

PULMONARY HYPERTENSION IN THE ADULT ICU : AN OVERVIEW ON CAUSES, EPIDEMIOLOGY, PROGNOSIS AND TREATMENT

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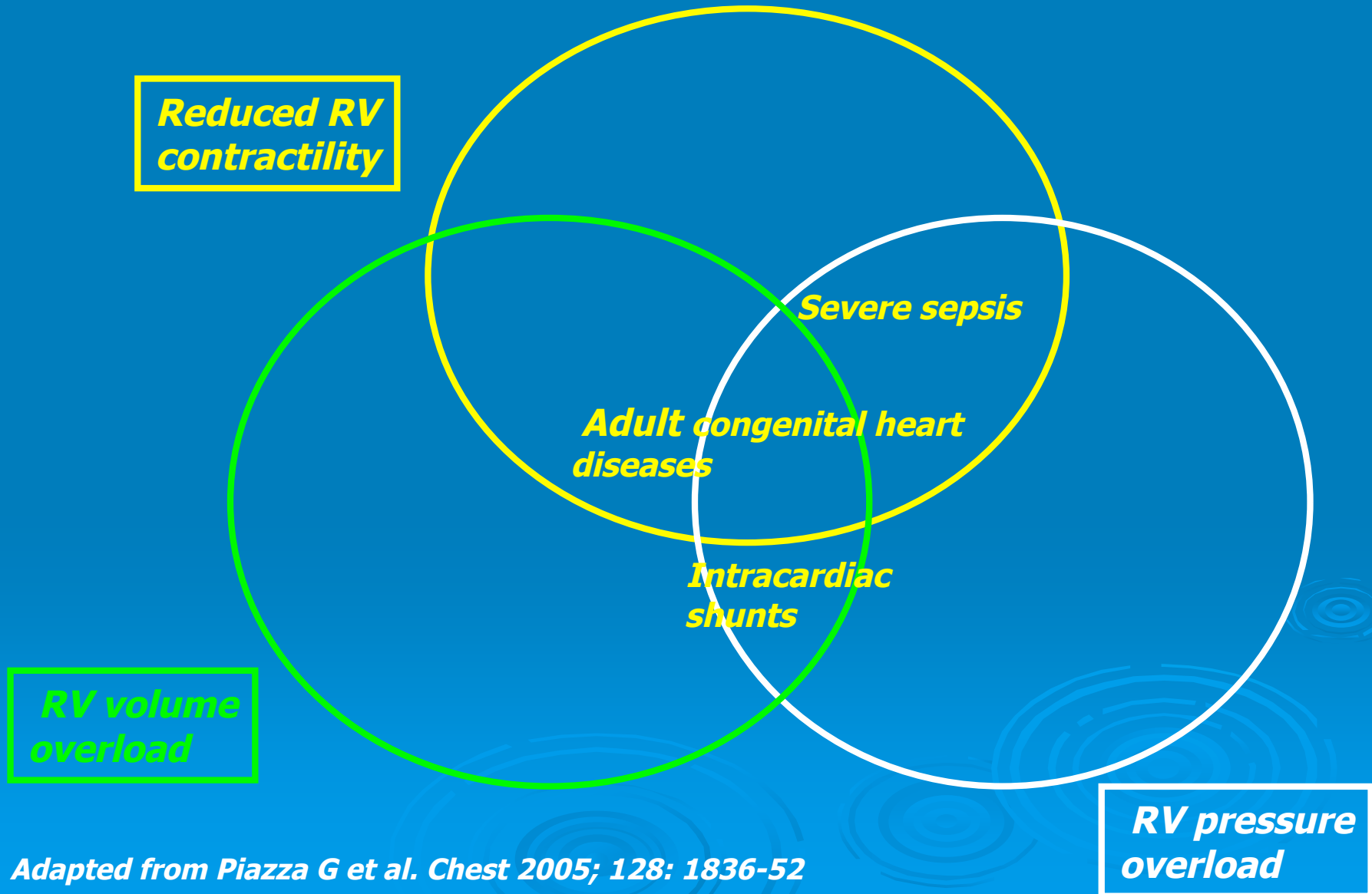
***OSPEDALE REGIONALE
LOCARNO
SWITZERLAND***



SGPH, MONTREUX, 2007

THE ACUTE RIGHT HEART SYNDROME: CAUSES

$$[P_{RA} > P_{LA}]$$

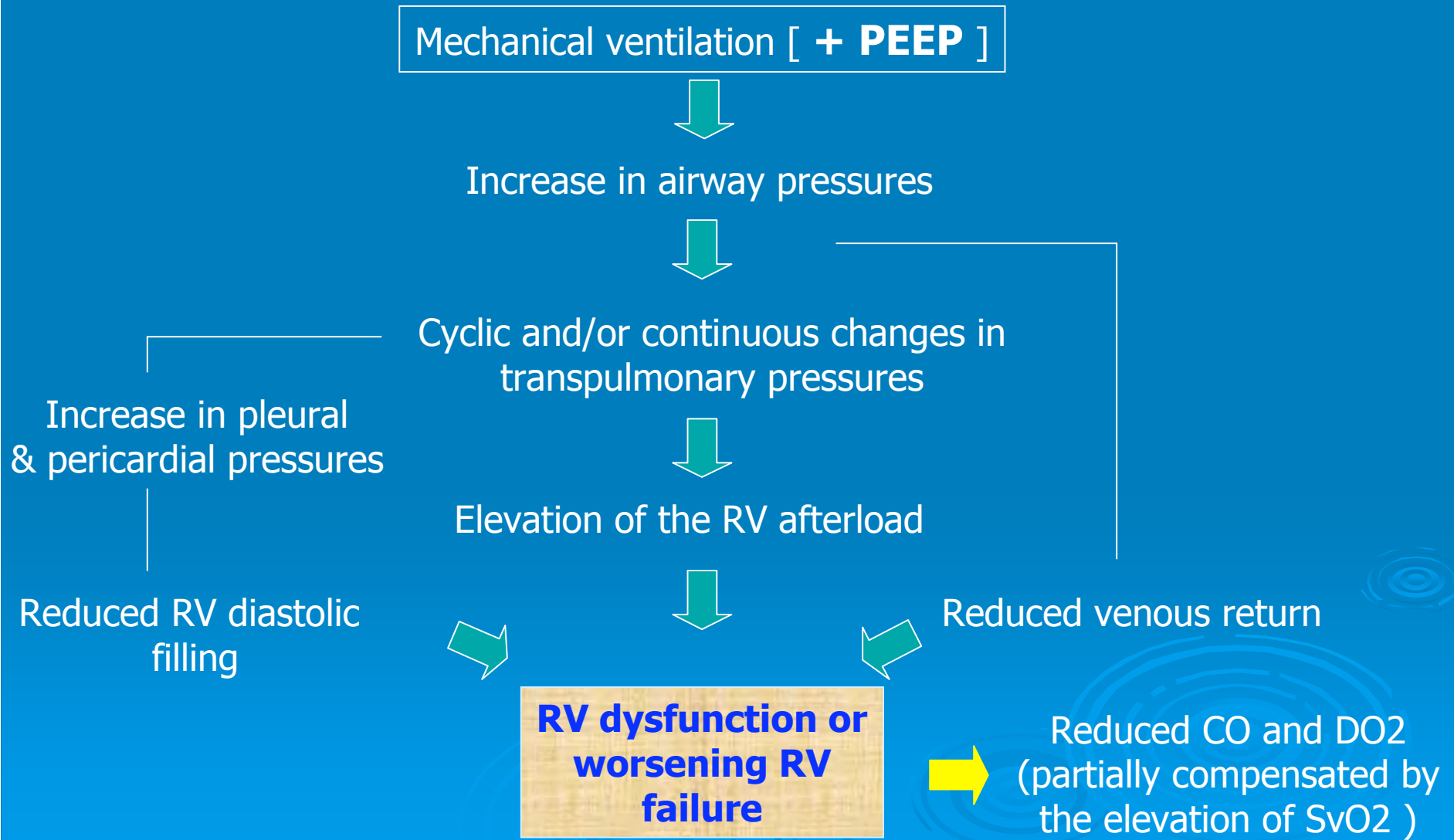


Adapted from Piazza G et al. Chest 2005; 128: 1836-52

CONDITIONS ASSOCIATED WITH RV PRESSURE OVERLOAD

- Acute pulmonary embolism
- Left-sided valvular disease, CM and dysfunction
- PH associated with lung diseases or chronic hypoxemia/CTEPH/PAH
- ALI/ARDS
- **Positive pressure ventilation**
- Pericardial diseases

Mechanical ventilation may deteriorate the RV function



EPIDEMIOLOGY AND PROGNOSIS

- **AECOPD AND COPD**
- **PULMONARY EMBOLISM IN AECOPD**
- **ALI/ARDS**
- **ACUTE EXACERBATIONS OF PAH**

AECOPD

	Group I (n = 15)			Group II (n = 20)		
	FiO ₂ = 0.21	FiO ₂ = 0.28	p	FiO ₂ = 0.21	FiO ₂ = 0.28	p
PaO ₂ , mmHg	40 ± 1	67 ± 3	< 0.001	49 ± 2	69 ± 3	< 0.001
CaO ₂ , ml/100ml	12.4 ± 0.6	17.4 ± 0.9	< 0.001	16.7 ± 0.7	18.9 ± 0.7	< 0.001
P \bar{V} O ₂ , mmHg	30 ± 1	43 ± 1	< 0.001	34 ± 1	43 ± 1	< 0.001
C \bar{V} O ₂ , ml/100ml	8.1 ± 0.5	12.8 ± 0.8	< 0.001	12.2 ± 0.5	14.6 ± 0.6	< 0.001
C \bar{V} O ₂ (ml/min/m ²)	4.4 ± 0.2	4.5 ± 0.2	NS	4.5 ± 0.2	4.4 ± 0.2	NS
SVI, ml/m ²	41.9 ± 2.3	40.5 ± 2.1	NS	37.7 ± 2.1	32.9 ± 1.6	< 0.005
RVS _{WI} , gm.m/beat/m ²	17.2 ± 1.6	16.8 ± 1.2	NS	15.3 ± 1.5	13.0 ± 1.1	< 0.01
PAR, mmHg/l/min	4.2 ± 0.3	4.4 ± 0.3	NS	3.8 ± 0.3	4.3 ± 0.4	< 0.05
CI x CaO ₂ (ml/min/m ²)	493 ± 26	672 ± 37	< 0.001	634 ± 26	629 ± 30	NS

The acute hypoxic vasoconstriction may not be the primary determinant of an elevated PAP in COPD-patients during an exacerbation ; other phenomena may account for the increase in PAP .

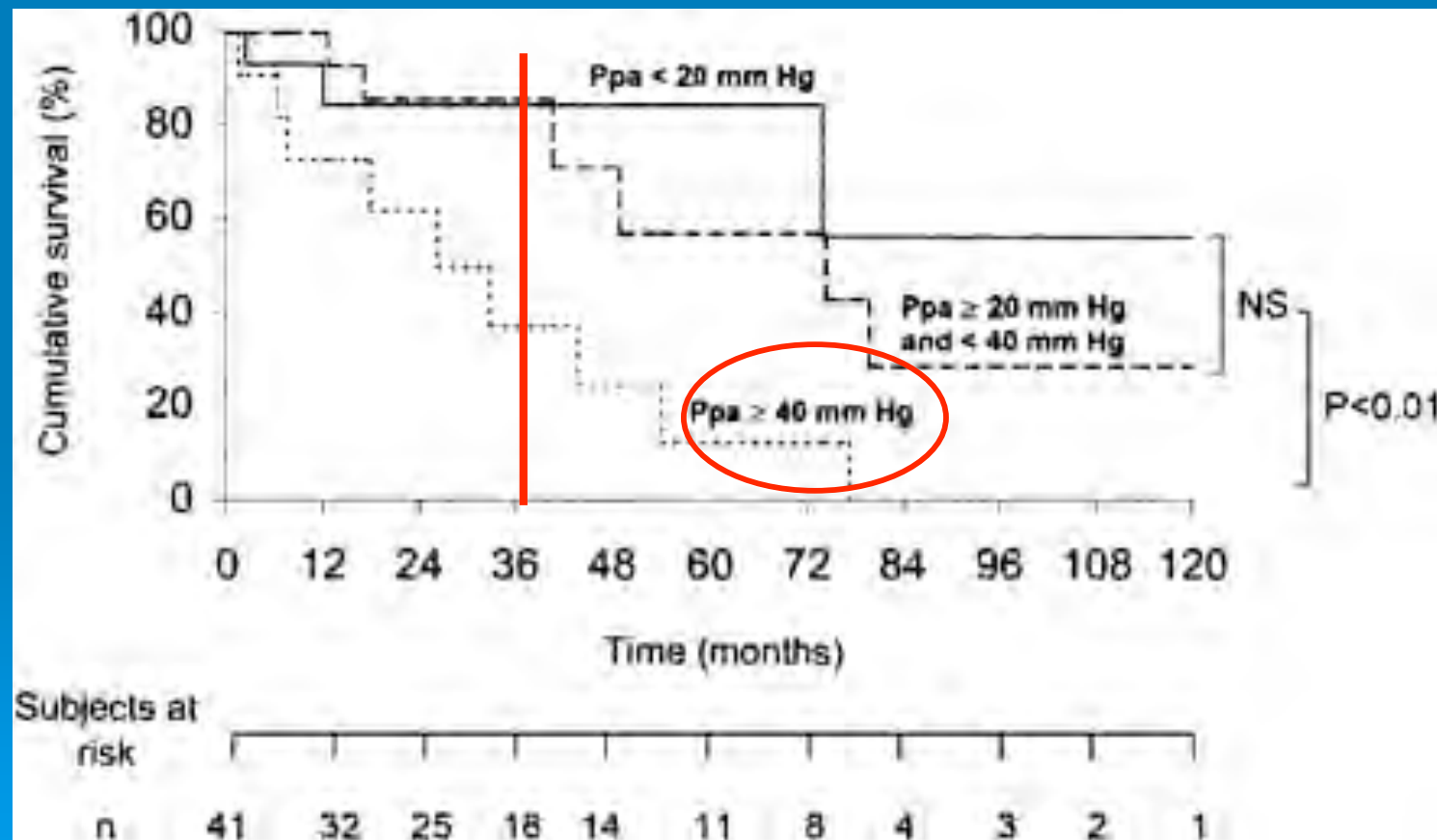
For definition of abbreviations, see table 1.

*DeGaulte JP, Domenighetti G, Naeije R, Vincent JL, Treyvaud D, Perret C
Am Rev Respir Dis. 1981; 124:26-30*

"OUT OF PROPORTION " PH [mPAP \geq 40 mmHg at rest] in COPD PATIENTS

Seems to be a rare disease: 1.1% of 998 pts routinely investigated during a stable condition. Pts are usually severely hypoxaemic but not severely hypercapnic

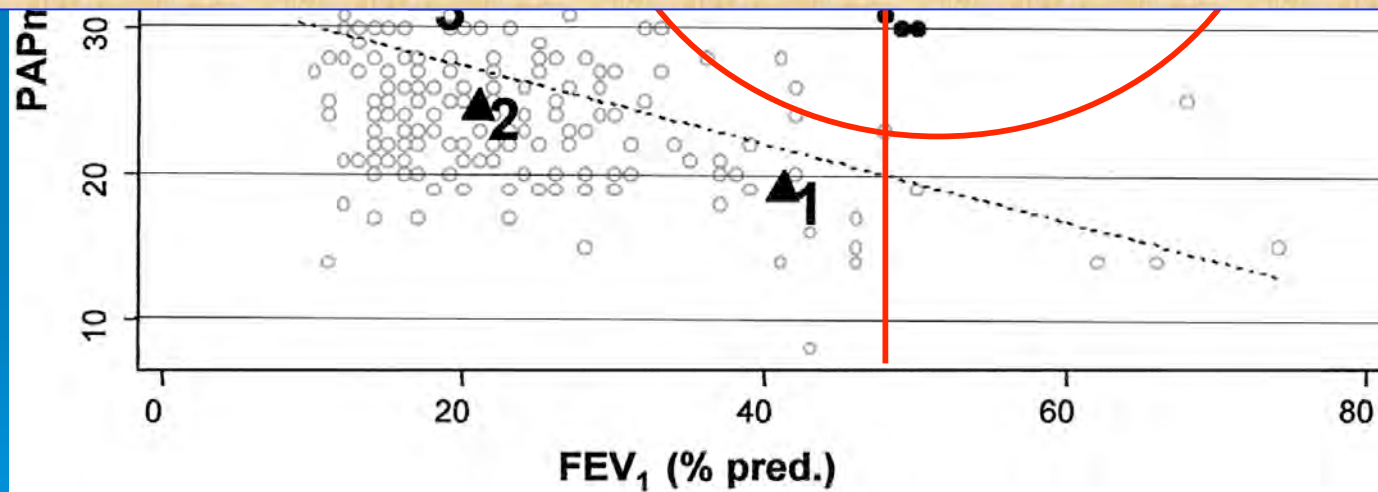
Chaouat A et al AJRCCM 2005; 172 : 189-194



Pulmonary Hemodynamics in Advanced COPD Candidates for Lung Volume Reduction Surgery or Lung Transplantation



The out of proportion PH in COPD-patients merits further investigations, being the incidence rate probably higher than that reported by the Strasbourg group. One basic question here would be to know if this type of PH need to be treated with the new vasodilators in order to improve prognosis.

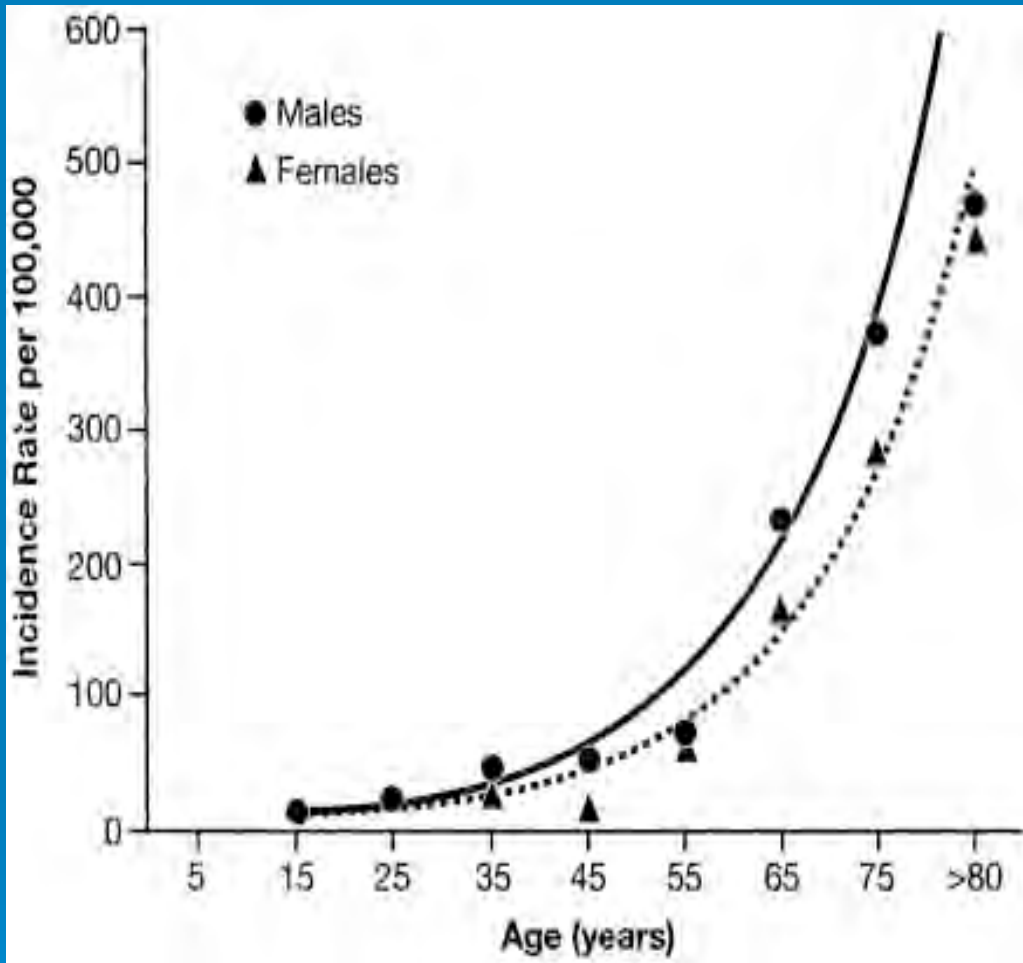


n=215

Group 4: n= 16 = 7,4 %

Thabut, G. et al. Chest 2005;127:1531-1536

ACUTE PULMONARY EMBOLISM



*White RH. Circulation
2003; 107: 1-4-1-8*

Incidence rate
per year
according to
age and gender

PULMONARY EMBOLISM AS A CAUSE OF EXACERBATION IN COPD-PATIENTS

A study showed a prevalence of 25% in 197 COPD-patients admitted for a severe exacerbation (highly selected group; one center study; ventilated COPD-pts were excluded from the analysis)

Tille-Loebund A et al Ann Intern Med 2006; 144: 390-396

Another study (**Should pulmonary embolism be suspected in exacerbation of chronic obstructive pulmonary disease?** *Rutschmann O et al Thorax 2007; 62: 121-125*) demonstrated in 123 consecutive pts

MESSAGES:

- TRUE PREVALENCE RATE IS UNKNOWN
- NO SYSTEMATIC SEARCH OF PE IN AECOPD IS REQUIRED

48 pts who
without clinical



Immobilization >7 d	12 (6)	5 (10)	1.75 (0.85-3.59)	0.177
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* There were 49 patients with PE and 148 patients without PE. COPD = chronic obstructive pulmonary disease; PE = pulmonary embolism.

† For severity of COPD, data were missing for 12 patients with PE.

‡ Data were missing for 37 patients overall.

§ Data were missing for 2 patients without PE.

| Data were missing for 18 patients.

ALI/ARDS

Some facts:

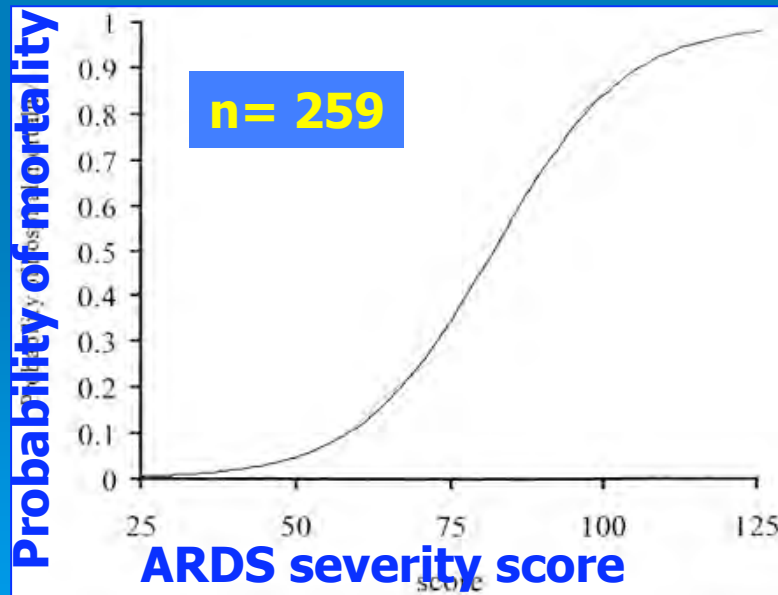
- Acute Cor pulmonale [and PAH] may have an incidence up to 25% in ARDS-patients submitted to a protective ventilation [*Jardin et al. 2003; Vieillard-Baron A et al. 2001*]
- Many factors contribute to PAH [and Cor P.] in ALI/ARDS
- There is some evidence that PAH [and Cor pulmonale] *per se* significantly affects outcome in ARDS [*Monchi M et al. 1998*]

Early Predictive Factors of Survival in the Acute Respiratory Distress Syndrome

A Multivariate Analysis

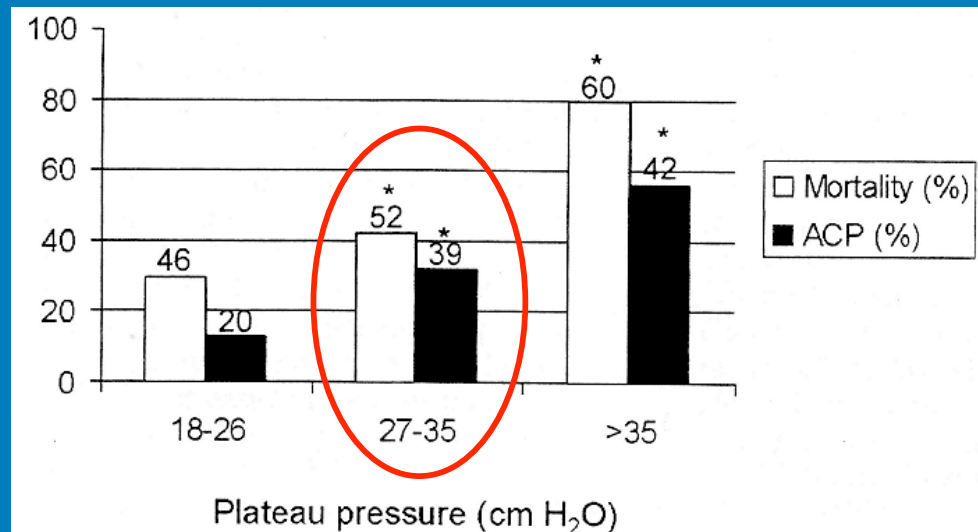
Monchi M et al

Am. J. Respir. Crit. Care Med. 1998, 158: 1076-1081



Among the hemodynamic parameters, only the right ventricular dysfunction retained a significant relationship. Patients who had a P_{RA} higher than the PWP had an OR of 5.1, as compared with those who had a P_{RA} lower or equal to PWP.

INTERACTION BETWEEN PLATEAU PRESSURES, MORTALITY RATE AND INCIDENCE OF ACUTE COR PULMONALE IN ARDS



n=352

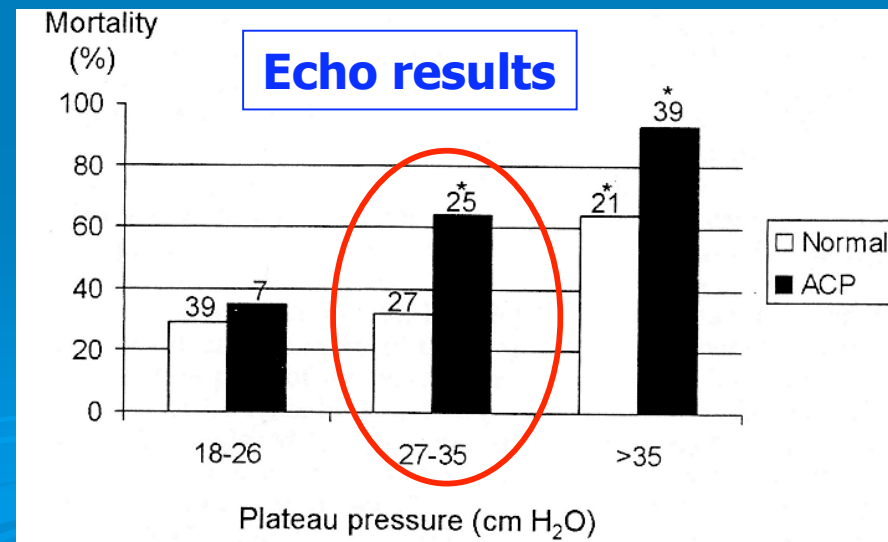
Group I: n=154(18-26cmH₂O)

Group II: n=123 (27-35)

Group III: n=75 (>35)

QUESTIONS :

- Is the threshold for a safe plateau pressure depending on the presence or not of acute cor pulmonale?
- Should the Ppl be kept below 27 cm H₂O in ARDS-patients ?



RVF ASSOCIATED WITH END STAGE PULMONARY VASCULAR DISEASE

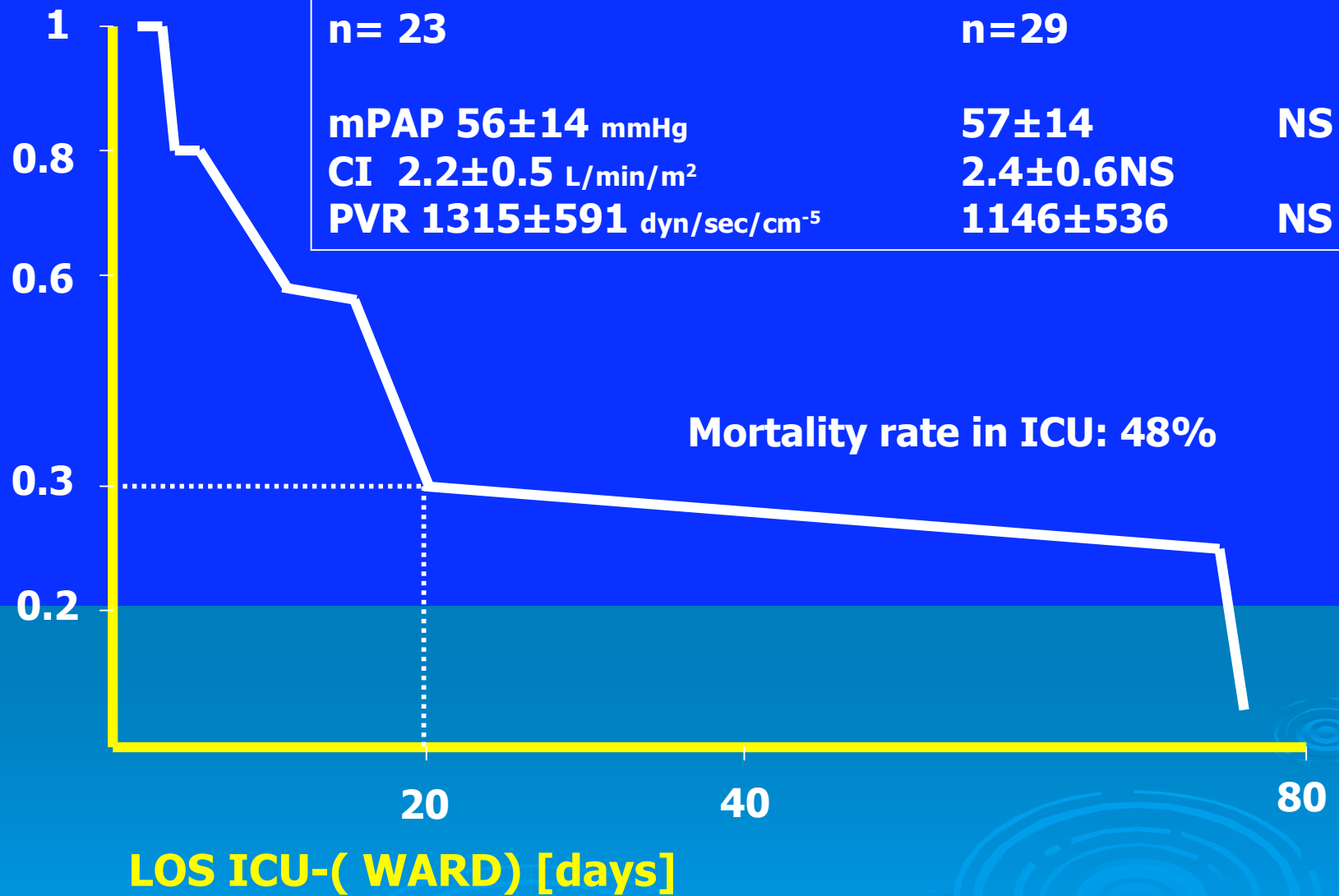


SURVIVAL AND PROGNOSTIC FACTORS OF ACUTE EXACERBATIONS OF PULMONARY HYPERTENSION

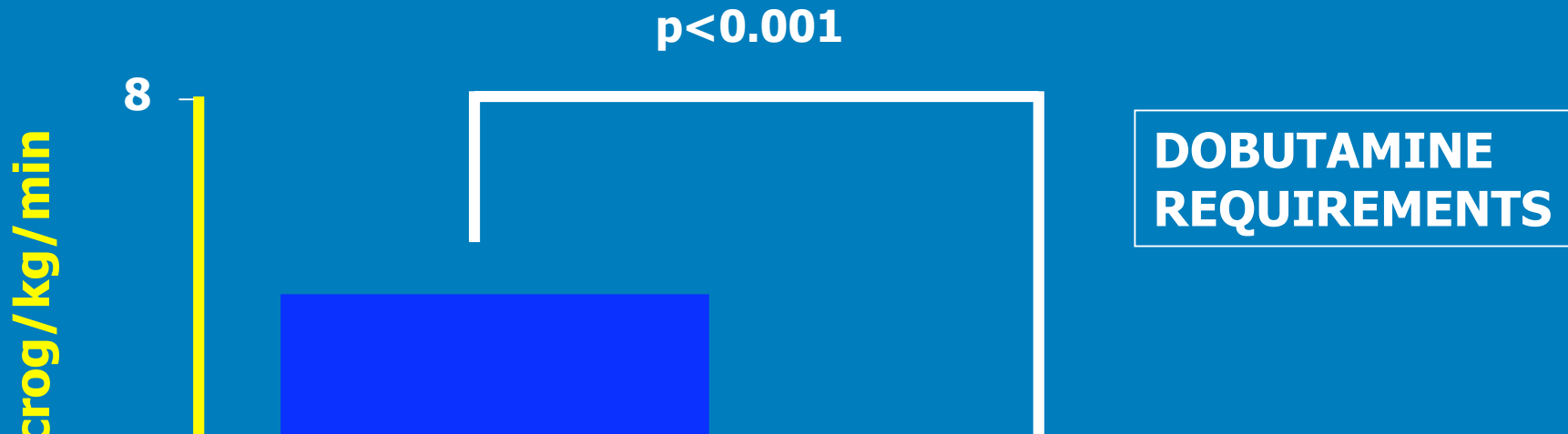
Sztrymf B et al. Poster presentation at the ATS, San Francisco, 2007

- **82 episodes in 46 pts (mean age 50 +/- 16 yrs)**
- **PH known since 4.2 +/- 3.6 yrs**
- **Causes: iPAH/CTEPH/SSc - associated/HIV / portopulmonary**
- **Treated with new drugs or combinations**

CUMULATIVE SURVIVAL [%]



Sztrymf B et al. Poster presentation at the ATS, San Francisco, 2007



CONCLUSION: THE ACUTE ON CHRONIC RH SYNDROME IS A DEVASTATING CONDITION IN PTS WITH PREEXISTING PH REQUIRING THE ICU

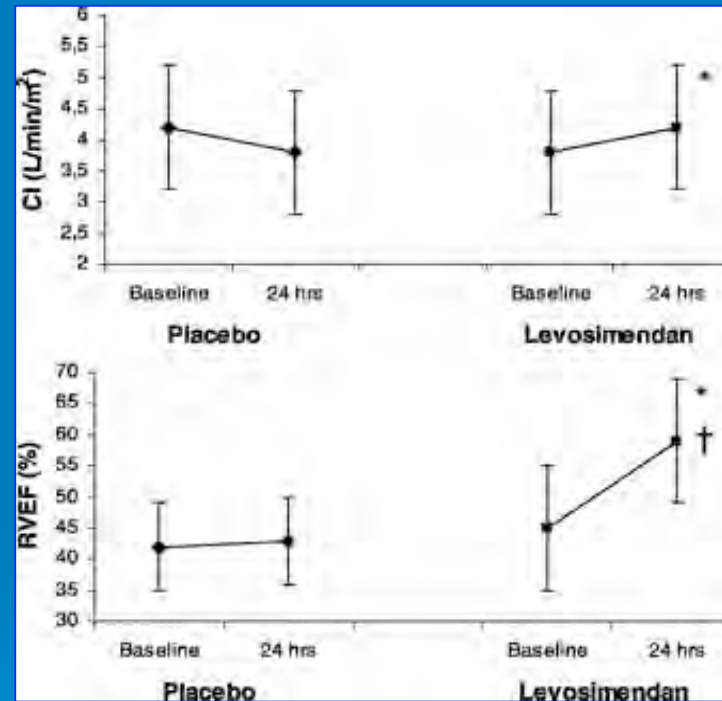
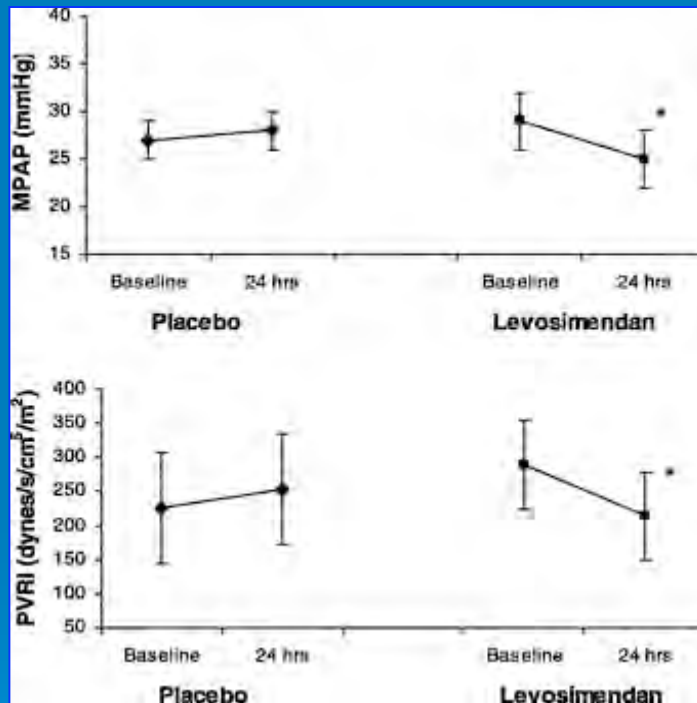
Sztrymf B et al. Poster presentation at the ATS, San Francisco, 2007

The acutely decompensated right ventricle: general therapeutic hints after addressing the primary cause of hemodynamic deterioration

- OXYGEN TREATMENT [different strategies according to the underlying pathology]
- MECHANICAL VENTILATION
- IMPROVEMENT OF LV FILLING [VOLUME]
- ↗ OF RV AND LV CONTRACTILE STRENGTH [INOTROPES]
- MAINTENANCE OF SYSTEMIC BLOOD PRESSURE [PRESSORS]
- MISCELLANEOUS THERAPY: DIURETICS, ACO

Effects of levosimendan on right ventricular afterload in patients with acute respiratory distress syndrome: a pilot study

Morelli A et al, Crit Care Med 2006; 34: 2287-2293



35 patients with ARDS associated with septic shock. Lev.: 0.2 $\mu\text{g}/\text{kg}/\text{min}$ for 24 hours
n = 18 (Lev)
n = 17 (PL)

PULMONARY VASODILATORS IN ICU

- **Parenteral Vasodilators:** i.v. epoprostenol; i.v iloprost
- **Inhaled vasodilators**

Preferred because of selective pulmonary vasodilation

- iNO [*Bhorade S et al. AJRCCM 1999;159: 571-579*] ,
- PGI₂ and analogues [*Hache M et al. Can J Anaesth 2001;48: 924-929. Domenighetti et al. Crit Care Med 2002*]
- **Oral vasodilators, mainly as a crossover therapy**
 - First line: Sildenafil, 12.5-25-50 mg tid [*Case reports*]
 - Medium-long term treatment: Bosentan 62.5-125 mg bid
- **Combination therapies: i.e. iNO / iPGI₂ + Sildenafil**