VILI
co vlastně poškozuje plíce při UPV?

Jan Máca

Akutně.cz, 2018

Ventilace

17 - 29 tis. dechů v klidu/den

≈

8.5 - 14.5 tis. litrů směsi plynů

VALI

poškození plic na UPV

VILI

poškození plic prokazatelně v souvislosti s UPV

"Often, as new knowledge progresses, old knowledge is abandoned or forgotten." Luciano Gattinoni

Mead 1970
Stress distribution in lung, theoretical model (30/140 cm H_2O)

Webb, Tierney 1974
pulmonary edema due to iPPV with high inflation pressures, protection by PEEP

Tremblay 1997, Ranieri 1999
↑ PEEP → ↓ LI

ARDS network (ARMA) 2000
6ml vs. 12ml/IBW - 31.0 percent vs. 39.8 percent, P=0.007

ALVEOLI (Brower) 2004, LOV (Meade) 2008, ExPress (Mercat) 2008
PEEP studie

Talmor 2008
P_L guided MV - ↑ P/F, C_{RS}

ACURASYS (Papazian) 2010, PROSEVA (Guerin) 2013
myorelaxace, pronace

EOLIA (Combes) 2018
ECMO

koncepty

Lachmann 1992 - editorial
Open up the lung and keep the lung open

Gattinoni 2005
The „baby lung“

Amato 2015
Driving pressure

Protti/Gattinoni/Marini 2016
Mechanical power, Driving energy

Co poškozuje plíci při UPV?

Co poškozuje plíci?

barotrauma/volumotrauma

atelektrauma

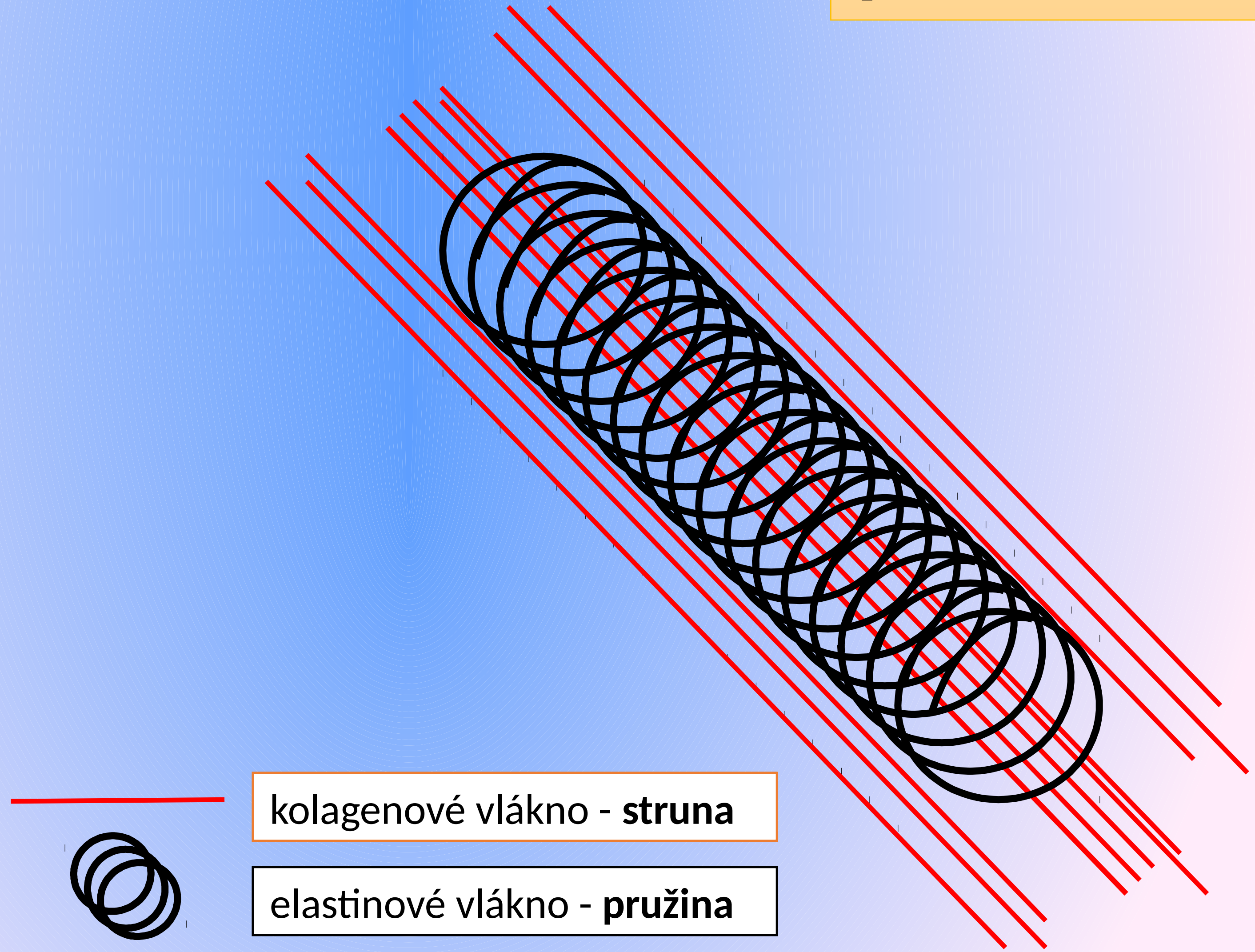
repeated alveolar collapse and expansion (RACE)

SBALI/P-SILI

HALI

fyziologické poznámky

plicní skelet



kolagenové vlákno - **struna**

elastinové vlákno - **pružina**

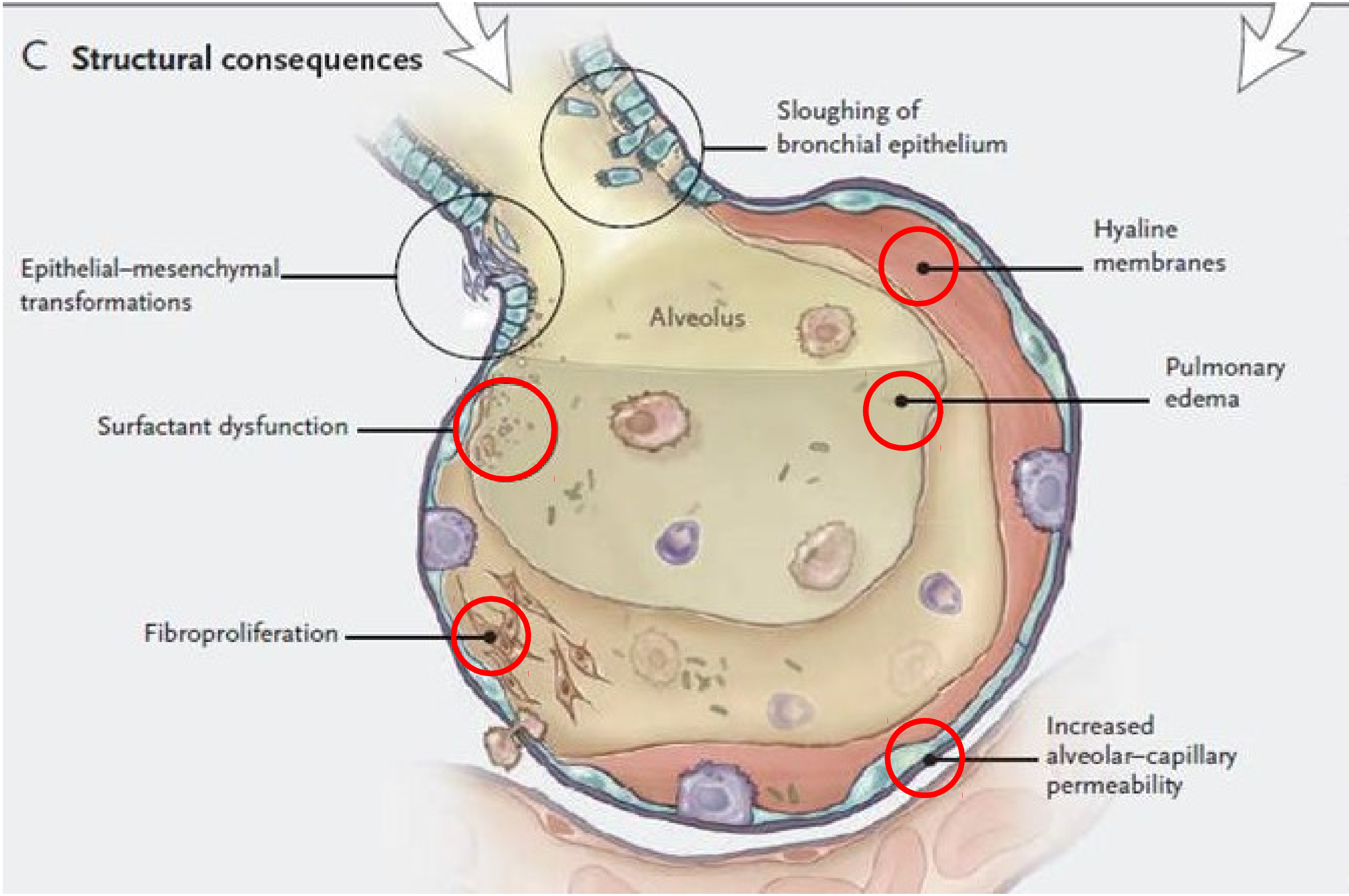
Princip VILI

patologická mechanická stimulace plic při PPV

poš

mechanotransdukce

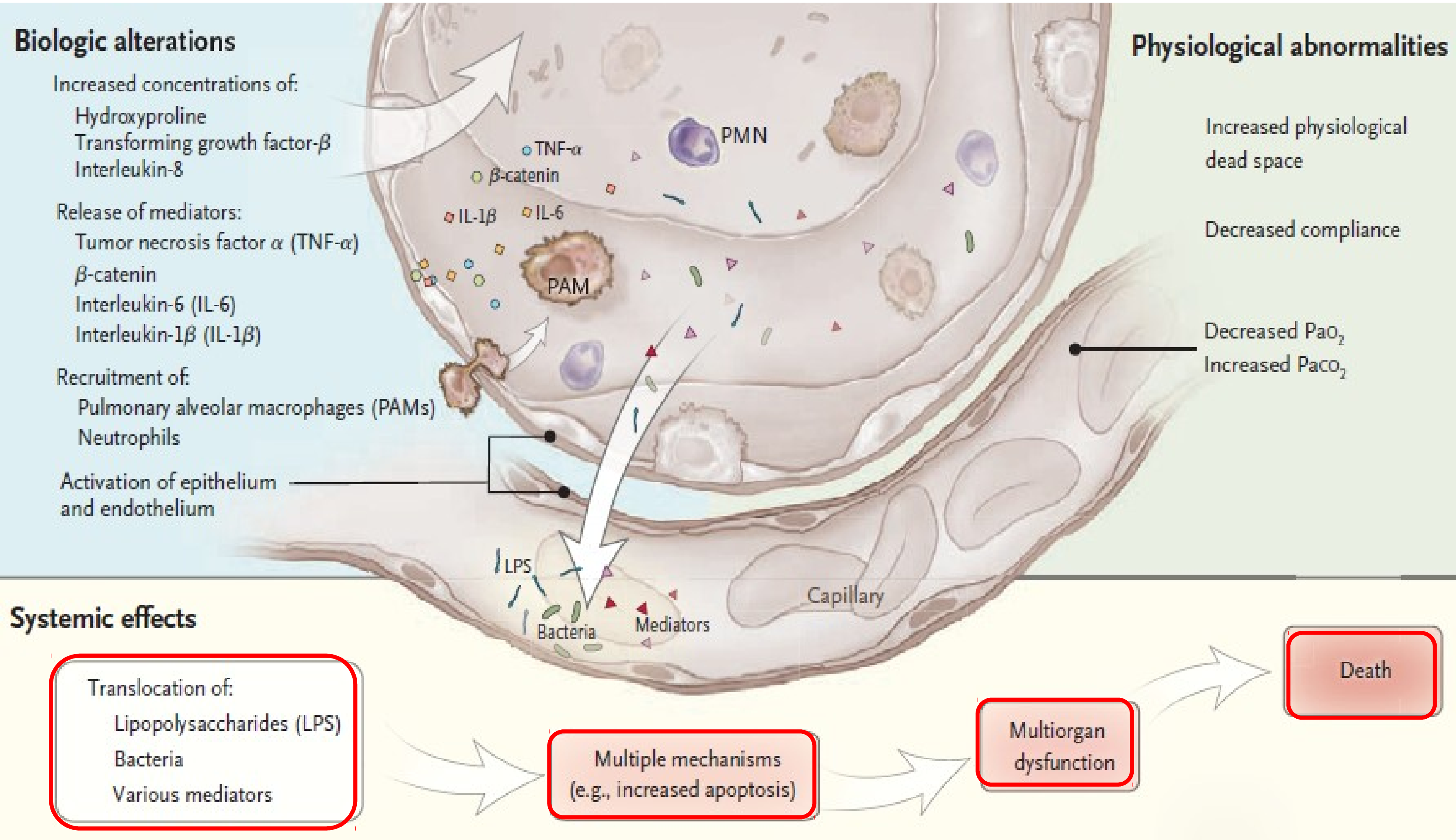
biotrauma


C Structural consequences
Sloughing of bronchial epithelium
Epithelial–mesenchymal transformations
Hyaline membranes
Alveolus
Pulmonary edema
Surfactant dysfunction
Fibroproliferation
Increased alveolar–capillary permeability

VILI/biotrauma

- **vznik a progrese protrahovaného plicního zánětu (dysbalance pro/proti)**
- **systémová propagace proinflamatorního stavu**

SIRS/sepse, MODS



Biologic alterations
Increased concentrations of:
Hydroxyproline
Transforming growth factor-β
Interleukin-8
Release of mediators:
Tumor necrosis factor α (TNF-α)
β-catenin
Interleukin-6 (IL-6)
Interleukin-1β (IL-1β)
Recruitment of:
Pulmonary alveolar macrophages (PAMs)
Neutrophils
Activation of epithelium and endothelium
TNF-α
β-catenin
IL-1β
IL-6
PMN
PAM
LPS
Bacteria
Mediators
Capillary
Physiological abnormalities
Increased physiological dead space
Decreased compliance
Decreased Pa_{O_2}
Increased Pa_{CO_2}
Systemic effects
Translocation of:
Lipopolysaccharides (LPS)
Bacteria
Various mediators
Multiple mechanisms (e.g., increased apoptosis)
Multiorgan dysfunction
Death

Co poškozuje plíci?

barotrauma/volumotrauma

Co poškozuje plíci?

barotrauma/volumotrauma

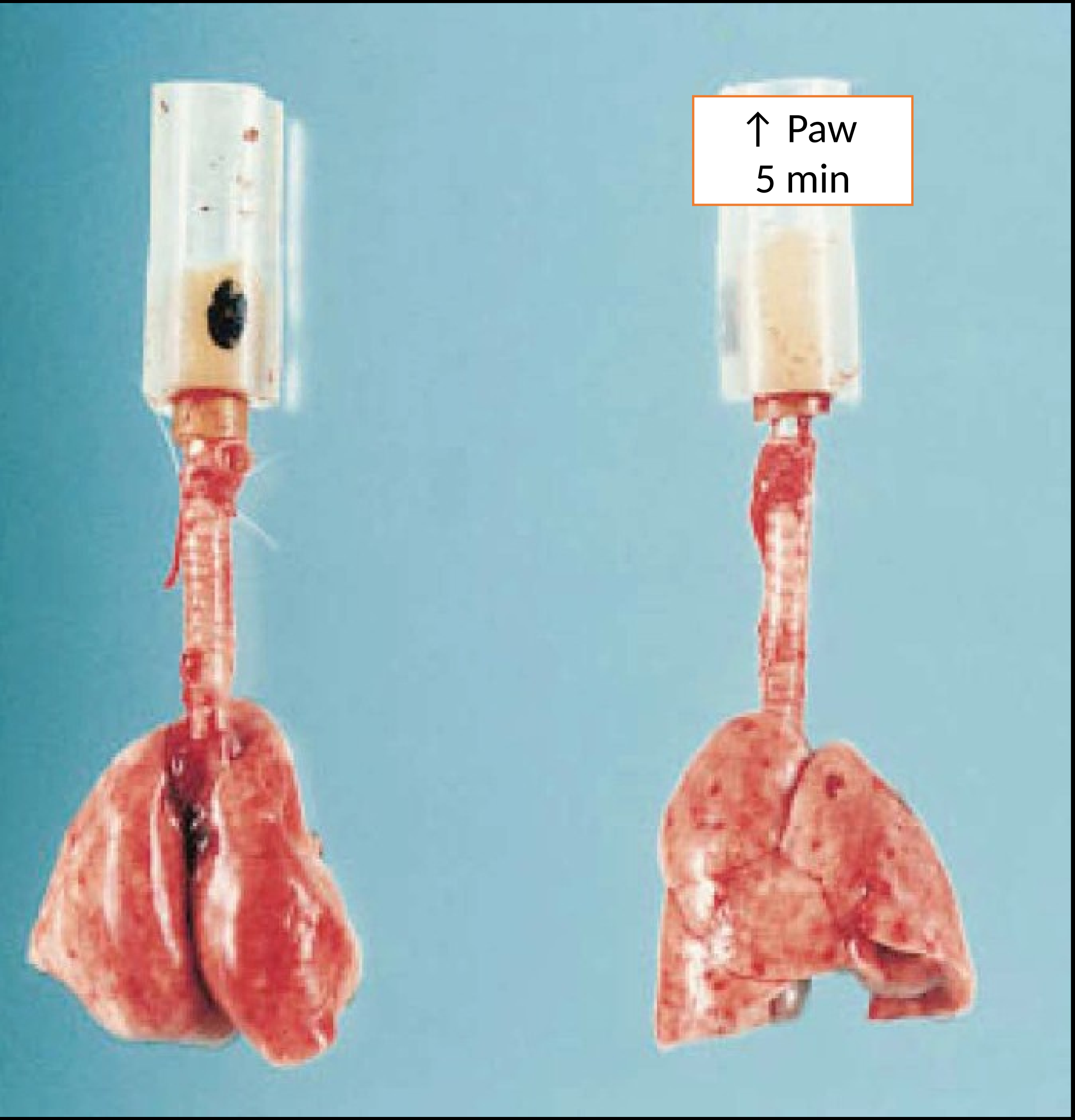
stress/strain

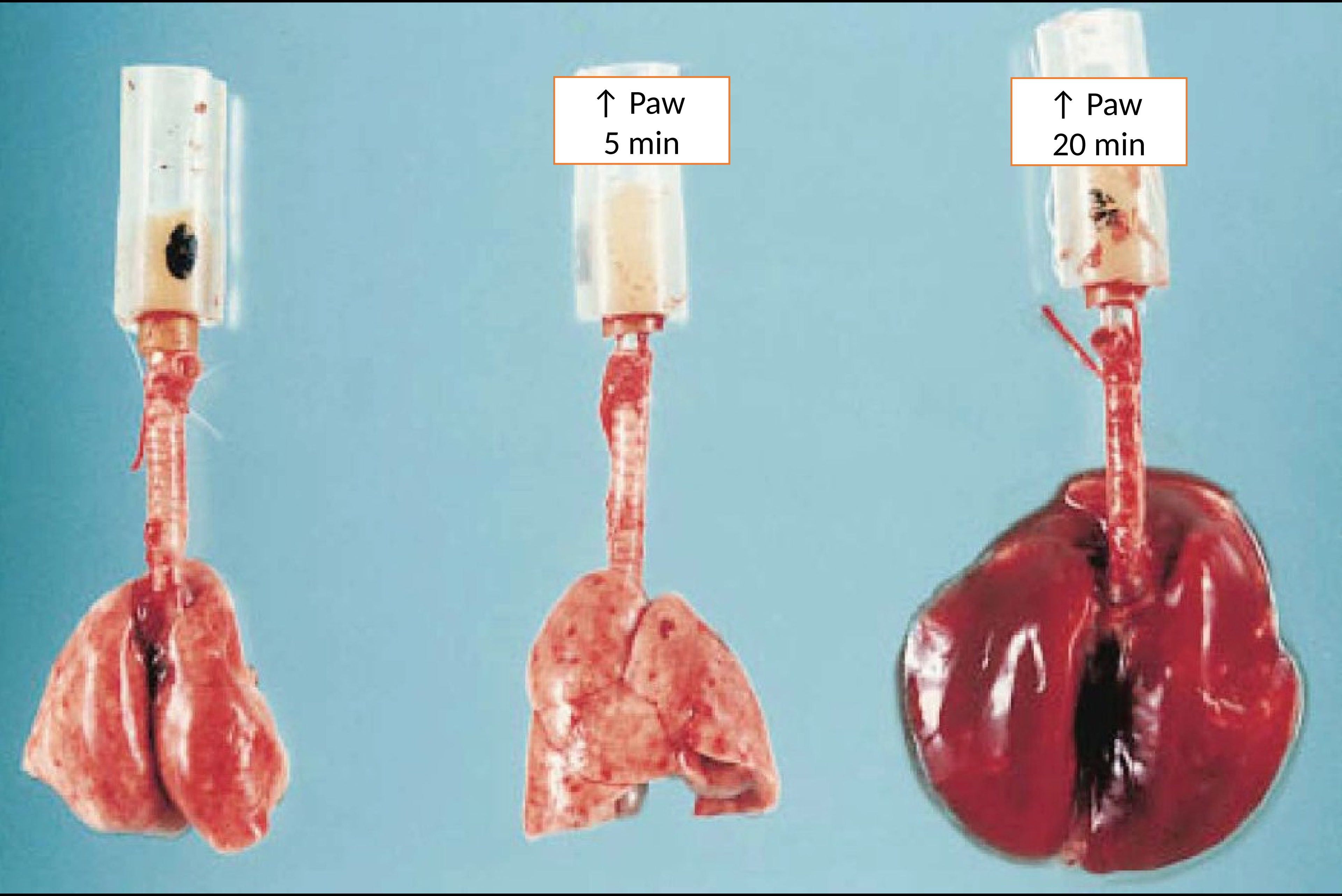
Paw (PIP, $P_{plateau}$), **P_L** ($P_{plateau}$-P_{es})

Vt

Rats, 45 cmH_2O

Rats, 45 cmH_2O

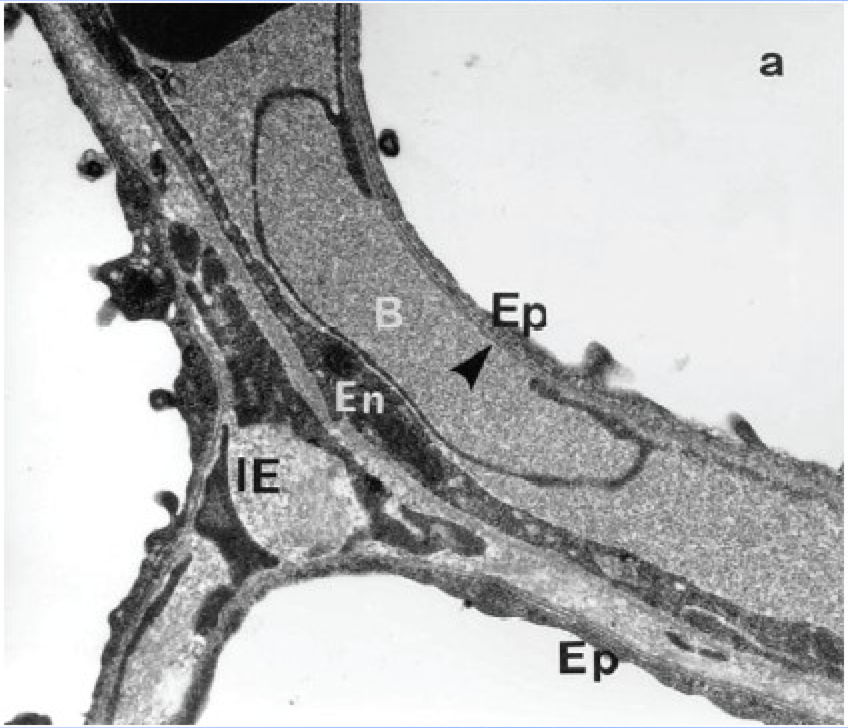


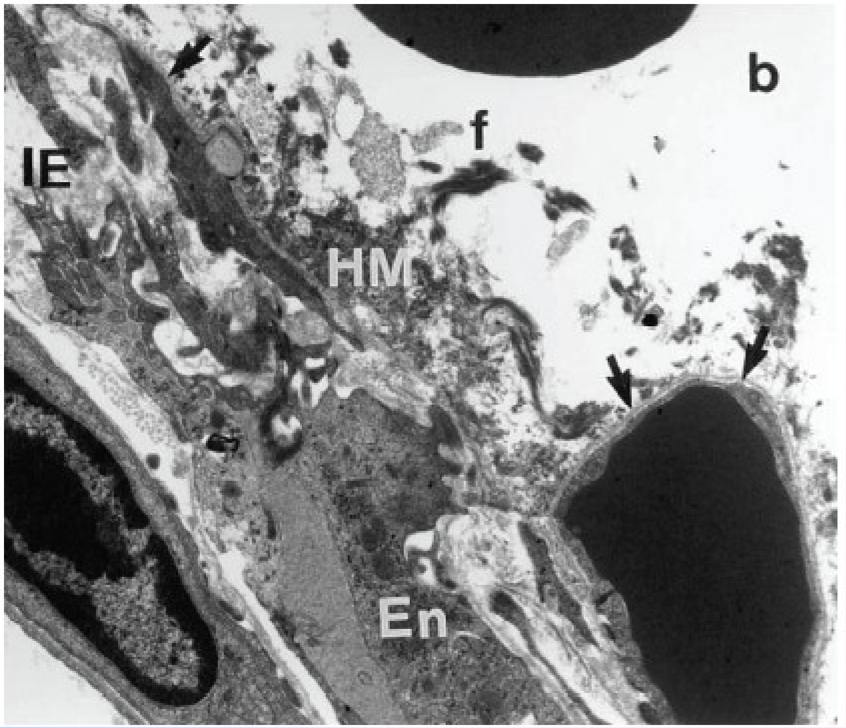


Dreyfuss 1998

Co poškozuje plíci?

Rats, 45 cmH_2O





5min

20min

Dreyfuss 1998

stress/strain

stress

stress is the **pressure** within lung structures to counteract the applied **transpulmonary pressure (P_L)**

accepted **surrogate** is the **airway plateau pressure (Pplateau)**, with the suggested limit **30 cmH_2O**

The „baby lung“ koncept, Gattinoni

stress

$$P_L = P_{AW} \times \frac{E_W}{E_{RS}}$$

Depending on chest wall elastance, **P_L associated with Paw 30 cmH_2O** can be estimated between 28 and 8 cmH_2O

The „baby lung“ koncept, Gattinoni

strain

strain is defined as the **ratio between tidal volume** and the **baseline gas volume of EELV (FRC) – baby lung**

Vt/FRC (Vt/EELV, Vt/V0)

limit 1.5

The „baby lung“ koncept, Gattinoni

stress/strain

stress = K x strain

$$PL = Espec \times \frac{Vt}{FRC}$$

Co poškozuje plíci?

Co je škodlivější?

stress

strain

Co poškozuje plíci?

Co je škodlivější?

↑Vt/ ↑PIP

MV

↑Vt/↓PIP

SB

↓Vt/↑PIP

strapping

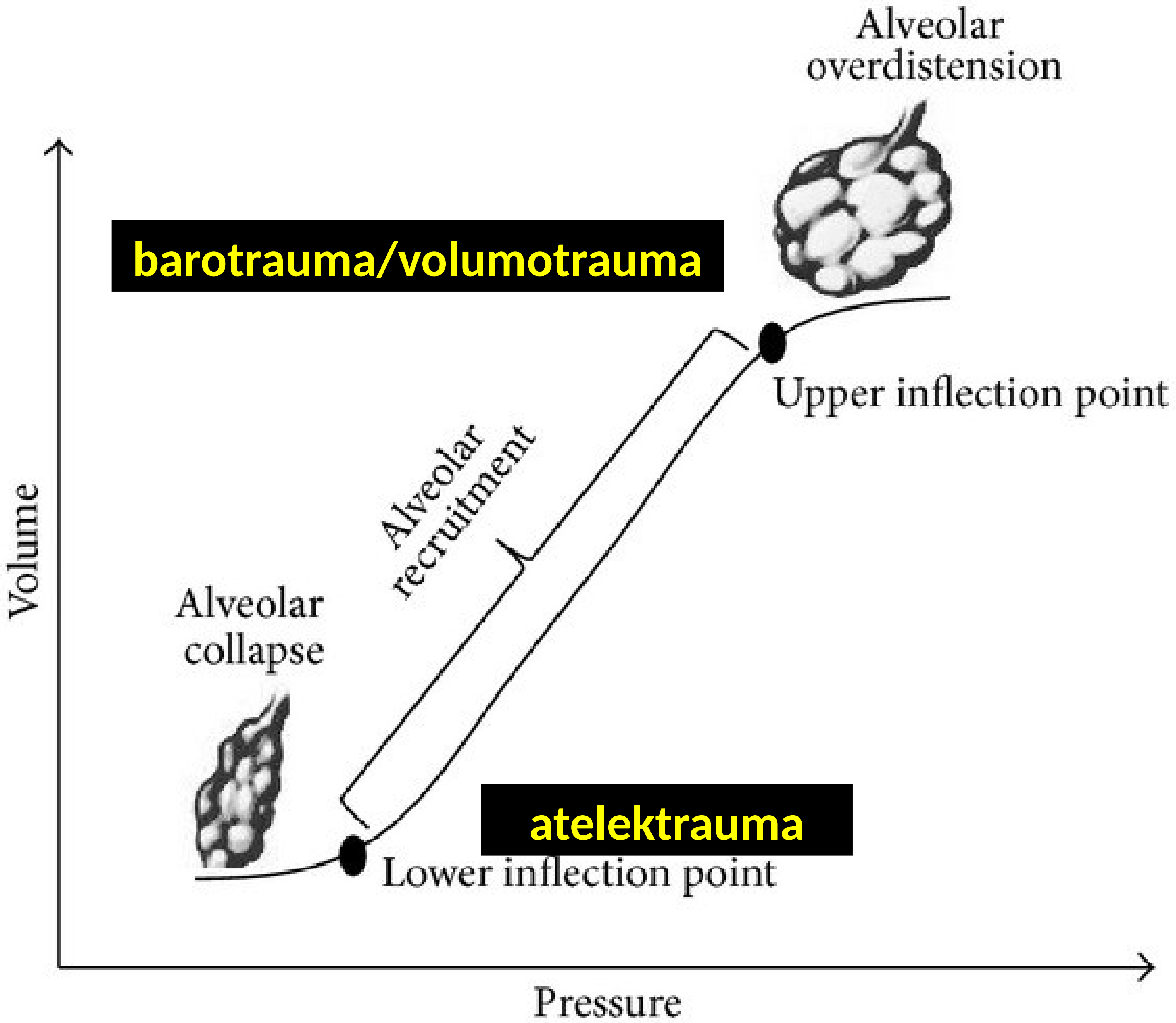
strain

Co poškozuje plíci?

atelektrauma

Co poškozuje plíci?

- **shear forces, tensile forces**
  - rekurentní kolaps alveolů (RACE)
  - hranice mezi provzdušněnými a nevzdušnými oblastmi (nehomogenity)



Alveolar overdistension
barotrauma/volumotrauma
Upper inflection point
Alveolar recruitment
Volume
Alveolar collapse
atelektrauma
Lower inflection point
Pressure

stress/strain/atelektrauma

Strain rate

**Stress raisers
(lung inhomogenities)**

strain rate

strain = Vt/FRC

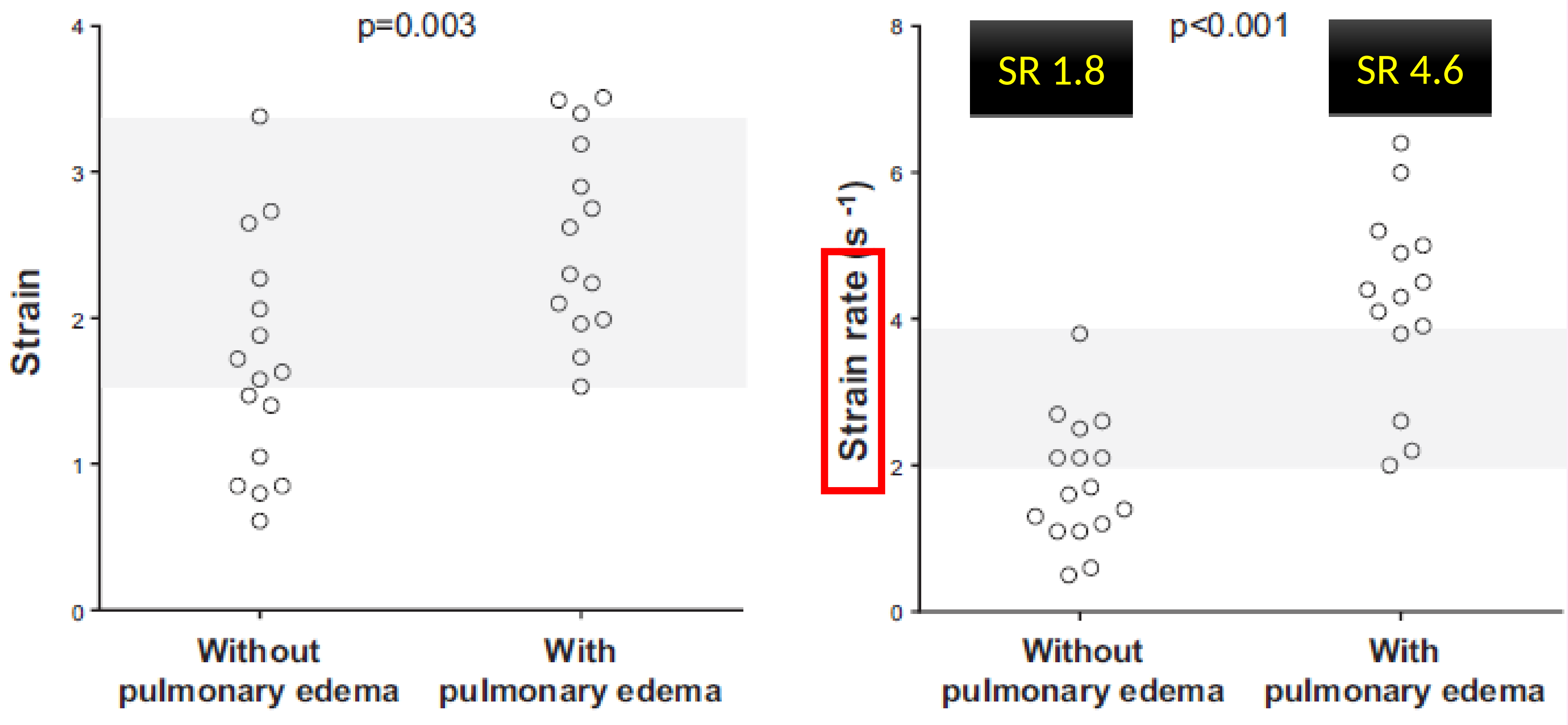
strain/Ti

strain/Ti

Role of Strain Rate in the Pathogenesis of Ventilator-Induced Lung Edema

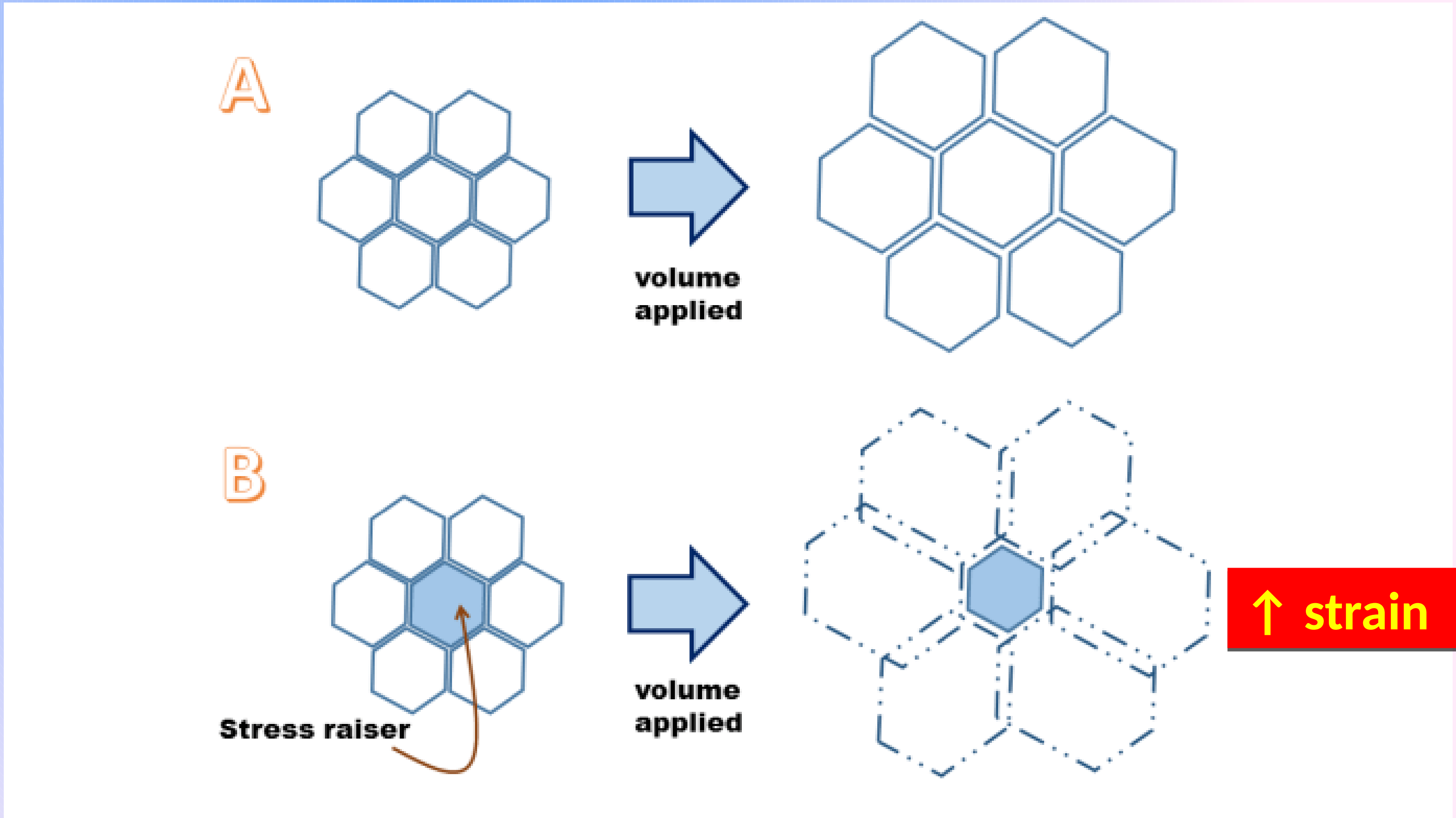
Alessandro Protti, MD[1]; Tommaso Maraffi, MD[2]; Marta Milesi, MD[2]; Emiliano Votta, PhD[3]; Alessandro Santini, MD[2]; Paola Pugni, MD[2]; Davide T. Andreis, MD[2]; Francesco Nicosia, MD[2]; Emanuela Zannin, PhD[3]; Stefano Gatti, MD[4]; Valentina Vaira, MD, PhD[2,5,6]; Stefano Ferrero, MD[5,7]; Luciano Gattinoni, MD, FRCP[1,2]

2016



stress raisers

plicní nehomogenity
hranice okrsků s rozdílnou poddajností



↑ strain

SBALI/P-SILI

Spontánní ventilace na UPV

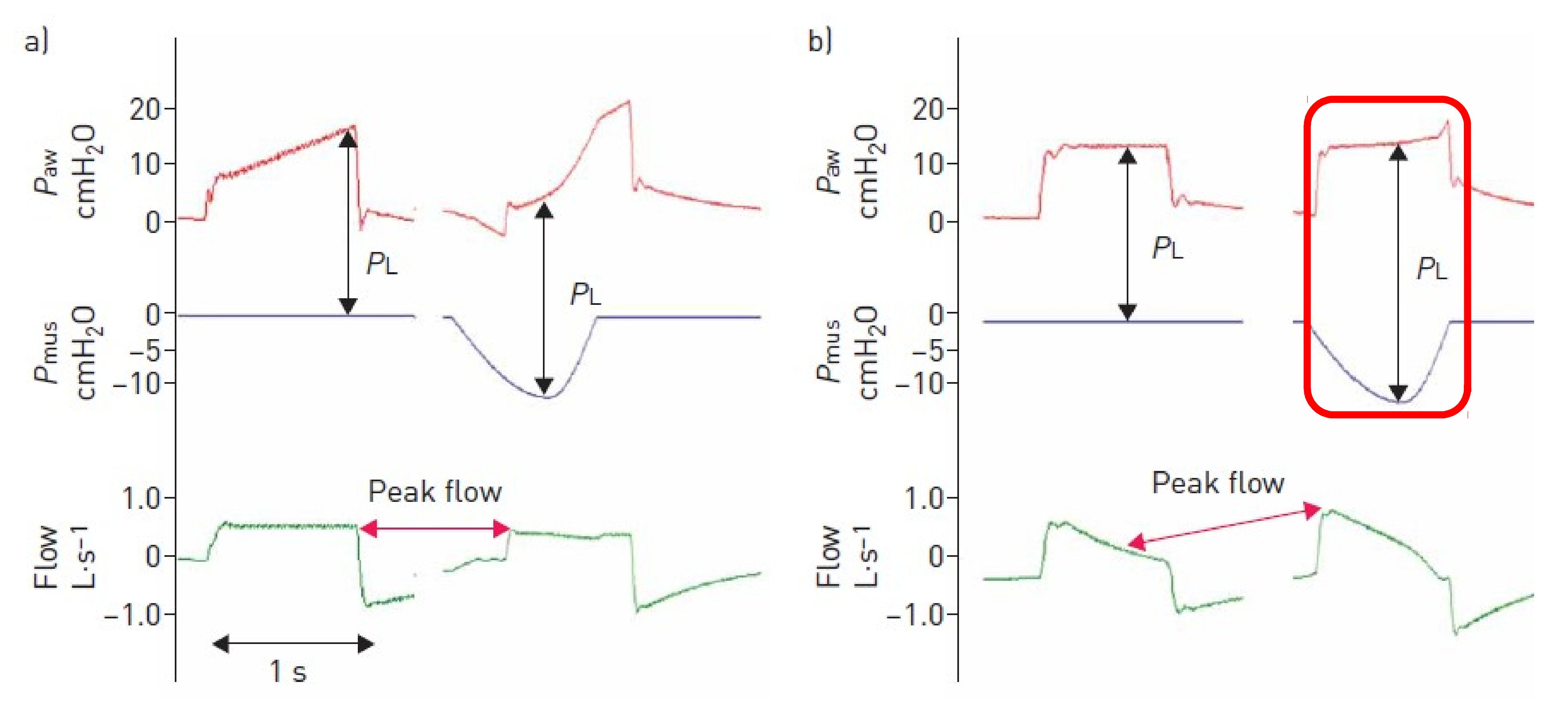
výhody

- ↑ ventilace dependentních oblastí při nižších Pplateau
- prevence atrofie inspiračních svalů

nevýhody

- **↑ P_L, pressure swings**
- zátěž pro expirační svaly při potřebě vyšší MV (agitace, teplota, plicní patologie,…)
- ↑RR, ↓Vt, ↑dynamické hyperinflace, ↑WOB, ↑O_2 konzumpce

Spontánní ventilace u ARDS



VCV

PCV

Rittayamai N, 2015

Spontánní ventilace na UPV

doporučena

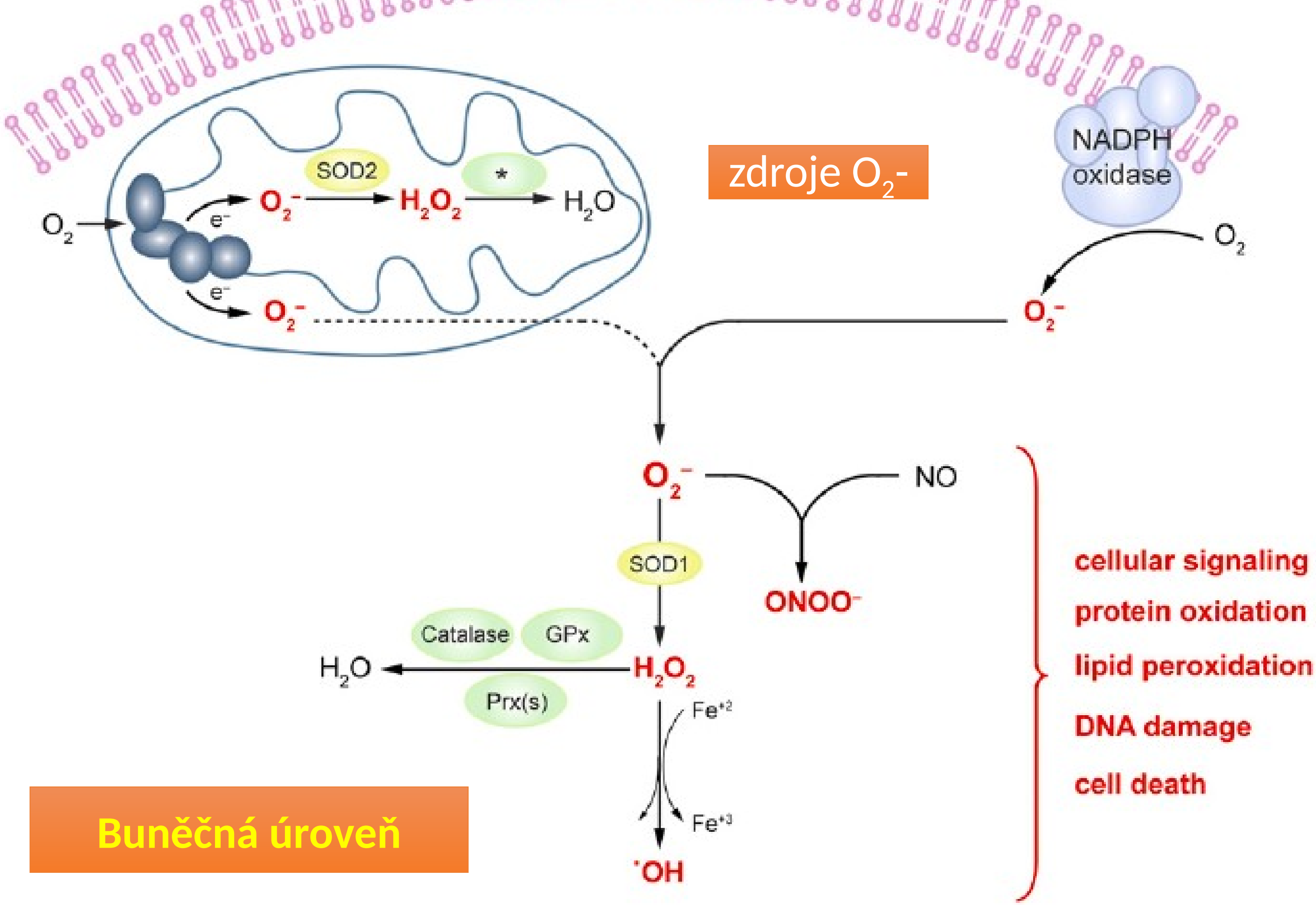
Lehké formy ARF/ARDS

nedoporučena

Těžké formy ARF/ARDS

Hyperoxic acute lung injury

ROS/RNS a hyperoxií indukované plicní poškození (HALI)



zdroje O_2-

Buněčná úroveň

ROS (H_2O_2)

normální hladiny - facilitace buněčné adaptace na hyperoxii

excesívní koncentrace

→ **oxidace proteinů a lipidů**
→ **poškození DNA**
→ geneze **RNS** (peroxinitrit)
→ aktivace PHD cesty aktivace degradace HIF-1α → **↓ produkce růstových faktorů** (VEGF)

protrahovaný stav → aktivace apoptózy a nekrózy

hyperoxie - HALI

- tracheobronchitis
- snížení mukociliárního transportu
- redukce imunitní odpovědi (AM)
- atelektázy (V/Q) – a) redukce tvorby surfaktantu, b) ↑ viskozity bronchiálního hlenu, c) absorpční atelektázy
- inflamace
- plicní edém
- intersticiální fibróza

Míra poškození je úměrná koncentraci a délce působení O_2

Crapo JD: Morphologic changes in pulmonary oxygen toxicity. *Annu Rev Physiol* 1986; 48:721–731

pokud je **$FiO_2 < 0.5$**, poškození je jen výjimečně

Hyperoxie - poznámky

HALI je nerozlišitelné od základního onemocnění

> 48 hodin, > 0.5 FiO_2, změny podobné ARDS

u ARDS může být souběh hyperoxie (plic) a hypoxie (systému)

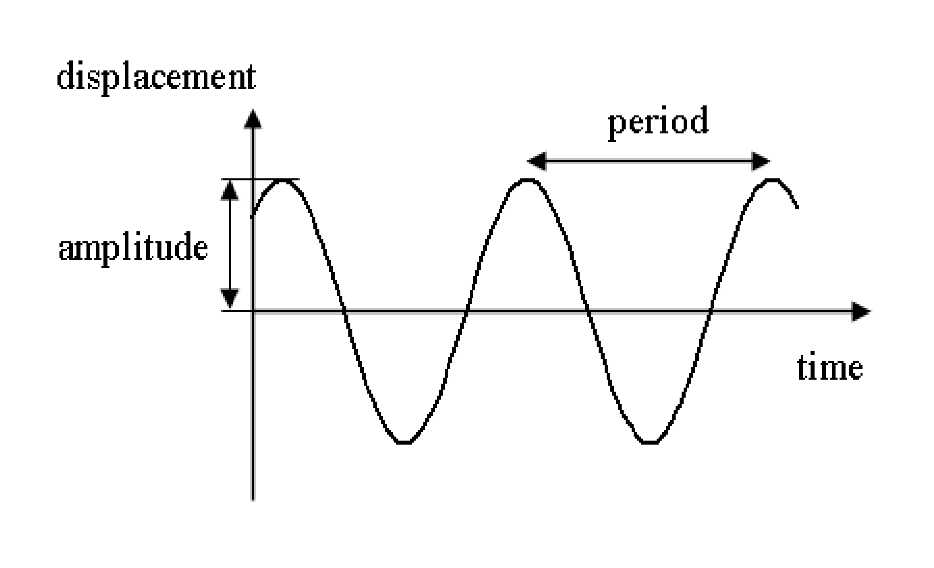
VILI koncepty

open lung concept

Lachmann 1992

open lung concept

- ↑ vzdušnost plíce
- zlepšení oxygenace/eliminace CO_2
- ↓ PVR

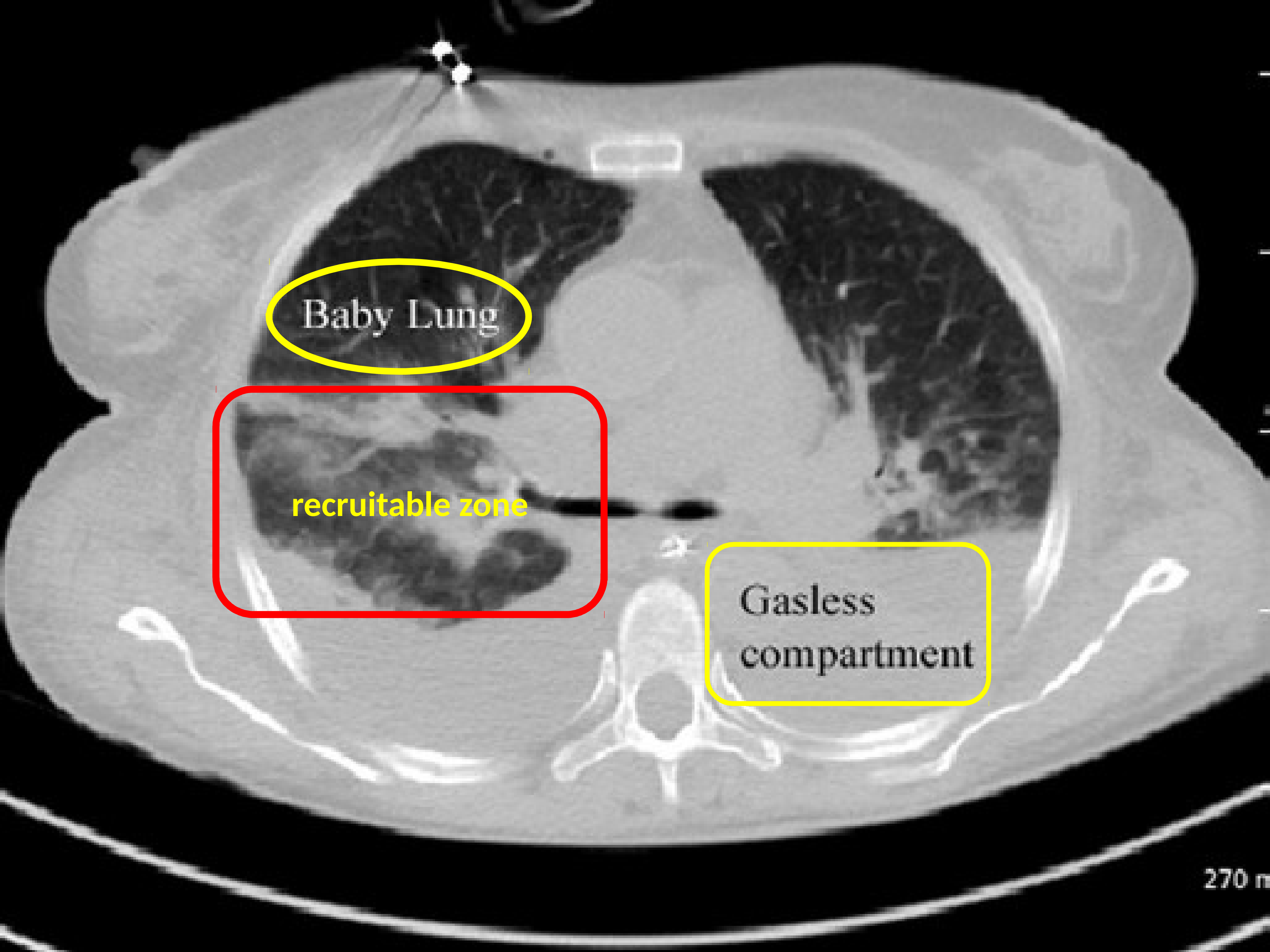


ventilace nízkou amplitudou mechanické stimulace

….produce minimal pressure swings during the ventilatory cycle and keep the lung volume equal to or just above the FRC level - this to prevent a significant depletion of surface active material…

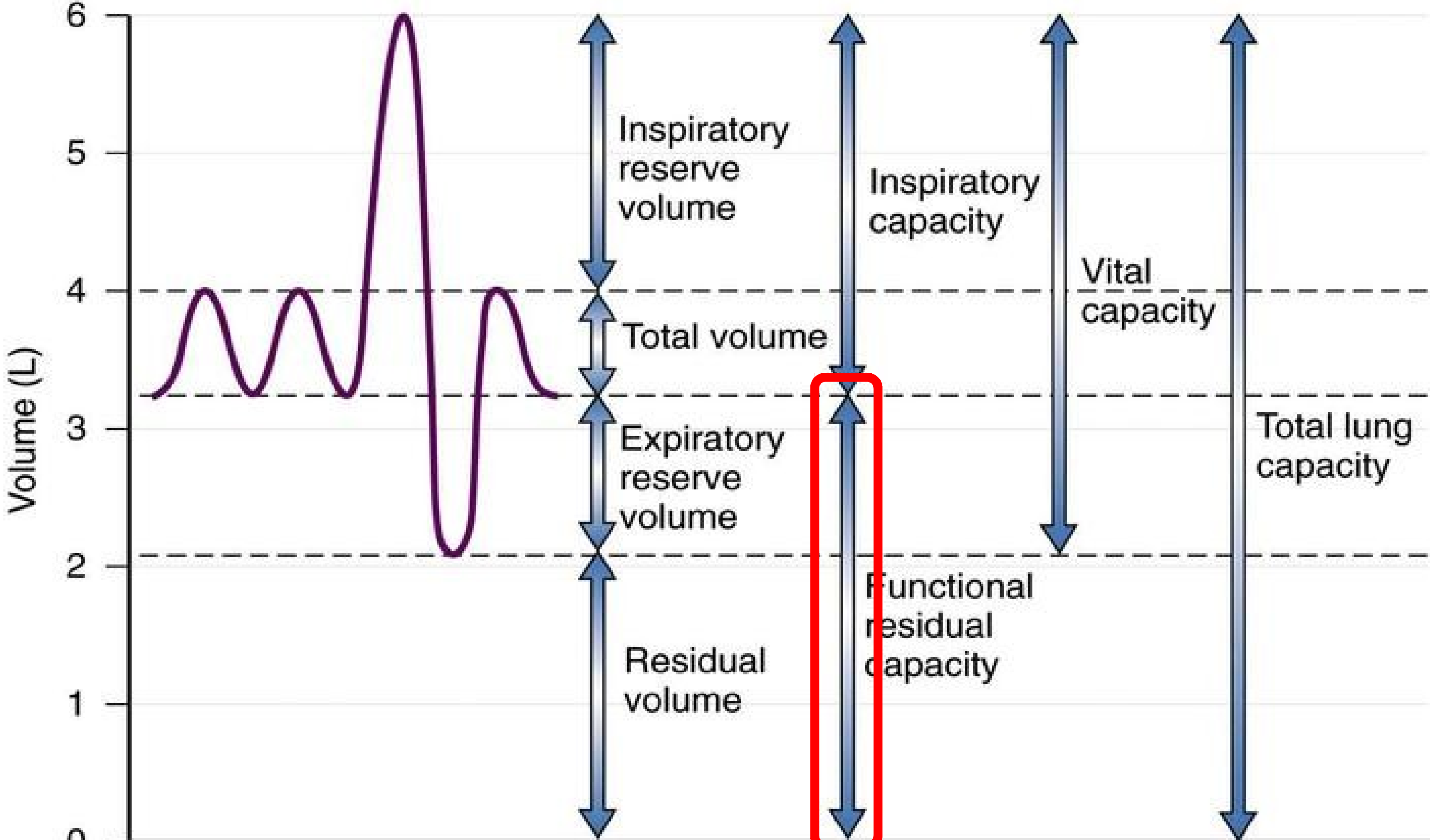
The „baby lung“ concept

Gattinoni 2005


Baby Lung
recruitable zone
Gasless
compartment

fyziologické poznámky

spirometrie



FRC ≈ EELV (MV) ≈ baby lung

The "baby lung" became an adult

Intensive Care Med (2016) 42:663–673
DOI 10.1007/s00134-015-4200-8

Luciano Gattinoni
John J. Marini
Antonio Pesenti
Michael Quintel
Jordi Mancebo
Laurent Brochard

the aerated ARDS baby lung

- **not stiff but small**
- **with near normal intrinsic mechanical characteristics**

Crs : FRC (EELV) ≈ 1 : 1

i.e. 20 ml/cmH_2O Crs ≈ 20 % of open ventilatable lung

The "baby lung" became an adult

Gattinoni 2016 ICM

stress

values even < 30 cmH_2O might cause lung damage

Paw values > 30 cmH_2O might not cause lung damage

strain

In a man with of 70 kg IBW, the **baby lung (FRC)**, may range from 200 to 300 ml to more than 1000 ml, depending on the ARDS severity

strain is completely different for each FRC

The "baby lung" became an adult

Gattinoni 2016 ICM

obecně uznávané limity protektivní ventilace

- **Vt 6-8ml/kg IBW**
- **Pplat 30cmH_2O**

mohou být u ARDS neprotektivní

...a mělo by se

Vt/FRC

driving pressure concept

Amato 2015

driving pressure

post hoc analysis

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

Marcelo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthur S. Slutsky, M.D., Laurent Brochard, M.D., Eduardo L.V. Costa, M.D., David A. Schoenfeld, Ph.D., Thomas E. Stewart, M.D., Matthias Briel, M.D., Daniel Talmor, M.D., M.P.H., Alain Mercat, M.D., Jean-Christophe M. Richard, M.D., Carlos R.R. Carvalho, M.D., and Roy G. Brower, M.D.

FEBRUARY 19, 2015

n = 3562, 9 studií

FRC ≈ functional lung size

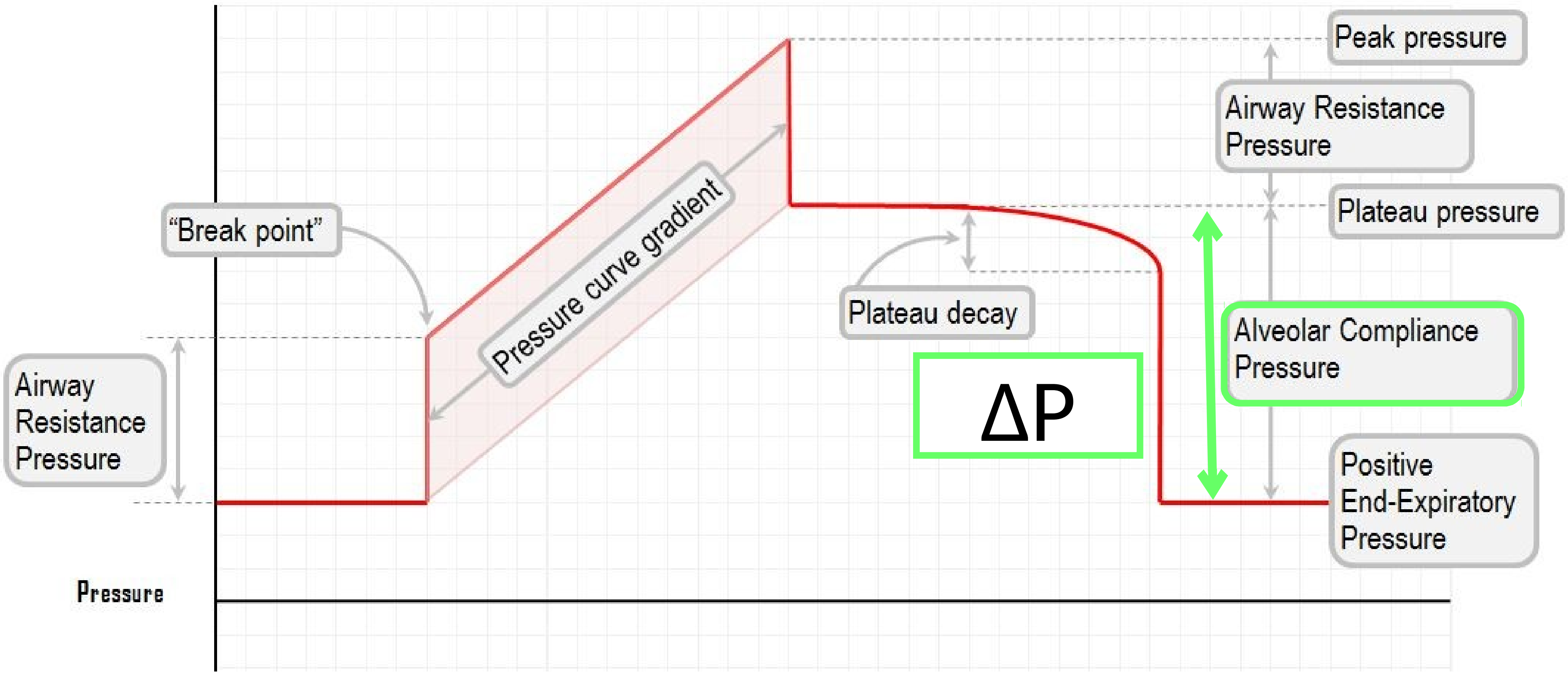
airway driving pressure

$$\Delta P = Vt/Crs$$

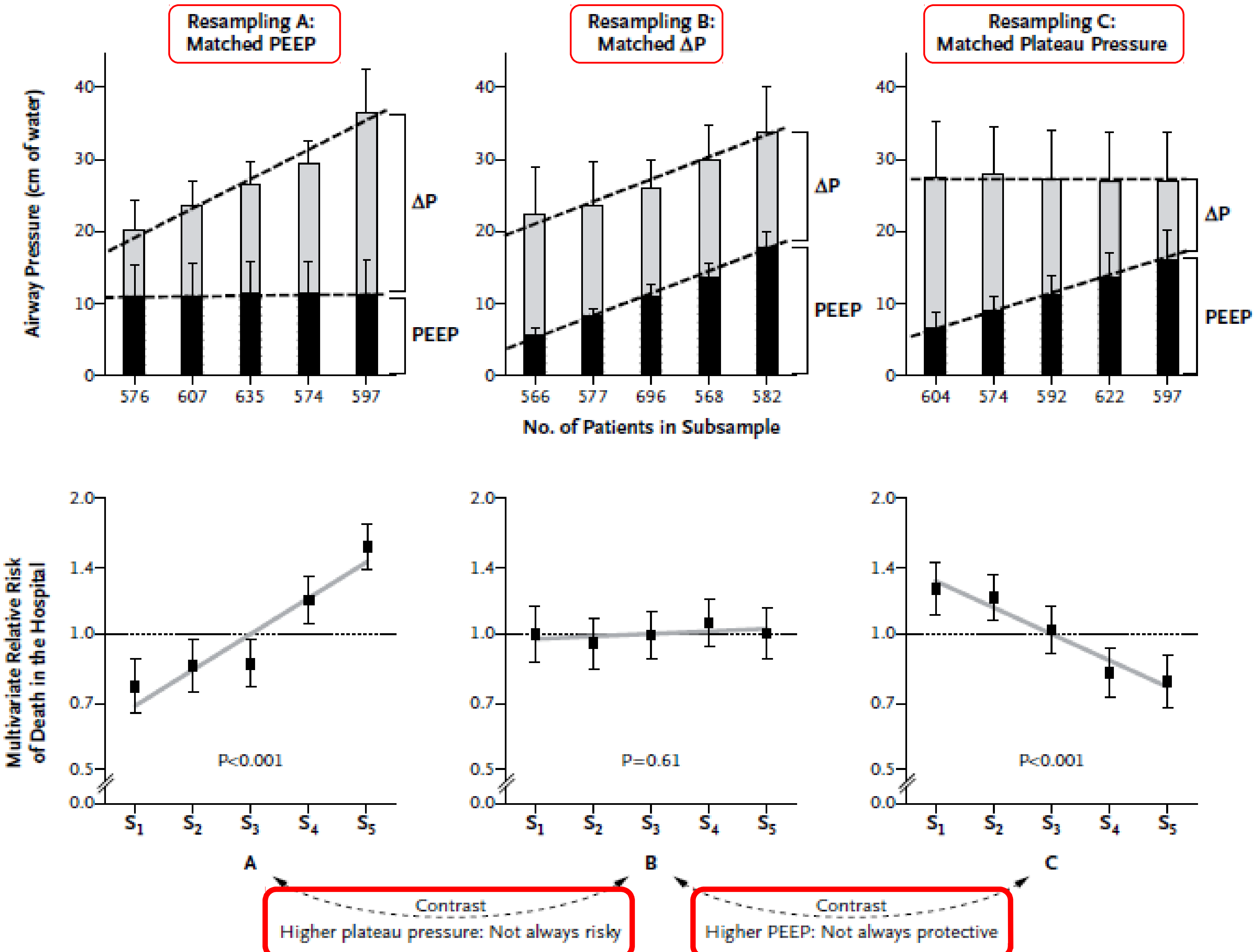
Vt normalized to the size of baby lung

JJ Marini

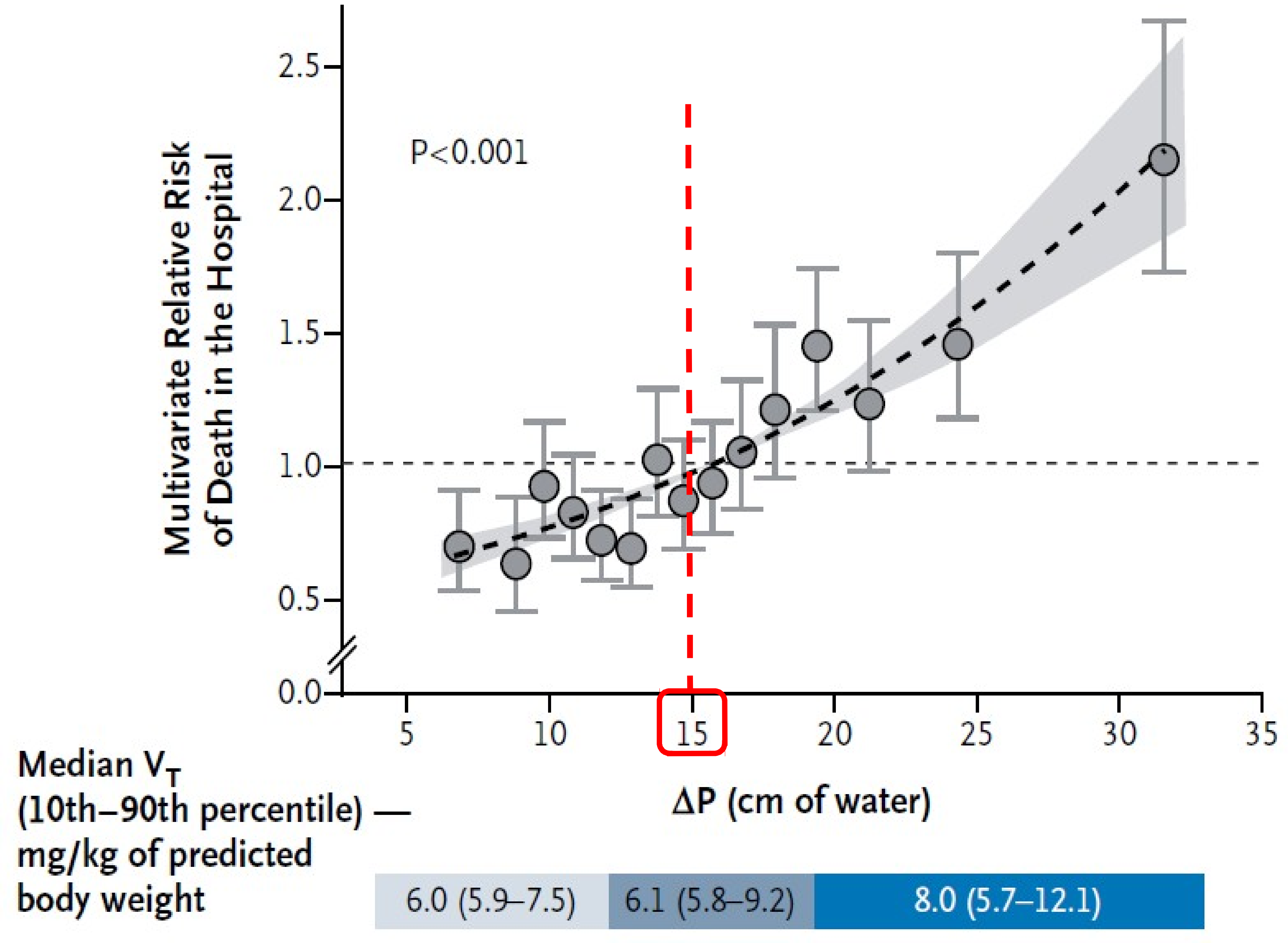
$$\Delta P = P_{plateau} - PEEP$$



Peak pressure
Airway Resistance Pressure
Plateau pressure
"Break point"
Pressure curve gradient
Plateau decay
Alveolar Compliance Pressure
ΔP
Airway Resistance Pressure
Positive End-Expiratory Pressure
Pressure



Resampling A: Matched PEEP
Resampling B: Matched ΔP
Resampling C: Matched Plateau Pressure
Airway Pressure (cm of water)
ΔP
PEEP
576
607
635
574
597
566
577
696
568
582
604
574
592
622
597
No. of Patients in Subsample
Multivariate Relative Risk of Death in the Hospital
P<0.001
P=0.61
P<0.001
A
B
C
Contrast
Higher plateau pressure: Not always risky
Contrast
Higher PEEP: Not always protective



Multivariate Relative Risk of Death in the Hospital
2.5
2.0
1.5
1.0
0.5
0.0
P<0.001
5
10
15
20
25
30
35
ΔP (cm of water)
Median V_T (10th–90th percentile) — mg/kg of predicted body weight
6.0 (5.9–7.5)
6.1 (5.8–9.2)
8.0 (5.7–12.1)

ΔP a predikce rozvoje VILI

ΔP je lepší než Vt a Pplateau

ΔP nezohledňuje

- junctional forces
- vascular flow and pressures
- intertidal opening and closing (RACE)
- frequency
- flow

Mechanical power

Protti/Gattinoni/Marini 2016

RESEARCH Open Access

Lung anatomy, energy load, and ventilator-induced lung injury

Alessandro Protti[1], Davide T. Andreis[2], Marta Milesi[2], Giacomo E. Iapichino[2], Massimo Monti[2], Beatrice Comini[2], Paola Pugni[2], Valentina Melis[2], Alessandro Santini[1], Daniele Dondossola[3], Stefano Gatti[3], Luciano Lombardi[4], Emiliano Votta[5], Eleonora Carlesso[2] and Luciano Gattinoni[1,2*]

ICME, 2015

View Full Size

Critical Care Medicine | May 2016

Mechanical Power and Development of Ventilator-induced Lung Injury

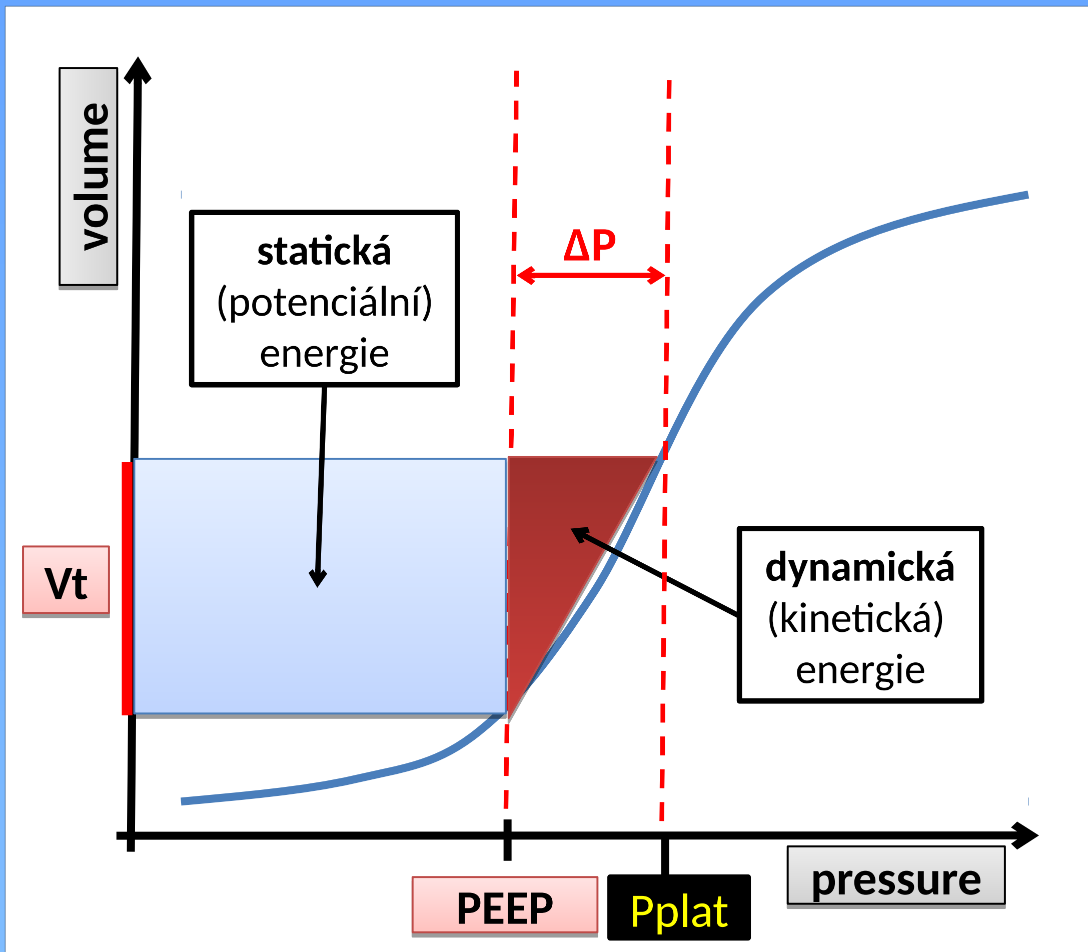
Massimo Cressoni, M.D.; Miriam Gotti, M.D.; Chiara Chiurazzi, M.D.; Dario Massari, M.D.; Ilaria Algieri, M.D.; Martina Amini, M.D.; Antonio Cammaroto, M.D.; Matteo Brioni, M.D.; Claudia Montaruli, M.D.; Klodiana Nikolla, M.D.; Mariateresa Guanziroli, M.D.; Daniele Dondossola, M.D.; Stefano Gatti, M.D.; Vincenza Valerio, Ph.D.; Giordano Luca Vergani, M.D.; Paola Pugni, M.D.; Paolo Cadringher, M.Sc.; Nicoletta Gagliano, Ph.D.; Luciano Gattinoni, M.D., F.R.C.P.

Mechanical power koncept

Critical Care Medicine | May 2016

Mechanical Power and Development of Ventilator-induced Lung Injury

Massimo Cressoni, M.D.; Miriam Gotti, M.D.; Chiara Chiurazzi, M.D.; Dario Massari, M.D.; Ilaria Algieri, M.D.; Martina Amini, M.D.; Antonio Cammaroto, M.D.; Matteo Brioni, M.D.; Claudia Montaruli, M.D.; Klodiana Nikolla, M.D.; Mariateresa Guanziroli, M.D.; Daniele Dondossola, M.D.; Stefano Gatti, M.D.; Vincenza Valerio, Ph.D.; Giordano Luca Vergani, M.D.; Paola Pugni, M.D.; Paolo Cadringher, M.Sc.; Nicoletta Gagliano, Ph.D.; Luciano Gattinoni, M.D., F.R.C.P.



Dynamická E + Statická E
=
Energie/dech

Energie/dech x DF
=
Celkový energy load/min

závěry

- **subjekty (prasata)**

- **MP větší než 12 J/min rozvinuly VILI**

- **velikost MP korelovala s hmotností plic, plicní elastancí a poklesem indexu PaO_2/FiO_2.**

- pod stanovenou hranicí se rozvinuly pouze **izolované** plicní denzity.

ORIGINAL

Ventilator-related causes of lung injury: the mechanical power

L. Gattinoni[1*], T. Tonetti[1], M. Cressoni[2], P. Cadringher[3], P. Herrmann[1], O. Moerer[1], A. Protti[3], M. Gotti[2], C. Chiurazzi[2], E. Carlesso[2], D. Chiumello[4] and M. Quintel[1]

ICM 8/2016

$$\mathrm{Power}_{rs} = \boxed{RR} \cdot \left\{ \boxed{\Delta V}^2 \cdot \left[\frac{1}{2} \cdot \boxed{EL_{rs}} + RR \cdot \frac{(1 + \boxed{I:E})}{60 \cdot I:E} \cdot \boxed{R_{aw}} \right] + \Delta V \cdot \boxed{PEEP} \right\}$$

The mechanical power increases:

- **Vt, ΔP, and flow (exponentially,exponent = 2)**
- **RR (exponent = 1.4)**
- **PEEP (linearly)**

syntéza statických a dynamických parametrů UPV

Effect of driving pressure on mortality in ARDS patients during lung protective mechanical ventilation in two randomized controlled trials

Claude Guérin[1,2,3*], Laurent Papazian[4,5,6], Jean Reignier[7], Louis Ayzac[8], Anderson Loundou[5], Jean-Marie Forel[9]
and on behalf of the investigators of the Acurasys and Proseva trials

CC 2016

mechanical power = ΔP × V_T × RR

horší přežití při

- **$Power_{rs}$ >12 J/min**

VILI
Co se s tím dá dělat?

Vt a Paw

Vt 6-8 ml/kg IBW, Pplateau < 30 cm H_2O

zvážit

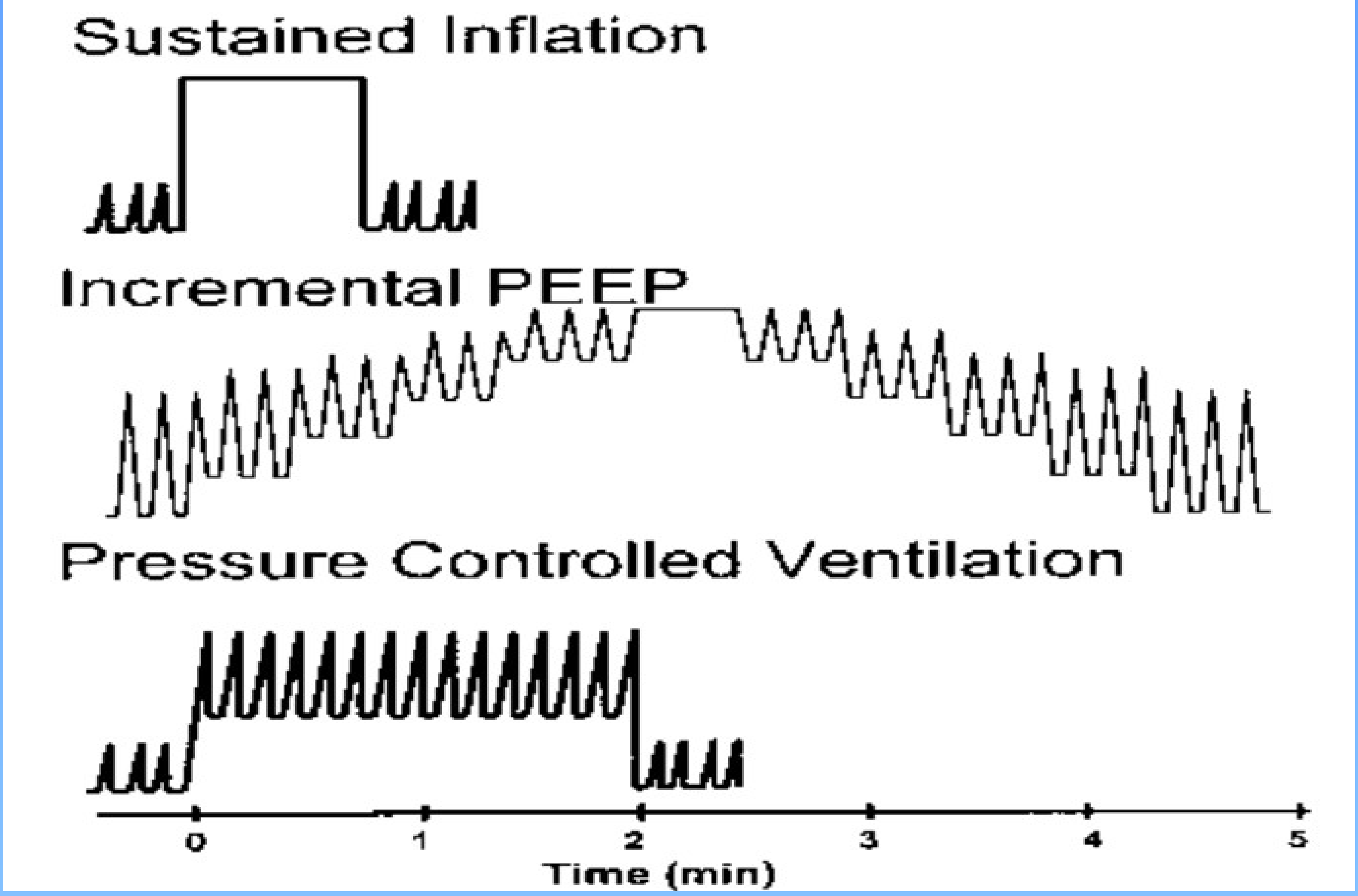
Vt/FRC (Crs) – baby lung (ARDS)

Strain < 1.5

recruitment manévry a **nastavení PEEP**

nadále kontroverzní témata

RM



Sustained Inflation
Incremental PEEP
Pressure Controlled Ventilation
0
1
2
3
4
5
Time (min)

RM

Summary and Recommendations

1. **Evidence is lacking** that the use of recruitment maneuvers improves patient outcomes.
2. A **stepwise recruitment maneuver is preferred** over sustained inflation.
4. Complications of recruitment (hypotension and desaturation) are common but temporary; complications such as barotrauma appear to be rare.
5. If a recruitment maneuver is effective, **sufficient PEEP is necessary to maintain the recruitment**.
6. **Evidence is not sufficient to recommend the routine use** of recruitment maneuvers as standard practice.

Nastavení PEEP

Podle výměny plynů — ALVEOLI 2004, LOV 2008

Podle poddajnosti — ExPress 2008

P-V křivka — Amato 1998

Ezofageální manometrie - PL — Talmor 2008

Stress index

EELV

UZ, EIT…

Nastavení PEEP

Summary and Recommendations: PEEP

1. **PEEP should be selected as a balance between alveolar recruitment and overdistention.**
2. **RCTs have failed to show a survival benefit** for the use of higher versus lower levels of PEEP.
4. Post hoc analysis of randomized controlled trials and a strong physiologic rationale support lower levels of PEEP for mild ARDS and higher levels of PEEP for moderate and severe ARDS: **5–10 cm H2O in mild ARDS, 10–15 cm H2O in moderate ARDS, and 15–20 cm H2O in severe ARDS**
5. Evidence is **not currently available to suggest that one approach to setting PEEP leads to better** outcomes than other approaches.

PRONACE

The NEW ENGLAND JOURNAL of MEDICINE

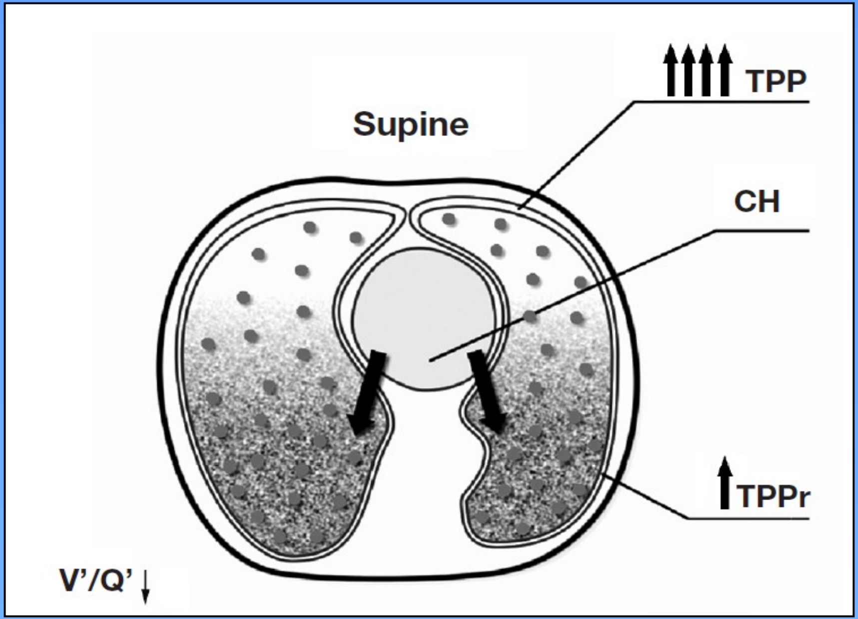
ORIGINAL ARTICLE

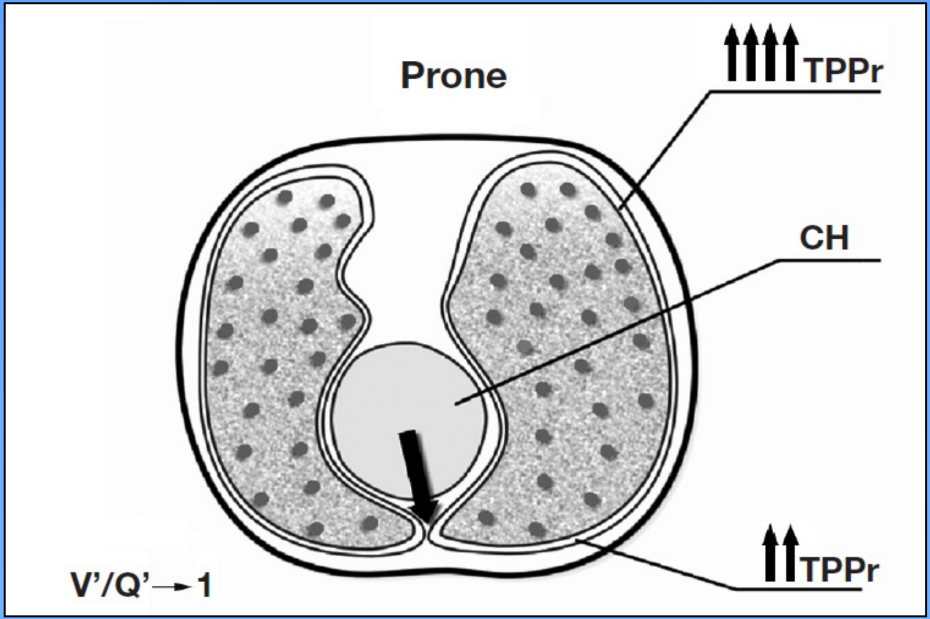
Prone Positioning in Severe Acute Respiratory Distress Syndrome

Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D.,
Jean-Christophe Richard, M.D., Ph.D., Pascal Beuret, M.D., Arnaud Gacouin, M.D.,
Thierry Boulain, M.D., Emmanuelle Mercier, M.D., Michel Badet, M.D.,
Alain Mercat, M.D., Ph.D., Olivier Baudin, M.D., Marc Clavel, M.D.,
Delphine Chatellier, M.D., Samir Jaber, M.D., Ph.D., Sylvène Rosselli, M.D.,
Jordi Mancebo, M.D., Ph.D., Michel Sirodot, M.D., Gilles Hilbert, M.D., Ph.D.,
Christian Bengler, M.D., Jack Richecoeur, M.D., Marc Gainnier, M.D., Ph.D.,
Frédérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D.,
Raphaele Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D.,
for the PROSEVA Study Group*

PROSEVA study, květen 2013, NEJM

efekt pronace - ARDSexp





- homogenizace P_{tp}
- zlepšení V/Q
- ↑ hydrostatika srdce
- ↑ clearance DC

Driving pressure

- airway ΔP <15 cmH_20 (Pplateau – PEEP)
- P_L (Ptp) ΔP <10 cmH_20

Mechanical power, driving energy, energotrauma

12 J/min?
role zatím nejasná

Doporučení

Léčit základní onemocnění

použít LPV

minimalizace stress/strain (↓Vt, ↓strain rate, ↓PL)
homogenizace plicního parenchymu (minimalizace atelektraumatu)
- **optimalizace PEEP, pronace, kontrola tekutinové bilance, RM,**

redukce pacient-ventilátorové dyssynchronie
- **myorelaxace, analgosedace**

redukce P-SILI (mild ARDS vs. severe ARDS)

titrace Vt spíše podle Crs (baby lung)

použít ΔP pod 15 cm H_2O jako cíl, titrace PEEP podle Crs vs. PL vs. ΔP

FiO_2 pod 0.6 (nejlépe 0.5)

Energotrauma jako endpoint (?), dynamická složka ventilace

Zdravá plíce

Nemocná plíce

LPV

LPV
uLPV
ECMO


děkuji za
pozornost