Turkey 21st National Congress of
Cardio-Vascular Thoracic Anesthesia & Intensive Care/ 23-35 April/2015

POST-THORACOTOMY ACUTE LUNG INJURY

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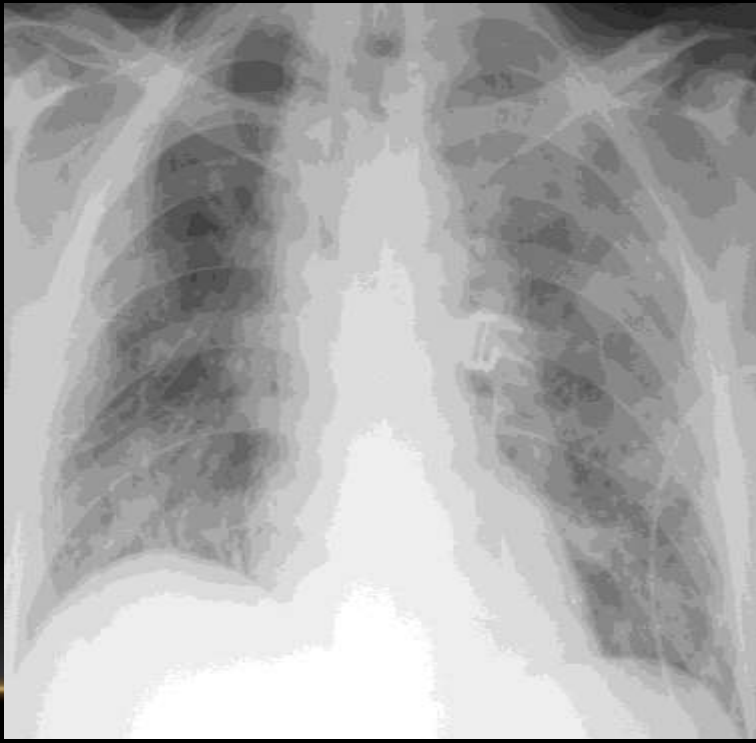
Dpt Anesthesiology Pharmacology & Intensive care

1. **Diagnostic criteria**
2. **Incidence & Risk factors**
3. **Pathogenesis**
4. **Lung protective strategies**

1. ALI/ARDS DIAGNOSTIC CRITERIA

1994 American-European CCM consensus - **2012 Berlin**

- Acute onset respiratory distress
- PaO_2:FiO_2 ≤300 mmHg (ALI), ≤200 mmHg (ARDS)
- CXR: Bi-unilateral infiltrates
- No circulatory overload/failure
  - LAP, PACP > 18 mmHg
  - LVEF < 40%, Mitral E/e’ >15
  - Response to diuretics, NTG
  - Valvular disease, Myoc. Ischemia



POSTOPERATIVE RESPIRATORY FAILURE

Respir. MUSCLE failure

BRONCHOPNEUMONIA

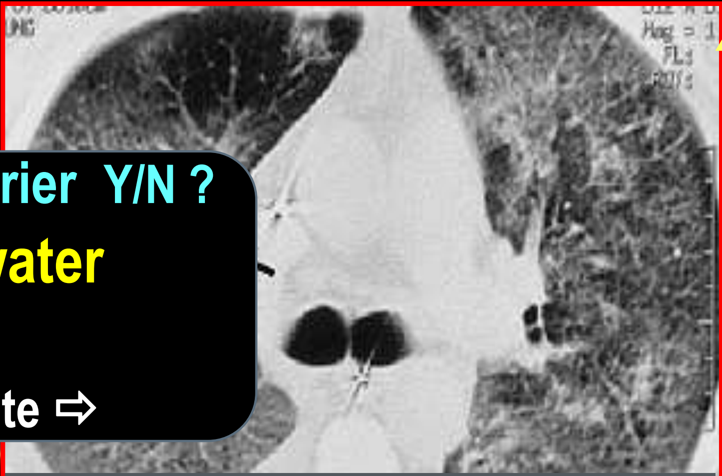
HYDROSTATIC edema

Leaky alveolar-capillary barrier Y/N ?

Extravascular lung water

Alveolar Fluid

⇦ Transudate vs Exudate ⇨



ALI / ARDS

Primary (>80%) vs Secondary

DIAGNOSIS: EARLY MARKERS OF ALI / ARDS

VS HYDROSTATIC EDEMA

Extravascular Lung Water Index

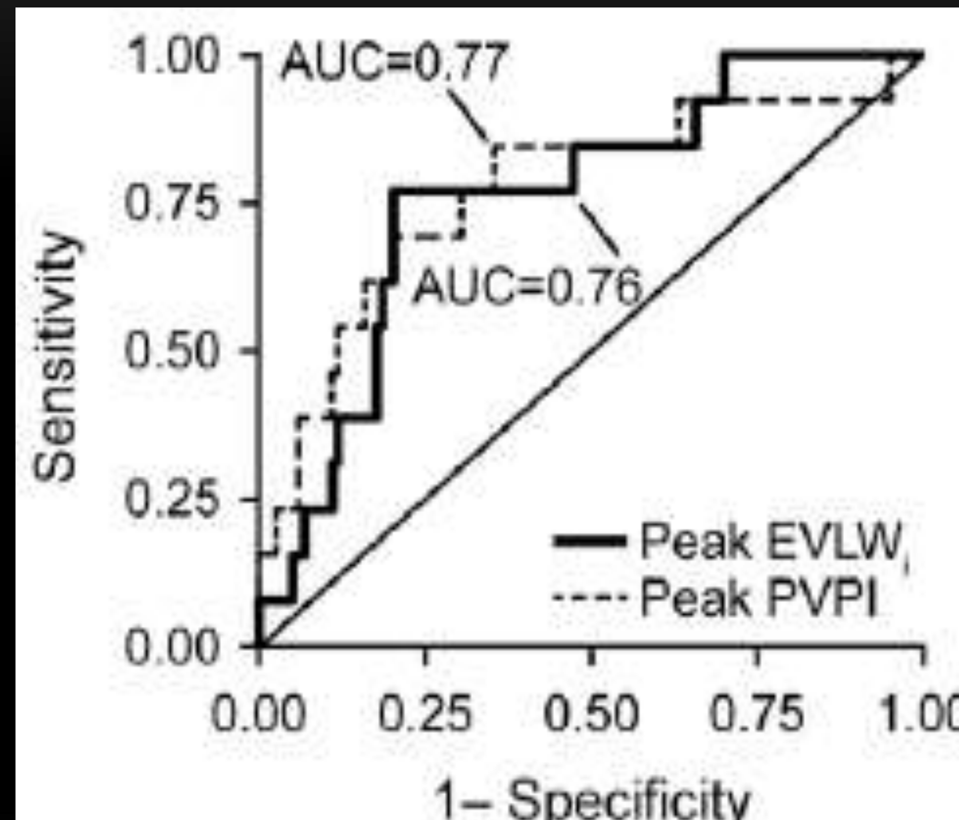
EVLWI ≥ 12.5-14 ml/kg

Ss 72-82%   Sp 64 – 82%

Pulm. Vasc. Permeability Index

PVPI ≥ 0.5-0.6

Ss 72-82%   Sp 64 – 82%



KOR D ET AL. *CRIT CARE MED* 2014

POST-THORACOTOMY ALI/ARDS

2. INCıDENCE - MORTALıTY

From 1984 - 2015
21 studies > 11'000 pts

			Lung Resection	Consensus 1994 criteria	Incidence (%)	Mortality (%)
Zeldin RA	1984	25	P	No	40	-
Verheijen-Breemhar	1988	243	P	No	4.5	27
Waller DA	1993	402	All	No	2.7	55
Turnage WS	1993	806	All	No	2.6	100
Hayes JP	1995	469	P	Yes	5.1	71
Parquin F	1996	146	P	No	15	9.1
Van der Werff YD	1997	197	P	No	12.2	100
Kutlu CA	2000	1139	All	Yes	3.9	64
				Yes	2.2	52
				Yes	4.2	37
				No	2.5	-
				Yes	n.a.	40
				Yes	2.5	40
				No	3.6	48
				No	3.1	25
Licker M	2009	558	All	Yes	0.9	20
Fernandez-Perez ER	2009	659	All	Yes	3.6	17
Marret E	2010	129	P	Yes	7.0	33
Blank RS	2011	129	P	Yes	7.0	-
Yao S	2013	364	P	Yes	2.7	30
Arslantas MK	2015	139	All	Yes	3.6	100

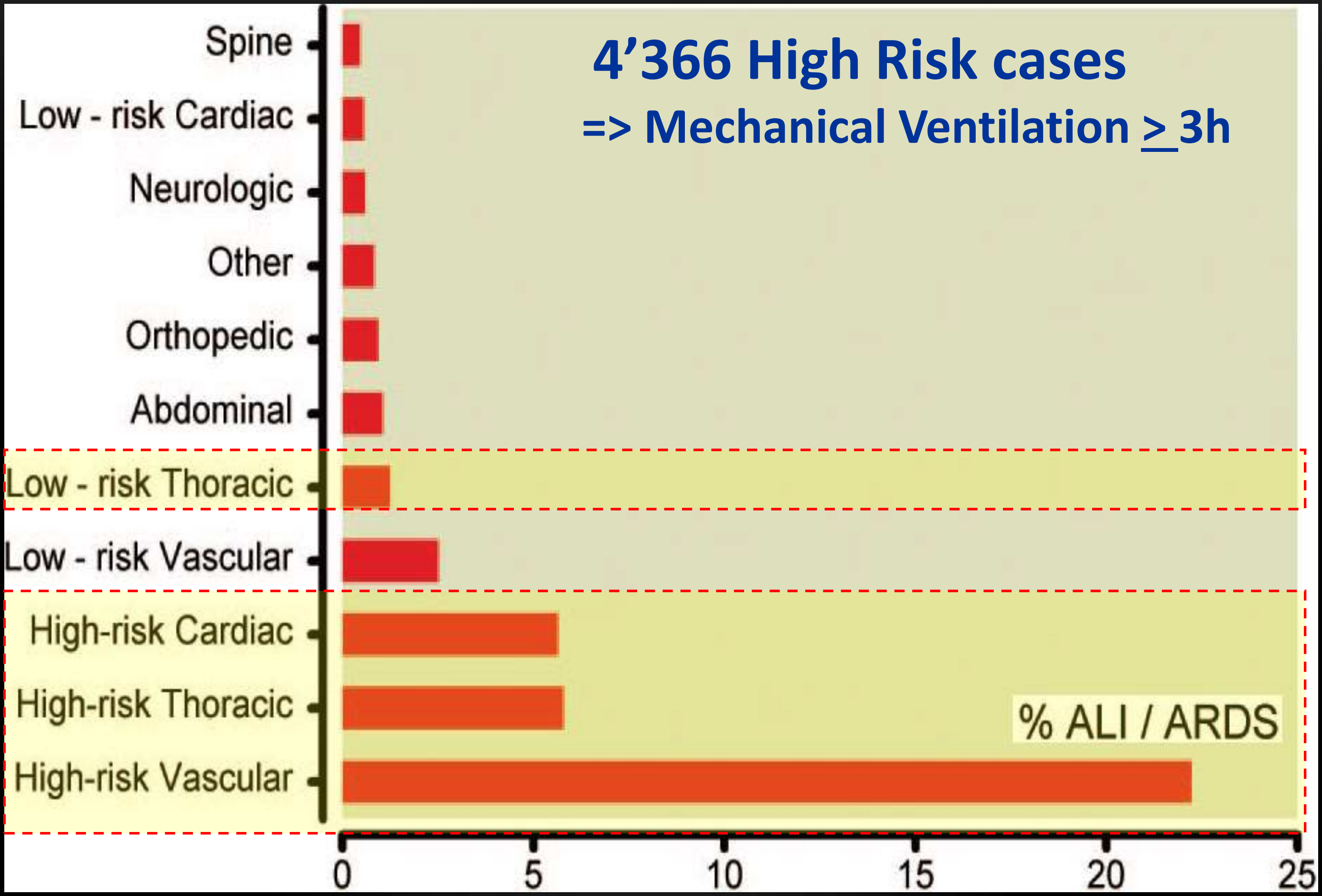
Pneumonectomy vs Lobe,Segm

Incidence 2.5 -7% 0.9 - 4.2%

> 80% within 3 days after surgery

Mortality 20 - 100%

POSTOP ALI / ARDS



ANESTHESIOLOGY 2011; 115:117-28

RISK FACTORS OF POST-THORACOTOMY ALI

MULTIVARIATE REGRESSION OF COHORT STUDIES

Risk Factors	Kutlu CA 2000 N = 1’139	Licker M 2003-09 N=879–1’138	Fernandez-P. 2000 -09 N=170- 659	Dulu A 2006 N = 2’192	Arslantas MK 2012 -13 N = 139	Yao s 2011-12 N=364
Male	+	-	n.a.	n.a.	-	
Age > 60	+	-	n.a.	n.a.	-	
Cancer	+	-	n.a.	n.a.	-	
Alcohol	n.a.	+	n.a.	n.a.	-	
Smoking	n.a.	-	-	-	+	
Chemotherapy	-	+	n.a.	n.a.	n.a.	
Low FEV_1	**n.a.**	-			n.a.	+
Pneumonectomy	+	+	n.a.	+	n.a.	
One Lung Vent.						
• V_T > 7 ml/kg	n.a.	+	+	n.a.	n.a.	
• High Driving P	n.a.	+	+	n.a.	n.a.	
Fluid balance +	n.a.	+	+	n.a.	+	+

Univariate analysis | **Right > Left Pneum.** | **Transfusion (FFP)**

OLV & BIORAISERS

INTERACTIONS BETWEEN TRANSFUSION, AGE, VENTILATION & POSTOPERATIVE ARDS

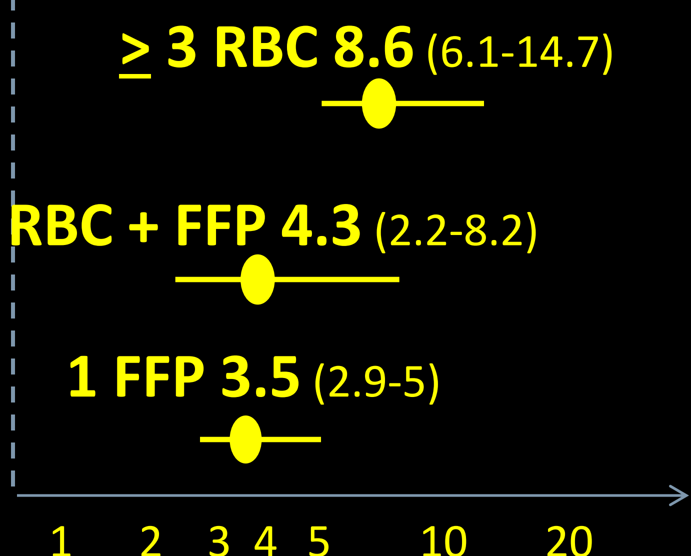
Systematic Review of 15 studies

Anesthesiology 2015 (accepted)

Risk of ARDS

V_T > 10 ml/kg + Transf.

43% ALI vs 1% V_T <7 no Transf



Variable	No ALI N = 1'285	ALI N = 58
Age, years	**62 ± 12**	**66 ±10***
V_T, ml/kg BWI	**7.6 ± 1.8**	**9.5 ± 2.5***
Pneumonia, n (%)	**4 (0.3)**	**5 (9)***
Transfusion, n (%)	**26 (2)**	**13 (22)***

POST-THORACOTOMY ALI / ARDS

- Diagnostic criteria
- Incidence & Risk factors
- **Pathogenesis**
  - Spontaneous V vs 2-LV vs 1-LV
  - Scenario
  - Ventilator-Induced Lung Injury
  - Key players
- Lung protective strategies

Pig Model of Thoracic Surgery
OLV - TLV - SB

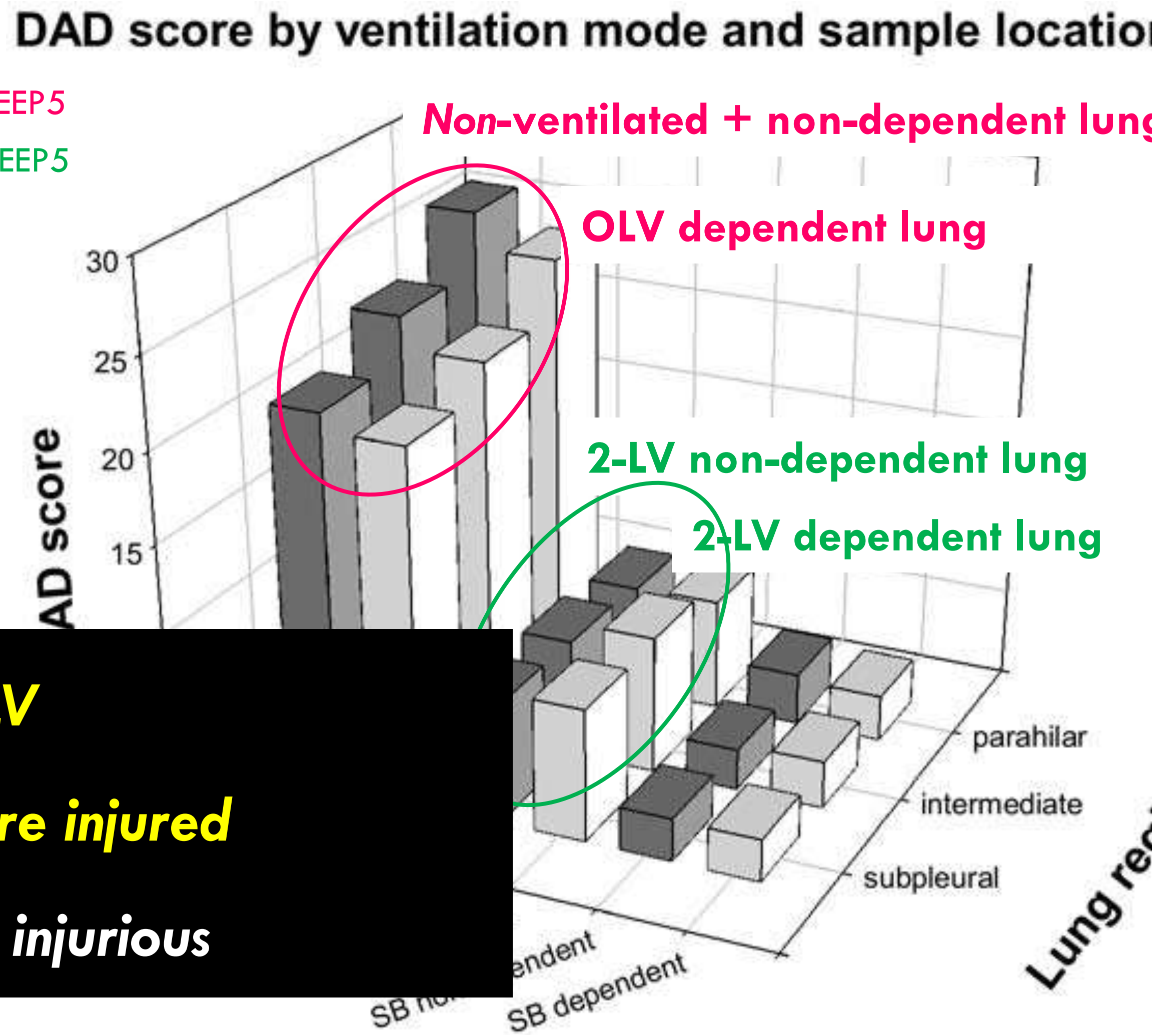
Kozian A et al.
J Cardiothor Vasc Anesth 2010

90 min ventil.+ thoracotomy:

- **One Lung Ventilation** V_T 10 ml/kg, PEEP5
- **Two-Lung Ventilation** V_T 10 ml/kg, PEEP5
- Spontaneous Breathing

Diffuse Alveolar Damage (DAD)

- Alveolar/interstitial edema
- Microhemorrhage
- PMN infiltration
- Microatelectasis
- Alveolar overdistension



OLV is more injurious than 2–LV

Ventilated & collapsed lungs are injured

Spontaneous breathing = least injurious

Collapsed L

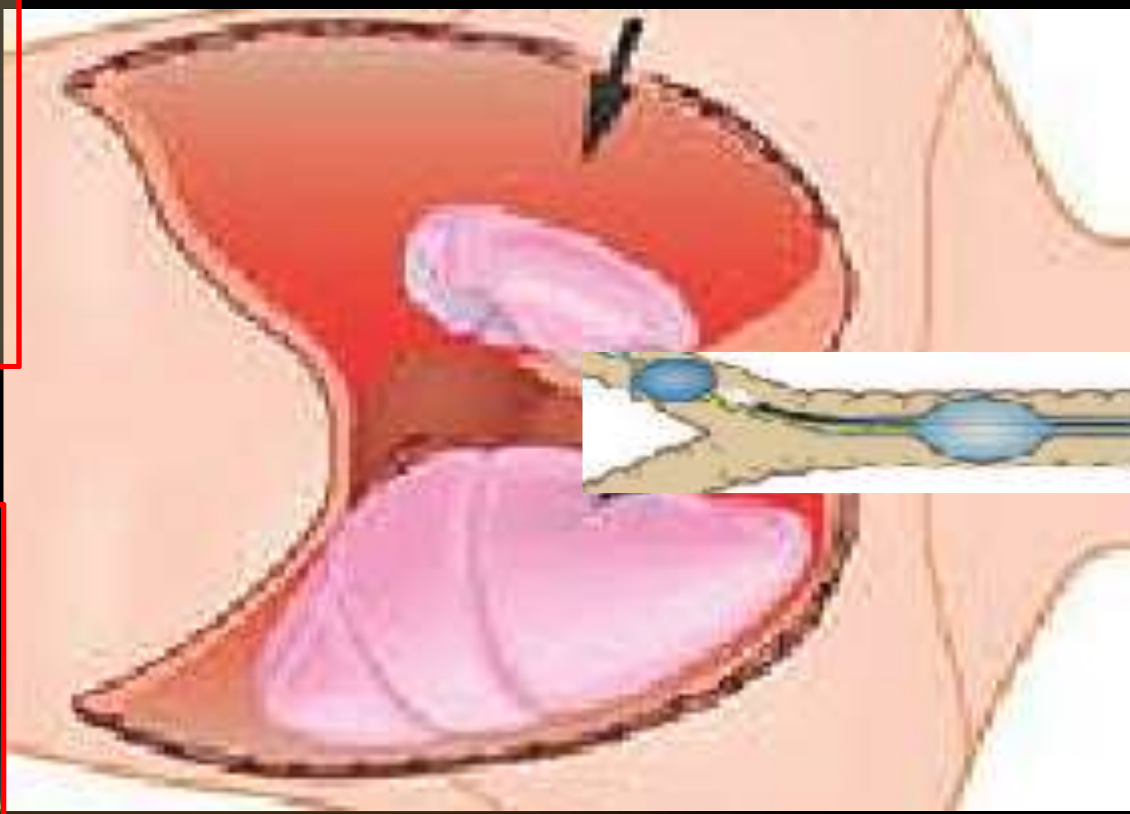
Ventilated L

INJURıOUS PATHWAYS OF POSTOP ALI

SCENARıO

Operated Lung *Deflated*

- ✓ **Lung disease** (cancer, infection)
- ✓ **Surgical manipulations**
  Pleura, vessel, parenchyma
- ✓ **Hypoxia →HPV, shunt**
- ✓ **Isch.-Reperf, Re-expansion**



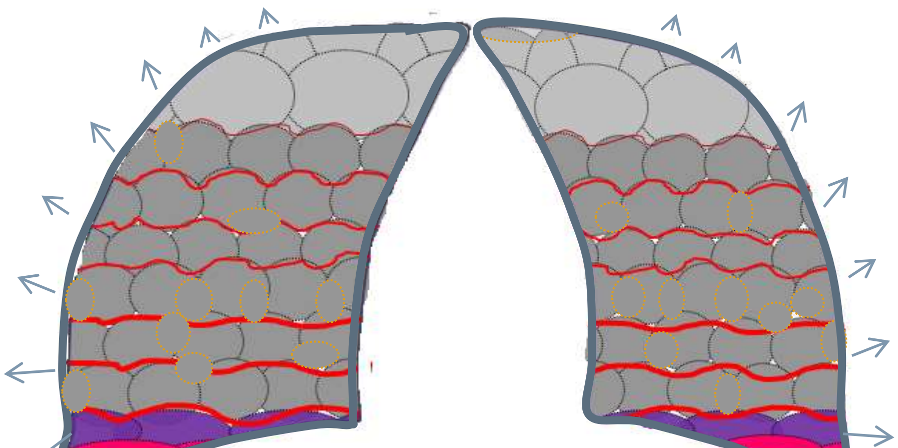
Non-operated Lung

Ventilated

- ✓ **Pressure / Volume control**
- ✓ **V_T, P_{PL}, PEEP I:E**
- ✓ **FIO_2** Normoxia - Hyperoxia

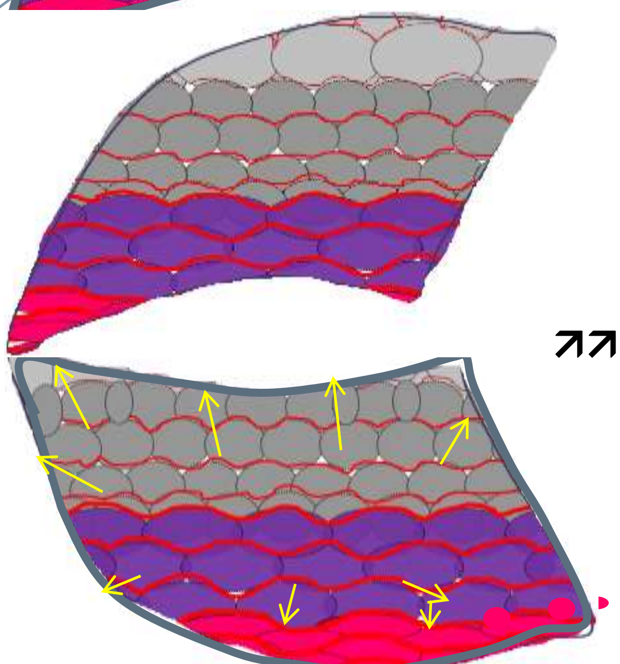
Lung : healthy, COPD,…

VENTıLATıON
SPONTANEOUS vs MECHANıCAL 1-2 L



Supine position
***Spontaneous* ventil.**
↓
Homogenous
Ventilation / Perfusion

Re-expansion ⇨ ↑ Ventilation / Perf.



↗↗ **V/Q** ***Dead space***

V/Q **0.9 – 1.5**

Low V/Q **< 0.9**

V/Q ~ 0 ***Atelectasis***

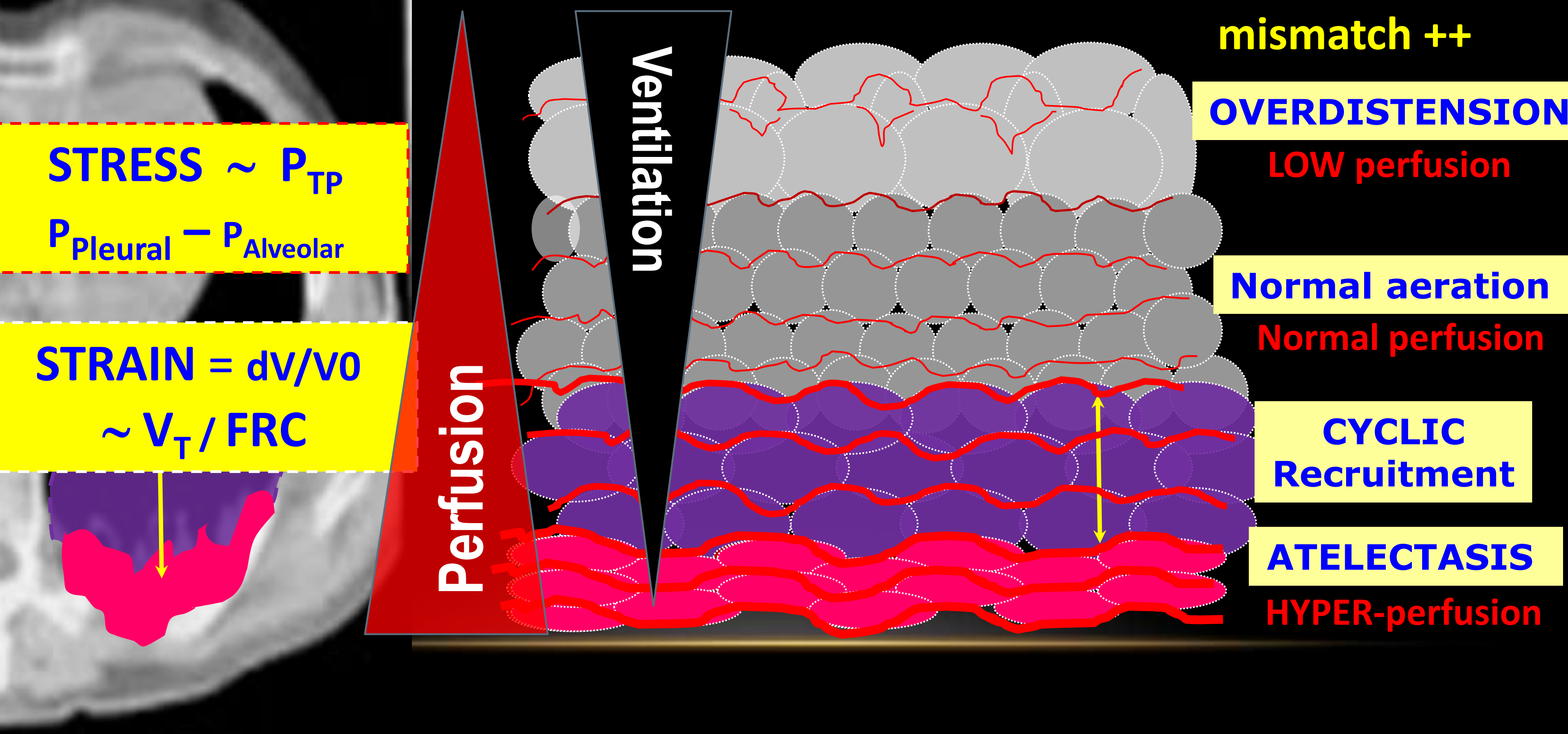
Collapsed lung
↑
Lateral position
***Mechanical* OLV**
↓
Heterogenous
Ventilation / Perfusion

CONCEPT OF VENTıLATOR-INDUCED LUNG INJURY
WET SPONGE MODEL

AERATION (V_T) : Heterogenous distribution

PERFUSION : Gravity dependent

Ventilation / Perfusion mismatch ++

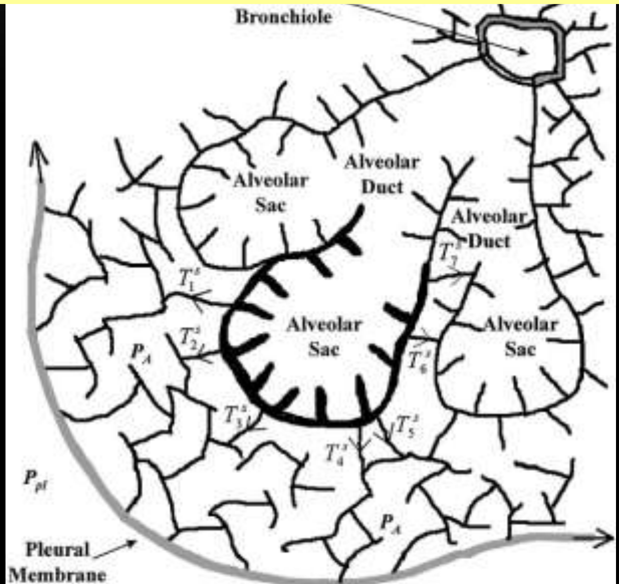


Adapted from Gattinoni L, Pesenti A. *Intensive Crit Care Dig* 1987 6:1–4

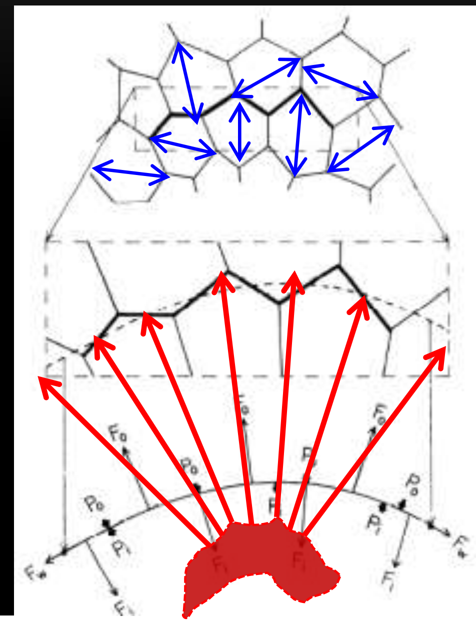
Stress distribution in lungs: a model of pulmonary elasticity

JERE MEAD, TAMOTSU TAKISHIMA, AND DAVID LEITH
Department of Physiology, Harvard University School of Public Health, Boston, Massachusetts

Homogeneous distribution of forces



P = Force/Surface



larger surface
Interdependent alveola
low P

Atelectasis
→ High tension

↗↗ SHEAR stress within alveolar units close to atelectasis

Mechano-chemical transduction
Inflammatory response

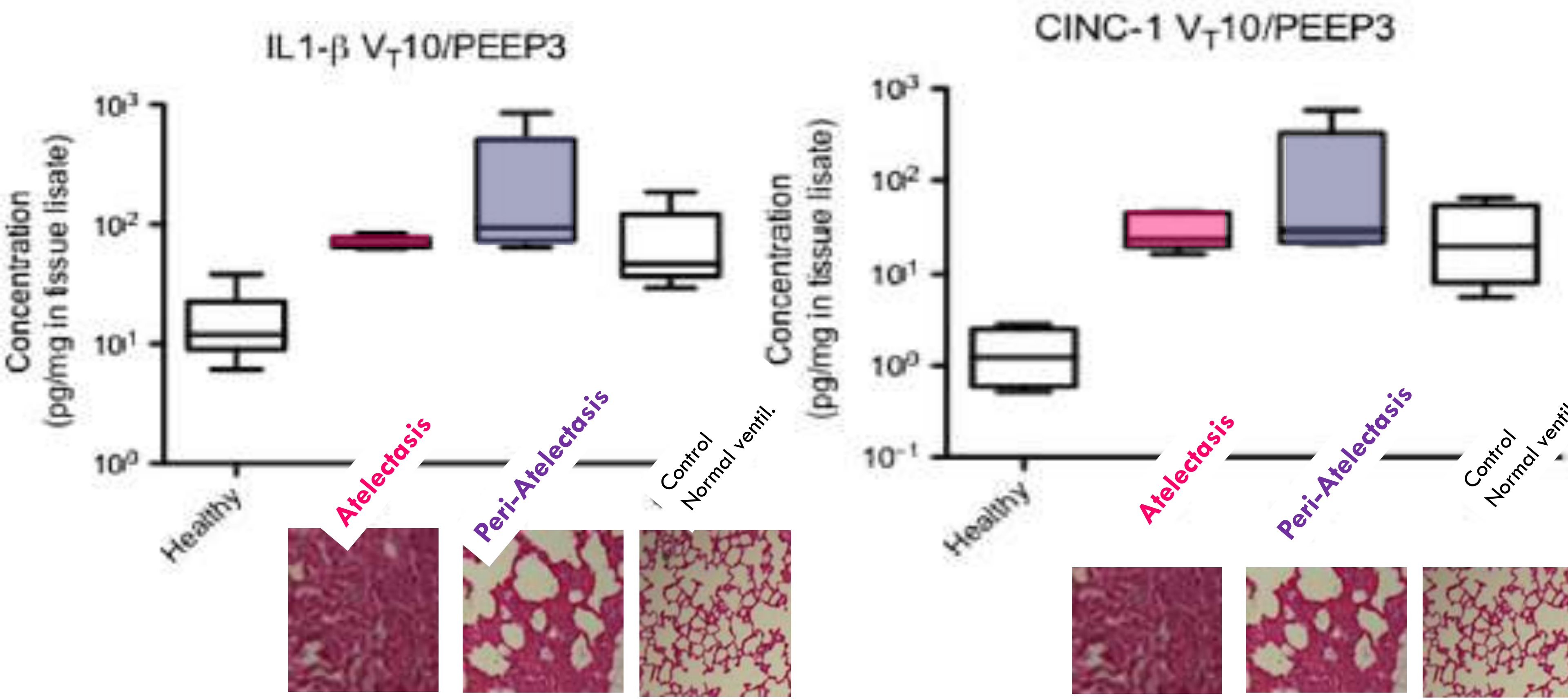
DIFFUSE Alveolar + Airway injuries

Tsushida S et al. *Am J Respir Crit Care Med* 2006;174: 279–89

Non-lobar atelectasis generates inflammation and structural alveolar injury in the surrounding healthy tissue during mechanical ventilation

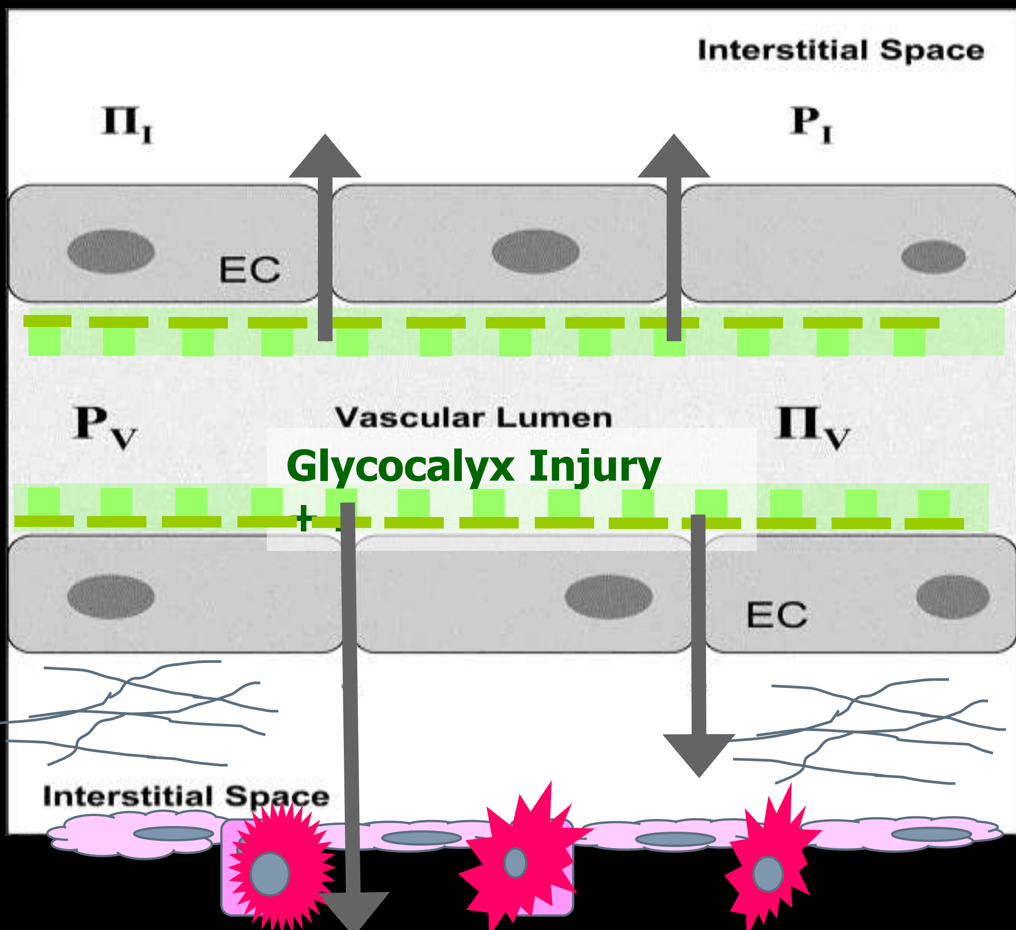
Jaime Retamal[1,2*], Bruno Curty Bergamini[3], Alysson R Carvalho[3], Fernando A Bozza[4], Gisella Borzone[5],

Retamal et al.
Critical Care 2014, 18:505



Inflammation in healthy lung parts ≥ than in atelectatic areas

PULMONARY CAPıLLARY LEAK SYNDROME



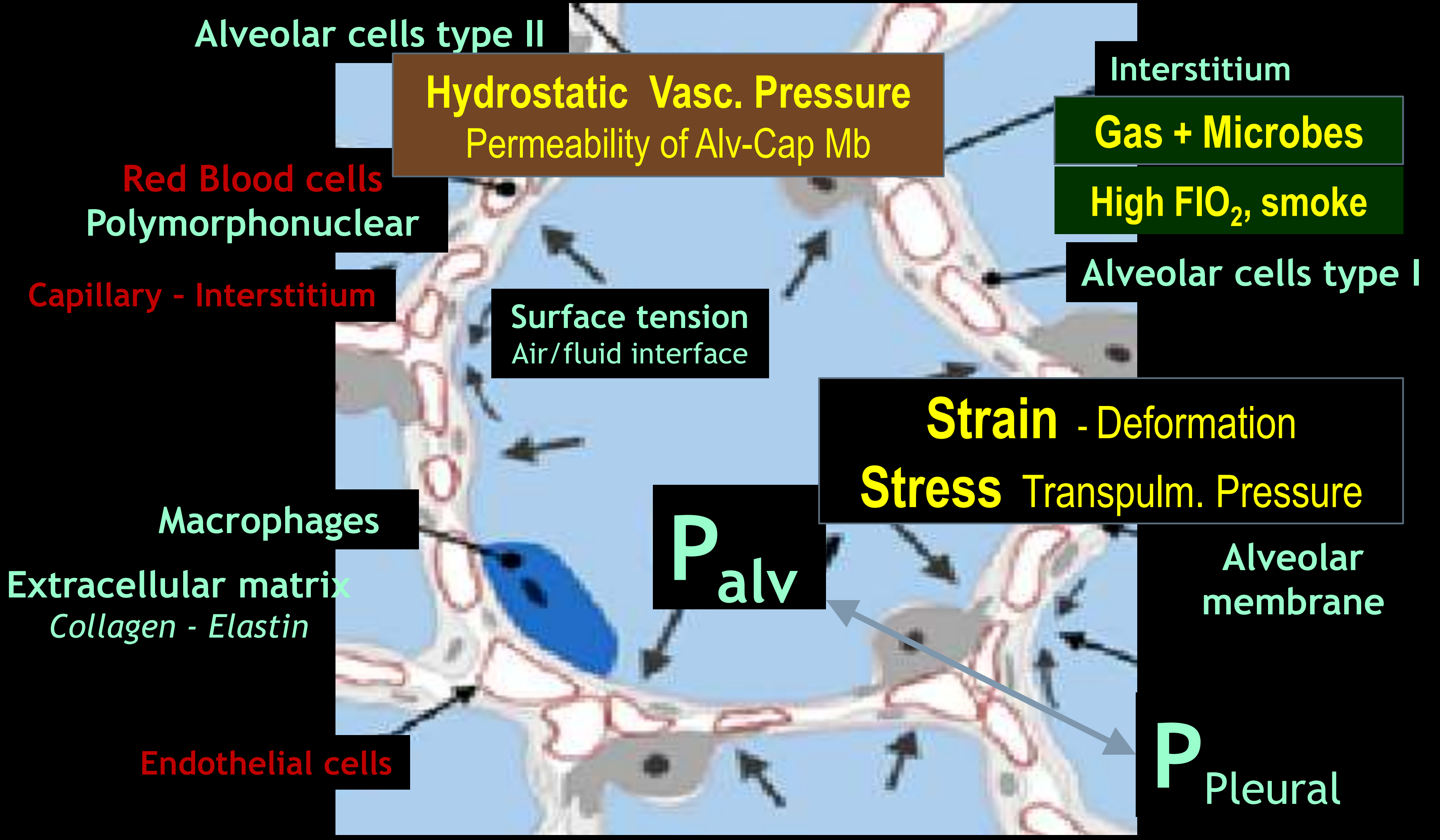
↑Hydrostatic Pressure
↑Alveolar Stress & Strain

Ventilation: ↑ V_T, ↑P_{TP}
Ischemia-Reperfusion
Sepsis, infection

Alveolar Inflammation

POST-THORACOTOMY ALI

PATHOGENESiS : KEY PLAYERS



1. *Definition*
2. *Incidence & Risk factors*
3. *Pathogenesis*

4. *Lung Protection*

- *Anesthesia*
- *Ventilation*
- *Hemodynamics*

4. LUNG PROTECTION IN THORACIC SURGERY ANESTHETICS: VOLATILS VS IV

Desflurane, Sevoflurane & **Isoflurane**

- **↓ Alveolar inflammatory responses**
  (TNF-α, IL-1, IL-6,…) *Anesthesiology* 2011;115:65-74
- **Bronchorelaxant** *Anesth Analg* 2005; 100:348-53

- **∅ Clinical outcome** *Cochrane* 2013 Modolo NS et al.
  poor quality of data
  Meta-analysis 20 RCTs, N=850 pts + OLV

THE COCHRANE COLLABORATION

4. LUNG PROTECTION MECHANICAL VENTILATION

- V_T
- PEEP
- ARM
  Alveolar Recruitment Maneuver
- FIO_2

Goals

- Gas Exchange
- No Harm

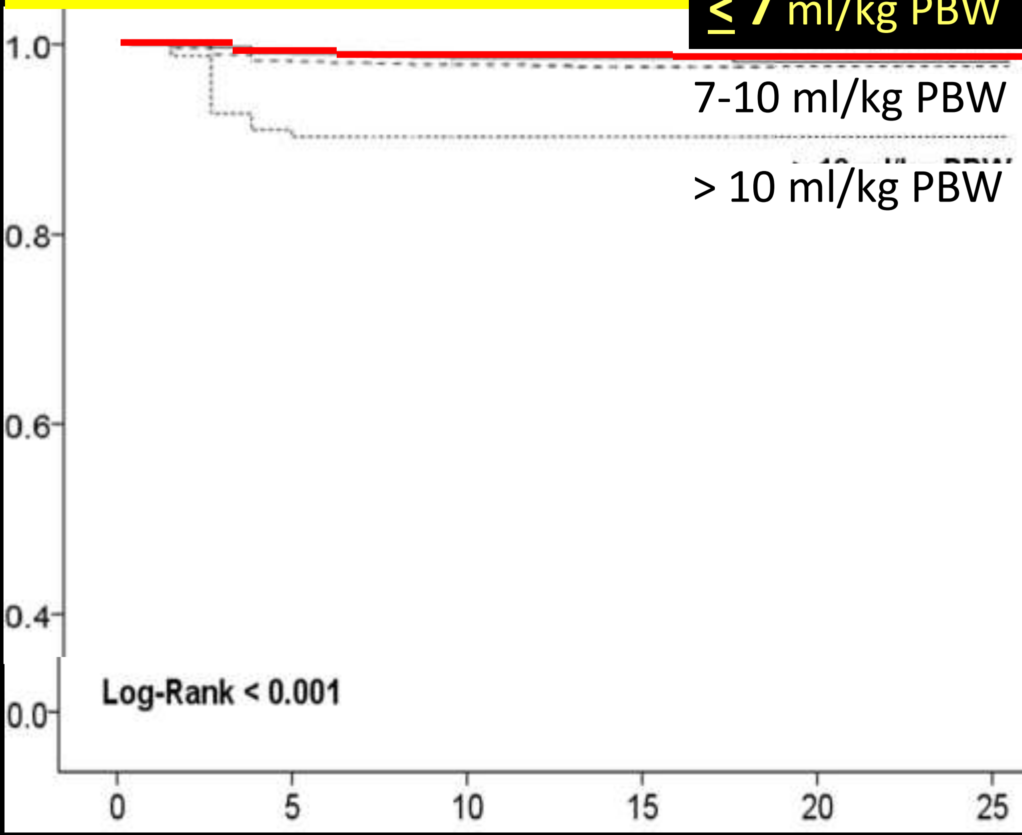
⇨ Open lung

Incidence of mortality and morbidity related to postoperative lung injury in patients who have undergone abdominal or thoracic surgery: a systematic review and meta-analysis

THE LANCET
2014 Nov 13

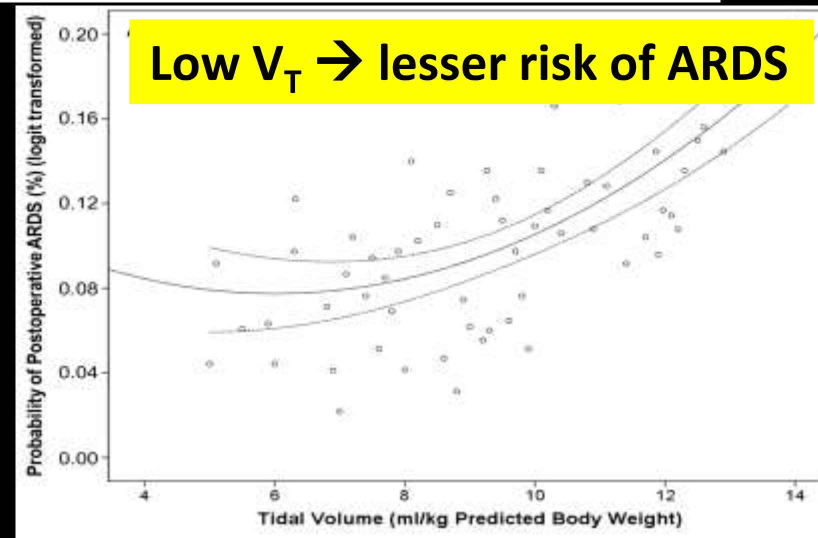
Ary Serpa Neto, Sabrine NT Hemmes, Carmen SV Barbas, Martin Beiderlinden, Ana Fernandez-Bustamante, Emmanuel Futier, Markus W Hı
Samir Jaber, Alf Kozian, Marc Licker, Wen-Qian Lin, Pierre Moine, Federica Scavonetto, Thomas Schilling, Gabriele Selmo, Paolo Severgnini,

Survival free of ARDS

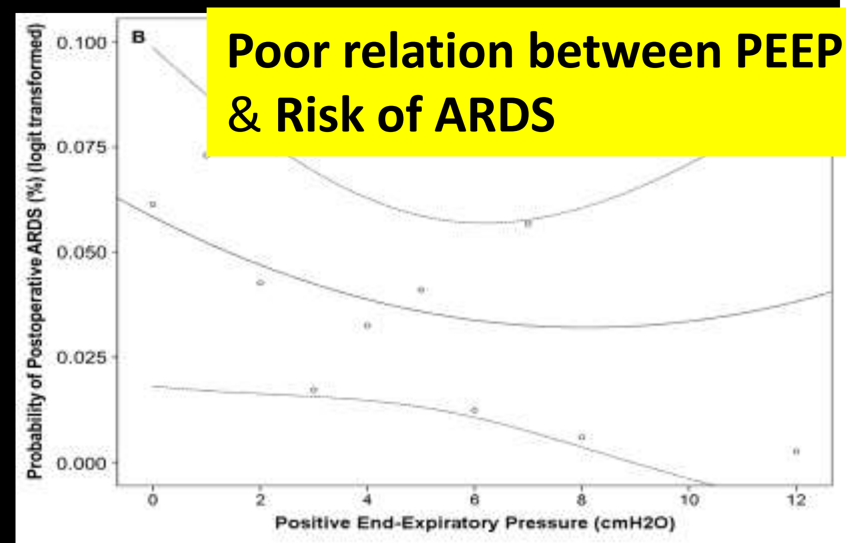


17 studies N=3’659
Abdominal & Thoracic procedures

Low V_T → lesser risk of ARDS



Poor relation between PEEP & Risk of ARDS

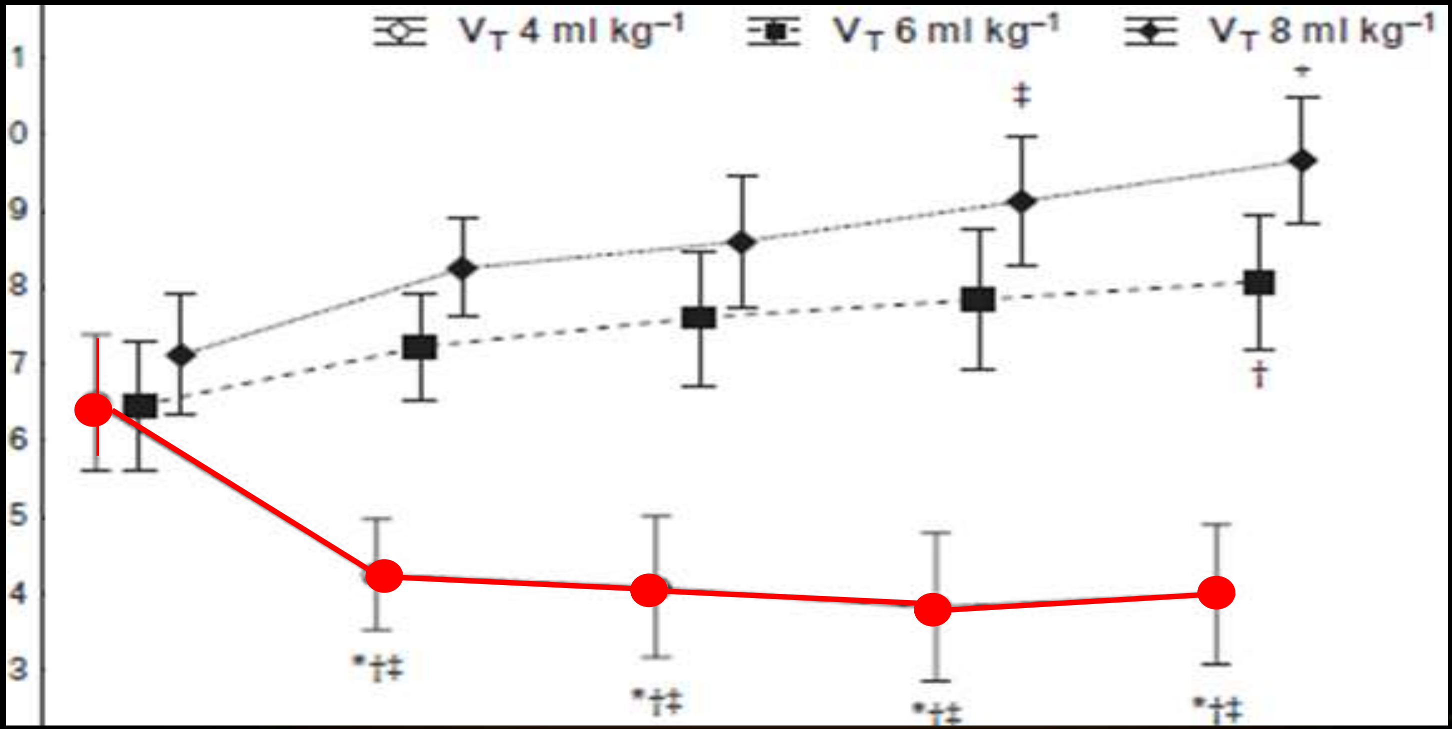


IMPACT OF V_T ON EVLWI

- 39 pts + VATS, OLV with V_T of **4** – 6 – 8 ml/kg PBW

  + PEEP 5 + ARM / 30 min

Extravascular Lung Water Index
ml/kg



EUR J ANAESTH 2014;31:466-73

LOW V_T : NOT ALWAYS FAVORABLE …

MASLOW AD. *J THORAC CARDIOVASC SURG* 2013;146:38-44

N=34, open thoracotomy, FEV_1 & DLCO > 40%, all TEA

VCV, $FIO_2 \geq 50\%$ I:E 1:1.7

N=16
High V_T 10 ml/kg IBW
RR 14 ZEEP

N= 16
Low V_T 5 ml/kg IBW
RR 14 PEEP 5

Rescue maneuver if SpO_2 <92%

1. FIO_2 100%
2. CPAP *operated* lung
3. Ventilate *operated* lung

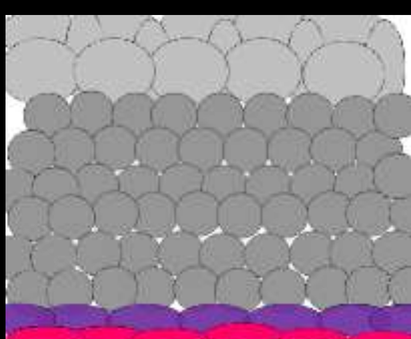
No Alveolar Recruitment !

Intraop crystalloids
3.9 ml/kg/h vs 2.6 ml/kg/h

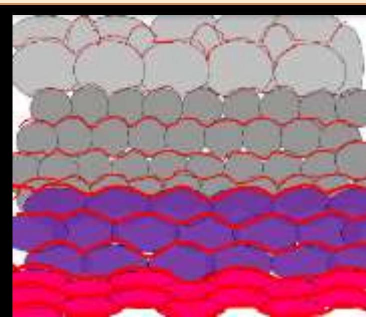
Lower V_D/V_{Alv}
Higher C_{Dyn}

Lower C_{dyn} & $P_{plateau}$
Higher $PaCO_2$

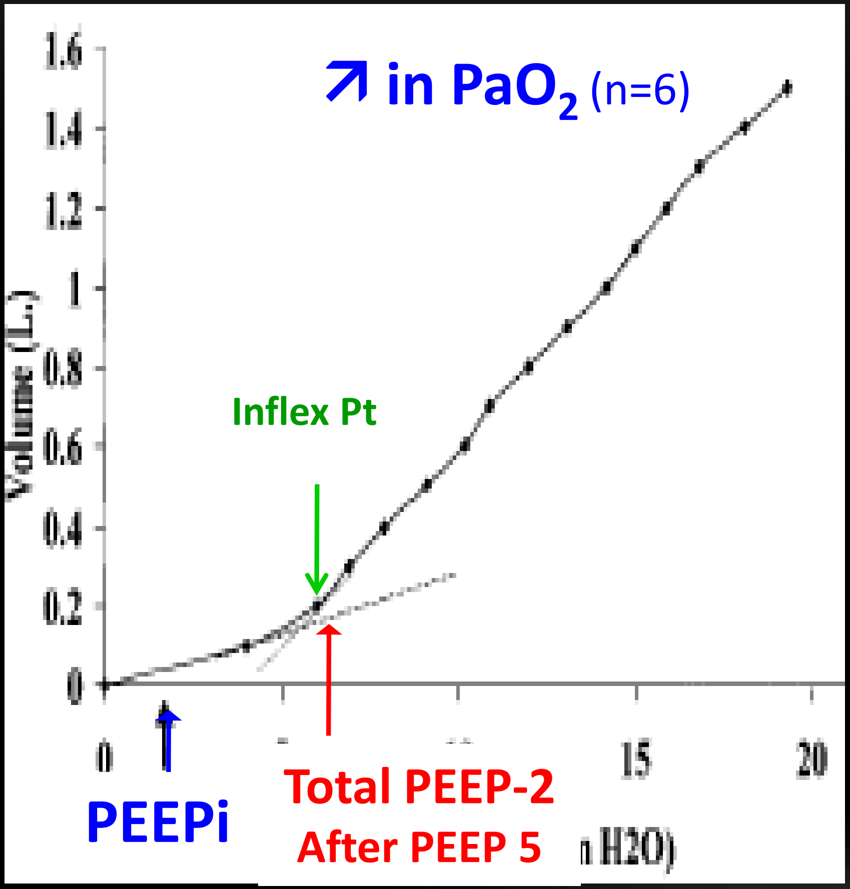
↗Atelectasis POD1-2

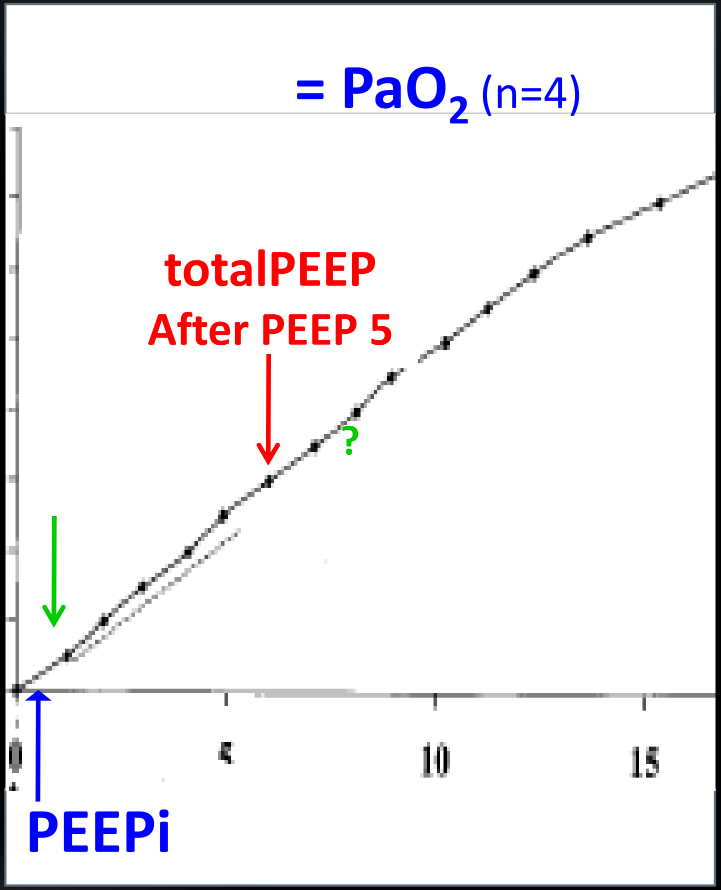


Similar SV
PaO_2/FIO_2
(30 min)



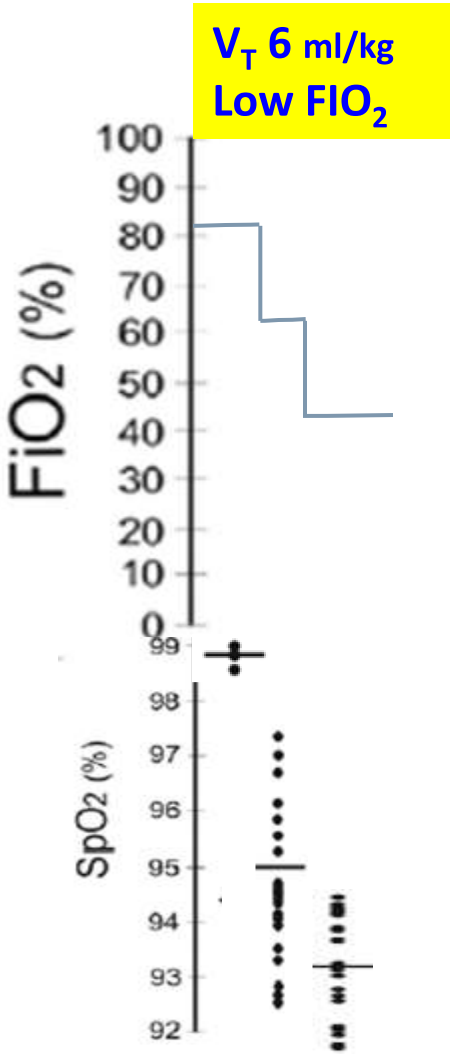
POST-THORACOTOMY ALI/ARDS
OPTIMAL PEEP ?

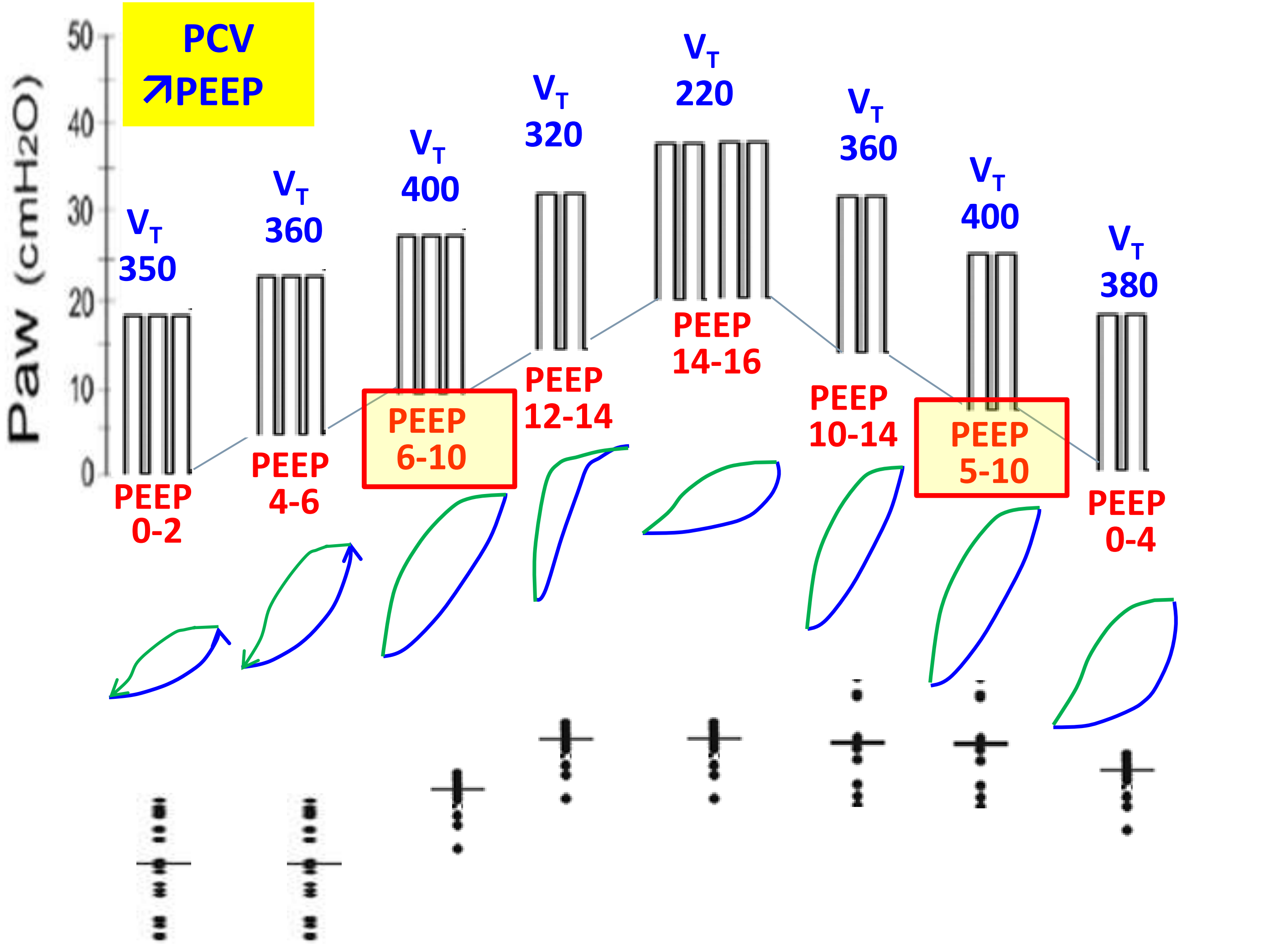




Slinger PD *Anesthesiology*. 2001;95:1096-102

ALVEOLAR RECRUıTMENT → OPTıMAL PEEP





CPAP ON THE OPERATED LUNG

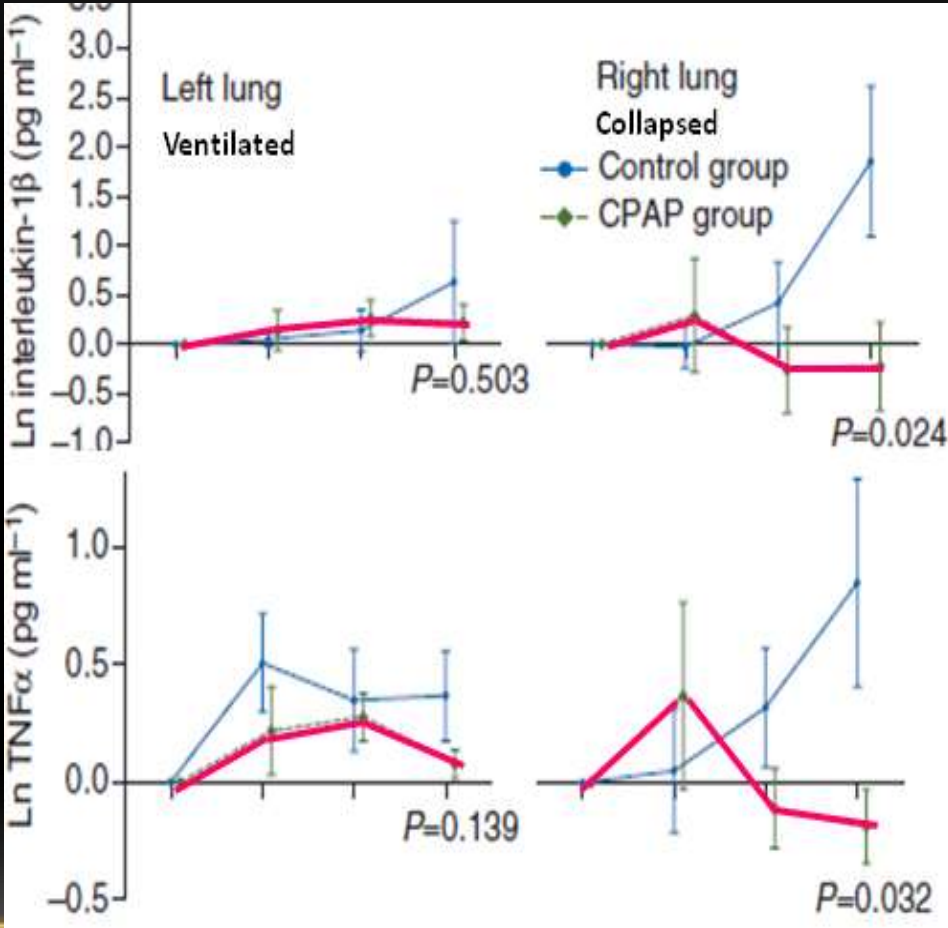
Br J Anaesth 2014;112:920-8

30 pts, oesophagectomy PLV:

V_T 6ml/kg, **PEEP5, ARM**

Restrictive fluids

Collapsed lung vs **CPAP**



CPAP

- **↓ Immune response**
- **↗ Oxygenation PaO_2**

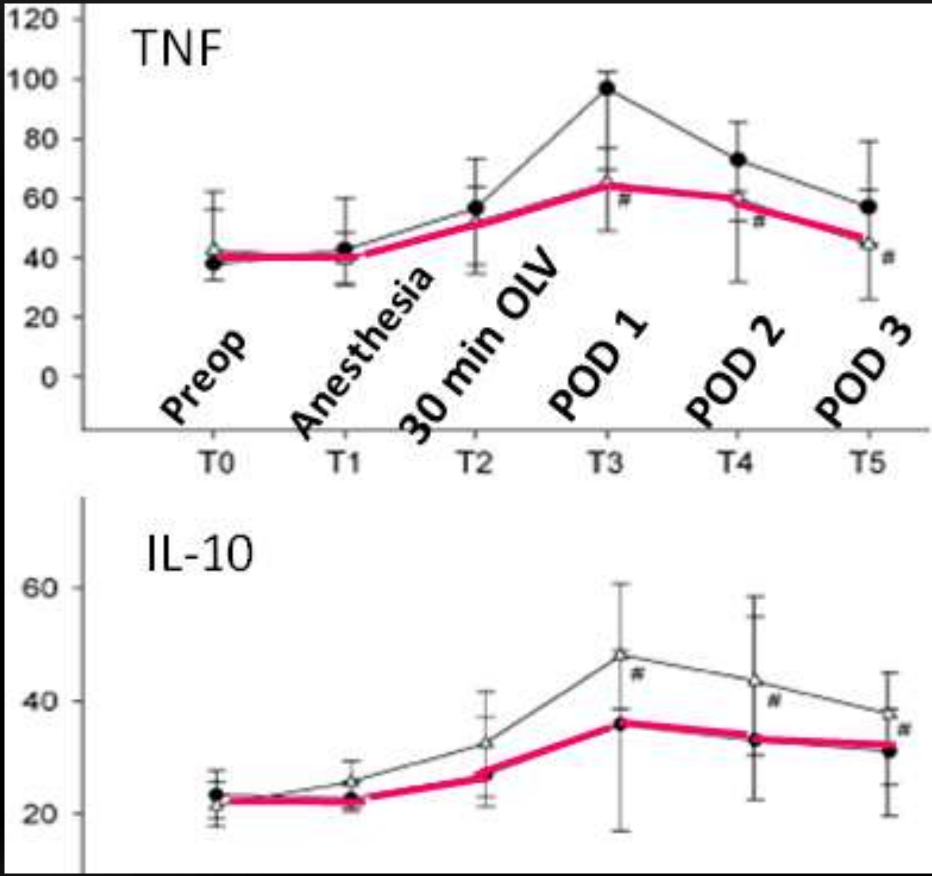
ANTI-INFLAMMATORY THERAPY

100 pts, lobectomy with OLV

V_T 6 ml/kg, PEEP 5, ARM

Control vs **Budesomide** **inhaled**

Preop inhaled corticoids attenuates pulmonary & systemic inflammation



Anaesthesia 2014;69:14-23

BIORAISERS

HYPEROXIA VS NORMOXIA

Pigs 3h OLV

V_T 8-10 ml/kg ZEEP

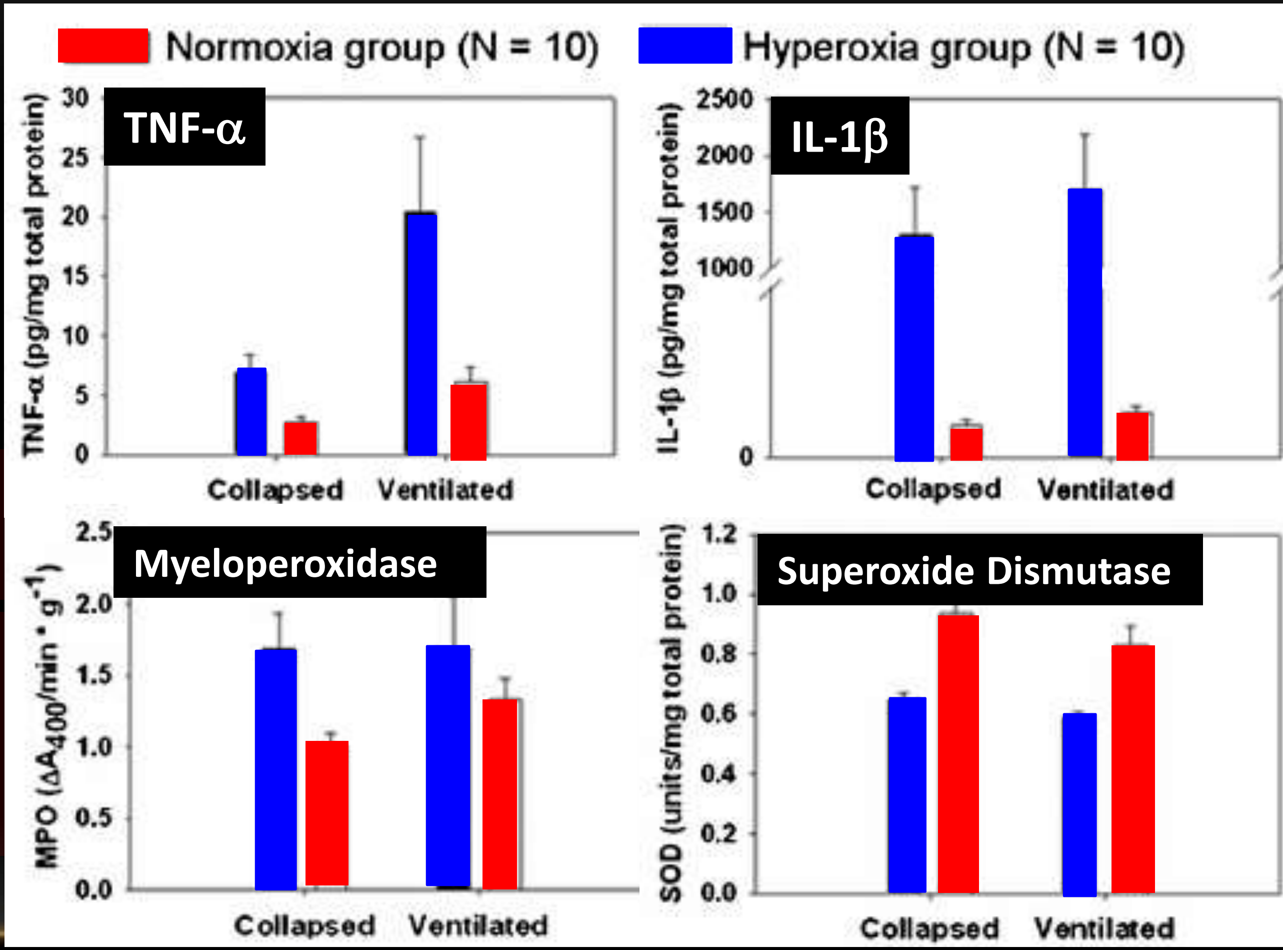
Normoxia FIO_2 < 50%

Hyperoxia FIO_2 100%

↓ Inflammatory response IL-1β, TNF-α,...

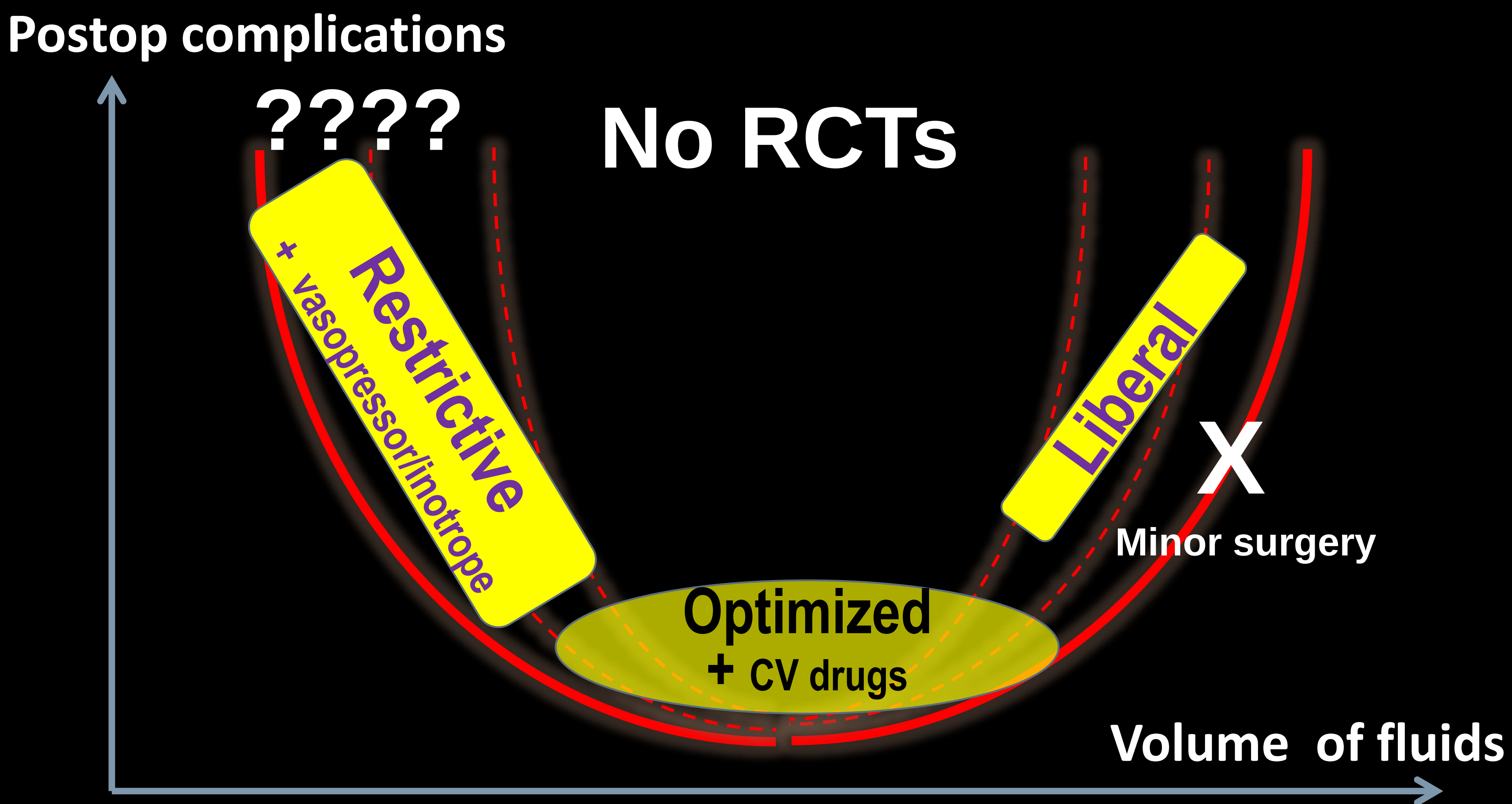
↓ Oxydative stress (MPO)

↑ Antioxidants (SOD)



Pediatric Pulmonology 2012; 47:979–86

OPTıMAL HEMODYNAMıC THERAPY
FLUıDS AND CV DRUGS



FLUiDS: LESS iS MORE…

Authors	Year	N	Lung resections	Fluids intra(-postop)		Endpoints
				With Postop Pulm. C	No PPC	
Blank	2011	129	Pneumon.	2.7 L (95%2.0-4.0) L	1.8 L (95%1.5-2.5) L	All PPC
Marret E	2010	129	Pneumon.	3.8 L (SD1.5)L*	2.5 L (SD1.3)	Major complic
Fernandez-Perez	2006	170	Pneumon.	2.2 L (IQ1.4-3.7)	1.3 L (IQ0.9-2.7)	ALI/ARDS*
Moller	[illegible]	[illegible]	[illegible]	[illegible]		All PPC
Bernard	[illegible]	[illegible]	[illegible]	[illegible]		…iac & PPC
Van der We…	[illegible]	[illegible]	[illegible]	[illegible]		…. edema
Parquin	[illegible]	[illegible]	[illegible]	[illegible]		…edema
Arslantas	2015	139	All	> 6ml/kg/h associated with PPC		
Alam	2007	152	All	2.8L (95%1.4-5)	2.5 L (95%1.4-4.5)	ALI/ARDS*
Licker	2003	879	All	2.6 ml/kg/h (95%2.3-2.9) *	2.0 ml/kg/h (95%CI1.7-2.3)	ALI/ARDS*
Ruffini	2001	1221	All	No association between fluid and complications		ALI/ARDS*
Kutlu	2000	1139	All	Fluid regimen not defined		ALI/ARDS*
Hayes	1995	469	All	Fluid regimen not defined		ALI/ARDS*

	No ALI	ALI
Intraoperative IV	1.9 L (1.2–2.5)	2.3 L (1.5–3.9)
Postop Fluid balance	1.5 L (1.4–1.6)	2.0 L (1.6–2.4)

HEMODYNAMıC CONTROL

- **INTRAOP**
  - **Fluids →Ringer-Lactate** (no saline)

    ± colloids (compensate BL)
    - **Restrictive** (normovolemia): **2–4 ml/kg/h in low risk pts**

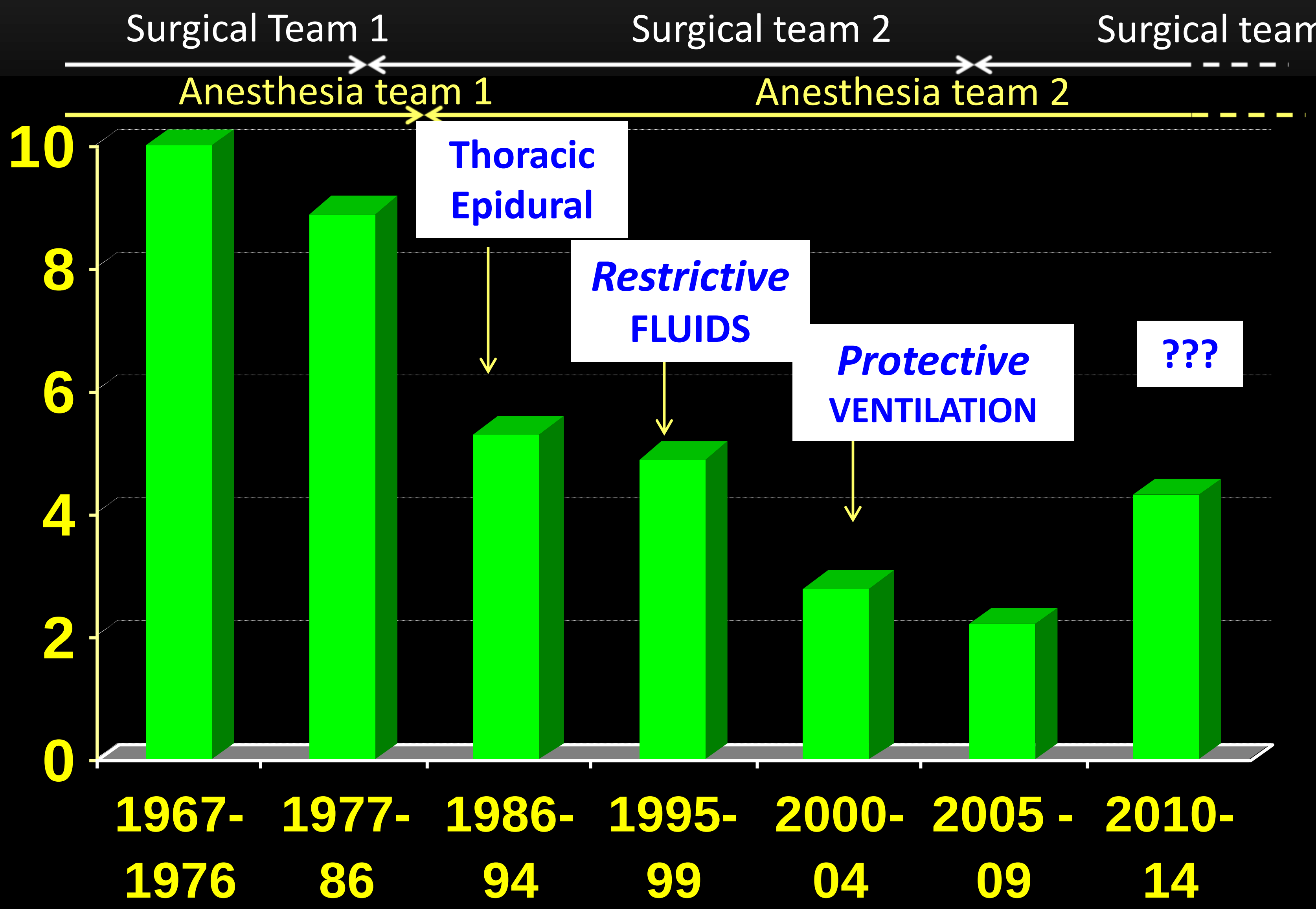
    or
    - **Goal-directed infusion in high risk pts** based on CO/SV monitoring (Doppler, PPV)
  - **Vasopressors: PHE, Ephedrine, NE infusion** (TEA)

3-6h postop in PACU

- **POSTOP**
  - ☞ **Fluid balance < 1.5L, Weight gain < 5%**
    - IV 0.5 L (5% Glucose 0.3% saline) + beverage, ½ solid food
  - ☞ **Mobilize without fainting, withdraw catheters, …**
    - Vasopressors or adjust circulatory volemia

Strategies to reduce mortality

Lung Cancer Surgery 1967 - 2015



CONCLUSIONS

Circulation

Avoid transfusion

Optimize/limit fluids ?

Hemodynamic targets

Beta-2 agonists inhaled ?

Ventilation 1-2 LV

V_T 4 – 8 ml/kg IBW

P_{inspir} < 25- 30 cm H_2O

Individualize PEEP ? CPAP

FIO_2 < 50-80% ?

Recruitment maneuver ?

Defense

Lung decontamination?

AB prophylaxis

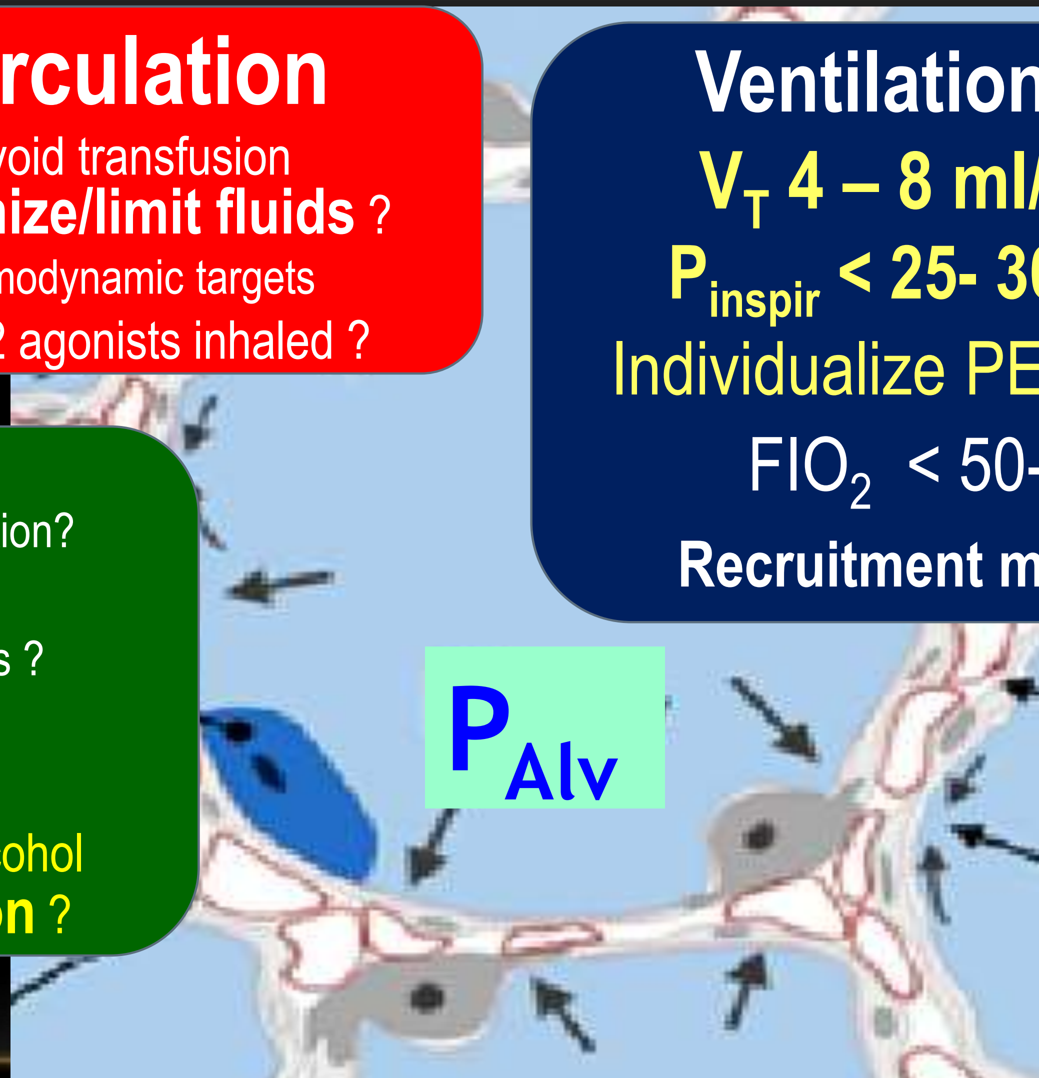
Inhaled Corticoids ?

IV Lidocaine ?

Nutrition ?

Stop smoking, alcohol

Prohabilitation ?

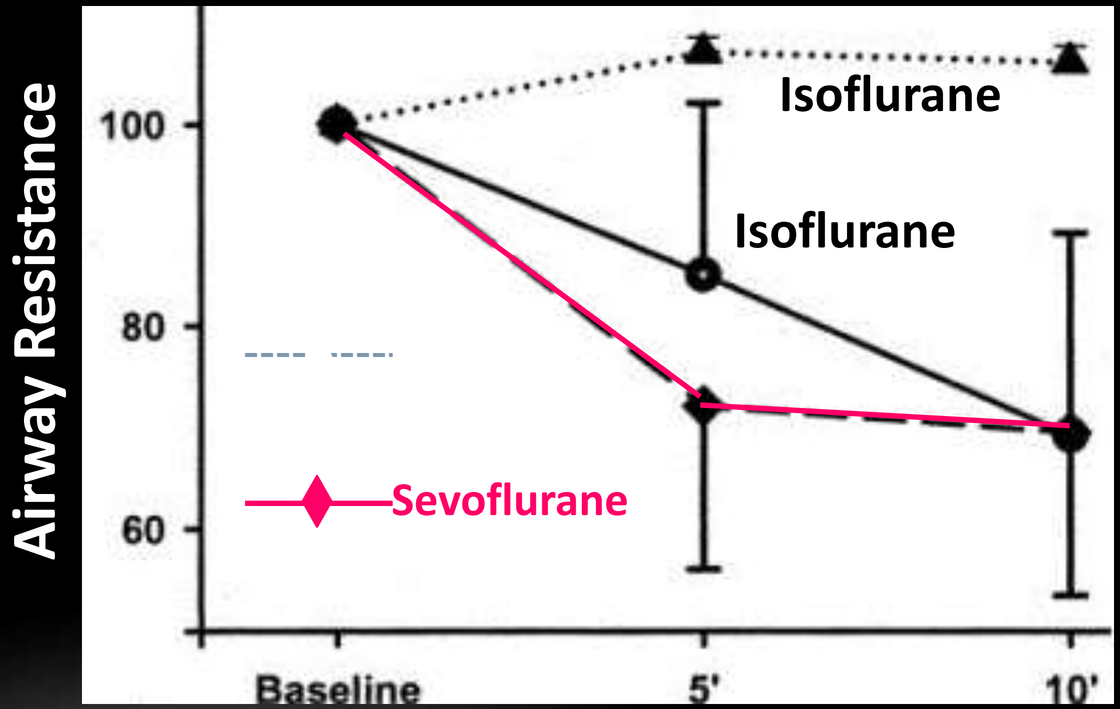



Thank You !
April 7, 2015
Mont Blanc 4’810 m
Mont Salève 1’330m

4. LUNG PROTECTION IN THORACIC SURGERY ANESTHETICS: VOLATIL VS IV

Sevoflurane / Iso ⇨ **bronchodilatation**

- in COPD (N=42)
- in healthy pts (N=43)

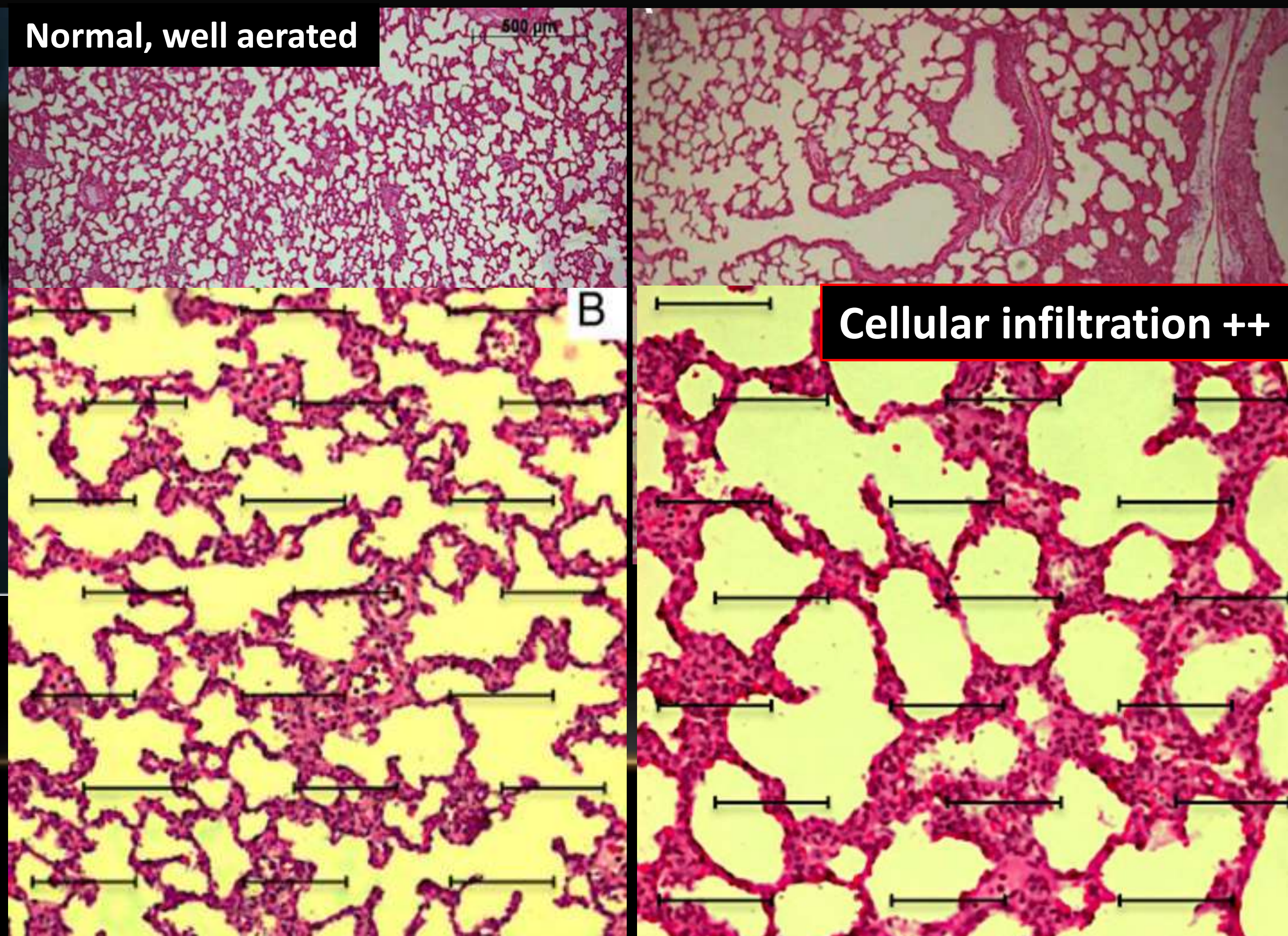


Volta CA et al. Anesth Analg 2005

INFLAMMATION INDUCED BY MECHANICAL VENTILATION

WHERE DOES IT OCCUR ?

Rat model of sub-lobar atelectasis, FIO_2 1.0 , V_T 10/ PEEP 3 or V_T 20 /ZEEP



Retamal et al.
Critical Care 2014, 18:505

DɪSCLOSURE

No conflict of interest