance) ↓ Lung volume ('baby lung') ↑ Chest wall elastance Fibrosing alveolitis (late)

Bersten AD. The acute respiratory distress syndrome. In Bersten AD., Soni N. (Eds). Oh's Intensive Care Manual 6th Ed. Butterworth Henemann Elsevier. 2009:375-385

Table 29.3 Pathophysiology of acute lung injury (ALI) and adult respiratory distress syndrome (ARDS)

Feature	Cause(s)
↑ Minute volume requirement	↑ Alveolar dead space (V_{Dphys}/V_t often 0.4–0.7) ↑ $\dot{V}CO_2$
↑ Work of breathing	↑ Elastance ↑ Minute volume requirement
Pulmonary hypertension	Pulmonary vasoconstriction (thromboxane A_2, endothelin) Pulmonary microvascular thrombosis Fibrosing alveolitis Positive end-expiratory pressure

Bersten AD. The acute respiratory distress syndrome. In Bersten AD., Soni N. (Eds). Oh's Intensive Care Manual 6th Ed. Butterworth Henemann Elsevier. 2009:375-385

Δ.Δ. ARDS

1. Καρδιογενές Πνευμονικό Οίδημα
2. Βαριά Πνευμονία
3. Κρυπτογενής Οργανού-μενη Πνευμονία (COP)
4. Διάχυτη Κυψελιδική Αιμορραγία (DAH)
5. Ιδιοπαθής Ηωσινοφι-λική Πνευμονία (IEP)
6. Πνευμονίτιδα εξ' Υπερευαισθησίας
7. Οξεία Διάμεση Πνευμονία (Hamman - Rich)
8. Πνευμονίτιδα του Λύκου
9. Κεγχροειδής Φυματίωση
10. Ταχέως εξελισσόμενος Καρκίνος (Λευχ., Λέμφ..)

Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

Παράγοντες που ορίζουν την έκβαση στο ARDS

1. Προχωρημένη Ηλικία
2. Χαμηλή PaO2/FiO2
3. Αύξηση του Vd/Vt
4. Υψηλή Pplateau (χαμηλή Compliance)
5. Εκταση πνευμονικών διηθήσεων
6. Χρονία ηπατική νόσος
7. Δυσλειτουργία οργάνου
8. Βαρύτητα της νόσου
9. Υπολευκωματιναιμία
10. Η παραμονή στο νοσοκομείο πριν το ARDS
11. APACHE II

Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

Στόχοι στο ARDS

i. Πρώϊμη διάγνωση και εκτίμηση
ii. Θεραπεία
    i. Φαρμακευτική
    ii. Μηχανική υποστήριξη αναπνοής (Μ.Α)
        i. Μη Επεμβατικός Μ.Α.
        ii. Επεμβατικός Μ.Α.

Marini J, 2010 The Essentilas, pp: 430-54, Doyle RL. AJRCCM 1995; 152:1818, Rubenfeld GD. NEJM 2005; 353:1685

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i. Πρώϊμη διάγνωση και εκτίμηση
ii. Θεραπεία
   i. Φαρμακευτική
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ΦΑΡΜΑΚΑ στο ARDS

- Δεν υπάρχει ειδική θεραπεία
- Θεραπεύουμε τη γενεσιουργό αιτία
- Οι υψηλές δόσεις κορτικοστεροειδών **δεν βοηθούν στην πρώϊμη φάση** του ARDS. Προς το παρόν **δεν βοηθούν και κατά την ινωδοπαραγωγική** φάση (3η φάση, 7-10 ημ.)
- Το αρνητικό ισοζύγιο βοηθά

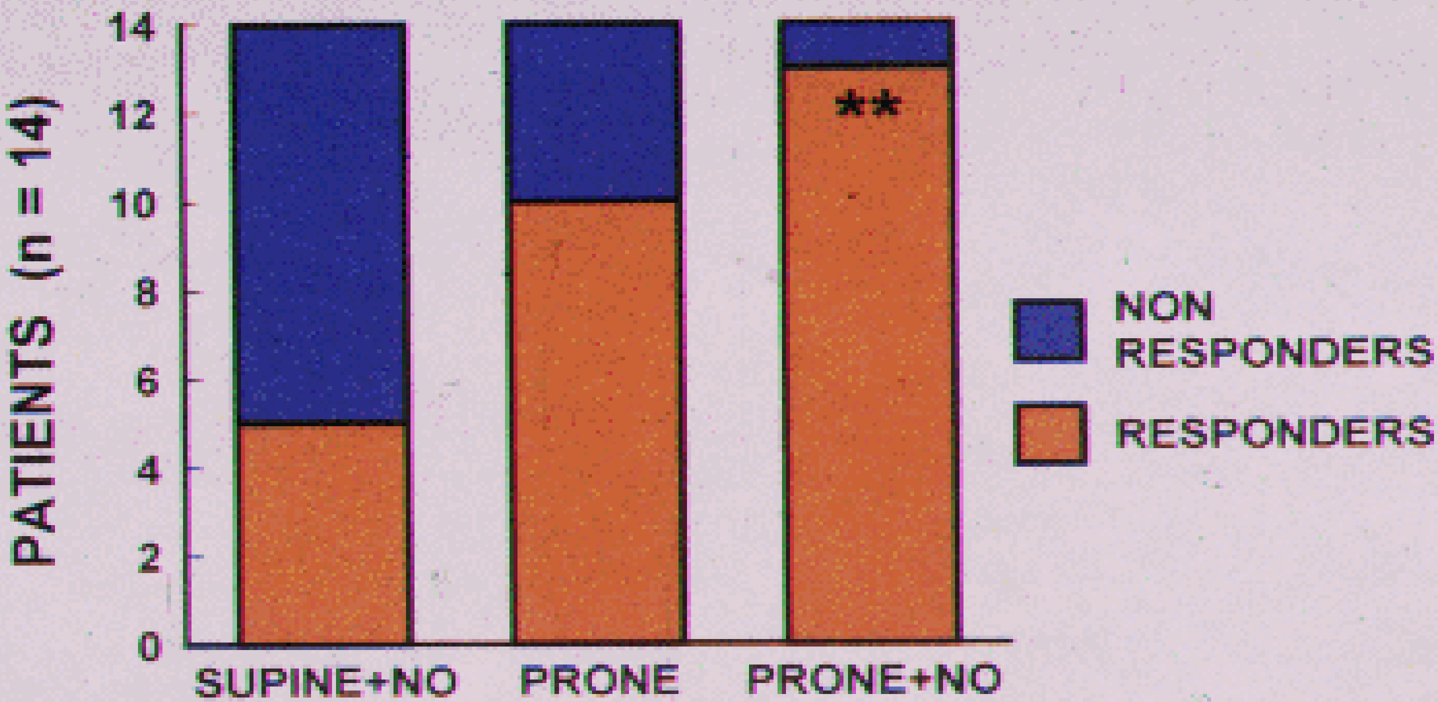
Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),:
Principles of Critical Care. McGraw-Hill. 2005: 515-547

Νόμος Starling

- $Q=K \times [(Pmv-Ppmv) - \sigma (\pi mv-\pi pmv)$

Marini J, Wheeler A. Critical Care Medicine. The essentials, 2010 pp: 430-54

Number of Patients who Respond to a Treatment
Responders: > 20% increment in PaO_2/FiO_2



** $p < 0.05$ respect Supine+NO

Blanch L, et al. Intensive Care Med 1997;23:S18.

Στόχοι στο ARDS

i. Πρώϊμη διάγνωση και εκτίμηση

ii. Θεραπεία

   i. Φαρμακευτική

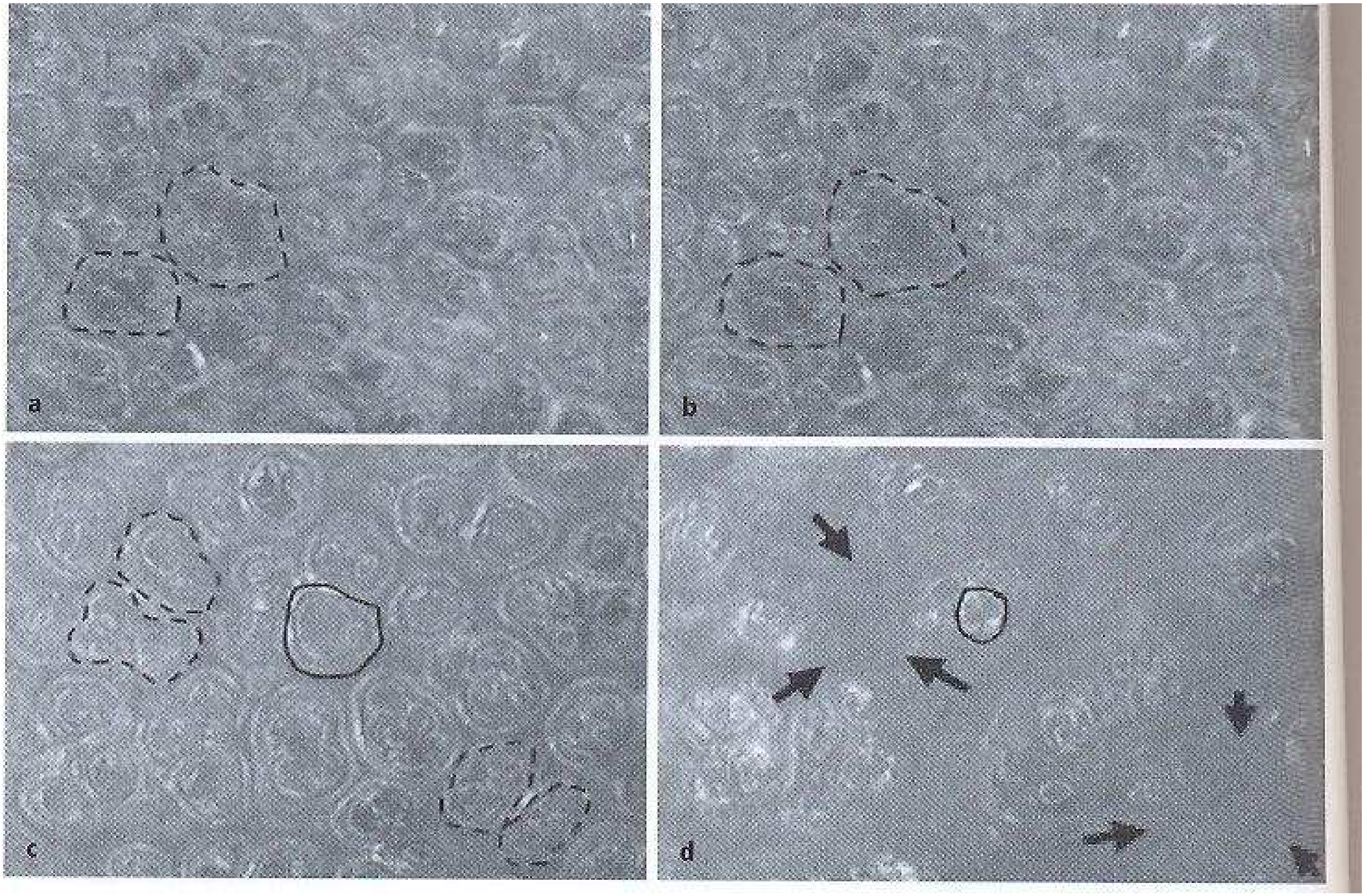
   ii. Μηχανική υποστήριξη αναπνοής (Μ.Α)

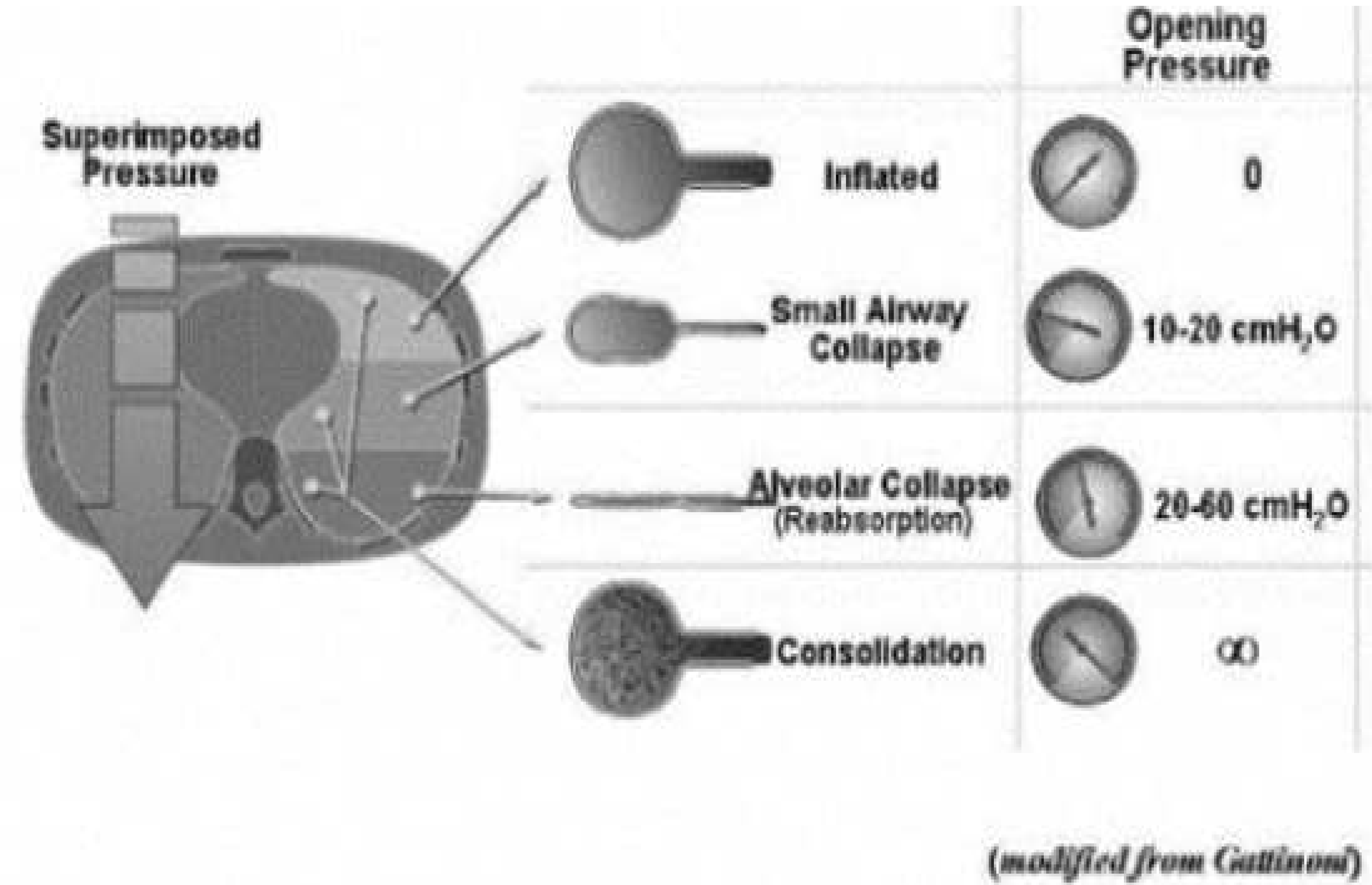
      i. Εκτίμηση

Marini J, 2010 The Essentilas, pp: 430-54, Doyle RL. AJRCCM 1995; 152:1818, Rubenfeld GD. NEJM 2005; 353:1685

ARDS - ΕΚΤΙΜΗΣΗ

- **ΕΤΕΡΟΓΕΝΕΙΑ**





Gattinoni L. AJRCCM 1987; 136:730-6

Ptrs = Palv - Ppl

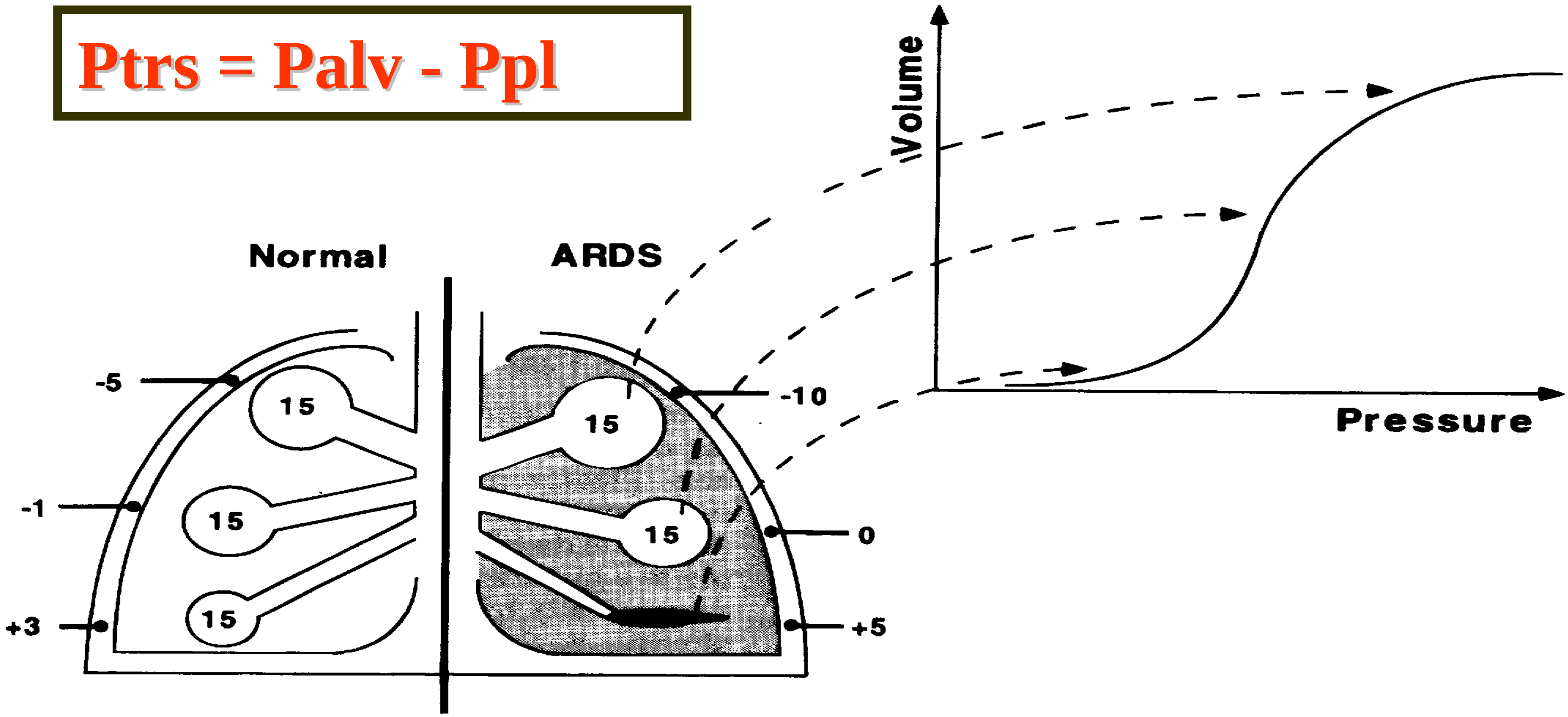


FIG. 9–4. Influence of the gravitational gradient of pressure on regional alveolar mechanics. Dependent alveoli at the base of the lung may remain collapsed at airway pressures that threaten to overdistend those in nondependent regions. Regional mechanics are especially heterogenous in the setting of ARDS. To counterbalance this gradient, higher regional PEEP in dependent areas or modified chest wall compliance in nondependent regions would be needed to improve the uniformity of distention and ventilation.

Marini J, Wheeler A. Critical Care Medicine. The essentials, 2010 pp: 430-54

ARDS – ΕΤΕΡΟΓΕΝΕΙΑ

i. **ΜΕΤΑΞΥ των ΠΕΡΙΟΧΩΝ του ΠΝΕΥΜΟΝΑ**
ii. **ΣΤΗ ΔΙΑΡΚΕΙΑ ΤΟΥ ΧΡΟΝΟΥ**
iii. **ΜΕΤΑΞΥ των ΑΣΘΕΝΩΝ**

Marini J, Wheeler A. Critical Care Medicine. The essentials, 2010 pp: 430-54

Στόχοι στο ARDS

i. Πρώϊμη διάγνωση και εκτίμηση
ii. Θεραπεία
   i. Φαρμακευτική
   ii. Μηχανική υποστήριξη αναπνοής (Μ.Α)
      i. Μη Επεμβατικός Μ.Α.
      ii. Επεμβατικός Μ.Α.

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Στόχοι στο ARDS

i. **Πρώϊμη διάγνωση και εκτίμηση**

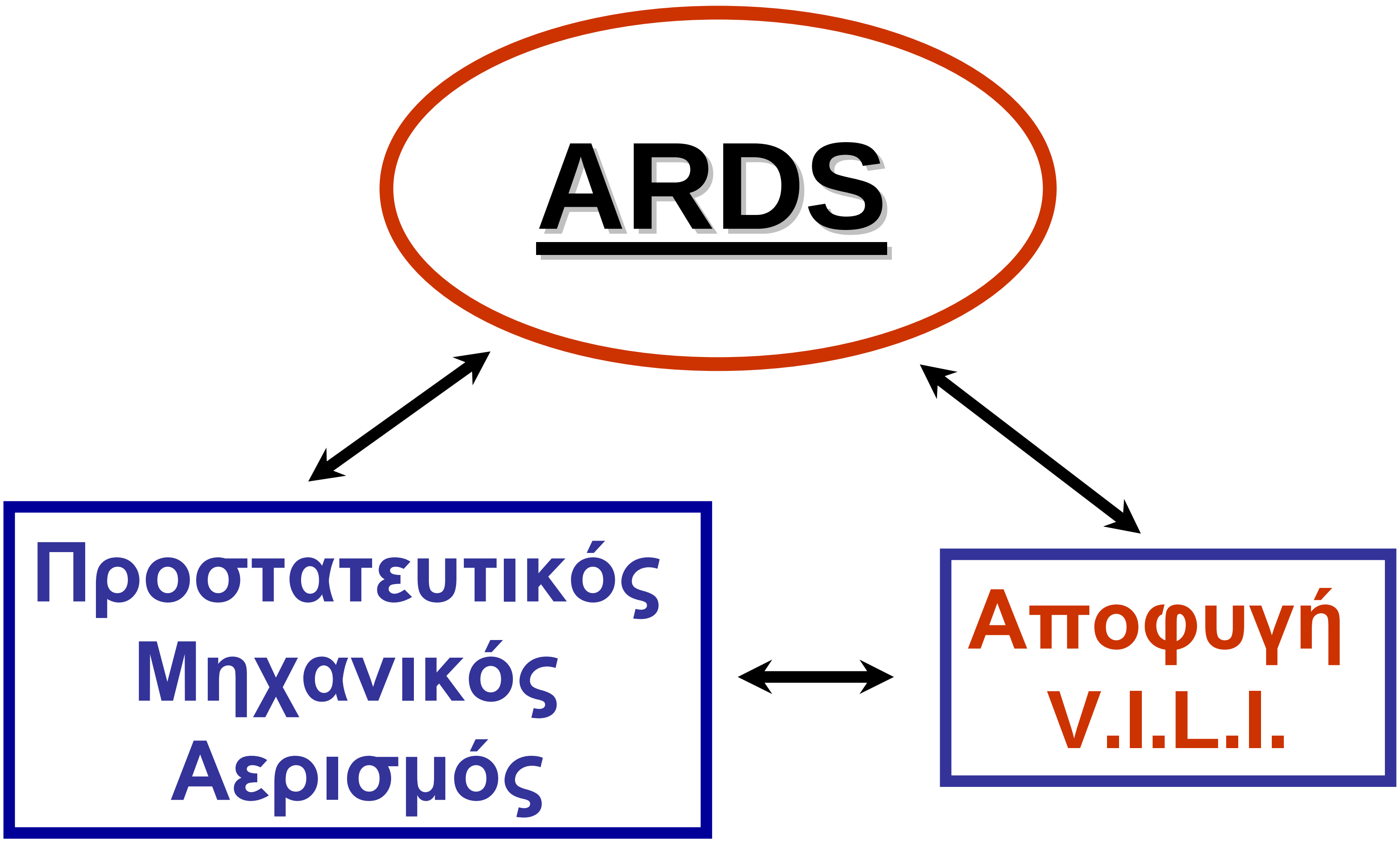
ii. **Θεραπεία**

  i. **Φαρμακευτική**

  ii. **Επεμβατικός Μηχανικός Αερισμός**

    i. **Εκτίμηση** (Raw, C, Ptrans, Poes, ..)

Marini J, 2010 The Essentilas, pp: 430-54, Doyle RL. AJRCCM 1995; 152:1818, Rubenfeld GD. NEJM 2005; 353:1685

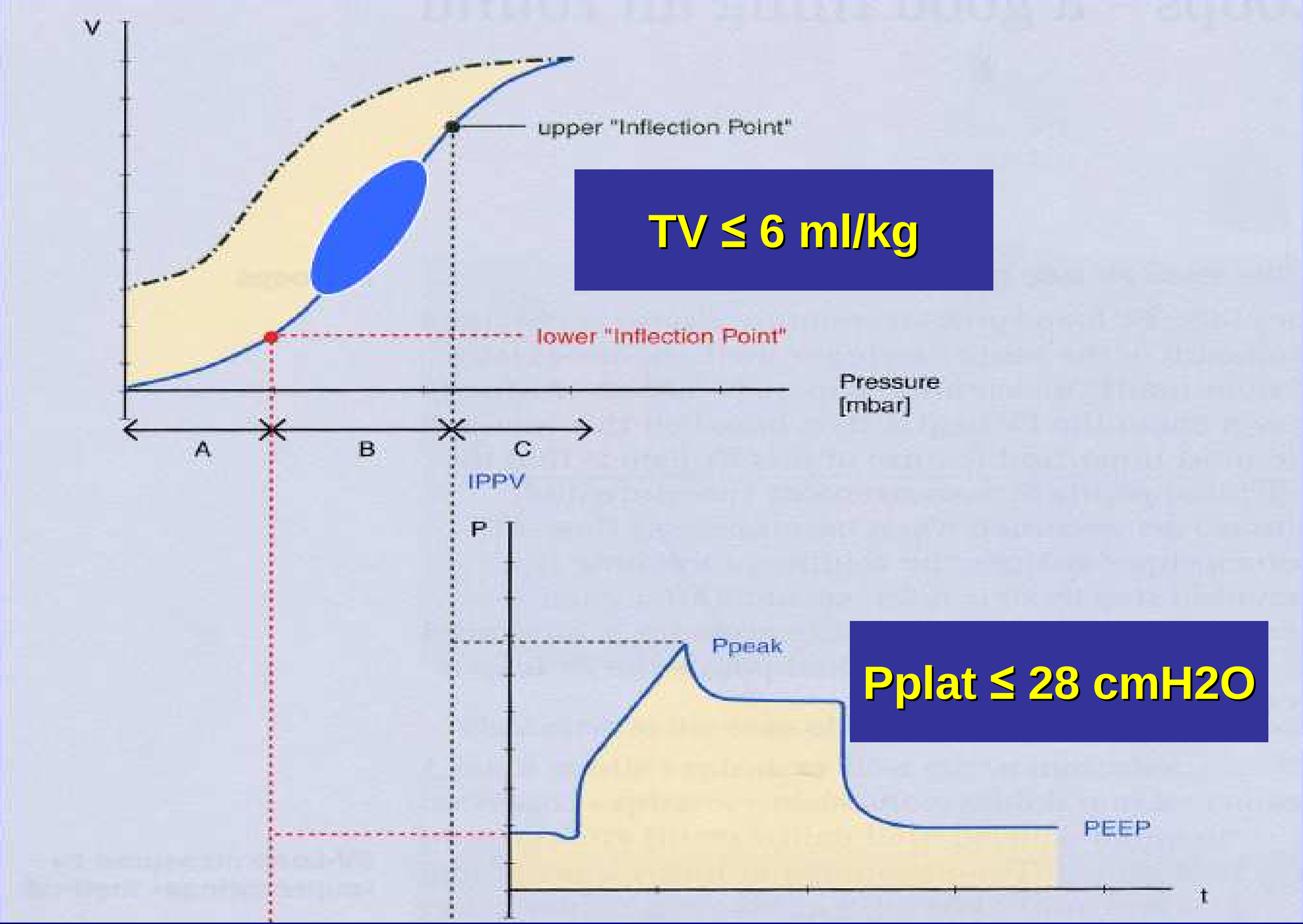


Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

Μηχανικός Αερισμός / ARDS

1. $FiO_2 \leq 0.6$ με $SaO_2 \geq 88\%$ ή $PaO_2 \geq 55$ mmHg

Marini J, Wheeler A. Critical Care Medicine. The essentials, 2010 pp: 430-54



TV ≤ 6 ml/kg

Pplat ≤ 28 cmH2O

TABLE 4. MAIN OUTCOME VARIABLES.*

Variable	Group Receiving Lower Tidal Volumes	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

ARDS NETWORK, NEJM 2000; 342:1301-08

The New England
Journal of Medicine

VOLUME 342 MAY 4, 2000 NUMBER 18

VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

Conclusions In patients with acute lung injury and the acute respiratory distress syndrome, mechanical ventilation with a lower tidal volume than is traditionally used results in decreased mortality and increases the number of days without ventilator use. (N Engl J Med 2000;342:1301-8.)

Μηχανικός Αερισμός στο ARDS

1. $FiO_2 \leq 0.6$ με $SaO_2 \geq 88\%$ ή $PaO_2 \geq 55$ mmHg
2. VT=6 ml/kg, I.B., Προστατευτικός Μ.Α.
3. Pplat < 28-30 cmH20
4. **Επαναστρατολόγηση κυψελίδων (Re)**
5. «Κατάλληλη» PEEP (inflection point, Poes)

Marini J, Wheeler A. Critical Care Medicine. The essentials. 2010;430-54

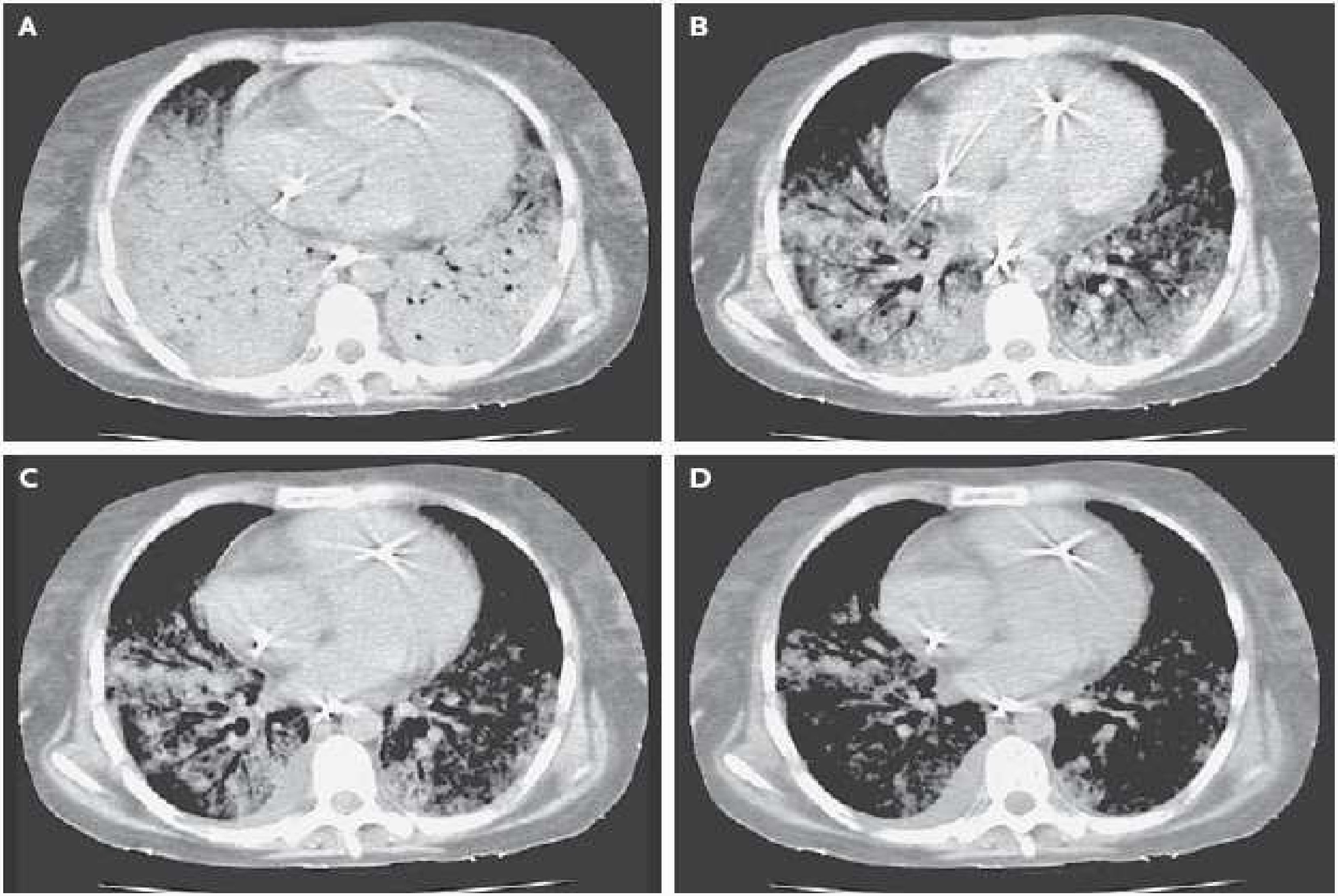


Figure 3. Effects of Recruitment Maneuvers to Promote Homogeneity within the Lung.

Panels A through D show the progressive resolution of infiltrates after application of inflations of increasing pressure. Reprinted from Borges et al.[40]

<u>Μηχανικός Αερισμός στο ARDS</u>

1. $FiO_2 \leq 0.6$ με $SaO_2 \geq 88\%$ ή $PaO_2 \geq 55$ mmHg
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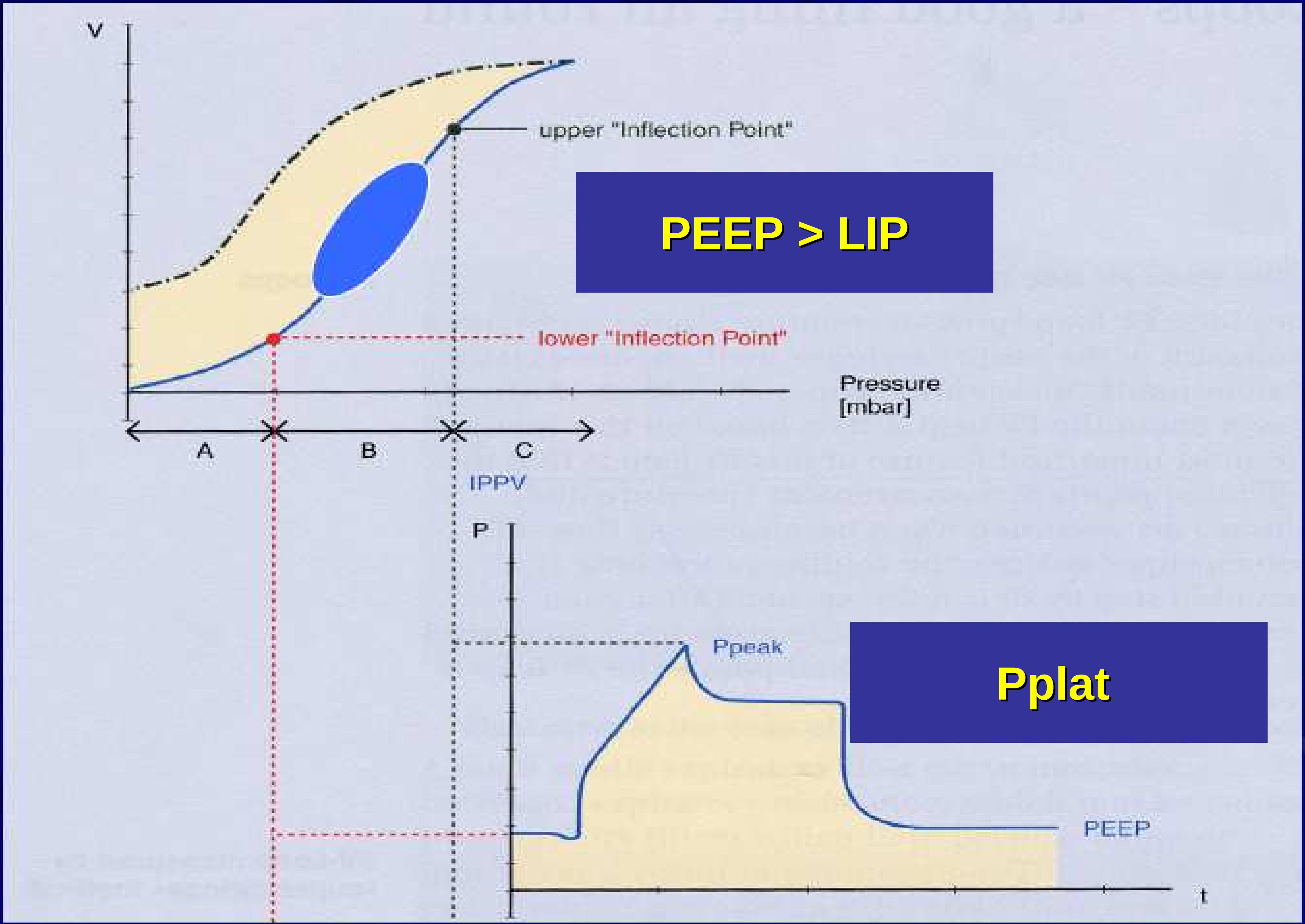
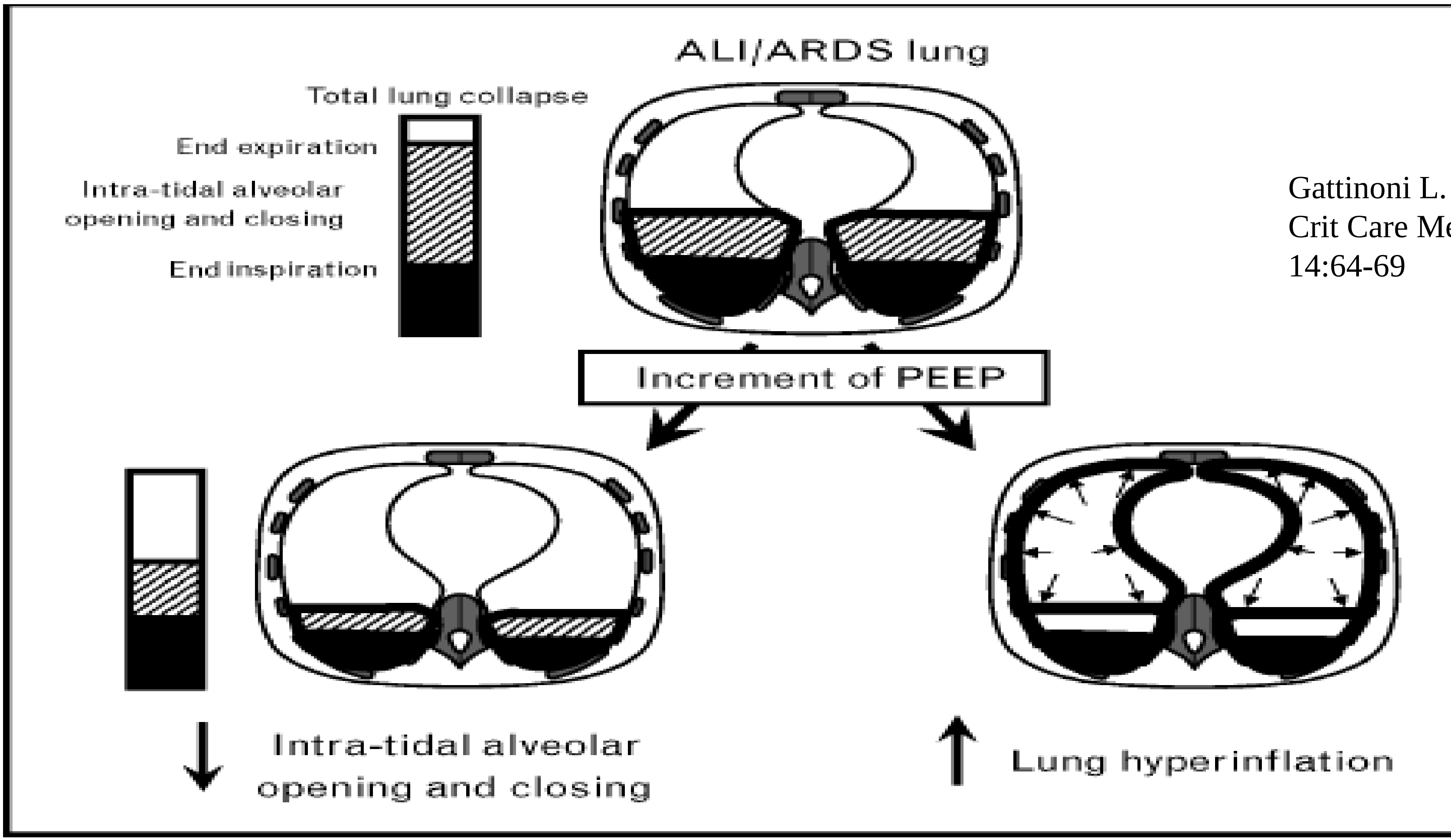
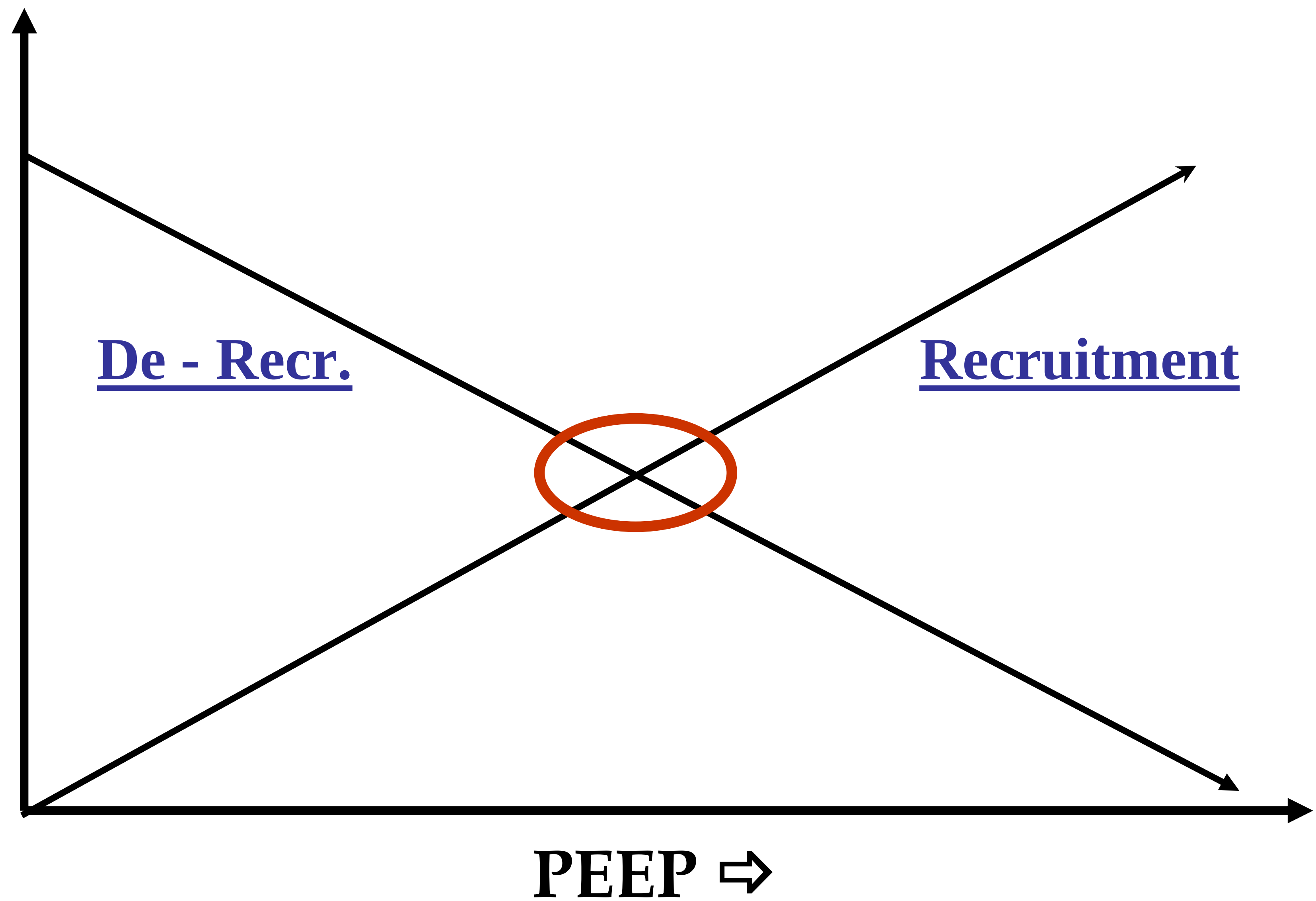

V
upper "Inflection Point"
PEEP > LIP
lower "Inflection Point"
Pressure
[mbar]
A
B
C
IPPV
P
Ppeak
Pplat
PEEP
t

Figure 1 Schematic representation of the effects of the increase of positive end-expiratory pressure (PEEP) on the lung parenchyma during acute lung injury/acute respiratory distress syndrome (ALI/ARDS)



Gattinoni L. Curr Op Crit Care Med 2008; 14:64-69



Ward NS, Levy MM. YearBook of Intensive Care @Emergency Medicine 2002; 297

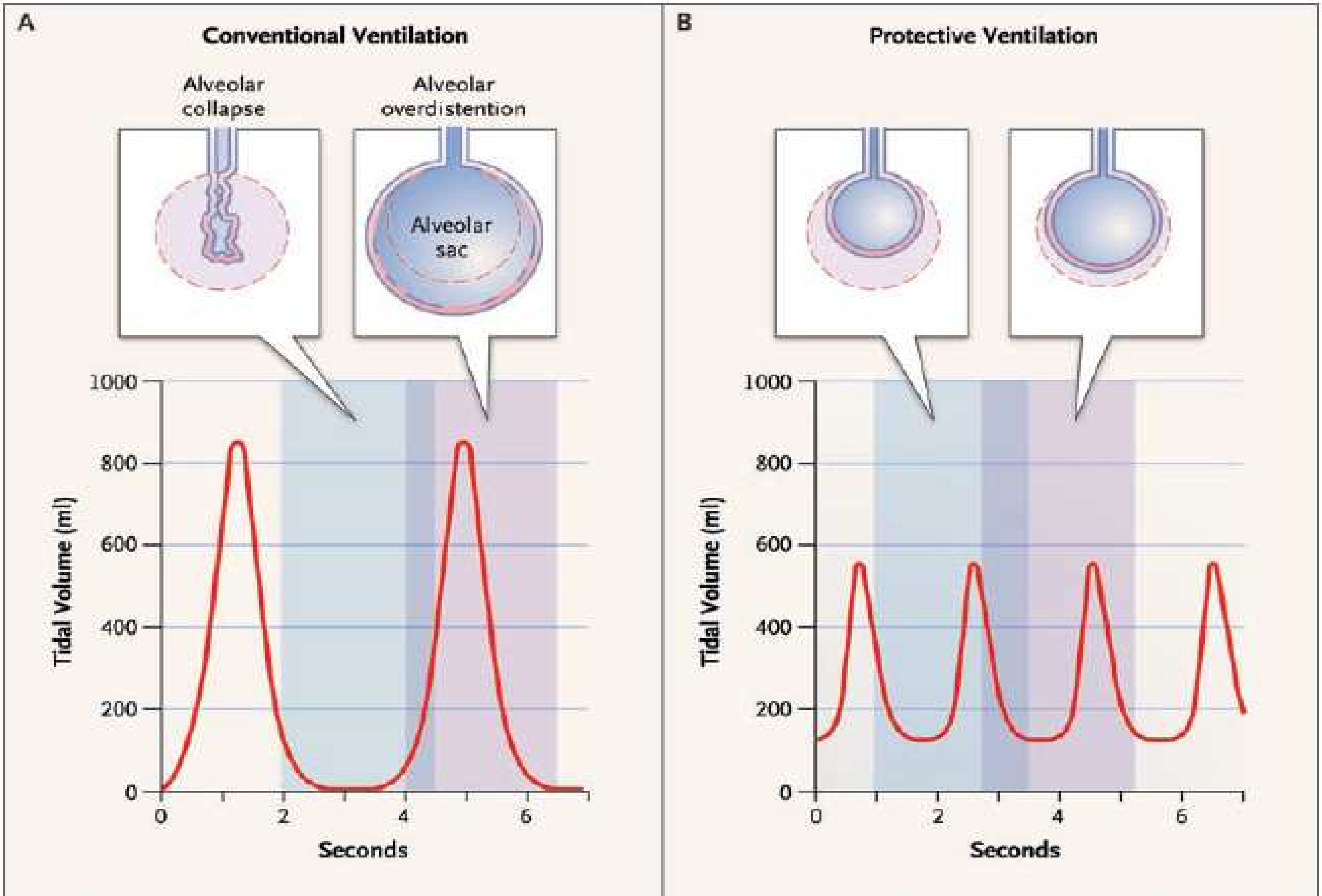


Figure 2. Conventional Ventilation as Compared with Protective Ventilation.

This example of ventilation of a 70-kg patient with ARDS shows that conventional ventilation at a tidal volume of 12 ml per kilogram of body weight and an end-expiratory pressure of 0 cm of water (Panel A) can lead to alveolar overdistention (at peak inflation) and collapse (at the end of exhalation). Protective ventilation at a tidal volume of 6 ml per kilogram (Panel B) limits overinflation and end-expiratory collapse by providing a low tidal volume and an adequate positive end-expiratory pressure. Adapted from Tobin.[18]

Malhora A. NEJM 2007; 357:1113-20

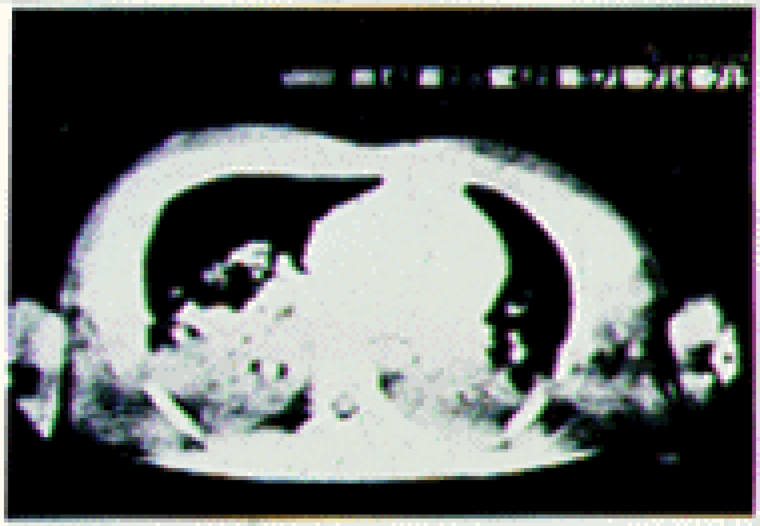
Μηχανικός Αερισμός στο ARDS

7. **Αν η οξυγόνωση δεν βελτιώνεται**

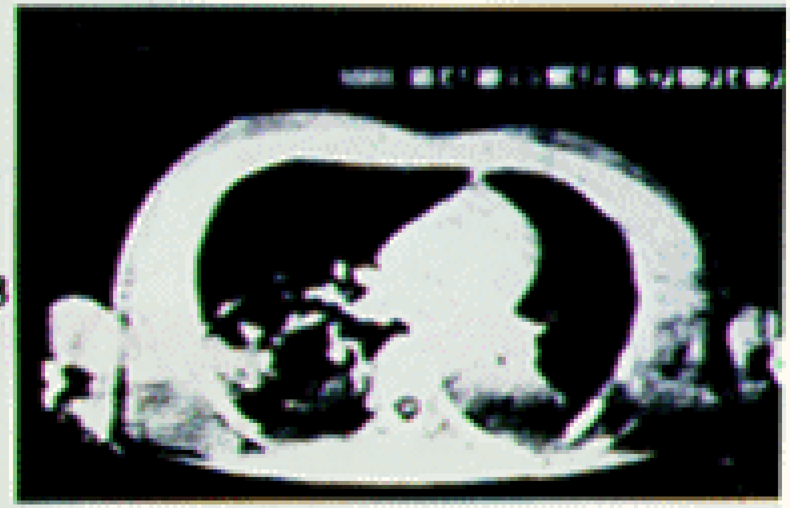
a. επιτρεπόμενη υπερκαπνία
b. I/E ≥ 1
c. υψηλή PEEP
d. **Open Lung Approach**
e. πρηνή θέση
f. Μηχανικός αερισμός υψηλής ταλάντωσης (HFO) ή εξωσωματική οξυγόνωσης (ECMO)

Marini J, Wheeler A. Critical Care Medicine. The essentials. 2010;430-54

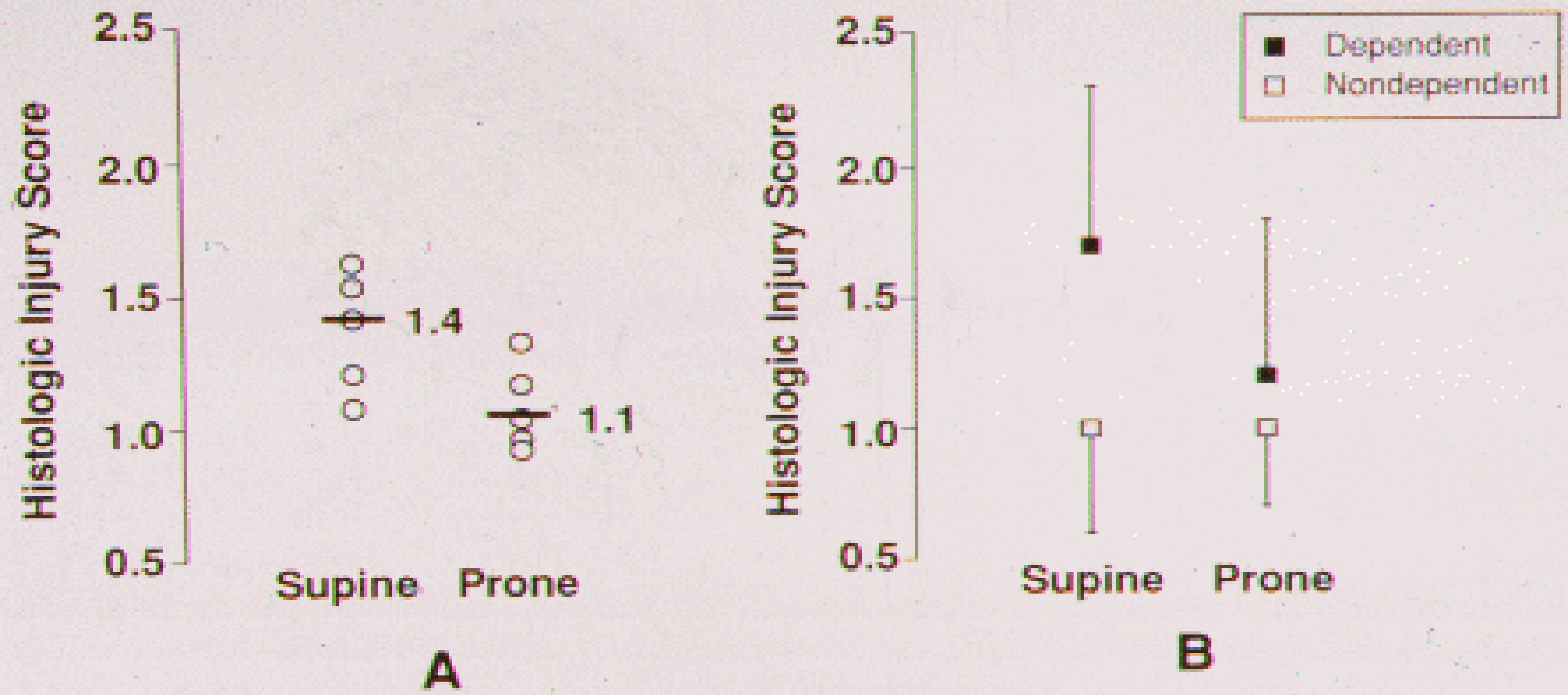
- **<u>ΠΡΗΝΗ ΘΕΣΗ στο ARDS</u>**



Gattinoni
Anesthesiology
69:824–832, 1988



Ventilator Induced Lung Injury
Supine vs Prone Position



- **Βλάβη στον Πνεύμονα**
  - **λόγω Αναπνευστήρα**
- **Vendilator-Induced Lung Injury (V.I.L.I.)**

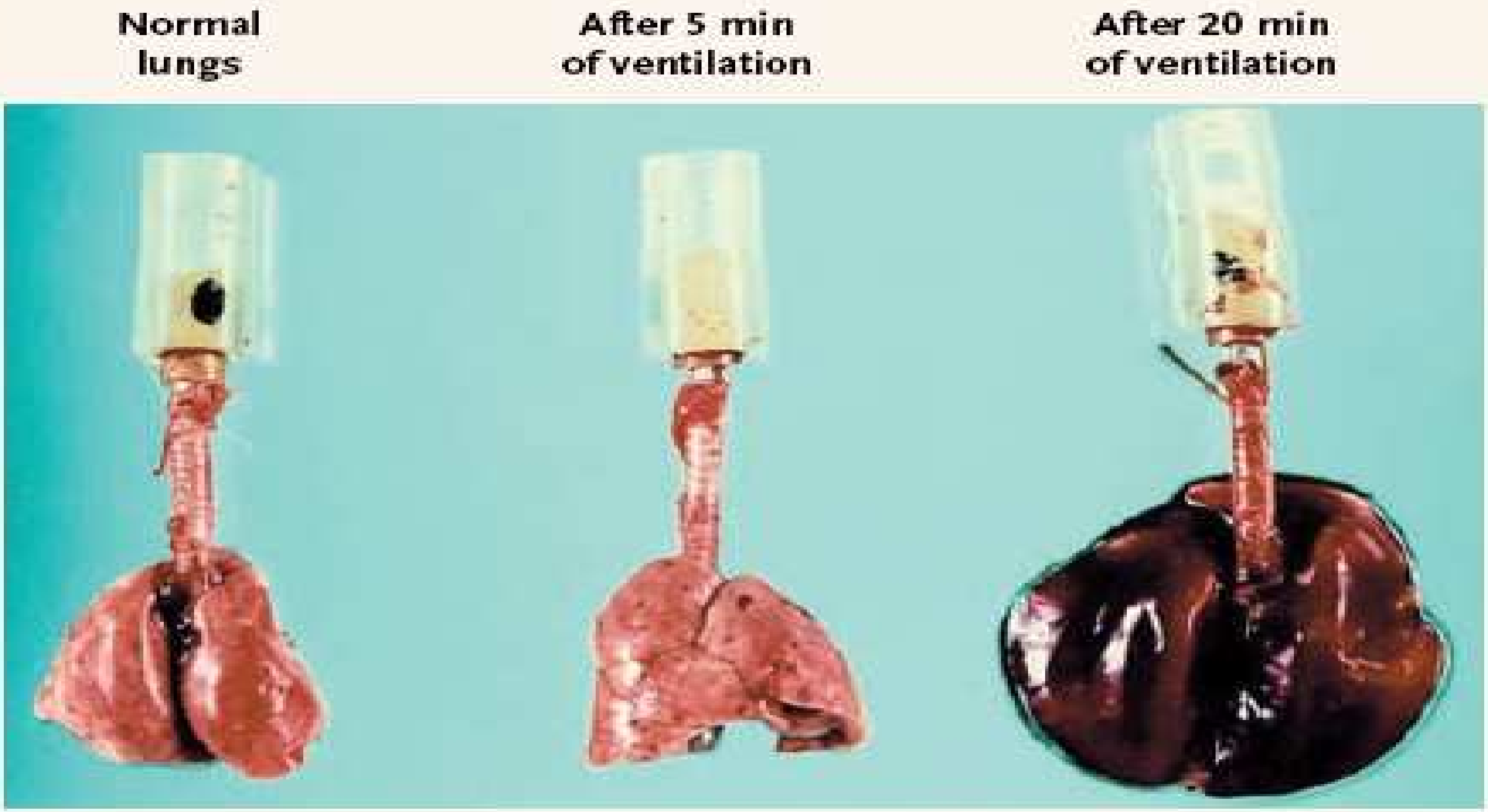


Figure 1. Normal Rat Lungs and Rat Lungs after Receiving High-Pressure Mechanical Ventilation at a Peak Airway Pressure of 45 cm of Water.
After 5 minutes of ventilation, focal zones of atelectasis were evident, in particular at the left lung apex. After 20 minutes of ventilation, the lungs were markedly enlarged and congested; edema fluid filled the tracheal cannula. Adapted from Dreyfuss et al.[8] with the permission of the publisher.

NEJM 2007;357 : 1113-20

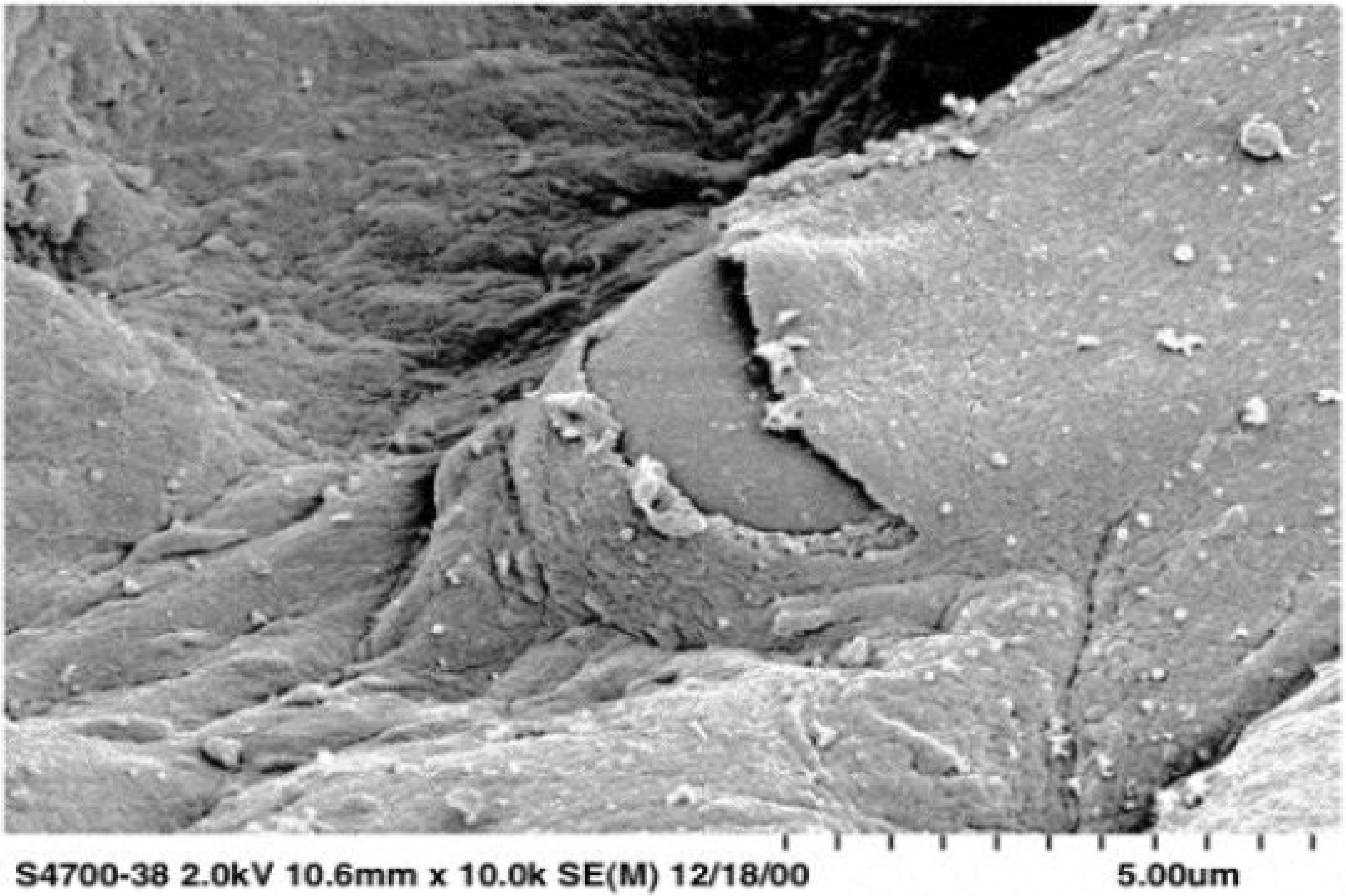


FIGURE 29-7 Stress fracture of the alveolar-capillary membrane resulting from ventilator-induced lung injury in a previously normal rat lung. Similar tears also have been demonstrated to occur in human patients with ARDS.

VlahakisNE. JAP 2000; 89:2490-6, Hotchkiss JR. CCM2002; 30:2368-70

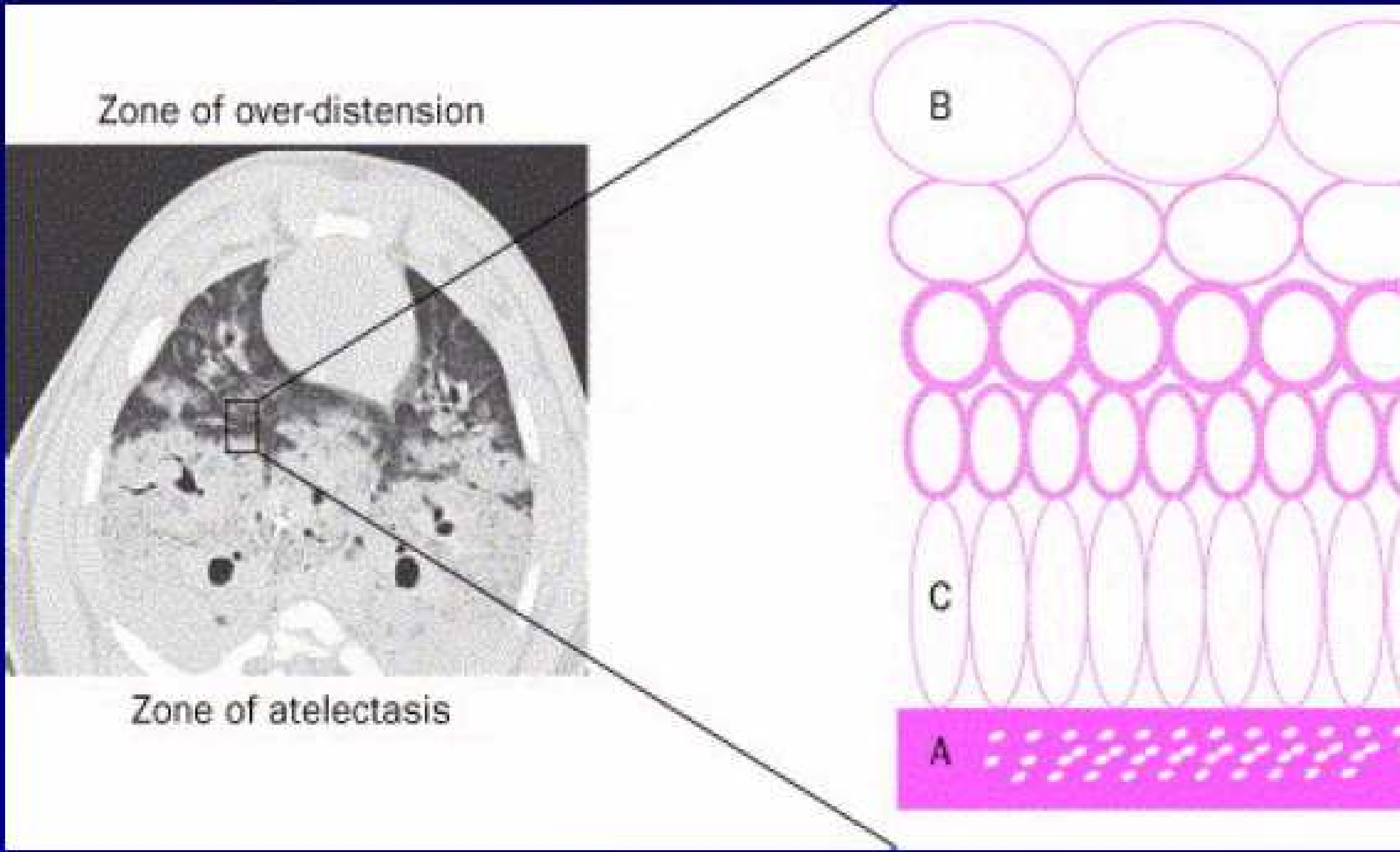
Ventilator Induced Lung Injury (VILI)

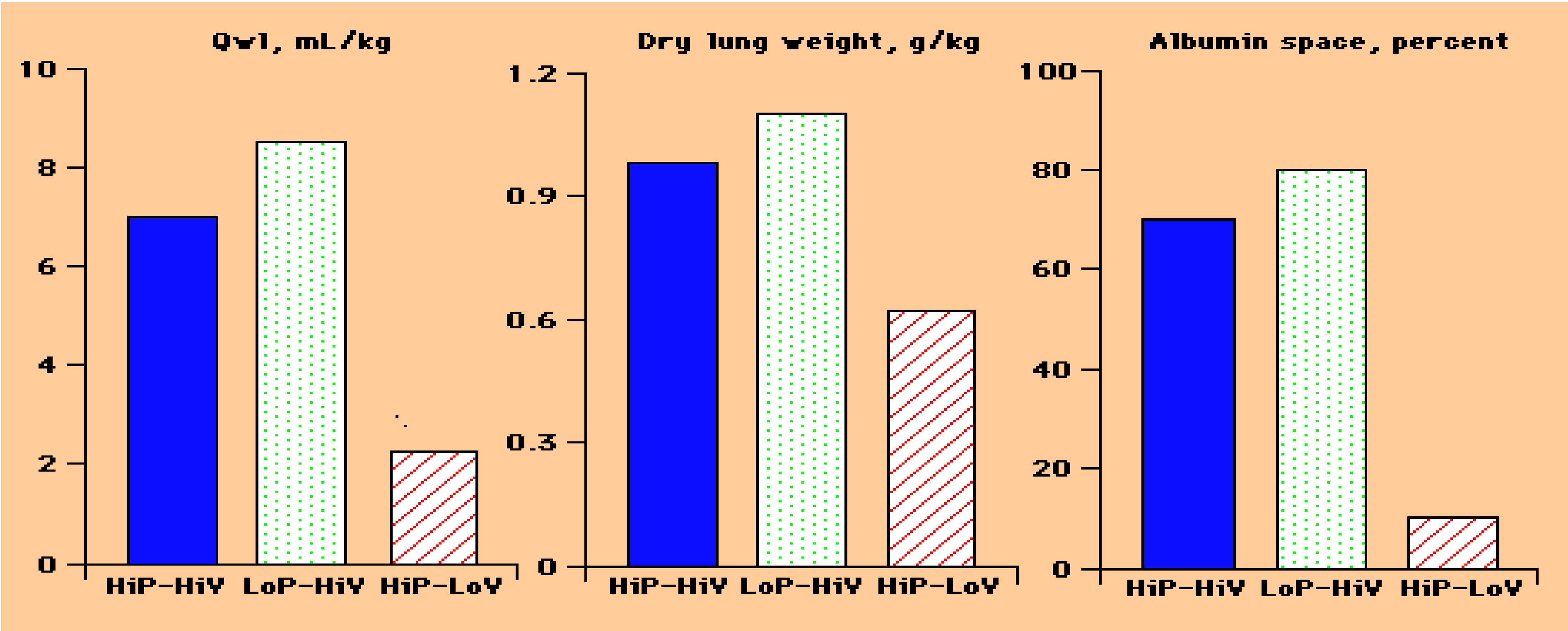
Hubmayr J Appl Physiol, 2005

- Περιοχική υπερδιάταση

- "Low Volume Injury" Περιοδική σύγκλειση-επανέκπτυξη μικρών αεραγωγών και κυψελίδων

- Αδρανοποίηση της Surfactant





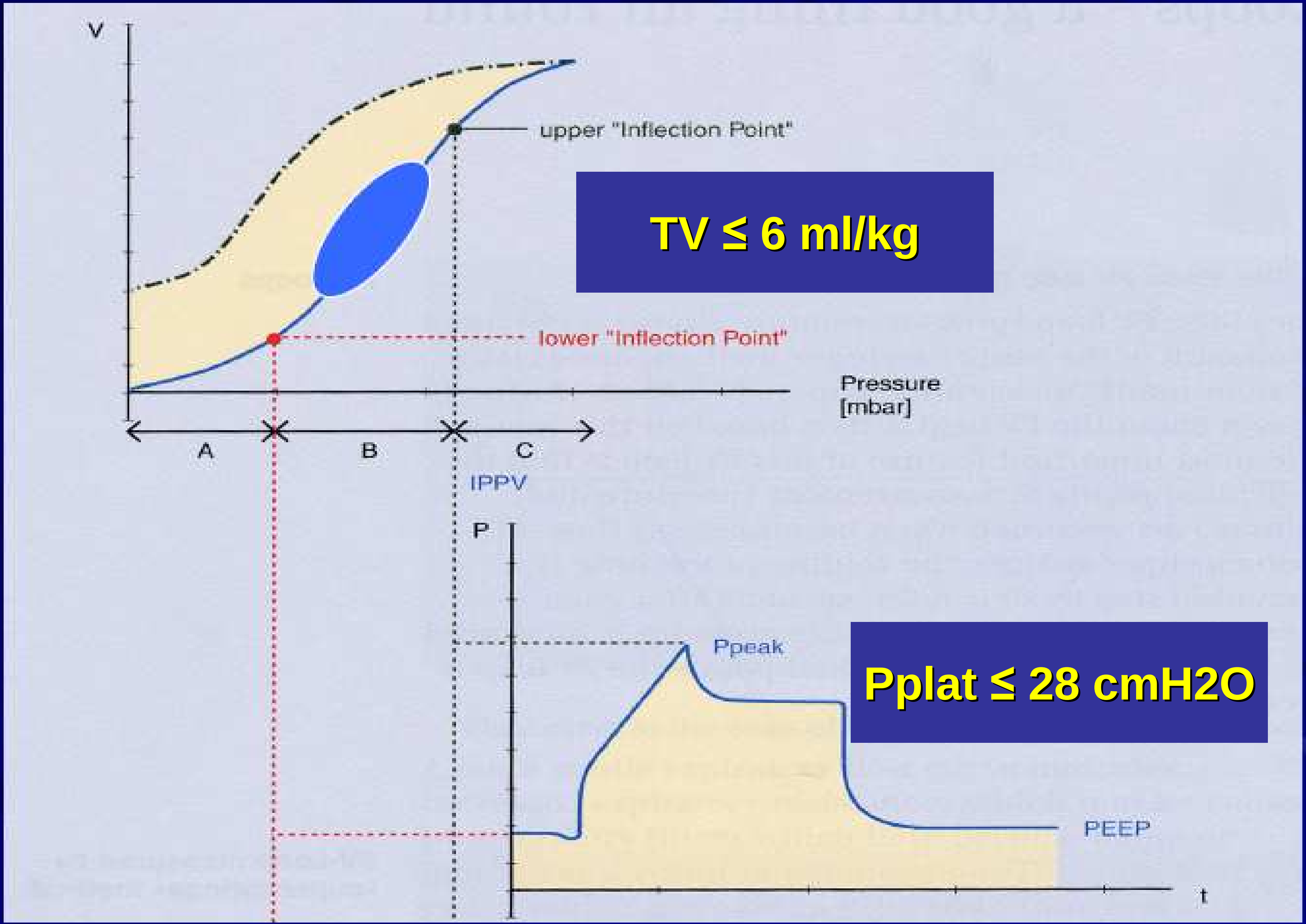
Lung injury with positive pressure and high volume ventilation The effects of various modalities of positive pressure ventilation in rats. Extravascular lung water (Qwl), dry lung weight, and albumin space are indicative of the development of lung injury. These abnormalities were induced in rats ventilated with high pressure and high tidal volume (HiP-HiV), low pressure and high volume (LoP-HiV), but not in those ventilated with high pressure and low volume (HiP-LoV). The HiP-HiV and LoP-HiV were always different from controls ($p < 0.0001$). Thus, ventilator-induced lung injury in this rat model appears to be more a function of high tidal volume than of high airway pressure. (Redrawn from Dreyfuss, D, Soler, P, Bassett, G, Saumon, G, Am Rev Respir Dis 1988; 137:1159).

- **<u>ΣΥΜΠΕΡΑΣΜΑΤΑ</u>**

ARDS: Η ΣΤΡΑΤΗΓΙΚΗ ΤΟΥ ΠΡΟΣΤΑΤΕΥΤΙΚΟΥ ΑΕΡΙΣΜΟΥ

1. **$FiO_2 \leq 0.6$ με $SaO_2 \geq 88\%$ ή $PaO_2 \geq 55$ mmHg**

Marini J, Wheeler A. Critical Care Medicine. The essentials. 2010;430-54



V
upper "Inflection Point"
TV ≤ 6 ml/kg
lower "Inflection Point"
Pressure
[mbar]
A
B
C
IPPV
P
Ppeak
Pplat ≤ 28 cmH2O
PEEP
t

ARDS: Η ΣΤΡΑΤΗΓΙΚΗ ΤΟΥ ΠΡΟΣΤΑΤΕΥΤΙΚΟΥ ΑΕΡΙΣΜΟΥ

4. Εκτίμηση της μηχανικής και P-V Curve
5. Επαναστρατολόγηση κυψελίδων (Re)
6. «Κατάλληλη» PEEP
7. Εμπόδισε το V.I.L.I.
8. Ελάττωσε τον Μ.Α. { Ελάττωσε τη f
Επιτρεπτή υπερCO2 }

Marini J, Wheeler A. Critical Care Medicine. The essentials. 2010;430-54

ARDS - Οξεία διάχυτη κυψελιδική βλάβη

A. Βαριά ανθεκτική υποO2 (Shunt: R to L)
B. Αυξημένη διαπερατότητα / Πνευμονικό οίδημα
C. Μειωμένη διατασιμότητα
D. Αμεσα Προστατευτικός Μηχανικός Αερισμός
E. Υψηλή Θνητότητα

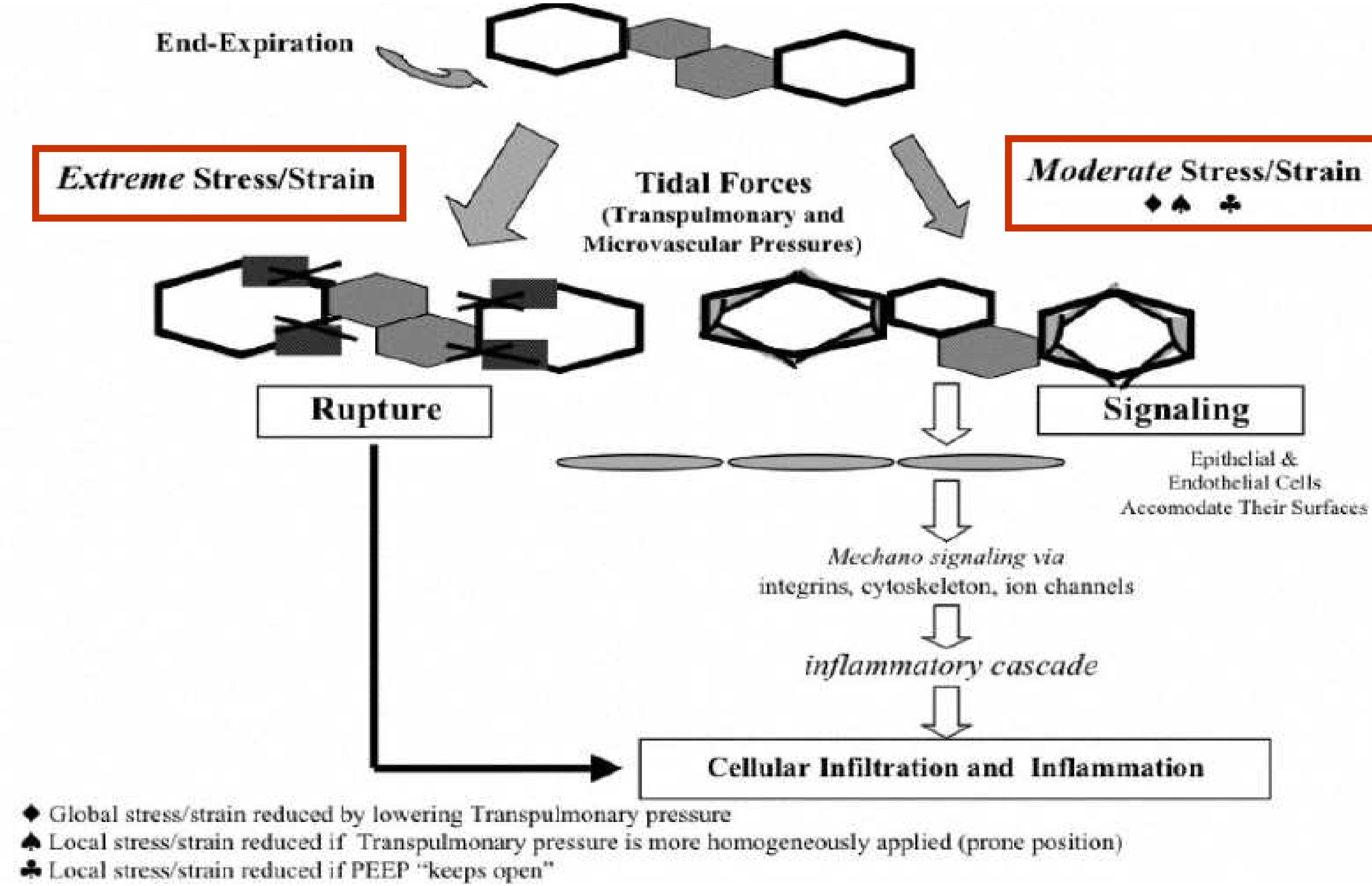
3 Στάδια για ανοικτό πνεύμονα

- **Κριτική πίεση ανοίγματος των αεραγωγών:** για να την υπερνικήσει κατά τη διάρκεια της εισπνοής
- **Opening pressure:** πρέπει να διατηρείται επαρκώς για μακρύ χρονικό διάστημα
- Στην εκπνοή; **critical time**, που θα απέτρεπε το κλείσιμο των κυψελίδων (auto-CPAP, PEEP…)

Marini J, Wheeler A. Critical Care Medicine. The essentials. 2010;430-54

Open Lung Approach
(Evaluate the Response)

- Not all patients are PEEP responsive.
  - Diffuse vs. Regional
  - Secondary vs. Primary
- If PEEP doesn't help, it may hurt.
  - Over Distension
  - Worsened V/Q
  - Redistributed Blood Flow
  - Elevations of P_{PA}



Marini J. CCM 2004; 32:250-5

ARDS: Η ΣΤΡΑΤΗΓΙΚΗ ΤΟΥ ΠΡΟΣΤΑΤΕΥΤΙΚΟΥ ΑΕΡΙΣΜΟΥ

1. $FiO_2 \leq 0.6$ με $SaO_2 \geq 88\%$ ή $PaO_2 \geq 55$ mmHg
2. VT=6 ml/kg, I.B., Προστατευτικός Μ.Α.
3. Pplat < 28-30 cmH20
4. Επαναστρατολόγηση κυψελίδων (Re)
5. «Κατάλληλη» PEEP (inflection point, Poes)

Marini J, Wheeler A. Critical Care Medicine. The essentials. 2010;430-54

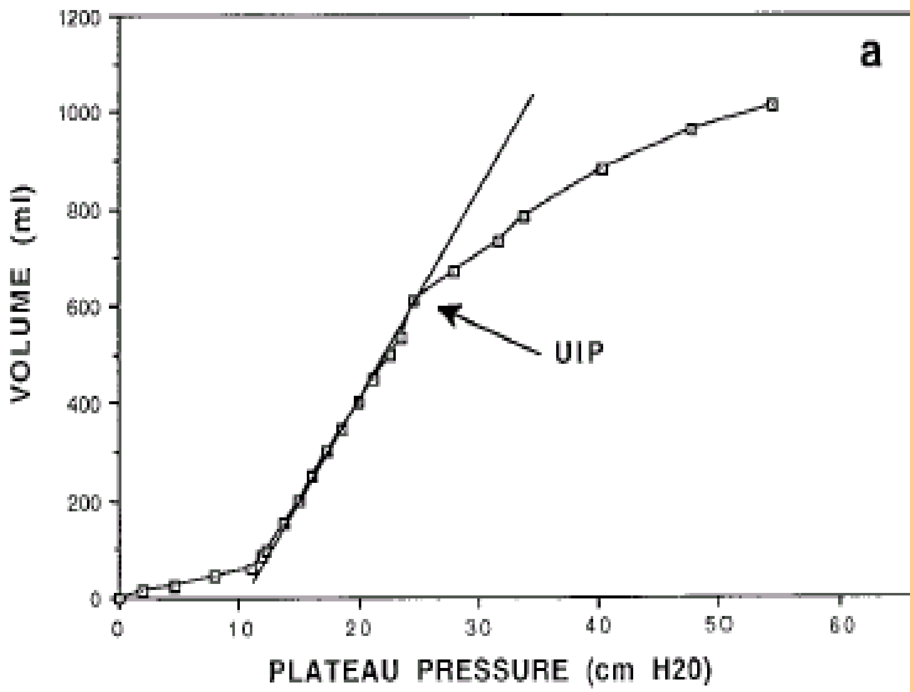
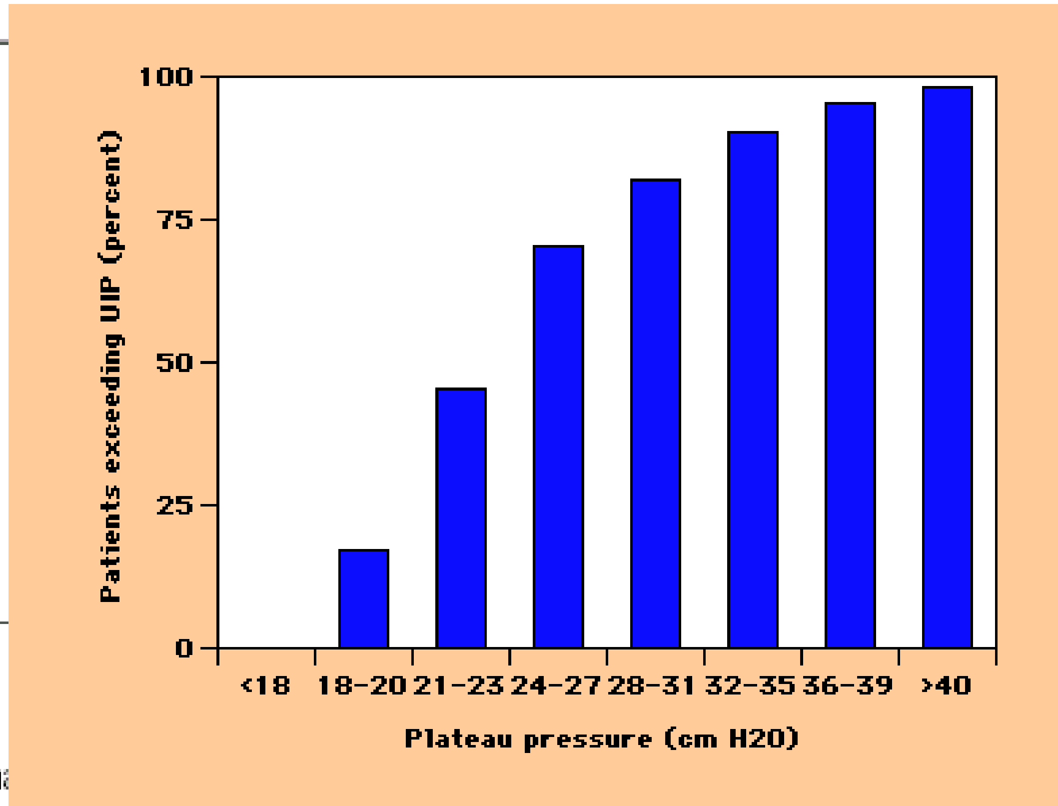


Figure 20. Importance of precise titration of VT during the mecha
of the respiratory system in a patient with ARDS. Note the lower i
intrinsic PEEP [PEEPi] measured in this patient). The upper inflectic
linearity. (*b*) Percentage of patients with ARDS whose end-inspirat
tion with PEEP set at the lower inflection point. To keep ventilatio
upper inflection points, in all patients required VT reduction to 5.5



Overdistension due to high plateau pressures
Percentage of patients exceeding the upper inflection point (UIP) of the static pressure volume curve as function of plateau pressure. (Redrawn from Roupie, E, Dambrosio, M, Servillo, G, Am J Respir Crit Care Med 1995; 152:121).

P transpulm. = P alv - P pl

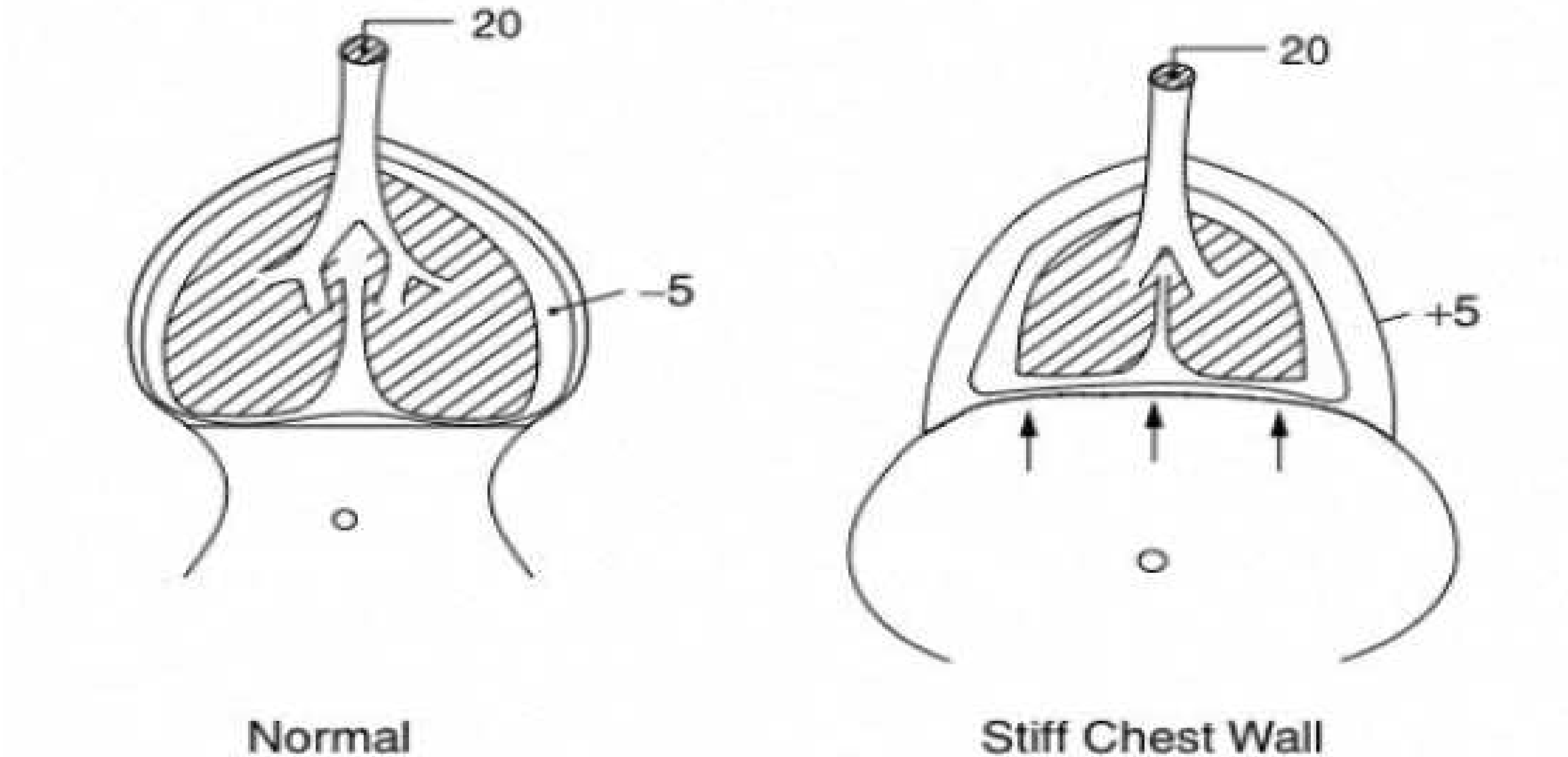


FIGURE 29-1 Influence of chest-wall compliance on transpulmonary pressure and lung volume. Any specified airway pressure is associated with less transpulmonary pressure in the presence of chest wall stiffness or expiratory effort.

Marini J, Wheeler A. Critical Care Medicine. The essentials. 2010;430-54

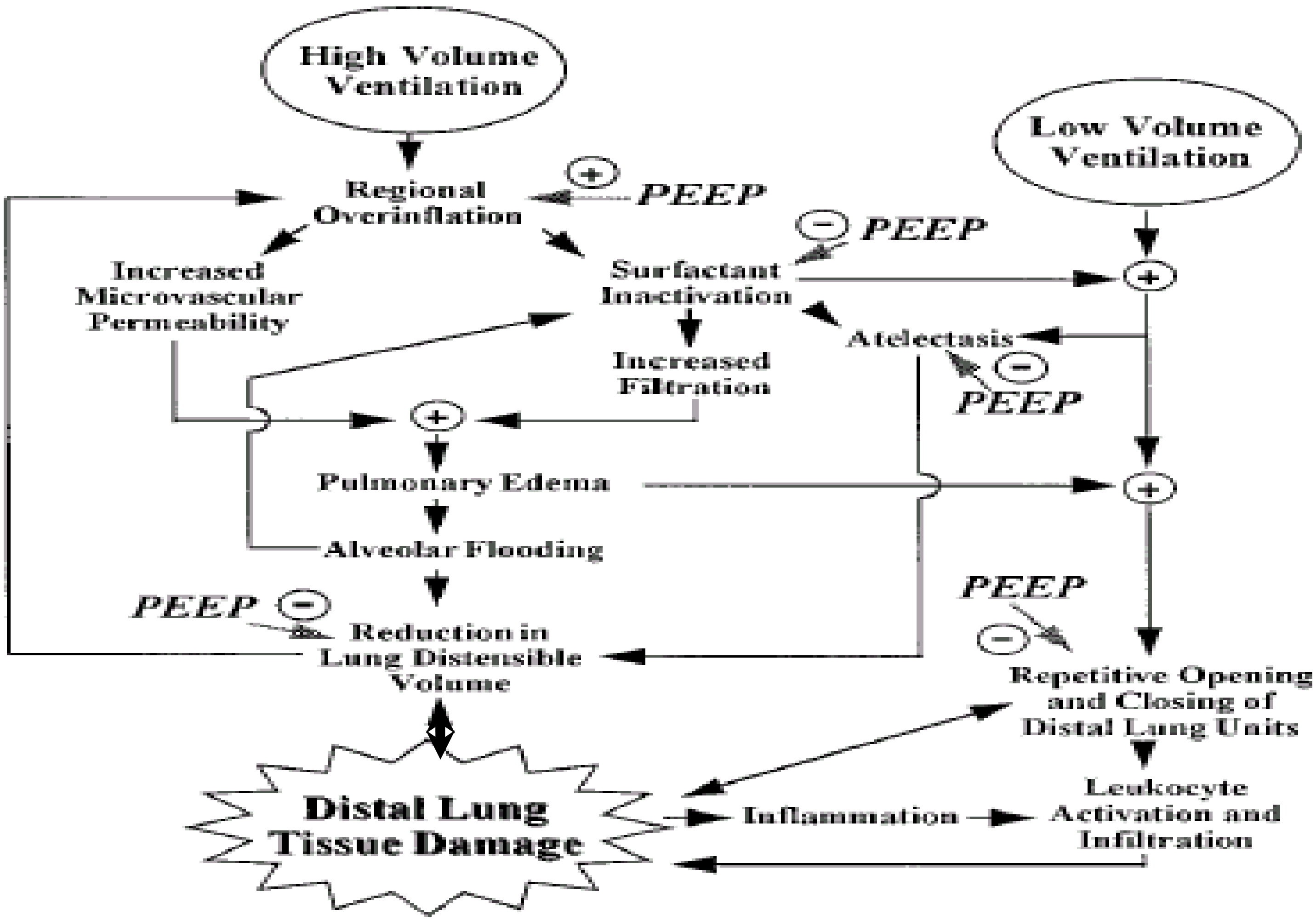
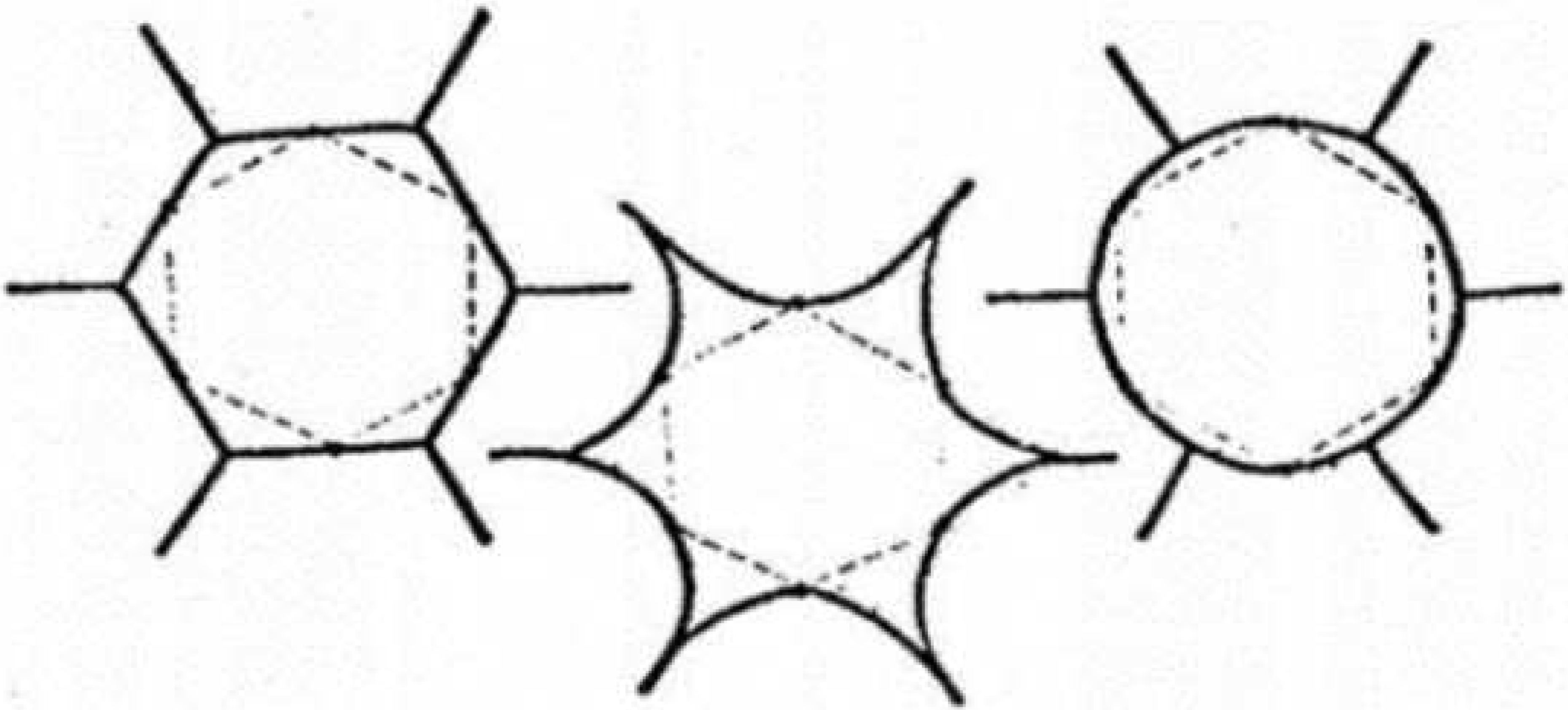
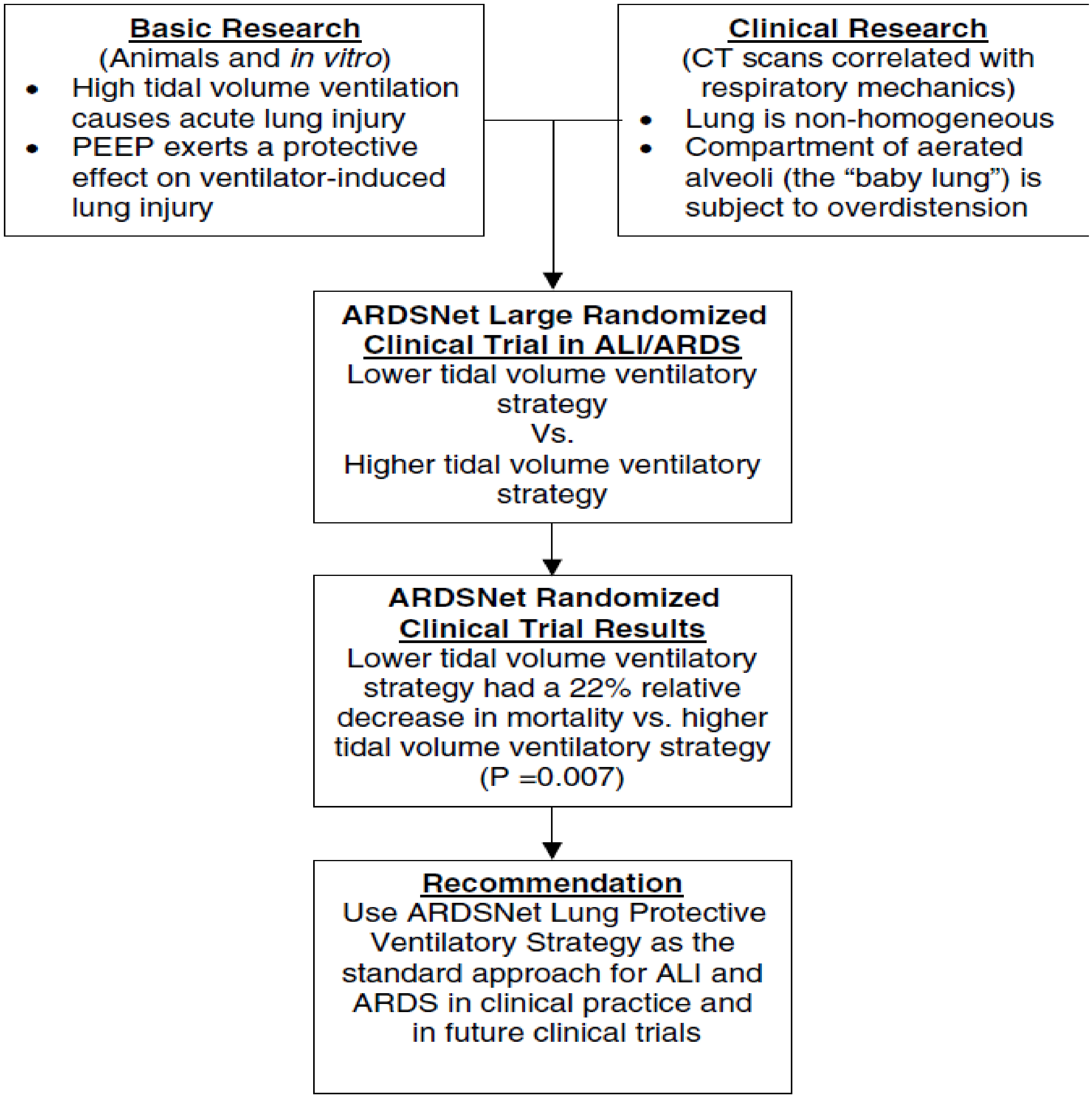


Figure 19. Flow diagram summarizing the contributors to mechanical ventilation–induced lung injury. PEEP generally opposes injury or edema formation (*minus sign*) except when it contributes to overinflation (*plus sign*).

Dreyfuss D, Saumon G. VILI. State of the Art. AJRCCM 1998; 157: 294



$$P_{eff} = P_{appl} (V/V_o)^{2/3}$$


Basic Research
(Animals and in vitro)
• High tidal volume ventilation causes acute lung injury
• PEEP exerts a protective effect on ventilator-induced lung injury
Clinical Research
(CT scans correlated with respiratory mechanics)
• Lung is non-homogeneous
• Compartment of aerated alveoli (the "baby lung") is subject to overdistension
ARDSNet Large Randomized Clinical Trial in ALI/ARDS
Lower tidal volume ventilatory strategy
Vs.
Higher tidal volume ventilatory strategy
ARDSNet Randomized Clinical Trial Results
Lower tidal volume ventilatory strategy had a 22% relative decrease in mortality vs. higher tidal volume ventilatory strategy (P =0.007)
Recommendation
Use ARDSNet Lung Protective Ventilatory Strategy as the standard approach for ALI and ARDS in clinical practice and in future clinical trials

Recruitment Maneuvers
Rationale

- Higher pressures are needed to open unstable lung units than to keep them open.
- High pressures must be sustained in order to apply effective leverage at the air-tissue interface.
- Periodic recruitment maneuvers may allow lower PEEP/tidal volume combinations.

Dangers of De-Recruitment

- No Inflammation or High Cycling Pressure → No Problem
- Acute Lung Injury

    Persistent Collapse
    - Ingrowth of Granulation Tissue
    - Neo-Vascular Cross Bridging

    Tidal Collapse & Re-Opening
    - Interdependence and Stress Fractures
    - Shear Stresses/Broncho Pulmonary Injury
    - High Alveolar Pressures Amplify Risks

Potential Mechanisms For Regional Damage

- **Collapse and Reopening**
  - **Interdependence Forces**
  - **Surfactant Depletion/Inactivation**
  - **Signal For Inflammation**
- **Persistent Collapse of Inflamed Tissue**
- **Perfusion Excess**
- **Increased Vascular Pressure**
- **Pooled Airway Fluids**

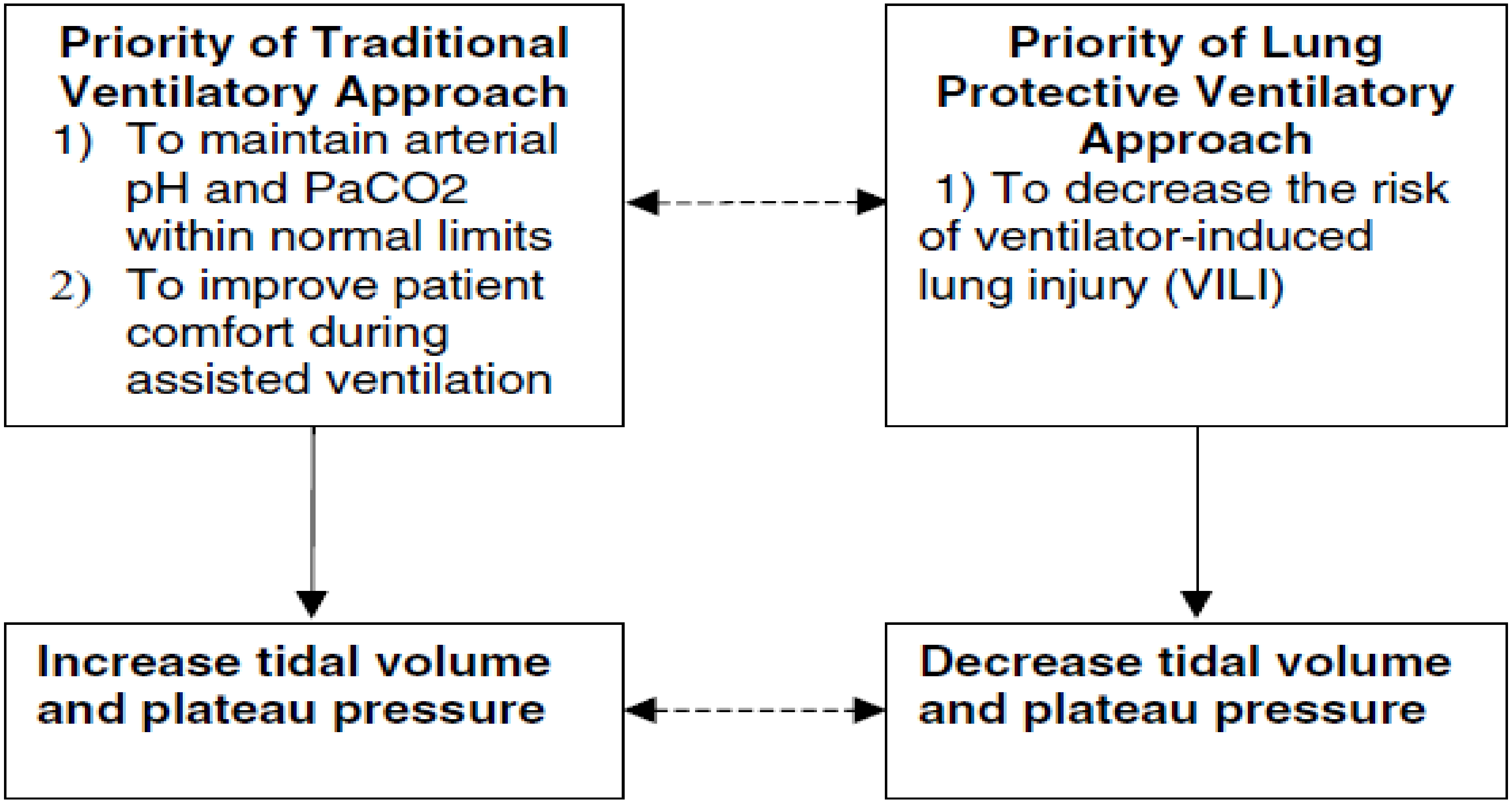


FIGURE 38-6 Schematic illustration that demonstrates how traditional and lung-protective approaches to mechanical ventilation of patients with ALI or ARDS have different priorities. The traditional approach gives higher priority to keeping arterial pH and Pa_{CO_2} normal (and possibly to keeping the patient more comfortable) than the lung-protective approach, which gives higher priority to prevention of ventilator-induced lung injury (VILI). Plateau pressure = static end-inspiratory pressure in the alveoli.

TABLE 38-6 Phase III Randomized Controlled Clinical Trials Using Lung-Protective Strategies

Authors	Year Published (Years of Enrollment)	Number of Subjects Enrolled	Mortality in Lower-Tidal Volume Group	Mortality in Higher-Tidal-volume Group	p Value
Amato et al[7]	1998 (1990–1995)	53	38%[a] (45%)[b]	71%[a] (71%)[b]	<0.0001 (0.37)
Brochard et al[8]	1998 (1994–1996)	116	46.5%[c]	37.9%[c]	0.39
Stewart et al[9]	1998 (1995–1996)	120	50.0%[d]	47%[d]	0.72
ARDSnet[3e]	2000 (1996–1999)	861	31.0%[f]	39.8%[f]	0.007

ARDS MV State of the Art Chest 2007 Mar

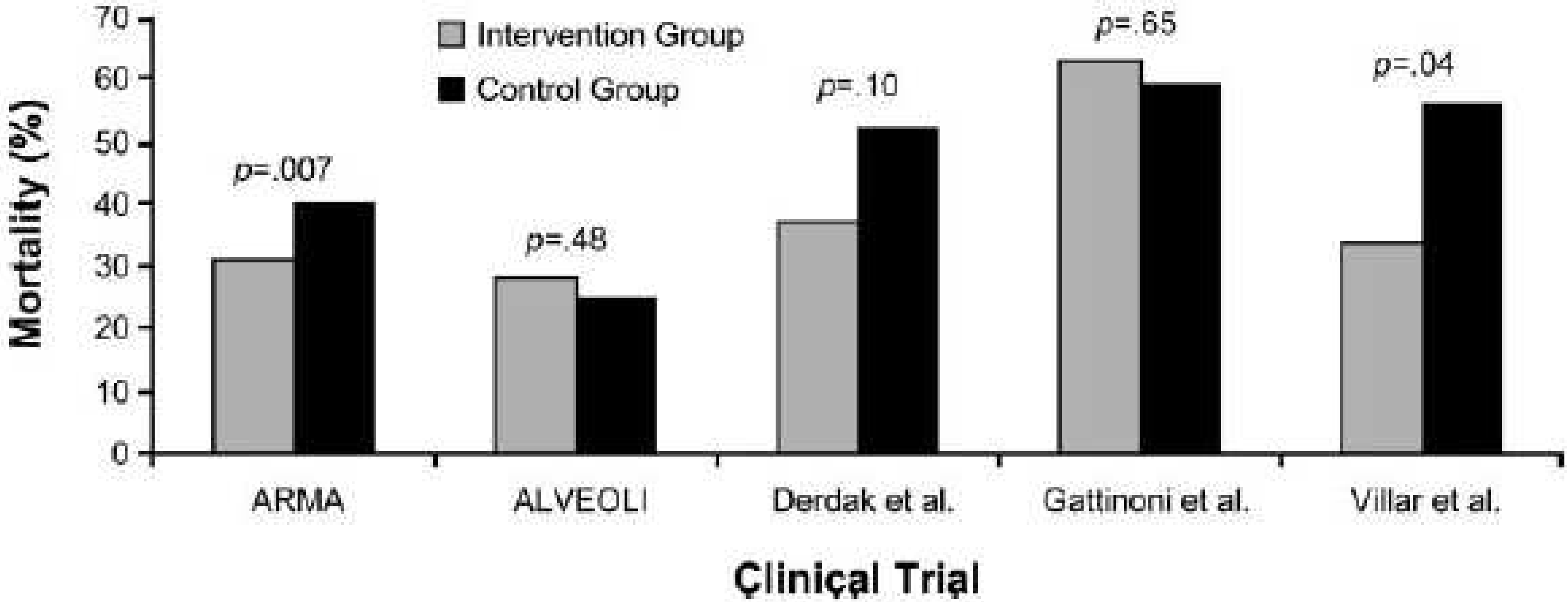


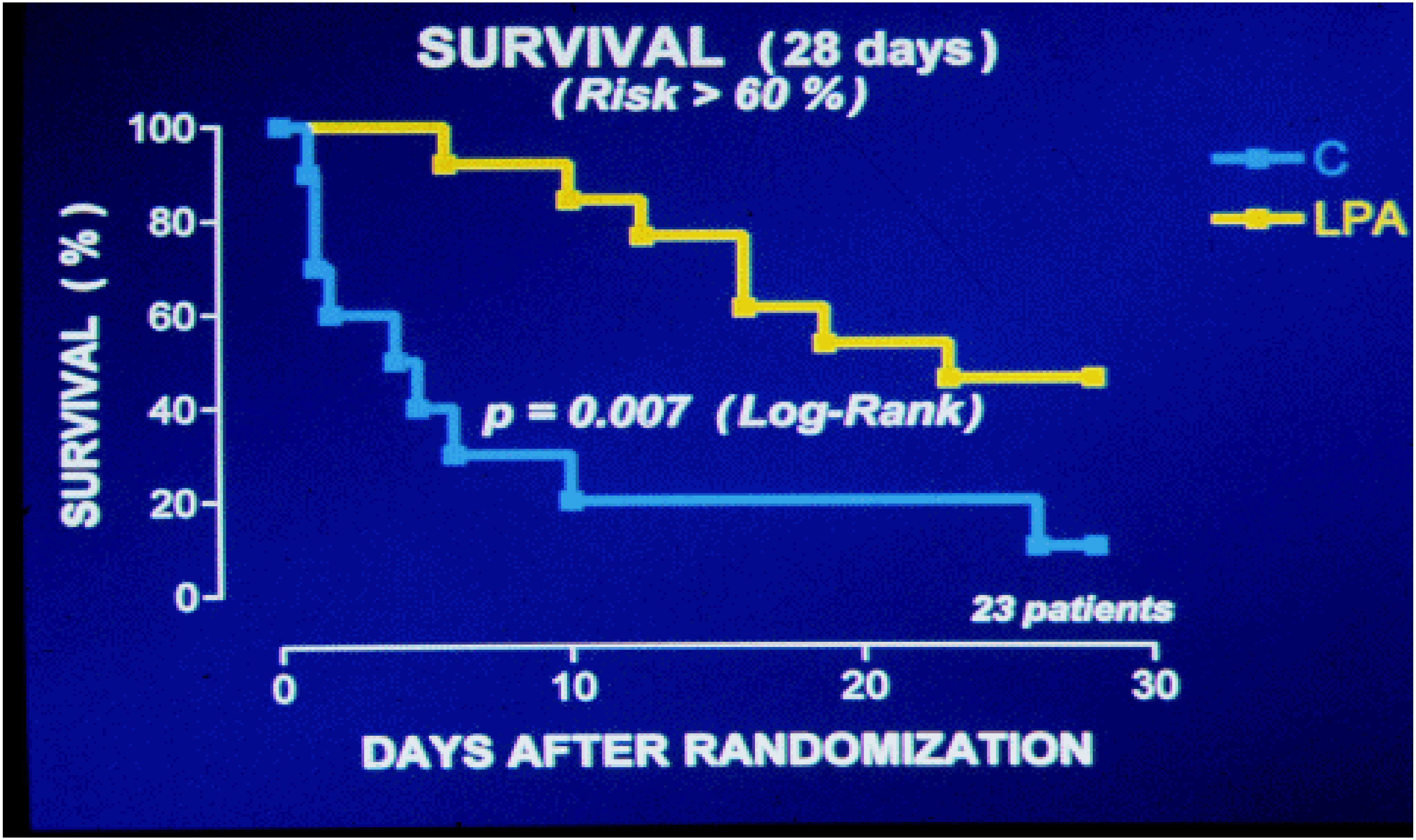
FIGURE 2. Mortality according to treatment group in representative randomized controlled trials evaluating strategies of mechanical ventilation in patients with ALI/ARDS. ARMA compared lower tidal volume ventilation with higher tidal volume ventilation and measured the in-hospital mortality rate.[14] ALVEOLI compared a high-PEEP protocol with lower PEEP and measured the in-hospital mortality rate.[35] Derdak et al[32] compared high-frequency oscillatory ventilation with conventional ventilation and measured the 30-day mortality rate. Gattinoni et al[49] compared prone positioning with conventional ventilation and measured the 180-day mortality rate. Villar et al[36] compared a protocol of lower tidal volumes with PEEP above the Pflex with higher tidal volumes and lower PEEP, and measured the in-hospital mortality rate.

ARDS MV State of the Art Chest 2007 Mar

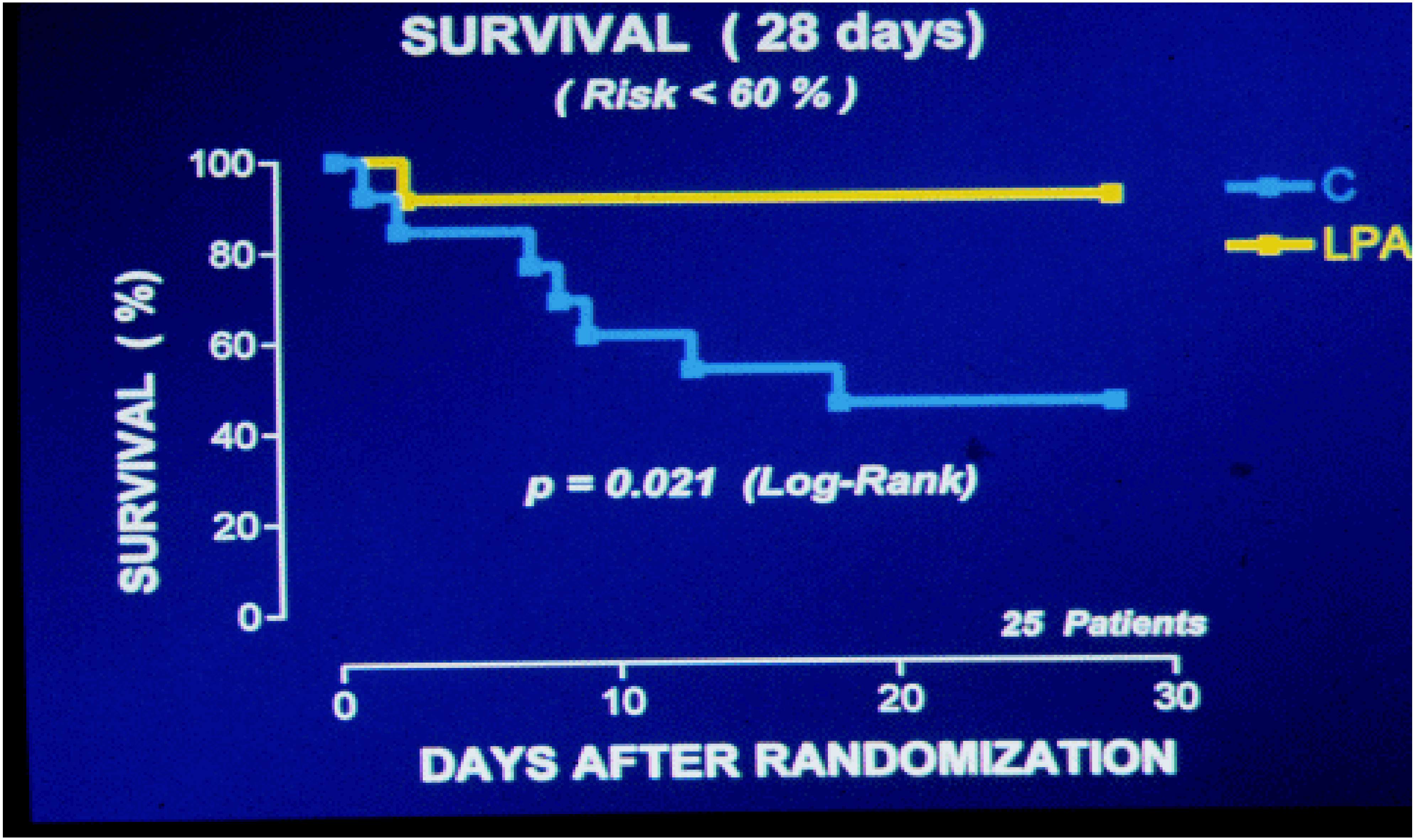
Key Results

(Amato)

	Conventional	Protective
Plateau (cmH_2O)	37	30
PEEP (cmH_20)	9	16
$PaCO_2$ (mmHg)	33	55
Barotrauma (%)	42	7
Mortality (%)		
28 Day	71	38
In-Hospital	71	45



SURVIVAL (28 days)
(Risk > 60 %)
100
80
60
40
20
0
SURVIVAL (%)
C
LPA
p = 0.007 (Log-Rank)
23 patients
0
10
20
30
DAYS AFTER RANDOMIZATION


SURVIVAL (28 days)
(Risk < 60 %)
SURVIVAL (%)
100
80
60
40
20
0
C
LPA
p = 0.021 (Log-Rank)
25 Patients
0
10
20
30
DAYS AFTER RANDOMIZATION

Key Determinants of ARDS Mortality

(Amato 1998)

- Mean PEEP in First 36 Hours
- Driving Pressure (P_{plat} - PEEP)
- Apache II Score

FIGURE 38-8 *A*. Schematic inspiratory static pressure-volume (P-V) curve of the respiratory system (lung and chest wall combined) in ARDS with a lower inflection point (LIP) at ~14 cm H_2O and an upper inflection point (UIP) at ~35 cm H_2O. The abscissa is recoil pressure of the respiratory system and the ordinate is lung volume above functional residual capacity (FRC). *B*. Same static P-V as in *A*, plus a dynamic P-V curve of 600 mL tidal volume starting at PEEP = 0, which is below the LIP. This tidal volume results in a plateau pressure of 25 cm H_2O, which is below the UIP. Static compliance (Cstat = $\Delta V/\Delta P$ = 600 mL/25 cm H_2O) is 24 mL/cm H_2O. *C*. PEEP of 15 cm H_2O has moved the starting point for the 600 mL tidal volume up the static P-V curve to a new FRC (*open arrow*), which is just above the LIP. The tidal volume results in a plateau pressure of 27.5 cm H_2O (*closed arrow*), which is well *below* the UIP. Cstat ($\Delta V/\Delta P$ = 600 mL/12.5 cm H_2O) is increased to 48 mL/cm H_2O, compared to *B*. *D*. Dynamic P-V curve of a 1000 mL tidal volume, starting at 14 cm H_2O PEEP, results in a plateau pressure of 38 cm H_2O (*closed arrow*). Note the decrease in Cstat ($\Delta V/\Delta P$ = 1000 mL/24 cm H_2O = 41.7 mL/cm H_2O) compared to Cstat derived from the tidal volume of 600 mL in *C*. The 1000 mL tidal volume's plateau pressure exceeds the UIP, which implies overdistension and is believed to put the lung at risk for ventilator-induced lung injury (see text). *(Reproduced with permission from Lanken PN: Acute respiratory distress syndrome, in Lanken PN, Hanson CW III, Manaker S (eds):* The Intensive Care Unit Manual. *Philadelphia.*

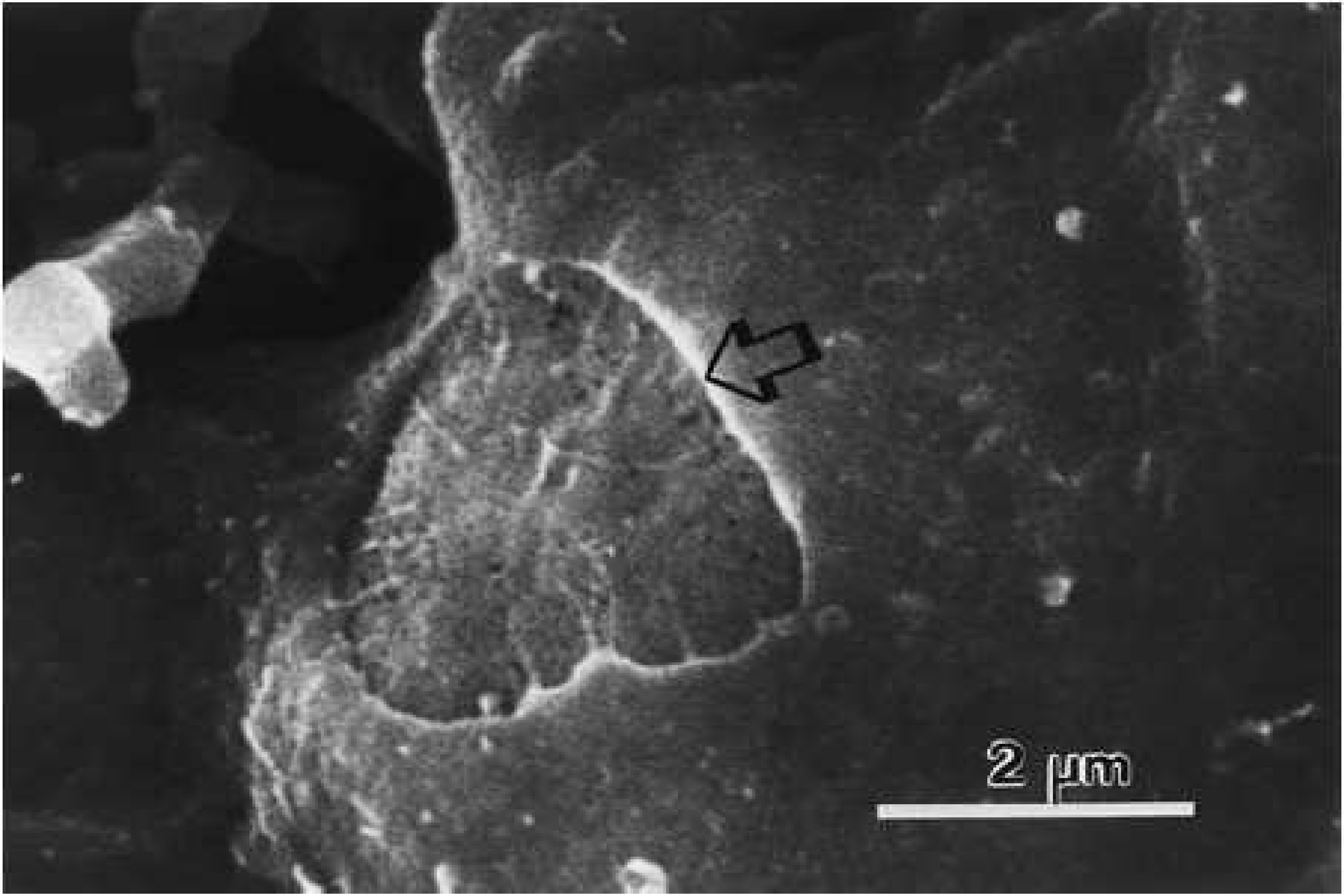

2 μm

FIGURE 38-9 Schematic diagram illustrating the conflicting priorities of higher- and lower-PEEP ventilator approaches and their hypothetical associated effects. Studies that use a higher PEEP approach may combine the higher PEEP with recruitment maneuvers, which are sustained inflations (e.g., 35 to 40 cm H_2O of continuous positive airway pressure for 30 seconds or more[4,7]). For a given low tidal volume, using a higher PEEP will result in a higher plateau (end-inspiratory) pressure than using a lower PEEP. Hypothetically, this higher plateau pressure, which represents the static end-inspiratory distending pressure in open alveoli, may increase the risk of ventilator-induced lung injury due to overdistension (see text and Chap. 17 for details).

due to overdistension (see text and Chap. 17 for details).

- **Ο κύριος παράγοντας του ΟΓΚΟ - ΤΡΑΥΜΑΤΟΣ, φαίνεται να είναι ο ΤΕΛΟ-ΕΙΣΠΝΕΥΣΤΙΚΟΣ ΟΓΚΟΣ (Pplat), μάλλον από τον TV ή την FRC**

Dreyfuss D and Saumon G, State of Art, AJRCCM 1998; 157:294

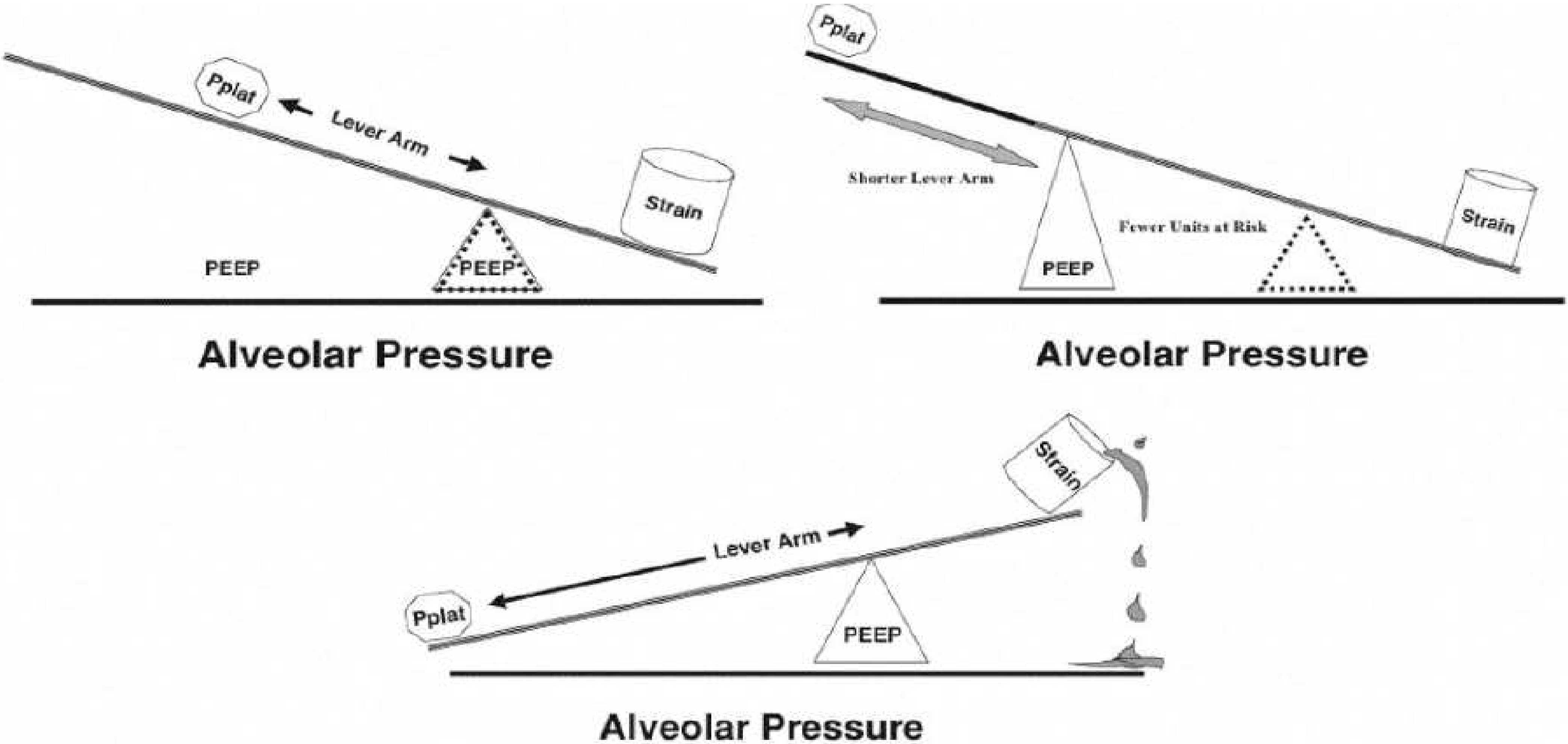


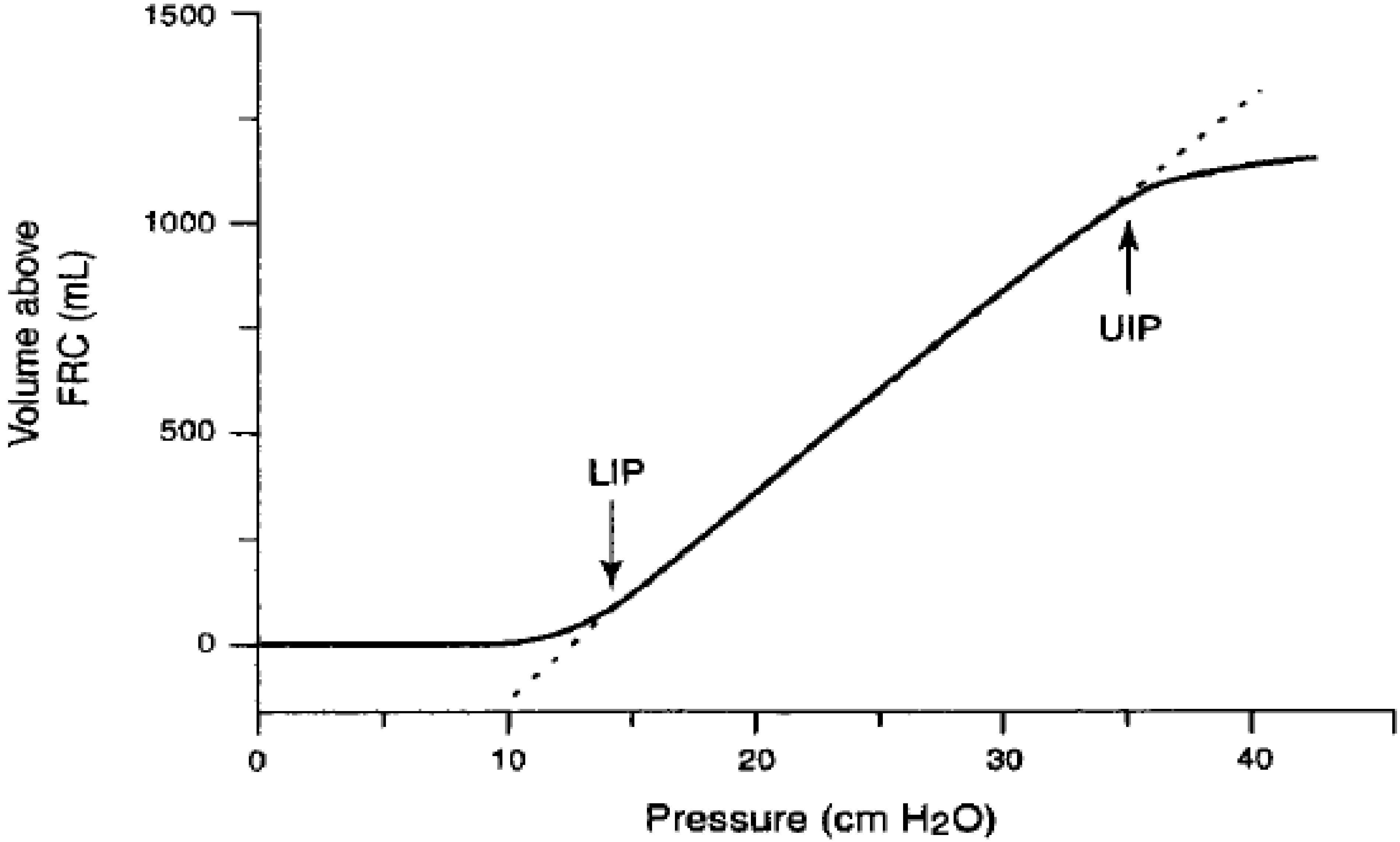
FIGURE 29-14 Conceptual relationship between plateau pressure, PEEP, and tissue strain. In the generation of tissue strain, the driving pressure for tidal volume (the difference between plateau pressure and PEEP) acts as a force lever arm, whereas PEEP acts as the fulcrum. (*Upper-left*) Levels of plateau pressure and PEEP produce strain within acceptable limits. (*Bottom-center*) Increasing plateau pressure while keeping PEEP at a level insufficient to hold open unstable units lengthens the lever arm and produces excessive tissue strain. (*Upper-right*) When PEEP is increased, the same high plateau pressure that caused damage previously is better tolerated in that fewer lung units are placed at risk after recruitment, and the lever arm of driving pressure is shortened.

Marini J, 2010 The Essentilas, pp: 430-54, Doyle RL. AJRCCM 1995; 152:1818, Rubenfeld GD. NEJM 2005; 353:1685

PEEP

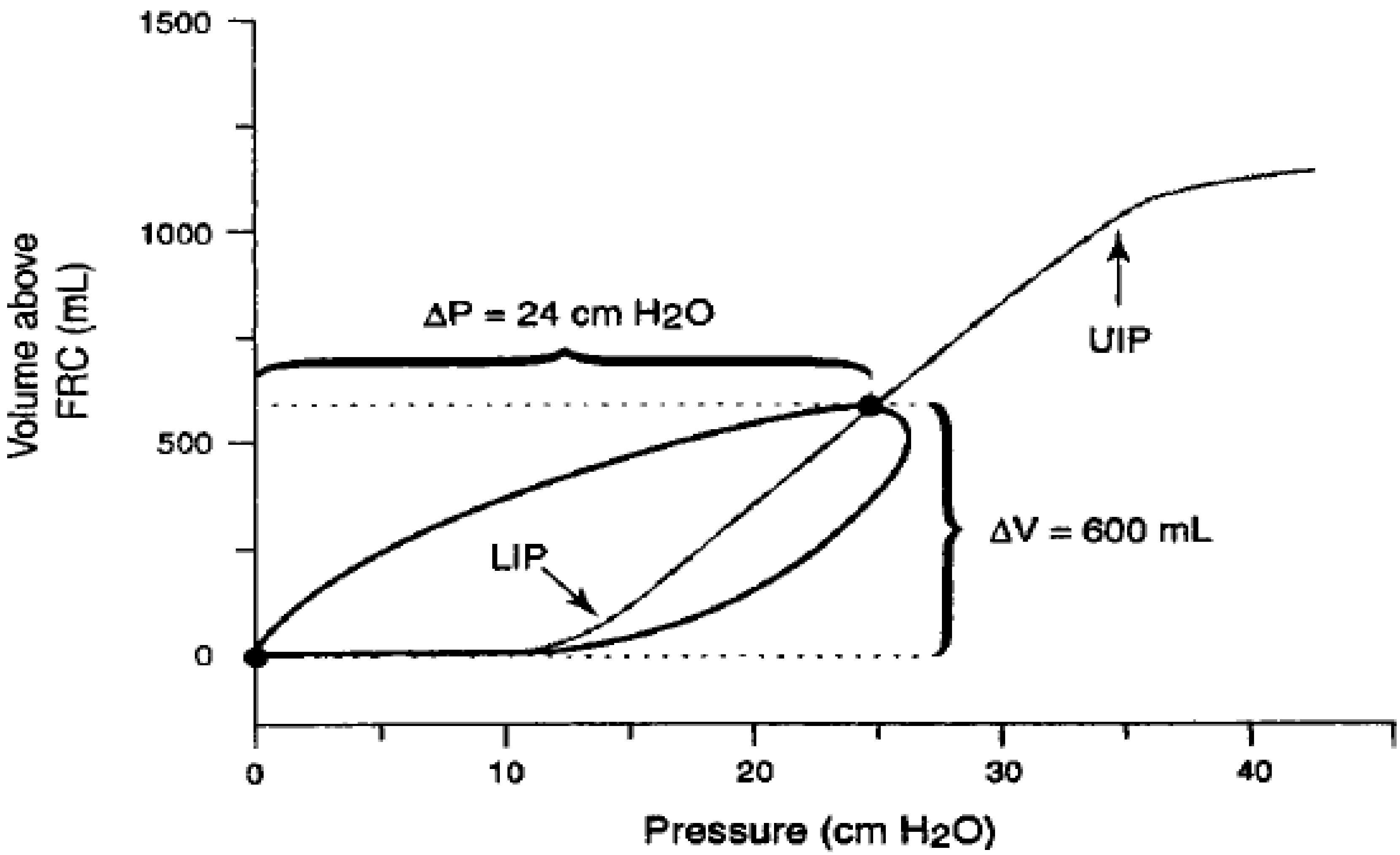
i. Διατηρεί την λειτουργία της **δραστικής surfactant** (large vs small aggregates)
ii. Εμποδίζει το **υπερβολικό χάσιμο της surfactant** προς τους small airways
iii. Ελαττώνει την συσσώρευση των **πρωτεϊνών** στον πνεύμονα και την ακόλουθη αδρανοποίηση της surfactant
iv. Εμποδίζει **Alveolar flooding**

Minerva Anesth 2006; 72:117-132



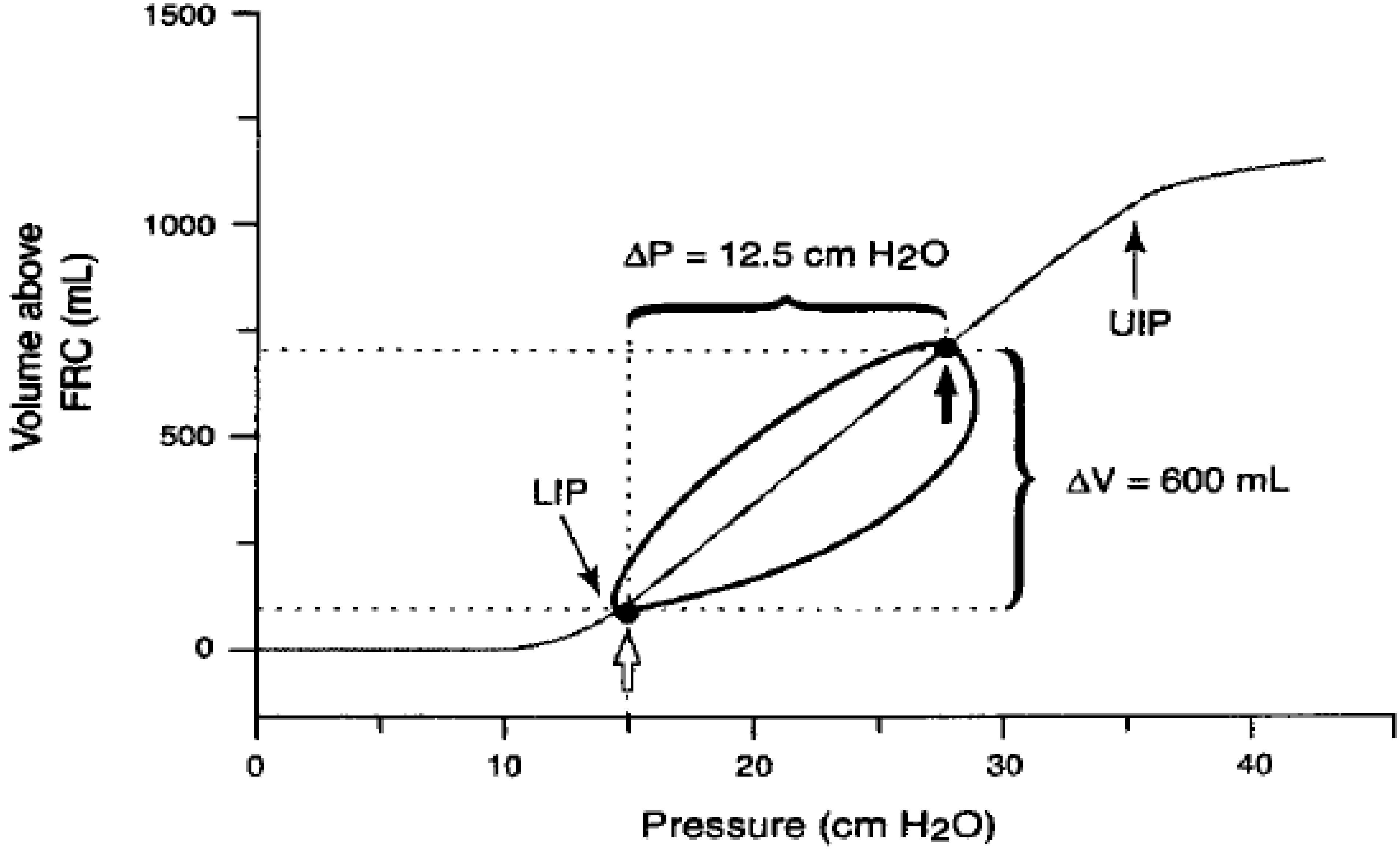
1500
1000
500
0
Volume above FRC (mL)
LIP
UIP
0
10
20
30
40
Pressure (cm H2O)

A



1500
1000
500
0
Volume above FRC (mL)
ΔP = 24 cm H2O
UIP
LIP
ΔV = 600 mL
0
10
20
30
40
Pressure (cm H2O)

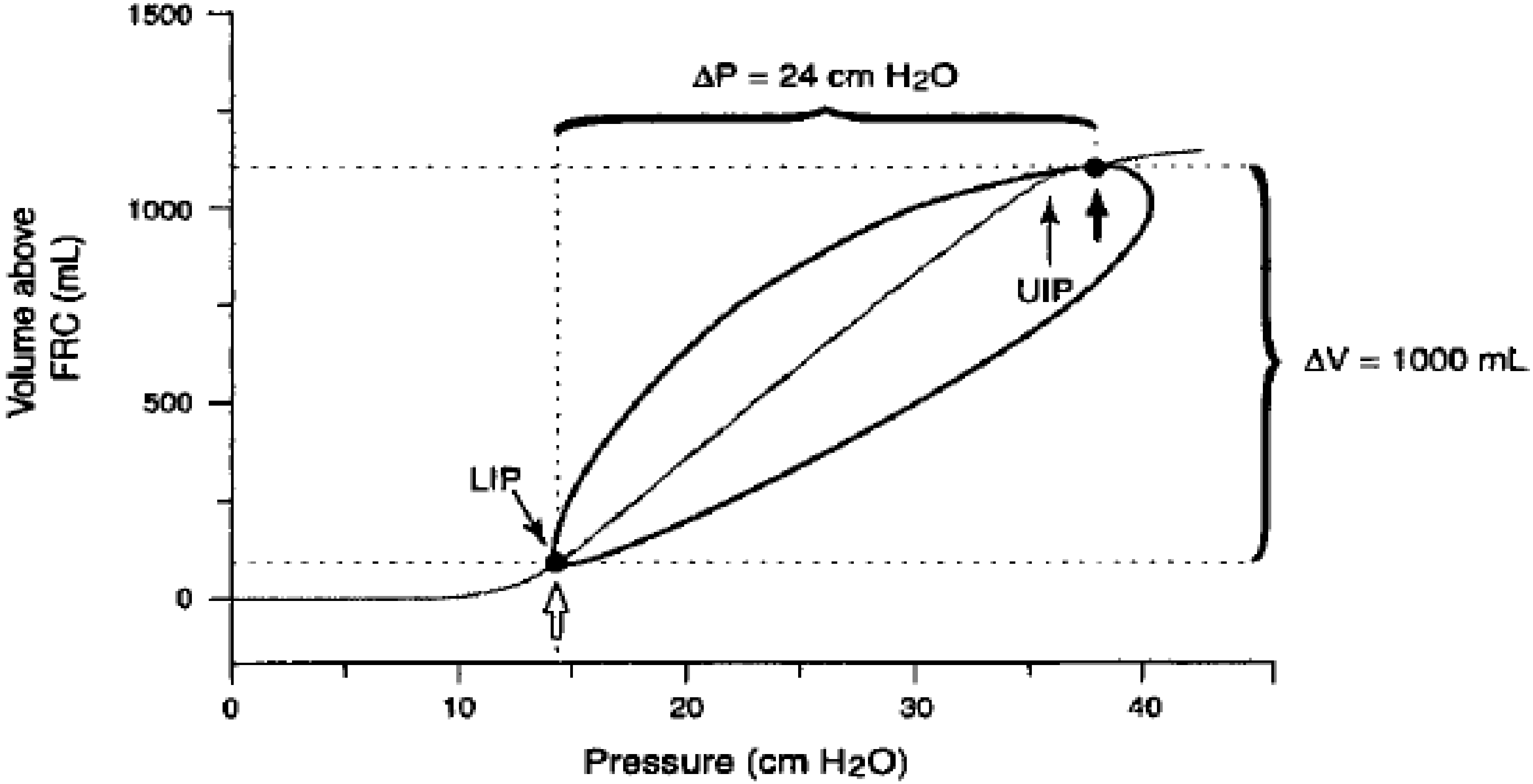
B



1500
1000
500
0
Volume above FRC (mL)
ΔP = 12.5 cm H2O
UIP
LIP
ΔV = 600 mL
0
10
20
30
40
Pressure (cm H2O)

C

Wood



ΔP = 24 cm H2O
ΔV = 1000 mL
Volume above FRC (mL)
1500
1000
500
0
LIP
UIP
0
10
20
30
40
Pressure (cm H2O)

D

Wood

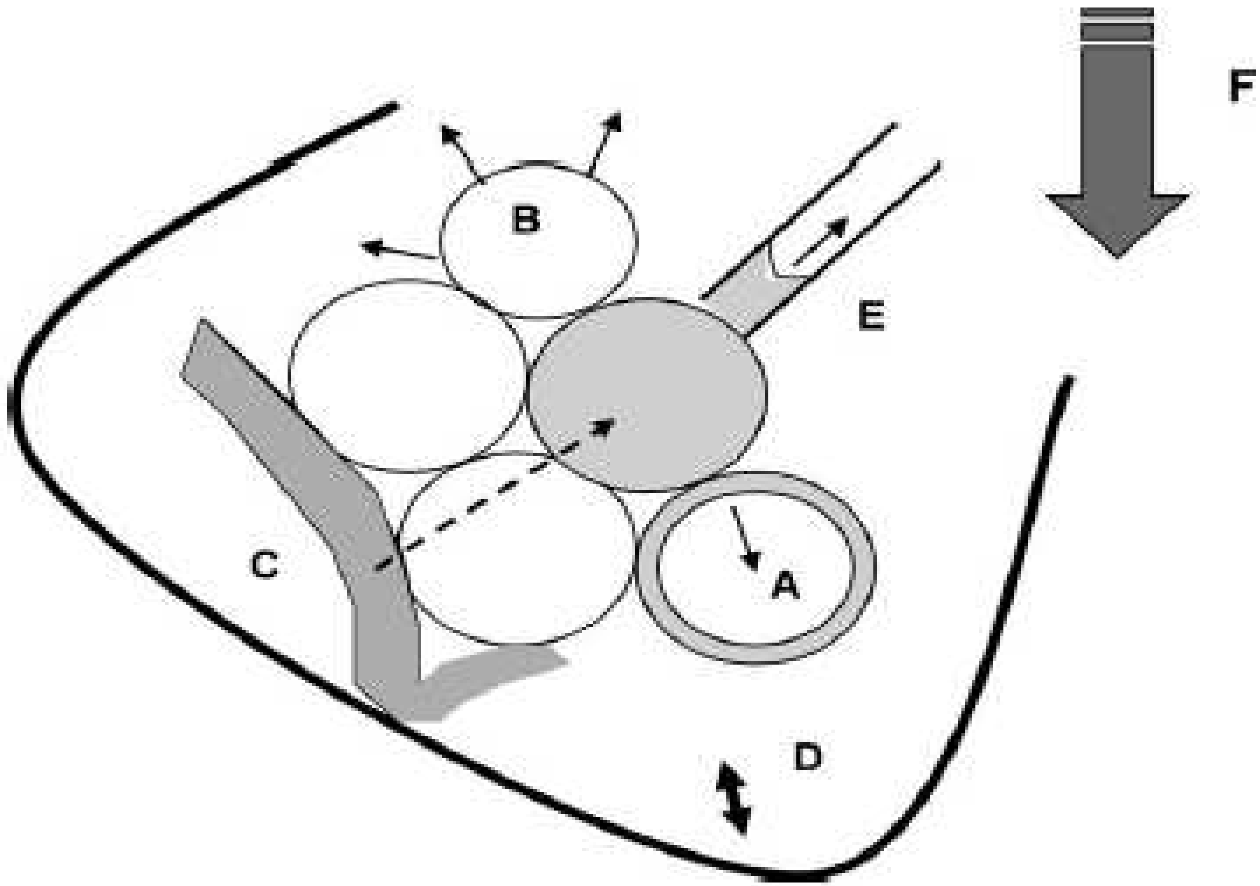
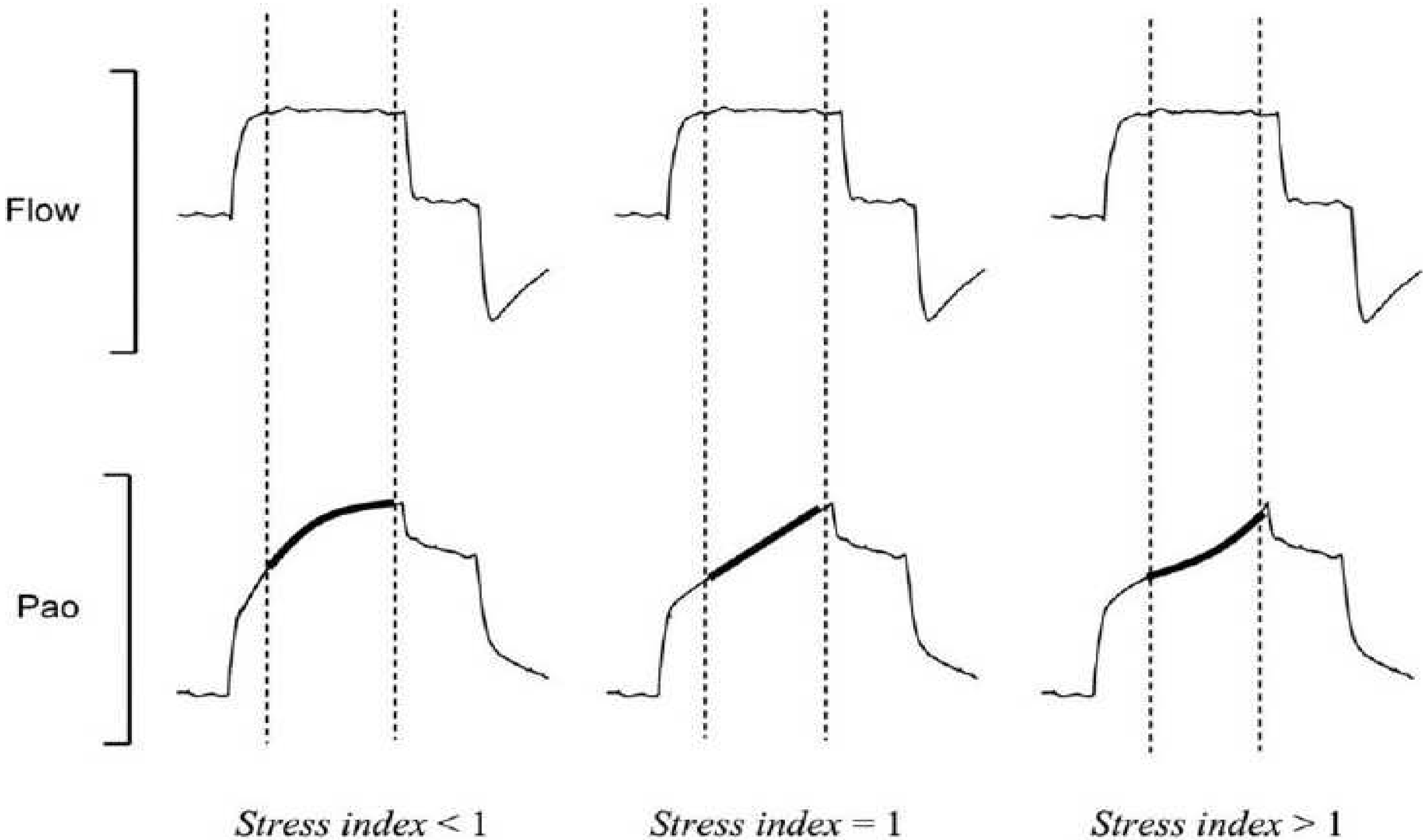


Figure 2. Forces at work to contain or propagate mobile airway fluid. (*A*) Surface tension; (*B*) interdependence; (*C*) hydrostatic vascular gradient; (*D*) pleural pressure; (*E*) capillary attraction, and (*F*) gravitational drainage.

Marini J. CCM 2010


Flow
Pao
Stress index < 1
Stress index = 1
Stress index > 1

ARDS

- Το ARDS αποτελεί σχετικά συνήθη αιτία οξείας αναπνευστικής ανεπάρκειας, υποO2 τύπου
- Στις USA η συχνότητα του ARDS τα τελευταία χρόνια έχει μειωθεί (39 περιπτώσεις / 100.000 άτομα το χρόνο)

Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

Table 1—*Randomized Controlled Trials Evaluating Strategies of Mechanical Ventilation for the Treatment of ARDS**

Study	Patients, No.	Intervention	Mortality Rates†	p Value
Amato et al[10]	53	≤ 6 mL/kg ABW; VT; < 20 cm H_2O Pdriving	38% vs 71%‡	0.001 •
Stewart et al[11]	120	≤ 8mL/kg IBW; VT; ≤ 30 cm H_2O Pplat	50% vs 47%	0.72
Brochard et al[12]	116	6–10 mL/kg IBW; VT; 25–30 cm H_2O Pplat	47% vs 38%§	0.38
Brower et al[13]	52	≤ 8 mL/kg PBW; VT; ≤ 30 cm H_2O Pplat	50% vs 46%	0.61
ARMA[14]	861	≤ 6mL/kg PBW; VT; ≤ 30 cm H_2O Pplat	31% vs 40%	0.007 •
Derdak et al[32]	148	HFOV	37% vs 52%‖	0.10
Bollen et al[33]	61	HFOV	43% vs 33%‖	0.59
ALVEOLI[35]	549	High-PEEP protocol	28% vs 25%	0.48
Villar et al[36]	103	5–8 mL/kg PBW; VT; PEEP of Pflex + 2 cm H_2O	34% vs 56%	0.04 •
Gattinoni et al[49]	304	Prone position 6 h/d for 10 d	63% vs 59%¶	0.65
Guerin et al[50]	791	Prone position 8 h/d	32% vs 32%‡	0.77
Mancebo et al[51]	136	Prone position 20 h/d	50% vs 62%	0.22

*ABW = actual body weight; VT = tidal volume; Pdriving = driving pressure; IBW = ideal body weight; Pplat = plateau pressure; PBW = predicted body weight; HFOV = high-frequency oscillatory ventilation.

†Values are given as the in-hospital mortality rates of intervention vs control group, unless otherwise noted.

‡28-day mortality rate.

§60-day mortality rate.

‖30-day mortality rate.

¶180-day mortality rate.

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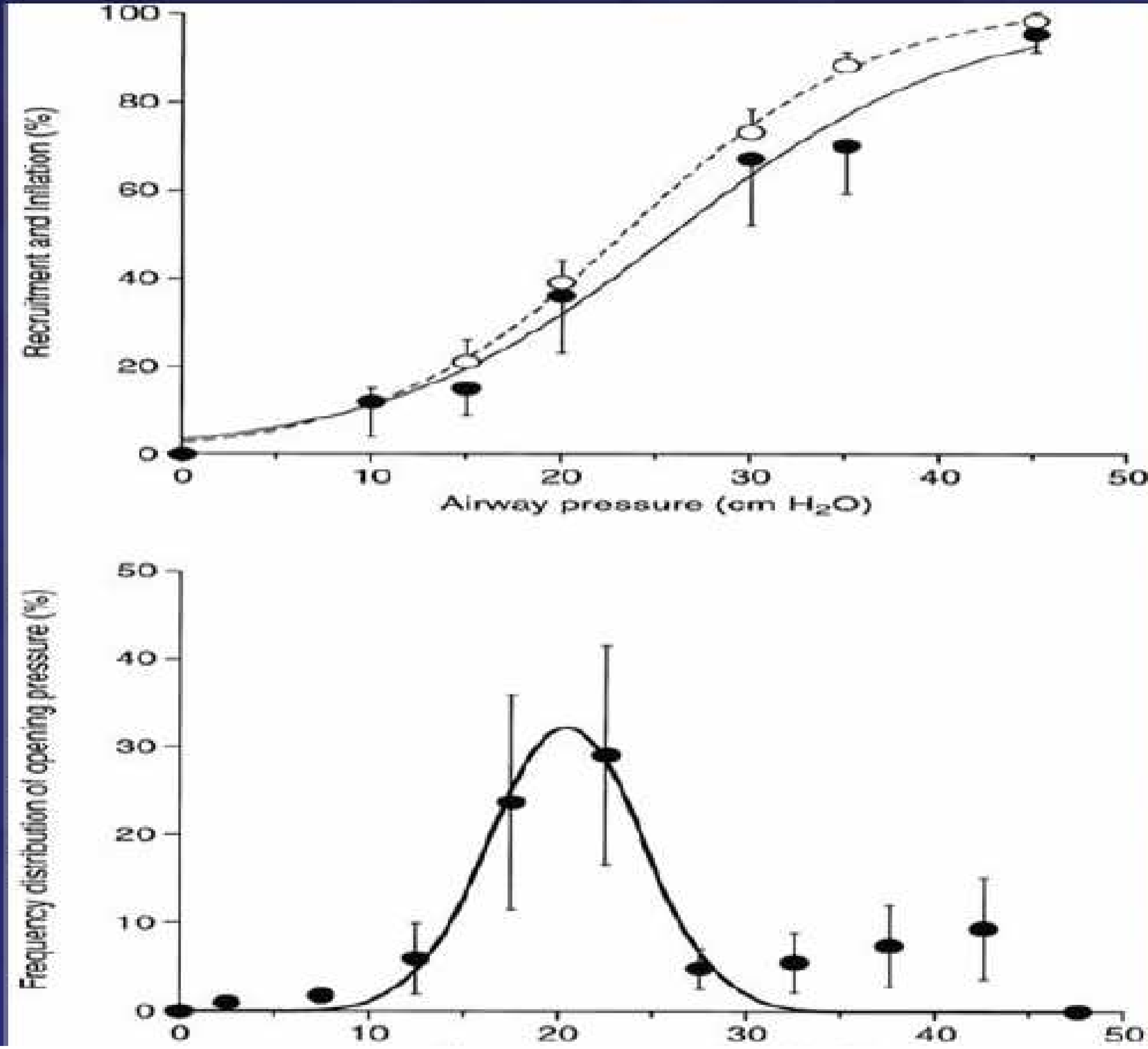
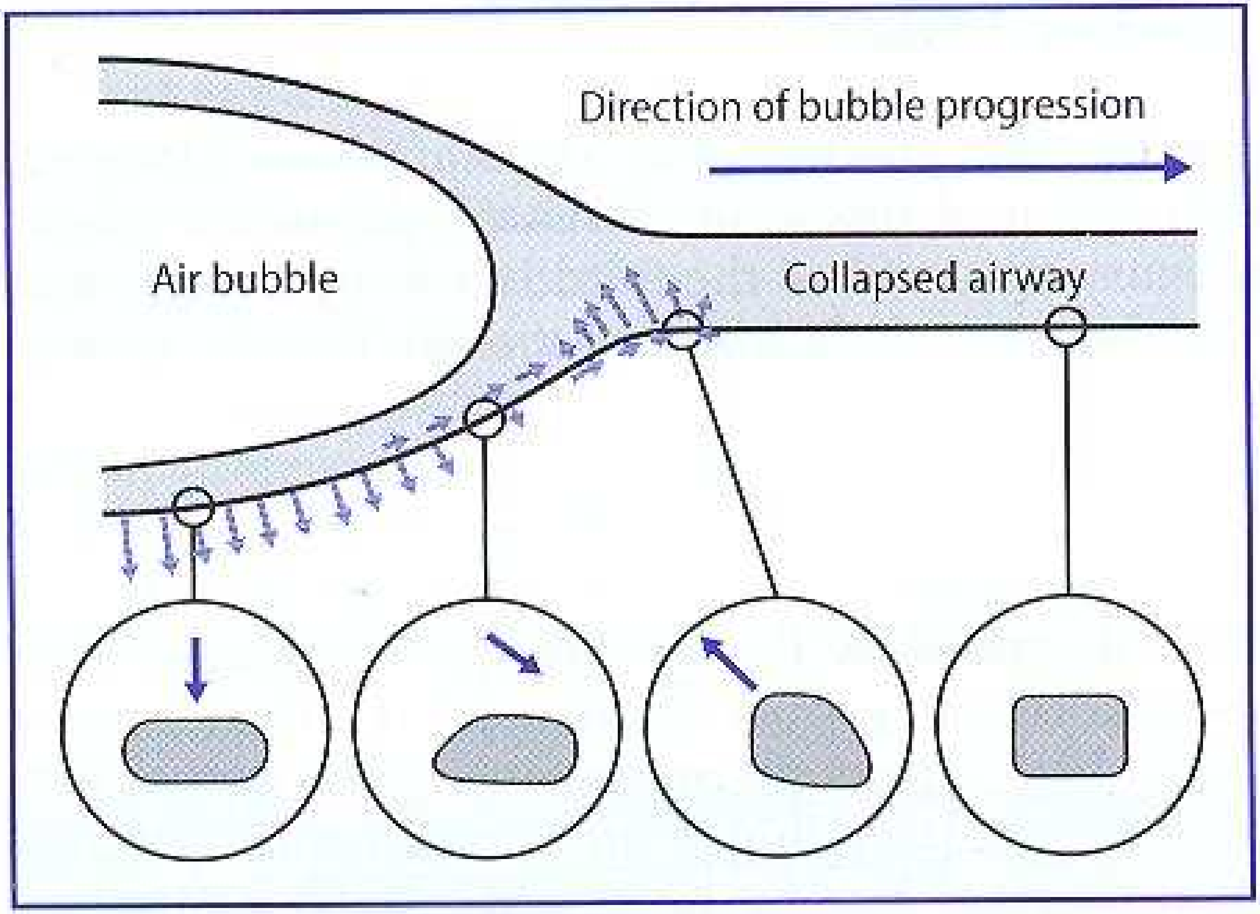
ΕΚΠΤΥΞΗ ΤΟΥ ΠΝΕΥΜΟΝΑ

"Pplat> 25cm H2O is required to reverse atelectasis…"

Crotti et al, Am J Respir Crit Care Med 2001.





Billek AM. JAP 2003; 94:1037-1044, Albert S. Yearbook of Intensive Care and Emergency Medicine 2008; 245-255

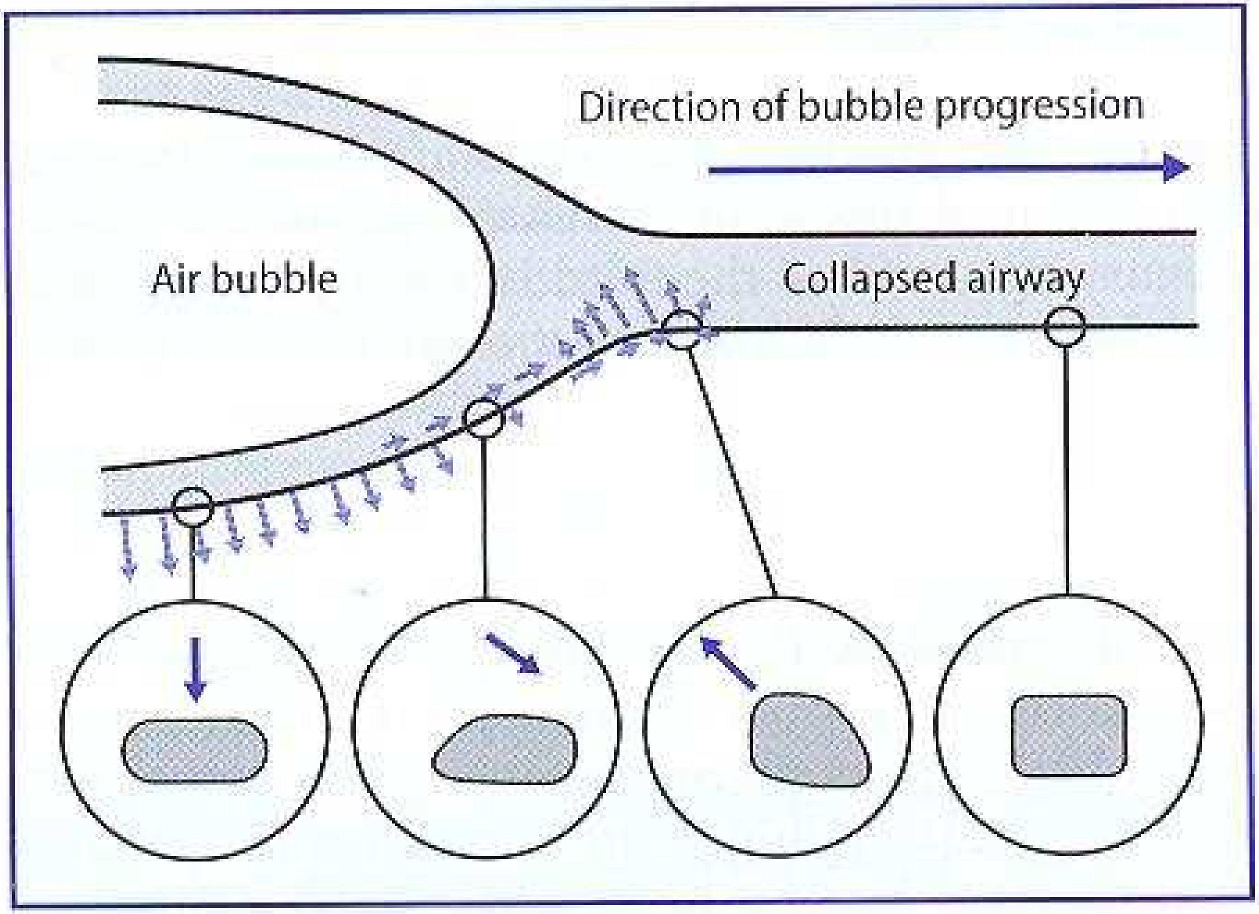


Fig. 4. Hypothetical stresses imparted on the epithelial cells of an airway during reopening. A collapsed compliant airway is forced open by a finger of air moving from left to right. A dynamic wave of stresses is imparted on the airway tissues as the bubble progresses. Circles show the cycle of stresses that an airway epithelial cell might experience during reopening. The cell far downstream is nominally stressed. As the bubble approaches the cell is pulled up and toward the bubble. After the bubble has passed, the cell is pushed outward. From [20] with permission.

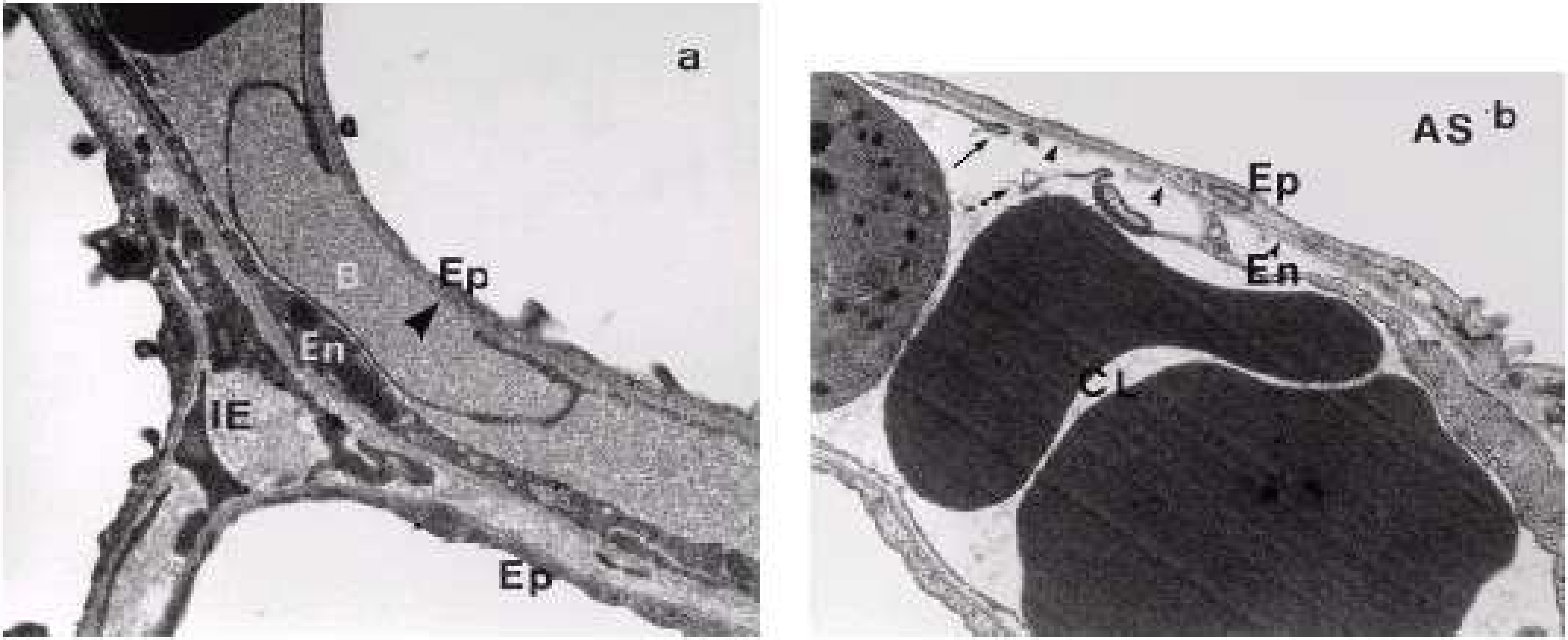
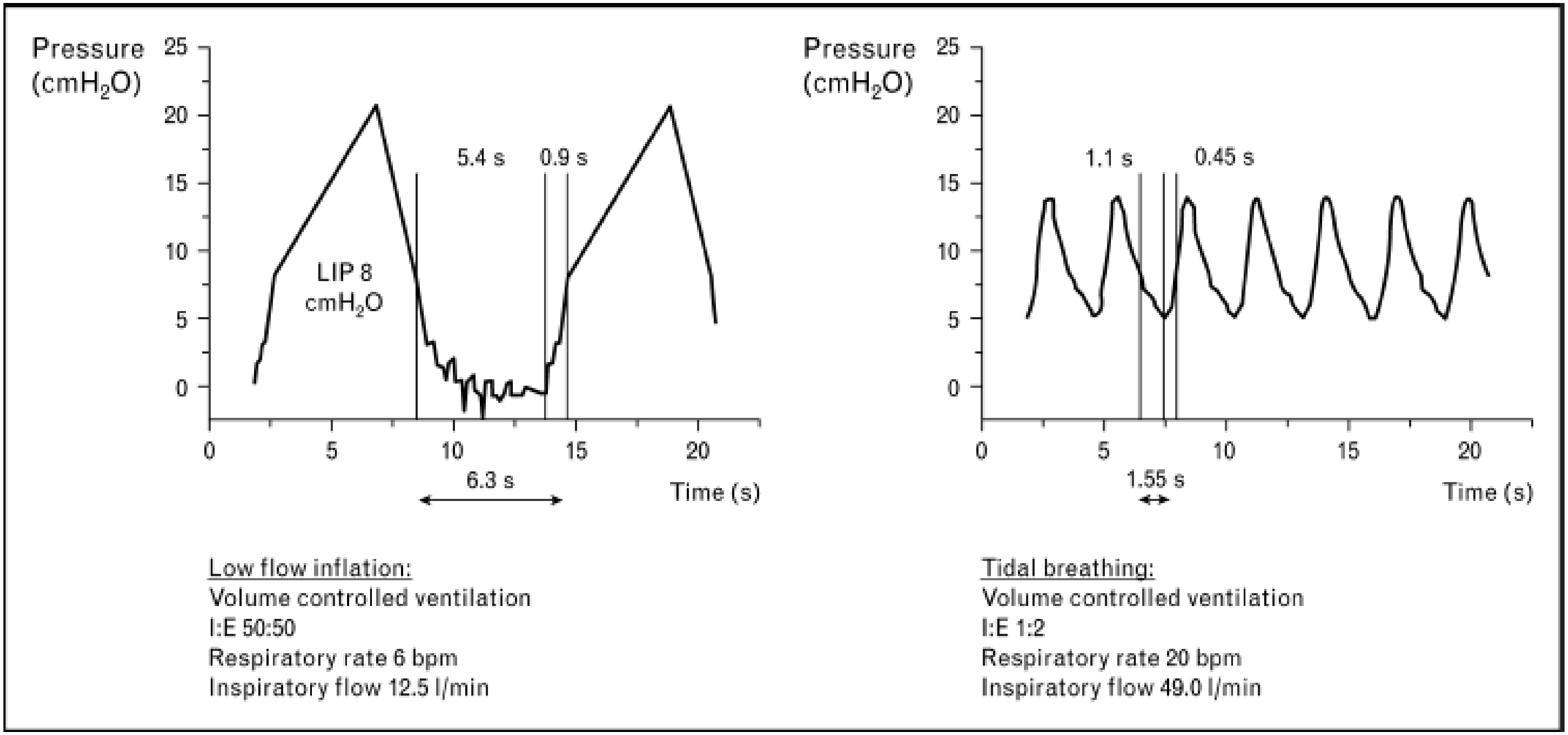


Figure 7. Early changes (5 min) in the ultrastructural appearance of the blood–air barrier after mechanical ventilation of a closed-chest rat at 45 cm H_2O peak airway pressure. (*a*) The thin part of an endothelial cell (En) is detached from the basement membrane (*arrowhead*) forming a bleb (B) filled with electron-dense material of the same density as the plasma. Epithelial type I cells (Ep) are intact. Note interstitial edema (IE). (*b*) The thin part of the endothelial cell is disrupted and floats in the capillary lumen (*arrows*) after becoming detached from the basement membrane (*arrowheads*). AS = alveolar space. *Panel a* was kindly provided by Dr. Paul Soler. *Panel b* is reproduced from D. Dreyfuss and G. Saumon. Ventilator-induced lung injury. *In* M. J. Tobin, editor. Principles and Practice of Mechanical Ventilation. McGraw-Hill, New York. 793–811, with permission.

Dreyfuss D, Saumon G. VILI. State of the Art. AJRCCM 1998; 157: 294

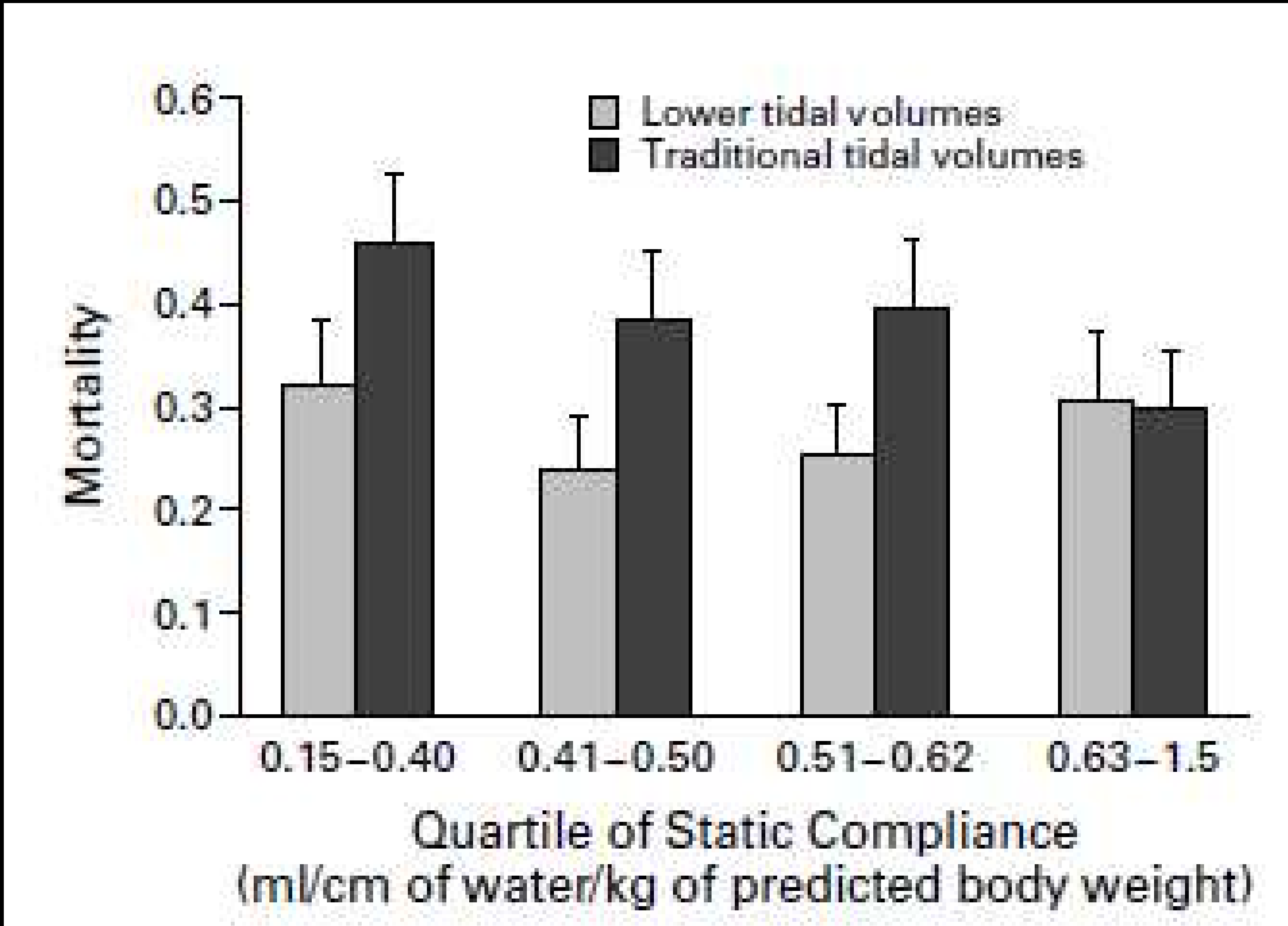
- **<u>Η σημασία της Αναπνευστικής συχνότητας στο ARDS</u>**

Figure 1 Alveolar pressure vs. time in an acute lung injury patient during slow inflation (left) and during tidal breathing (right)



In this patient the lower inflection point (LIP) is around 8 cmH_2O, which can be seen as the inflection in the pressure trace (indicated by arrows) during inspiration and expiration. During the slow inflation the pressure is below the LIP for more than 6 s. During therapeutic tidal ventilation at a rate of 20 breaths/min the corresponding time is only 1.5 s and this is a too short time for collapse to occur. bpm, breaths/min; I : E, inspiration : expiration. From [30] with permission.

Curr Op Crit Care Med
2008; 14:87-93

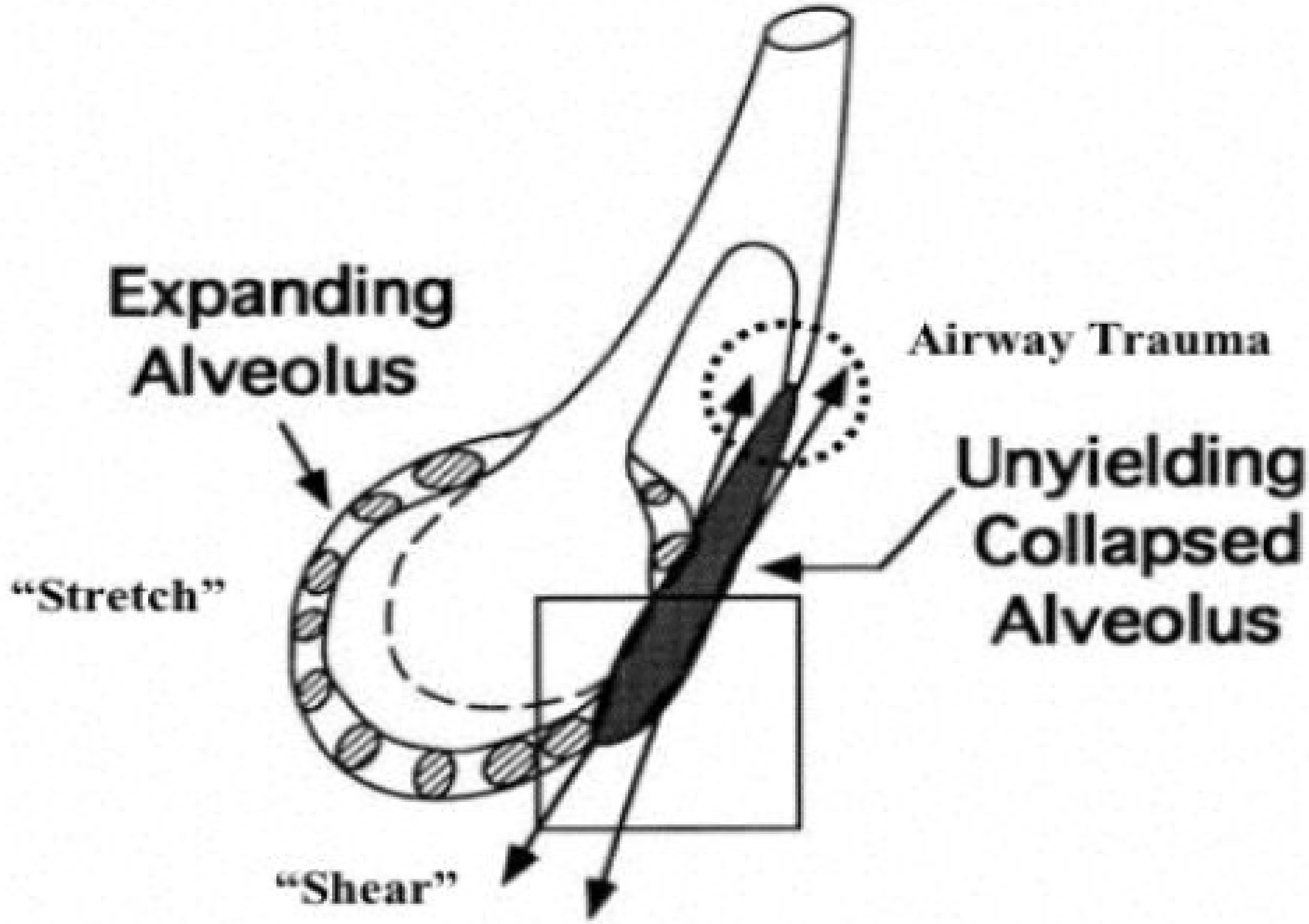


ARDS NETWORK, NEJM 2000; 342:1301-08

<u>Βασικές Θεραπευτικές Αρχές</u>

- **<u>ΚΡΙΣΗ ΟΞΥΓΟΝΩΣΗΣ</u>**
  - Μείωση του κινδύνου/οφέλους στον αερισμό, λόγω υπερκαπνίας vs υψηλών TV
  - Επαρκές Re
  - Μείωση του VO2 και των απαιτήσεων στον αερισμό
  - Πρηνή θέση

FIGURE 29-6 Forms of tissue stress that occur near the junctions of open and closed lung units.



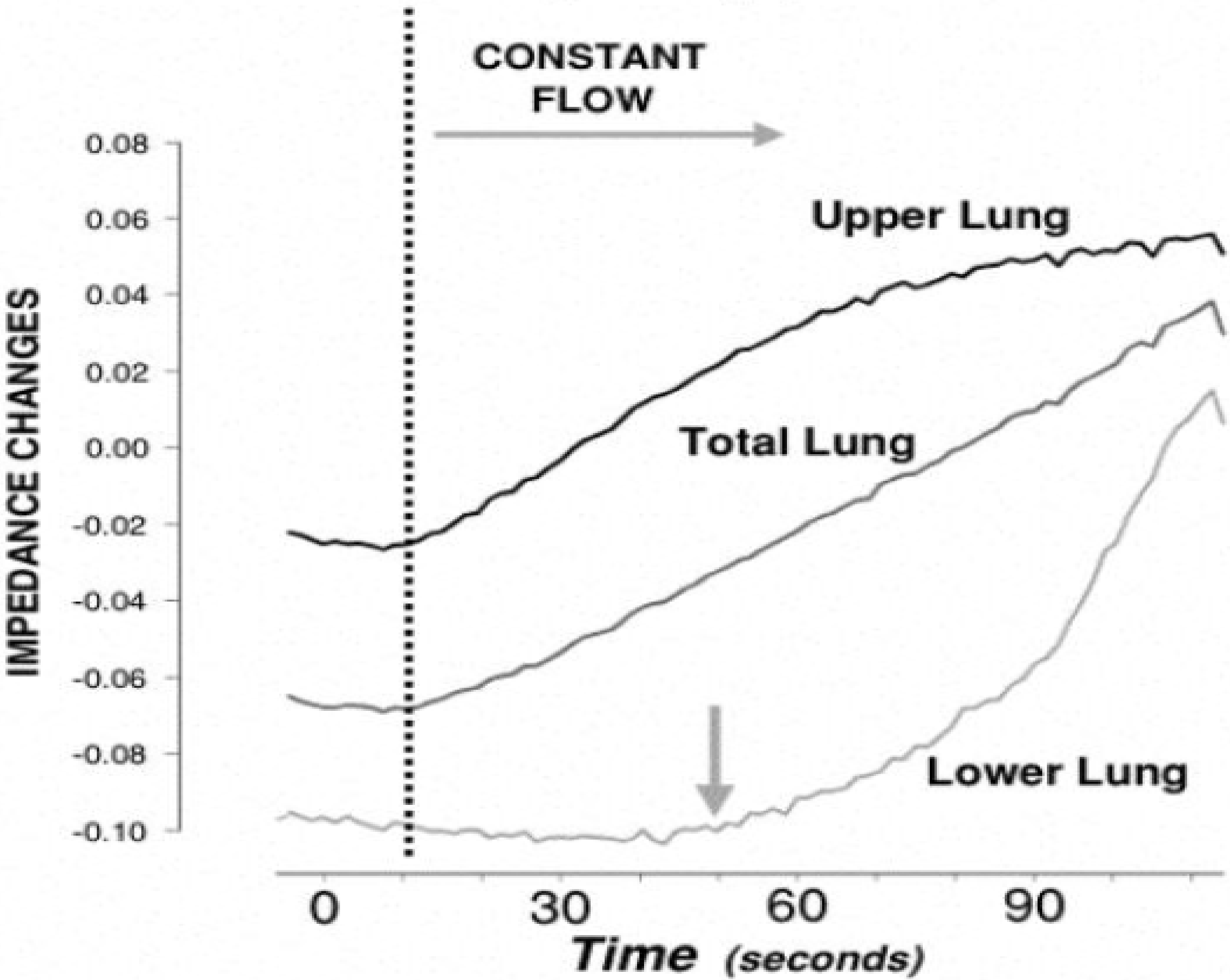
Marini J, Wheeler A. Critical Care Medicine. The essentials, 2010 pp: 430-54

NHLBI ARDS Network

- NIH-funded consortium σε 10 κέντρα, 24 Νοσοκομεία, 75 ΜΕΘ
- Σκοπός: RCTs; αποτελεσματική θεραπεία
- Key ARDSnet studies:
  – Ογκοι αναπνευστήρα
  – Στεροειδή
  – PEEP
  – Διαχείριση όγκου/τοποθέτηση Pwp

Υπερδιάτασις στο ARDS

- **Vei =** $$\frac{\text{VT x Pplat}}{\text{Pplat – PEEPi}}$$
- Υπόταση
- Βαρότραυμα



CONSTANT
FLOW
Upper Lung
Total Lung
Lower Lung
IMPEDANCE CHANGES
0.08
0.06
0.04
0.02
0.00
-0.02
-0.04
-0.06
-0.08
-0.10
0
30
60
90
Time (seconds)

FiO2 - PEEP

Table 1. Settings for Positive End-Expiratory Pressure (PEEP), According to the Required Fraction of Inspired Oxygen (FiO_2).*

FiO_2	PEEP
0.3	5
0.4	5–8
0.5	8–10
0.6	10
0.7	10–14
0.8	14
0.9	14–18
1.0	18–24

* Settings are from the ARDSNet trial.[19] The required FiO_2 is the lowest value that maintains arterial oxyhemoglobin saturation above 90%. After the corresponding level of PEEP is selected, arterial oxyhemoglobin saturation and plateau airway pressure should be monitored in the patient.

Table 1. Forces acting to contain or disperse alveolar biofluids

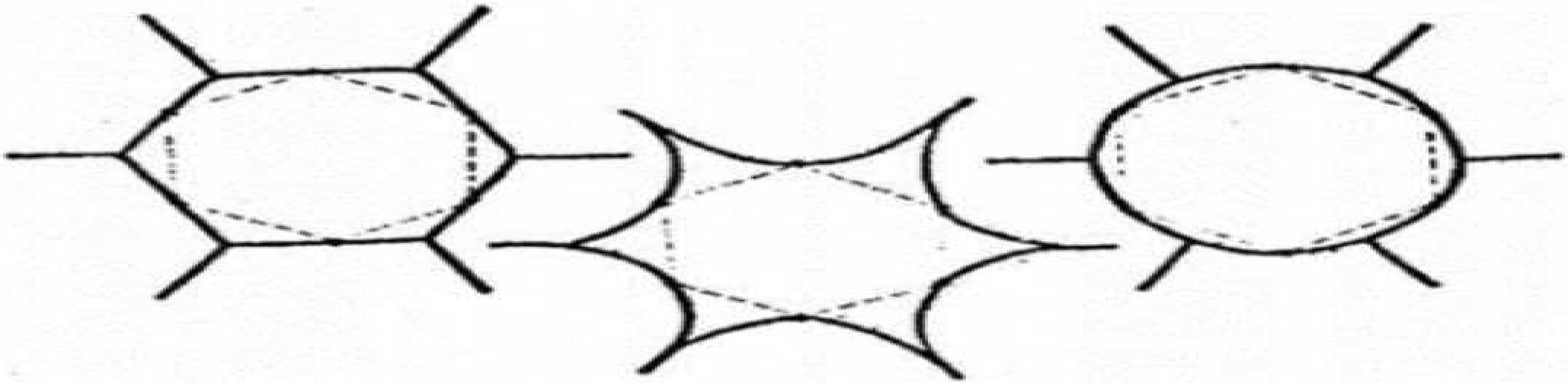
Containing Forces	Propagating Forces
Positive end-expiratory pressure	High tidal volume
High peak inspiratory flow[a]	High peak expiratory flow[a]
Interdependence	Expulsive efforts/airway suctioning
Surfactant	High surface tension
Lymphatic drainage	High microvascular pressure
Intact epithelial pumps	Increased permeability
Damaged side down	Damaged side up

Marini J. CCM 2010

FIGURE 38-4 Schematic representation of the alveolus under normal conditions (*left-hand side*) and during development of acute lung injury (ALI) and the acute respiratory distress syndrome (ARDS) (*right-hand side*). In the acute phase of the syndrome (*right-hand side*), there is sloughing of both the bronchial and alveolar epithelial cells, with the formation of protein-rich hyaline membranes on the denuded basement membrane. Neutrophils are shown adhering to the injured capillary endothelium and marginating through the interstitium into the air space, which is filled with protein-rich edema fluid. In the air space, an alveolar macrophage is secreting cytokines such as interleukins-1, -6, -8, and -10, (IL-1, 6, 8, and 10), and tumor necrosis factor-α (TNF-α), which act locally to stimulate chemotaxis and activate neutrophils. Macrophages also secrete other cytokines, including interleukins-1, -6, and -10. Interleukin-1 can also stimulate the production of extracellular matrix by fibroblasts. Neutrophils can release oxidants, proteases, leukotrienes, and other proinflammatory molecules, such as platelet-activating factor (PAF). A number of anti-inflammatory mediators are also present in the alveolar milieu, including interleukin-1–receptor antagonist, soluble tumor necrosis factor receptor, autoantibodies against interleukin-8, and cytokines such as interleukins-10 and -11 (not shown). The influx of protein-rich edema fluid into the alveolus has led to the inactivation of surfactant. MIF denotes macrophage inhibitory factor. (*Reproduced with permission from Ware et al.*[36])

Ventilation of ARDS
What Do We Know?

- ARDS is a heterogeneous problem.
  - Between patients
  - Over time
  - Between lung regions
- Response to interventions reflects this heterogeneity.
- Lung recruitment is essential to avoid VILI.
- The chest wall influences regional lung volumes and recruitability.



$$P_{eff} = P_{appl} (V/V_o)^{2/3}$$

FIGURE 29-4 Amplification of tension at the boundaries of open and collapsing lung tissue. Normally distended (*left*), collapsing (*center*), and overdistended (*right*) states of inflation. Because of interdependence, the tensions applied to a collapsing alveolus are amplified. A simple mathematical model predicts that the tensions resulting from an alveolar pressure (Pappl) produce a tension comparable with an effective pressure (Peff) described by the equation. At 30 cmH_2O applied pressure, the volume of an aerated alveolus (V) is approximately 10 times that of a collapsed alveolus (V_0). Thus the estimated pressure necessary to mimic the tensions at the interface is approximately 4.5 times as great as that applied (140 cmH_2O). (*Used, with permission, from J. Mead et al JAP 1970 Am J Respir Crit Care Med 163:1609–13, 2001.*)

V.I.L.I

- ***Shear Stress***

- "Traction exerted on the normal parenchyma surrounding atelectatic areas"

» Mead J, et al. JAP 1970; 28:596-608

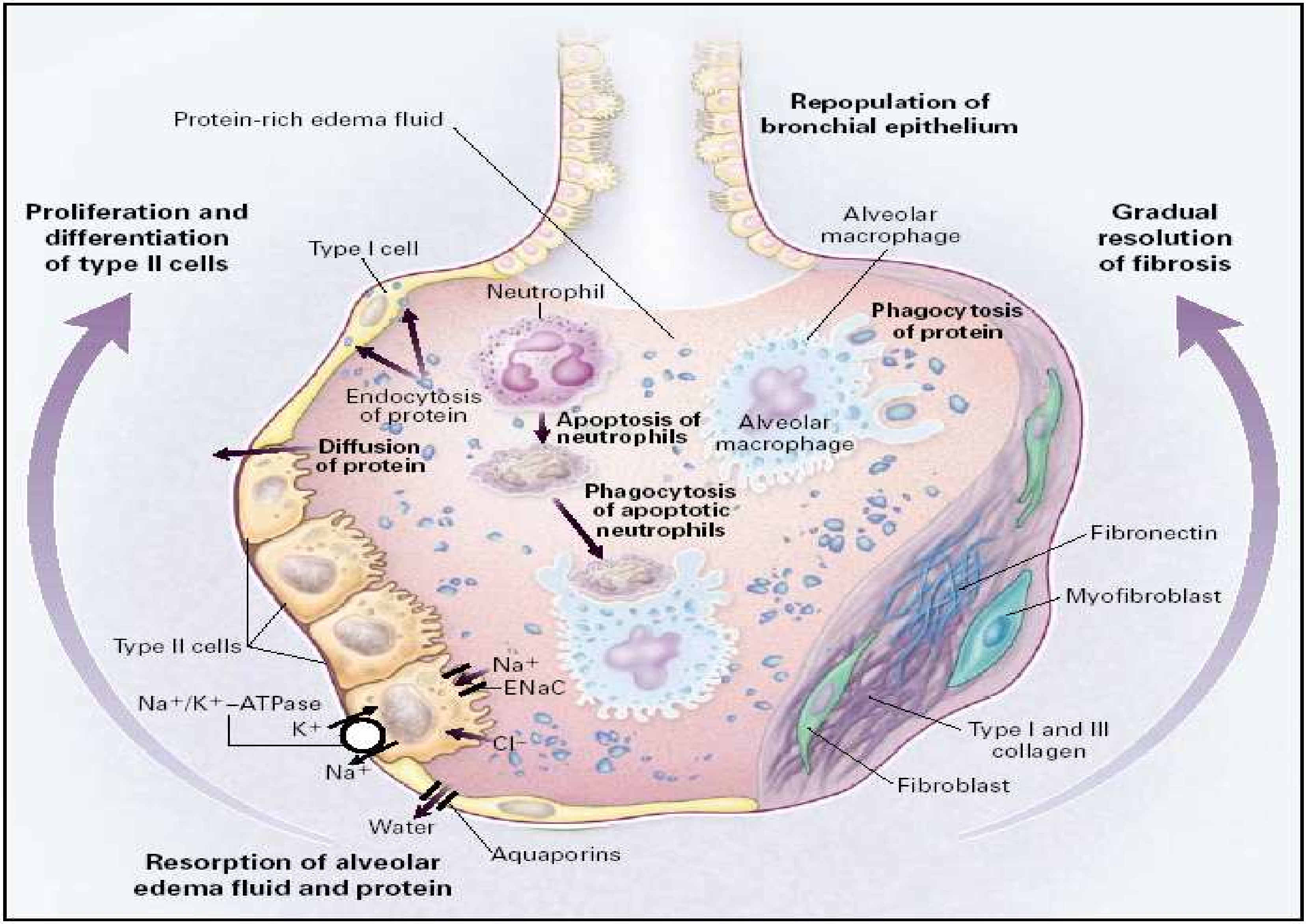
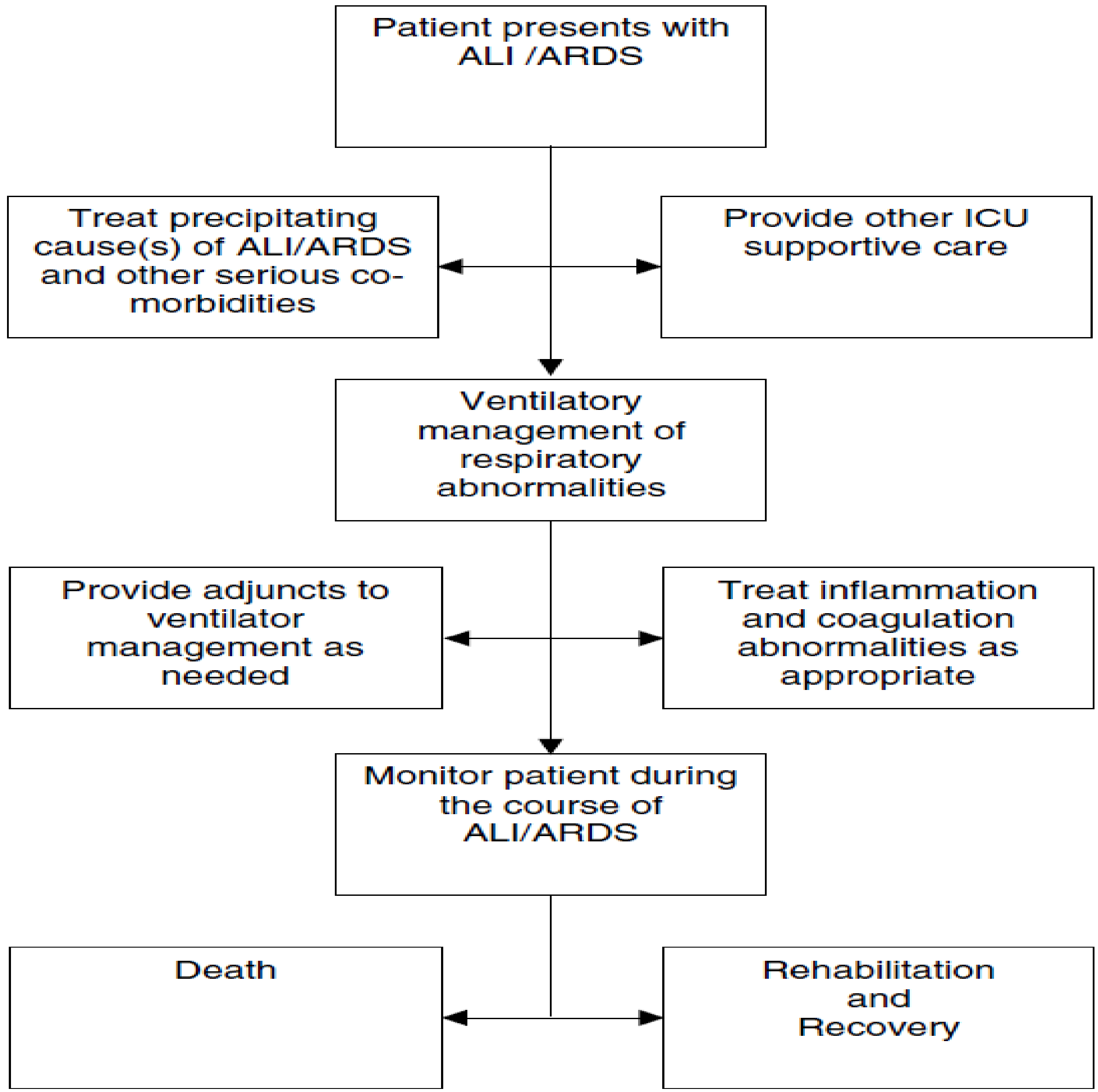


Figure 4. Mechanisms Important in the Resolution of Acute Lung Injury and the Acute Respiratory Distress Syndrome.



Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

Μηχανισμοί “Βλάβης”

1. Δομική αλλοίωση κυττάρου
2. Μεταβολική δυσλειτουργία
3. Τροποποιημένη λειτουργική απάντηση
4. Θάνατος κυττάρου από ισχαιμία

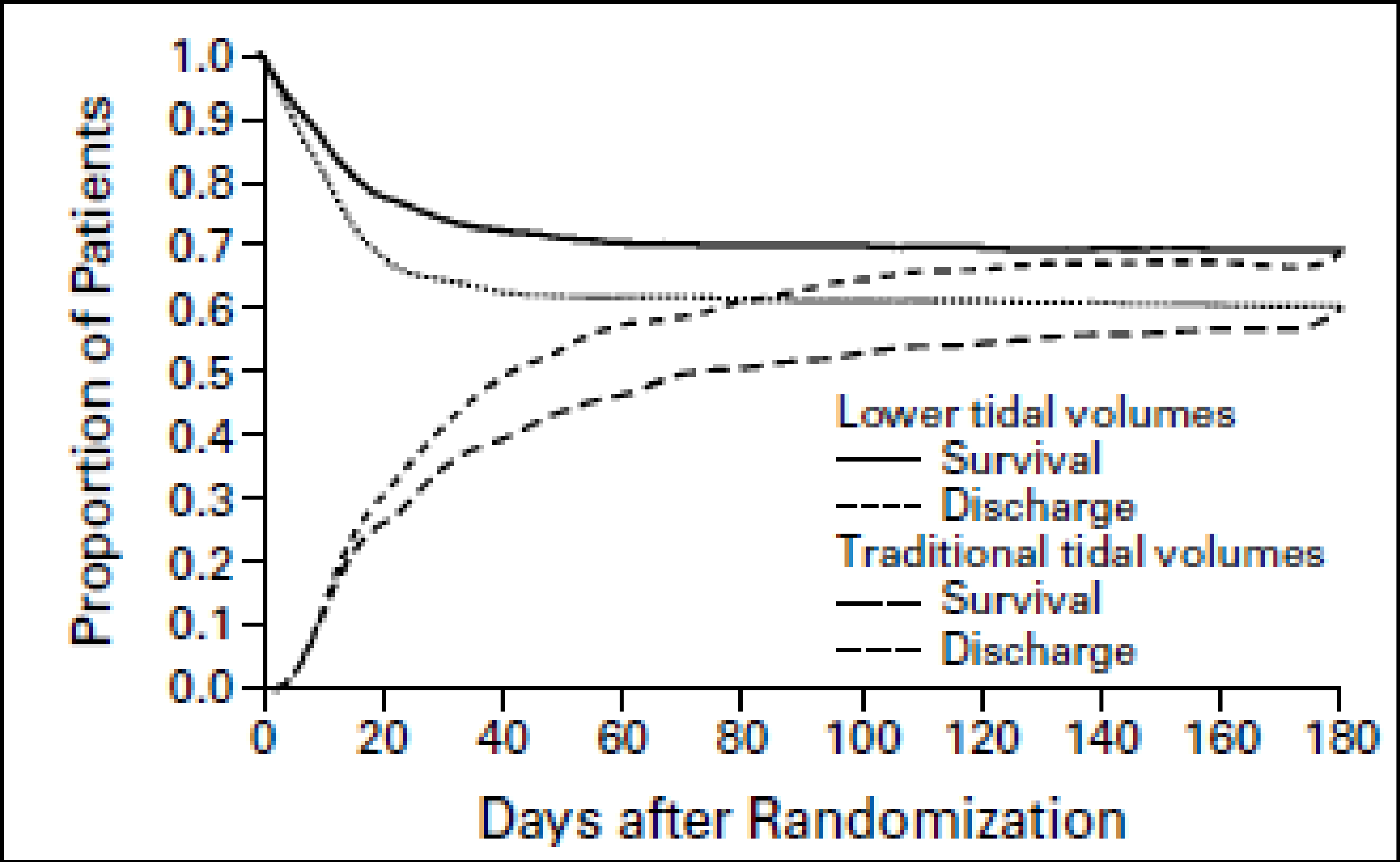
Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

ARDS

- **Φυσιολογικός πνεύμων – baby**
- **Ατελεκτασία**
- **Οίδημα**
- **Φλεγμονή -Πύκνωση**
- **Ινωση**

Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547

TV Lower vs Traditional in ARDS



ARDS NETWORK, NEJM 2000; 342:1301-08

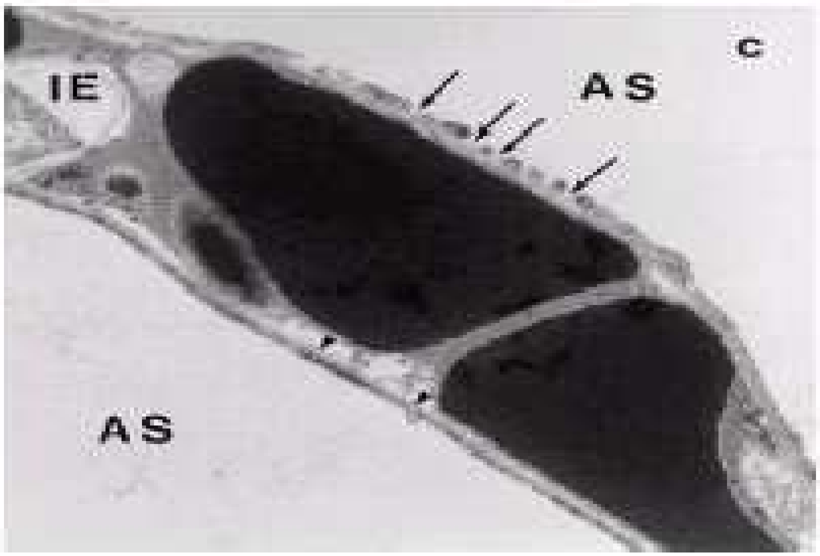
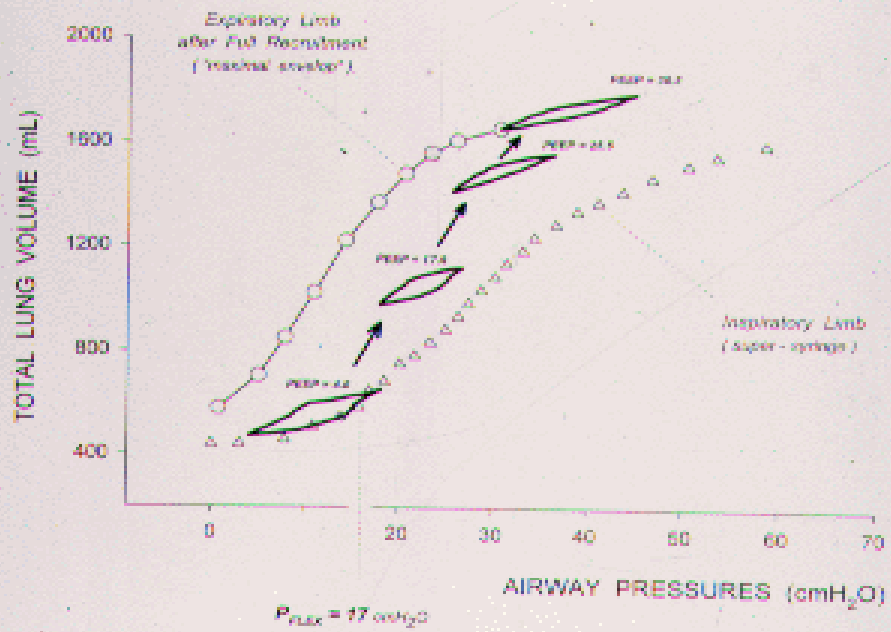


Figure 8. Changes in the ultrastructural appearance of the blood–air barrier after mechanical ventilation of a closed-chest rat for 20 min at 45 cm H_2O peak airway pressure. (*a*) Widespread destruction of epithelial cells leads to denudation of basement membranes (*arrowheads*). Many gaps in the capillary endothelium allow close contact between cytoplasmic processes of an intracapillary polymorphonuclear neutrophil (PN) and the basement membrane (*arrows*). (*b*) Very severe changes in the alveolar–capillary barrier result in diffuse alveolar damage. The epithelial layer is totally destroyed (*upper right quadrant*) leading to denudation of the basement membrane (*arrows*). Hyaline membranes (HM), composed of cell debris and fibrin (f), occupy the alveolar space. En = endothelial cells; IE = interstitial edema. (*c*) There are many gaps in an alveolar type I cell. The endothelial cell is detached from the basement membrane (*arrowheads* indicate the basement membrane). There is edema in the interstitium (IE). AS = alveolar space. *Panels a* and *c* are reproduced from D. Dreyfuss and G. Saumon (227), with permission. *Panel b* is reproduced from Dreyfuss and coworkers (4), with permission.

Dreyfuss D, Saumon G. VILI. State of the Art. AJRCCM 1998; 157: 294

PEEP and RECRUITMENT



Μηχανικός Αερισμός στο ARDS

1. **Εκτίμηση μηχανικής του πνευμονικού παρεγχύματος και του θωρακικού κλωβου**

Marini J, 2010 The Essentilas, pp: 430-54, Doyle RL. AJRCCM 1995; 152:1818, Rubenfeld GD. NEJM 2005; 353:1685

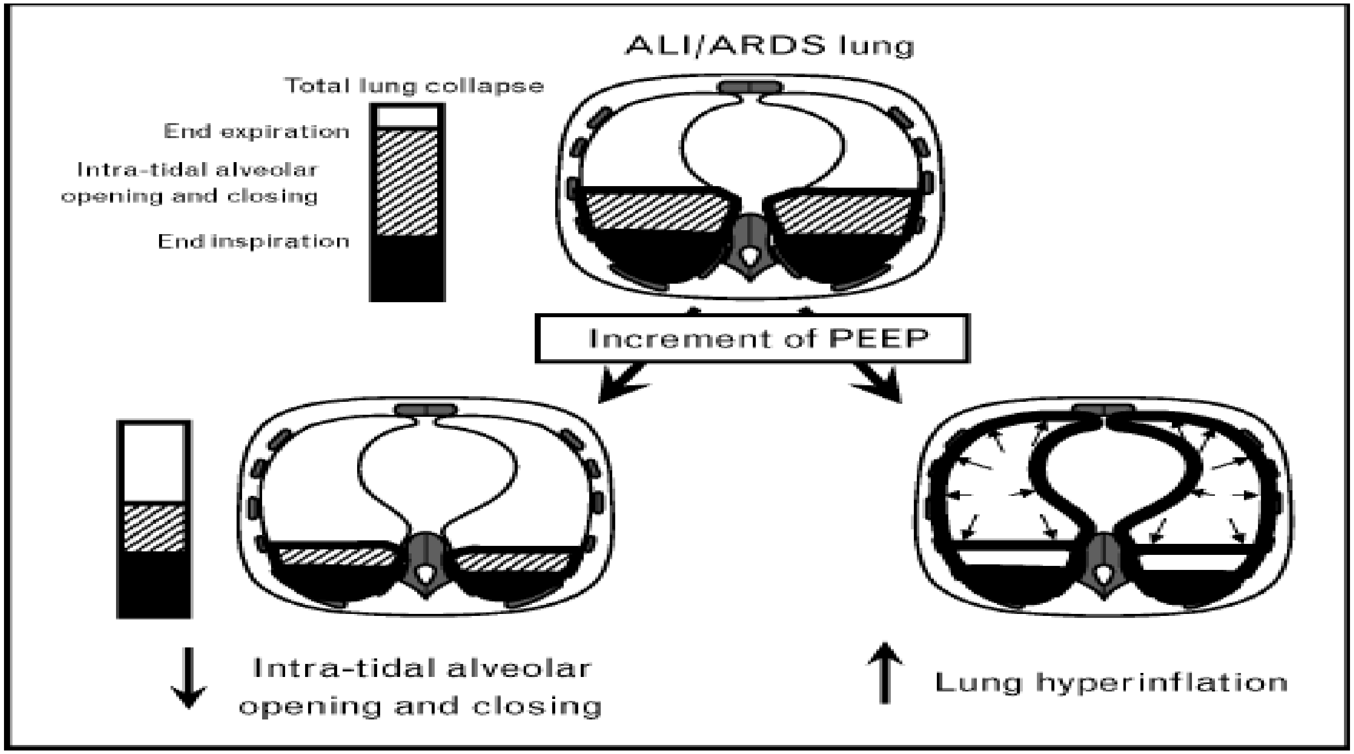
- **«Η σημασία του VILI έχει πρόσφατα δεχτεί μια ηχηρή εξήγηση από το ARDS Network, που έδειξε ελάττωση κατά 22% στη θνητότητα των ασθενών με ARDS, όταν λόγω ελάττωσης του TV, κατά τη διάρκεια του MV, το μηχανικό stress των πνευμόνων μειώθηκε»**

Richard JD, Current Opinion Critical Care 2002; 8:12

TABLE 38-4 Differential Diagnosis of Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS)

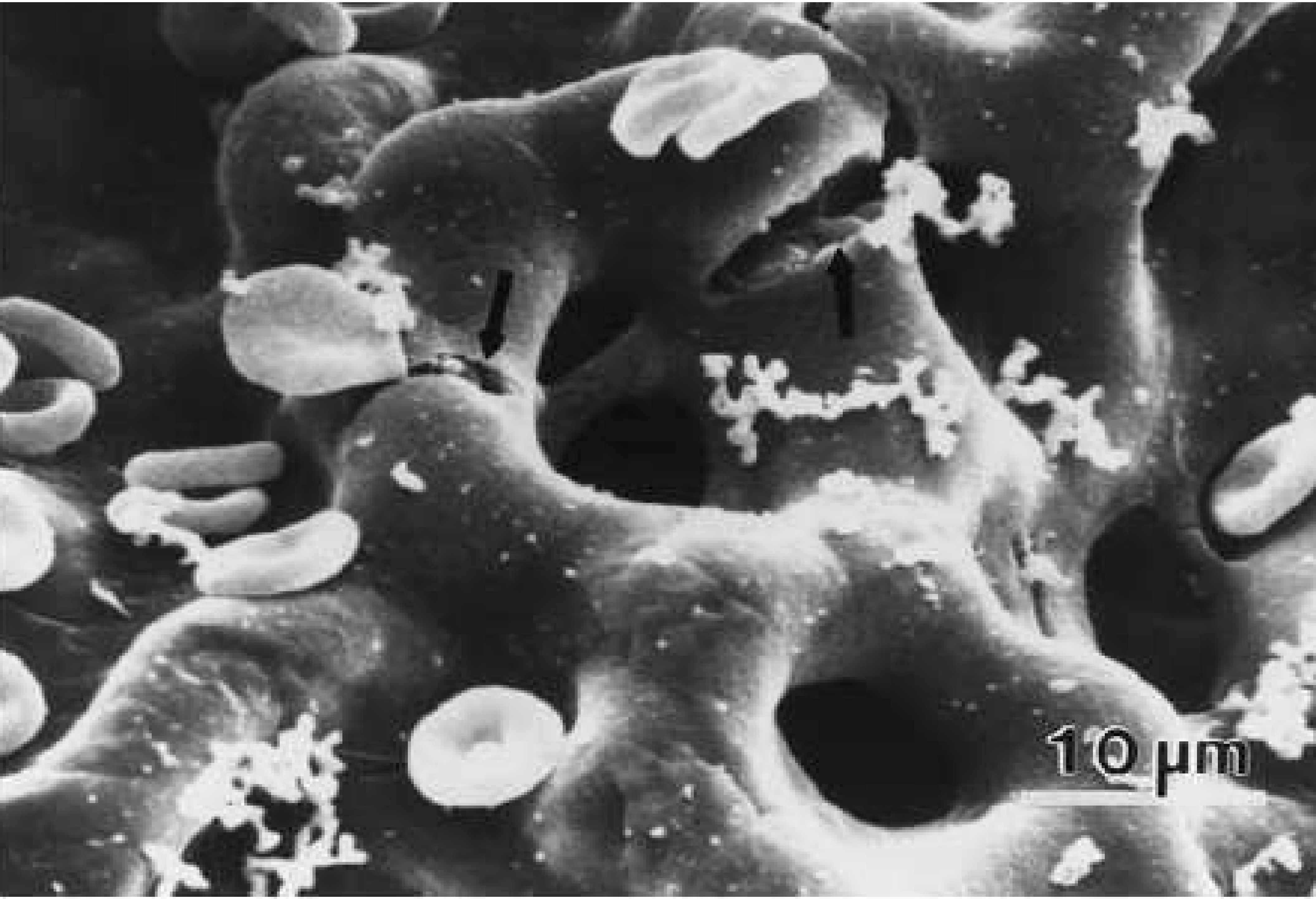
Disorder	Characteristics	Comments
Hypersensitivity pneumonitis	Typically slower onset than ARDS (over weeks) with progressive course; however it may present in an advanced state, mimicking ARDS; may respond to high-dose corticosteroid therapy and removal from offending agent	
Leukemic infiltration	May be rapid in onset during active disease states; usually leukemia is clinically apparent	
Drug-induced pulmonary edema and pneumonitis	May follow use of heroin, other opioids, overdose of aspirin, tricyclic antidepressants, or exposure to paraquat	May progress to overt ARDS
Acute major pulmonary embolus (PE)	Occurs acutely, occasionally accompanied by severe hypoxemia that may be resistant to O_2 therapy like ARDS, and by hypotension, requiring pressors, mimicking ARDS with sepsis; patients typically have risk factors for acute PE and may not have common precipitating causes of ARDS	Chest radiograph in ARDS should have bilateral infiltrates consistent with pulmonary edema; chest radiograph in acute major PE may have unilateral or no infiltrates; acute major PE needs a confirmatory study (e.g., pulmonary angiogram)
Sarcoidosis	The onset is not acute, but its clinical recognition may be; oxygenation is often impaired and the chest radiograph can be diffusely abnormal	Historical features and the frequent presence of hilar adenopathy in sarcoidosis usually eliminate confusion with ARDS
Interstitial pulmonary fibrosis	The onset is not acute, but its clinical recognition may be; oxygenation is often impaired and the chest radiograph can be diffusely abnormal	Prior chest radiographs and a history of chronic and progressive dyspnea characterize the collection of diseases causing interstitial pulmonary fibrosis

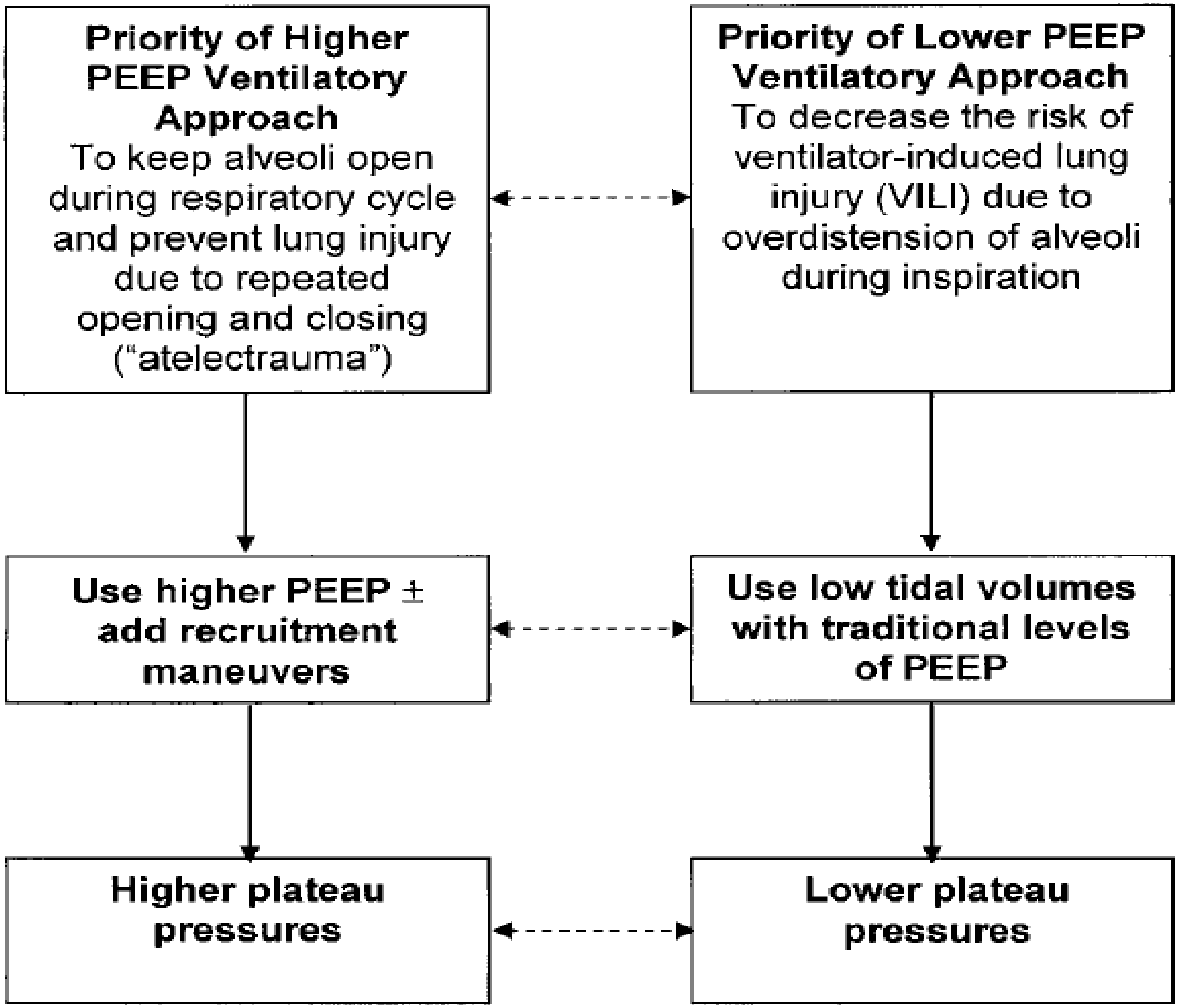
Figure 1 Schematic representation of the effects of the increase of positive end-expiratory pressure (PEEP) on the lung parenchyma during acute lung injury/acute respiratory distress syndrome (ALI/ARDS)



As shown in the upper panel, the ARDS lung is commonly characterized by the simultaneous presence of a normally aerated (white) and a collapsed (black) lung area. During each tidal breath, the end-inspiratory pressure will decrease the amount of collapsed lung by recruiting alveolar units. At the end of expiration, a portion of the recruited alveoli will collapse again, thereby generating a 'cycling alveolar opening and closing' process. The increase of PEEP during volume-controlled ventilation with a constant tidal volume may determine two opposite effects: on the one hand (lower left panel), it will decrease the amount of lung tissue undergoing cycling opening and closing by increasing the amount of alveolar units kept open at the end of expiration, and, on the other hand (lower right panel), it will augment the degree of hyperinflation of the normally aerated lung region.

Gattinoni L. Curr Op Crit Care Med 2008; 14:64-69


10 µm


Priority of Higher PEEP Ventilatory Approach
To keep alveoli open during respiratory cycle and prevent lung injury due to repeated opening and closing ("atelectrauma")
Priority of Lower PEEP Ventilatory Approach
To decrease the risk of ventilator-induced lung injury (VILI) due to overdistension of alveoli during inspiration
Use higher PEEP ± add recruitment maneuvers
Use low tidal volumes with traditional levels of PEEP
Higher plateau pressures
Lower plateau pressures

Wood

TABLE 38-9 NIH NHLBI ARDS Network Low-Tidal-Volume Ventilation Strategy

Part I. Ventilator set-up and adjustment

1. Calculate ideal body weight (IBW).[a]
2. Use assist/control mode and set initial tidal volume (TV) to 8 mL/kg IBW (if baseline TV >8 mL/kg).
3. Reduce TV by 1-mL/kg intervals every 2 hours until TV = 6 mL/kg IBW.
4. Set initial rate to approximate baseline minute ventilation (but not >35 bpm).
5. Adjust TV and respiratory rate (RR) to achieve pH and plateau pressure (Pplat) goals listed below.
6. Set the inspiratory flow rate above patient demand (usually >80 L/min); adjust flow rate to achieve goal of inspiratory : expiratory ratio of 1:1.0–1.3

Part II. Oxygenation goal: Pa_{O_2} = 55–80 mm Hg or Sp_{O_2} = 88–95%

1. Use these incremental F_{IO_2}-PEEP combinations to achieve oxygenation goal:

F_{IO_2}	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12
F_{IO_2}	0.7	0.8	0.9	0.9	0.9	1.0	1.0	1.0
PEEP	14	14	14	16	18	20	22	24

Βασικές Θεραπευτικές Αρχές

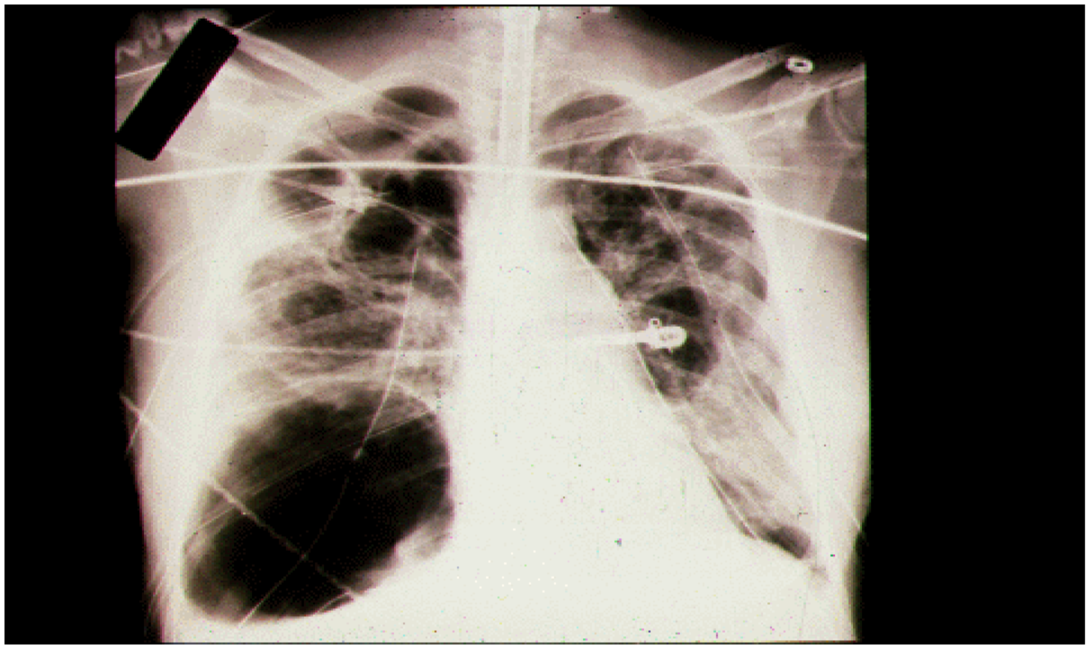
- **ΚΡΙΣΗ ΟΞΥΓΟΝΩΣΗΣ**
  - ΚΡΙΣΙΜΟΣ ΡΟΛΟΣ: ο χειρισμός της Ppeak, Pmean, PEEP (auto και PEEPi) στην επίτευξη ικανοποιητικής PaO_2/FiO_2
  - ΚΥΡΙΟ ΡΟΛΟ: οι Διαπνευμονικές πιέσεις στο collapse των αεραγωγών. Επίσης και mean Paw
- **Αποφυγή High TV / Low PEEP → VILI**
- **Αποφυγή overstretching**

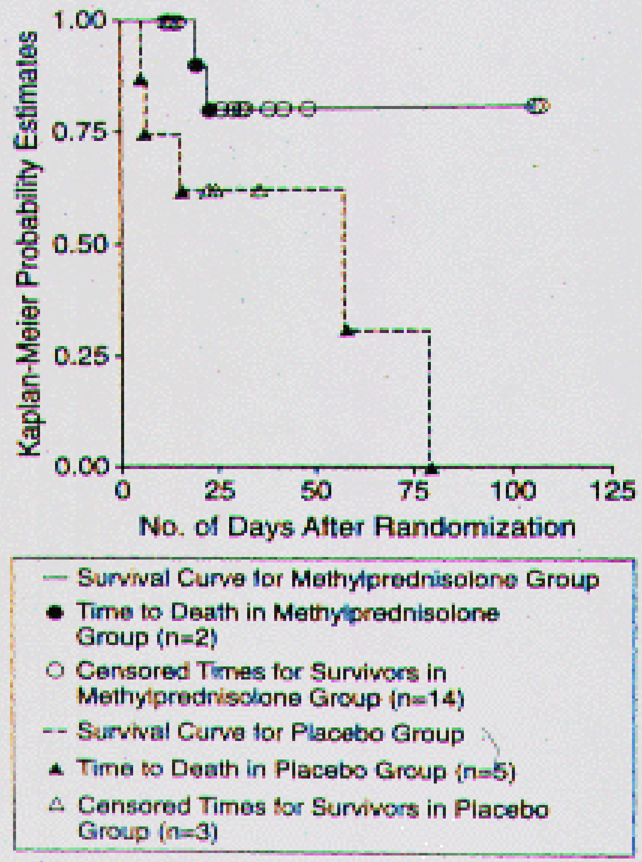
Open Lung Method

1. Optimal gas exchange
2. Low intrapulmonary shunting
3. Paw: minimal
4. Hemodynamic side-effects: minimal
5. Open up the atelectatic areas

- V.I.L.I.: ανάλογο της Ptransp
- Re: ουσιώδες στο να αποφύγουμε το V.I.L.I.
  – Το Θωρακικό τοίχωμα επηρεάζει τους όγκους, τις πιέσεις του πνεύμονα τοπικά και την Re

- Marini J

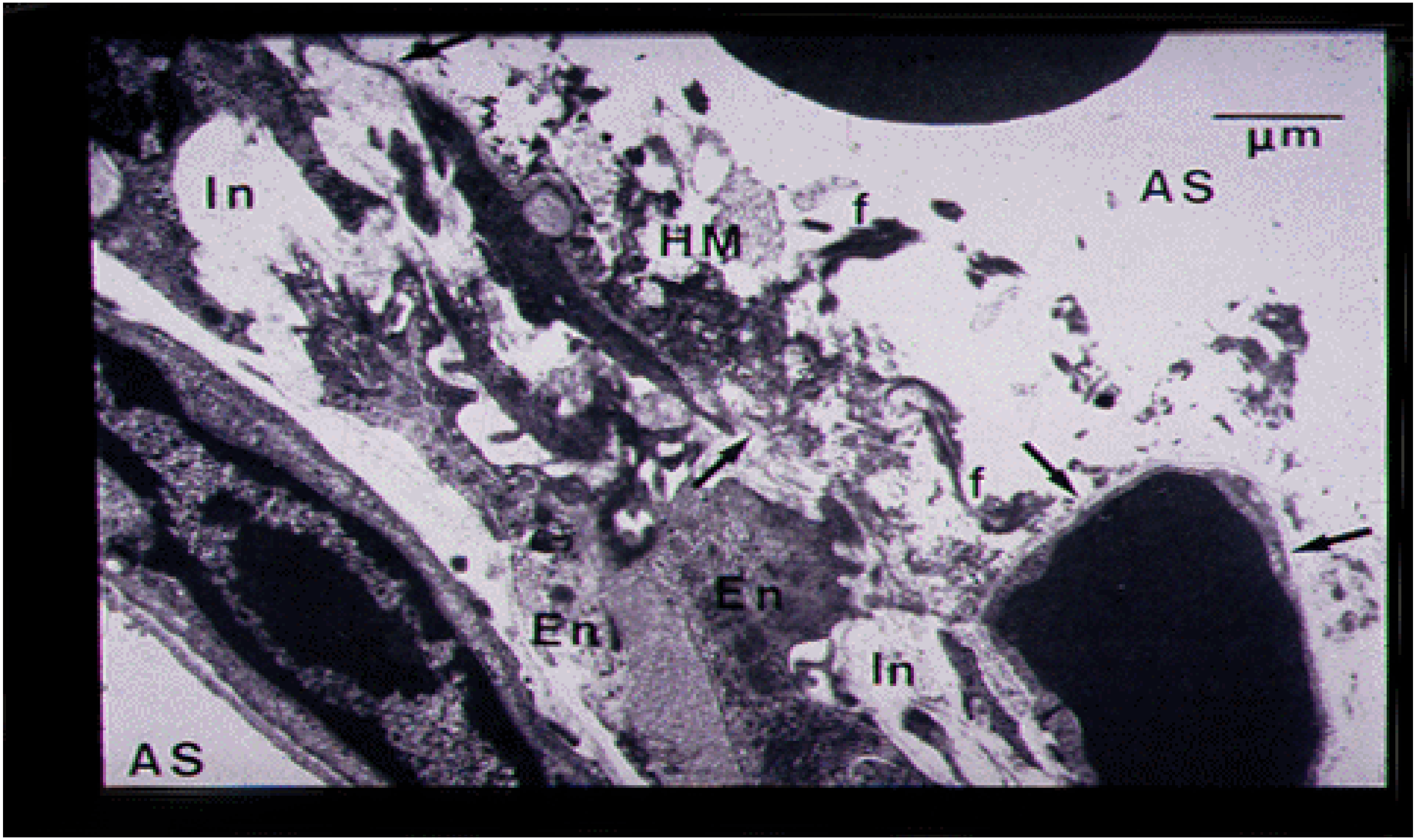




Meduri et al., 1998

- 5 RCTs εφαρμόζοντας υψηλή PEEP έδειξαν μία μείωση στην ενδονοσοκομειακή θνησιμότητα (p=0.03) και μία τάση στη θνησιμότητα στις 28 ημ. (p=0.06), χωρίς αύξηση του βαροτραύματος (Oba)
- 6 RCTs εφαρμόζοντας υψηλή PEEP έδειξαν μία μείωση στην ενδονοσοκομειακή θνησιμότητα (p=0.03) και στη θνησιμότητα στις 28 ημ. (p=0.06), χωρίς αύξηση του βαροτραύματος

Oba Y. Resp Med 2009; 103:1174-81
Phoenix SI, Anesthesiology 2009; 110:1098-105



VlahakisNE. JAP 2000; 89:2490-6, Hotchkiss JR. CCM2002; 30:2368-70

Open Lung Approach
(Evaluate the Response)

- Not all patients are PEEP responsive.
  - Diffuse vs. Regional
  - Secondary vs. Primary
- If PEEP doesn't help, it may hurt.
  - Over Distension
  - Worsened V/Q
  - Redistributed Blood Flow
  - Elevations of P_{PA}

ARDS

- Αρχική Βλάβη (ΠΜΝ, Ρίζες Ο2, Φλεγμονή)

↓

- Βλάβη Πνεύμονα
  - Βαριά ΥποΟ2
  - Stiff Lungs
  - Αμφω σκιάσεις

↓ **M.A.**

- Εκβαση

- ΜΗΧΑΝΙΣΜΟΙ ΒΛΑΒΗΣ

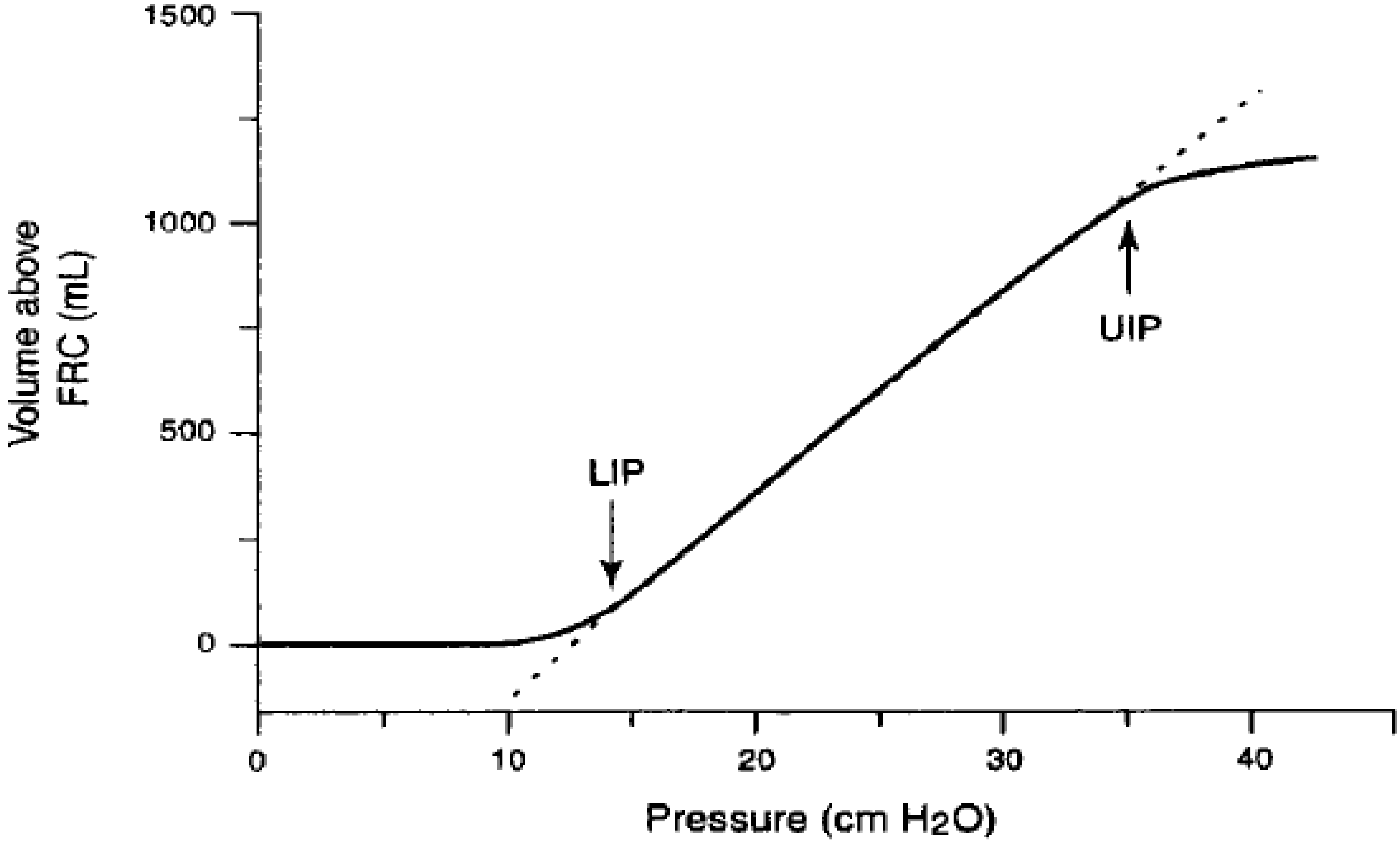
↓

- V/Q Ανομοιογένεια
- Μηχανική πνεύμονα

↓

- V.I.L.I

Christie J., Lanken P. ALI and the ARDS. In Hall J., Schmidt G., Wood L (Eds),: Principles of Critical Care. McGraw-Hill. 2005: 515-547


1500
1000
500
0
Volume above
FRC (mL)
LIP
UIP
0
10
20
30
40
Pressure (cm H2O)

A

Κλινικά Χαρακτηριστικά/ARDS

– Δύσπνοια, ταχύπνοια, κυάνωση και ανθεκτική υποξυγοναιμία, χαμηλή διατασιμότητα
– Αναπτύσσονται 48-72 ώρες μετά το οξύ συμβάν

Marini J, 2010 The Essentilas, pp: 430-54, Doyle RL. AJRCCM 1995; 152:1818, Rubenfeld GD. NEJM 2005; 353:1685

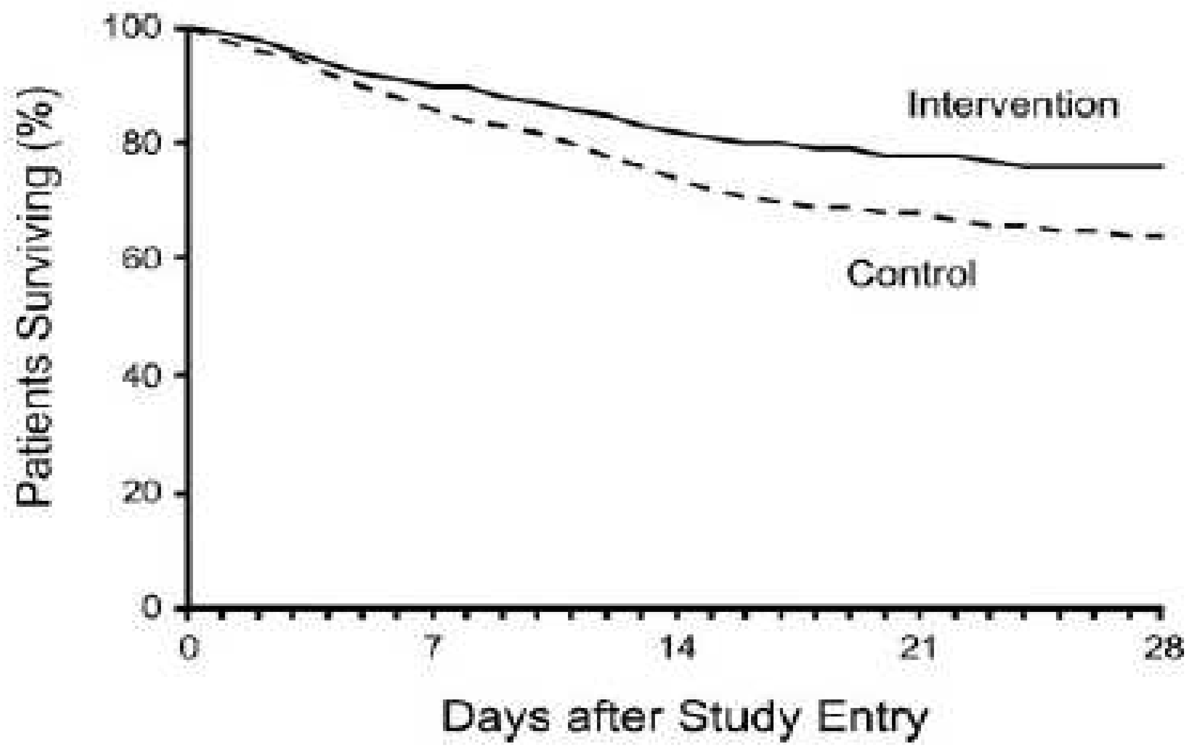


FIGURE 1. Kaplan-Meier analysis of survival during the first 28 days after randomization in patients with ALI and ARDS. The in-hospital mortality rate was 31.0% in the group treated with lower tidal volumes compared with 39.8% in the group treated with traditional tidal volumes ($p = 0.007$; 95% CI for the difference between groups, 2.4 to 15.3%). A Kaplan-Meier analysis of survival during the first 180 days after study entry is presented in the publication by the Acute Respiratory Distress Syndrome Network.[14]

ARDS NETWORK, NEJM 2000; 342:1301-08