PRONE POSITION IN ARDS
DECUBITUS VENTRAL DANS LE SDRA

Bordeaux le 15 Novembre 2013

JARCA

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Disclosure of conflict of interests

- NONE

ARRD 1974 C. Bryan. Comments of a devil advocate

WHAT IS THE RATIONALE ?

1. Oxygenation

Early clinical observations showing dramatic improvement of oxygenation in patients with severe ARDS with the proning SESSION

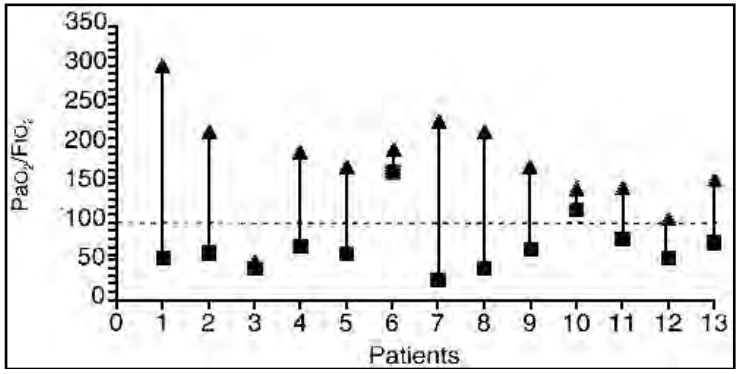
Trauma or secondary ARDS ***Low PEEP high FIO2***

Pt.	Gender (M/F)	Age (yr)	Diagnosis	Complication	Outcome
1	M	33	Multiple trauma	ARDS	Survived
2	F	56	Septicemia	DIC, MOF	Survived
3	F	42	Septicemia	ARDS, DIC	Died
4	M	46	Septicemia	ARDS, MOF	Died
5	M	29	Severe burn	Septicemia	Died
6	M	35	Severe burn	Pneumonia	Survived
7	M	66	Aspiration	Aspiration pneumonia	Survived
8	M	19	Multiple trauma	ARDS	Died
9	M	20	Intoxication	Pneumonia	Survived
10	F	25	Septicemia	ARDS	Survived
11	F	28	Multiple trauma	ARDS	Survived
12	M	60	Intoxication	Aspiration Pneumonia	Survived
13	M	61	Septicemia	ARDS, MOF	Survived

Pt., patient; ARDS, acute respiratory distress syndrome; DIC, disseminated intravascular coagulation; MOF, multiple organ failure.

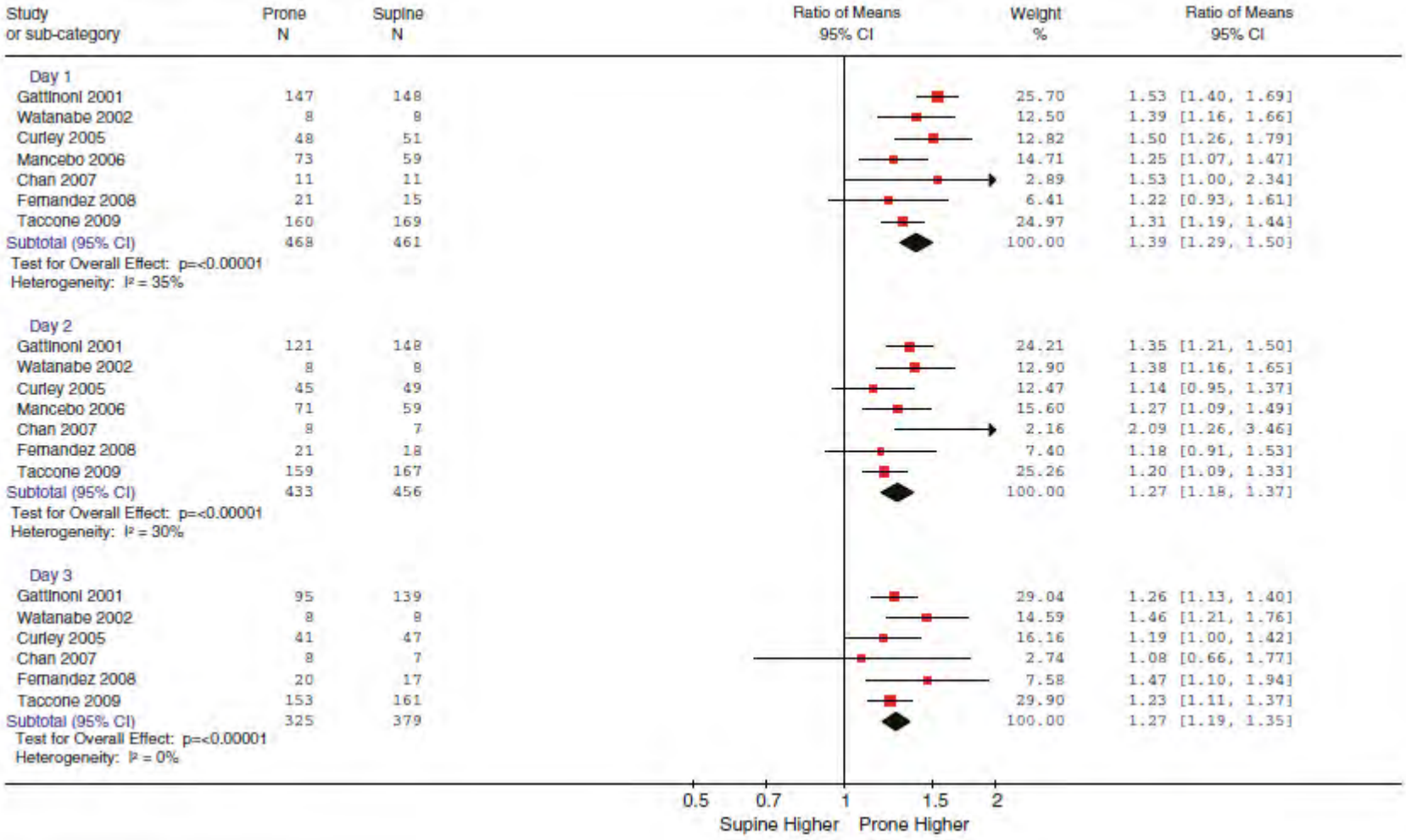
Pt.	$\dot{V}_E$ (L/min)		FIO_2		PEEP (cm H_2O)		PaO_2 (torr)		P(a-a)O_2 (torr)		OI (torr)	
	Before	Prone	Before	Prone	Before	Prone	Before	Prone	Before	Prone	Before	Prone
1	12.2	12.8	1.0	0.4	5	5	52	43	606	167	55	300
2	10.6	10.6	1.0	0.5	5	4	33	35	618	213	62	218
3	8.9	10.6	1.0	1.0	7	2	56	50	616	613	41	50
4	16.6	18.0	0.9	0.4	8	7	41	29	537	177	71	197
5	12.5	11.4	1.0	0.55	10	10	49	59	604	235	68	177
6	11.5	11.5	0.5	0.3	5	5	42	38	232	116	165	200
7	12.1	13.2	1.0	0.85	5	5	42	33	644	137	27	229
8	14.4	15.1	1.0	0.4	10	10	57	42	615	154	41	220
9	10.2	10.1	0.75	0.5	6	6	35	32	450	236	67	177
10	8.0	7.9	0.55	0.5	5	9	44	38	283	245	117	146
11	9.7	9.5	0.75	0.5	10	10	47	50	429	235	80	143
12	13.7	14.0	1.0	0.8	9	10	41	38	616	447	56	106
13	15.5	15.2	0.95	0.75	9	10	50	42	556	377	75	155
Mean	11.99	12.30	0.88	0.53	7.08	7.15	45.3	40.7	524	258	71.2	178.3
± SD	2.56	2.77	0.18	0.20	2.18	2.82	7.4	8.4	136	141	35.8	61.9
p Value	NS		<.0001		NS		<.05		<.0001		<.0002	

Pt., patient. To convert torr to kPa, multiply the value by 0.1333.

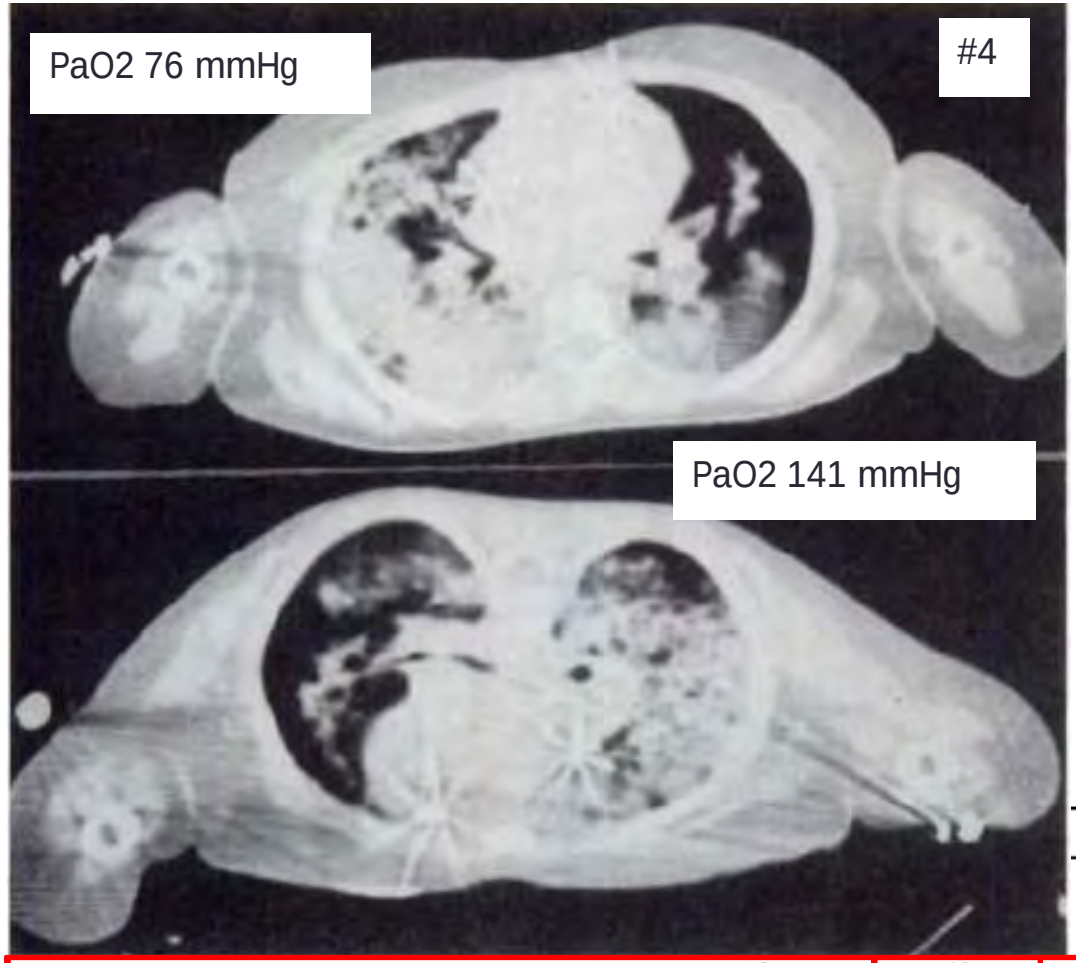


"We conclude that treatment in the prone position has a dramatic positive effect on the gravely impaired gas exchange seen in connection with severe acute lung insufficiency. As the first means of treatment, it should also be used before more complex treatment modalities such as nitric oxide and ECMO". Mure et al. CCM 1997

Better oxygenation in the proning ARM



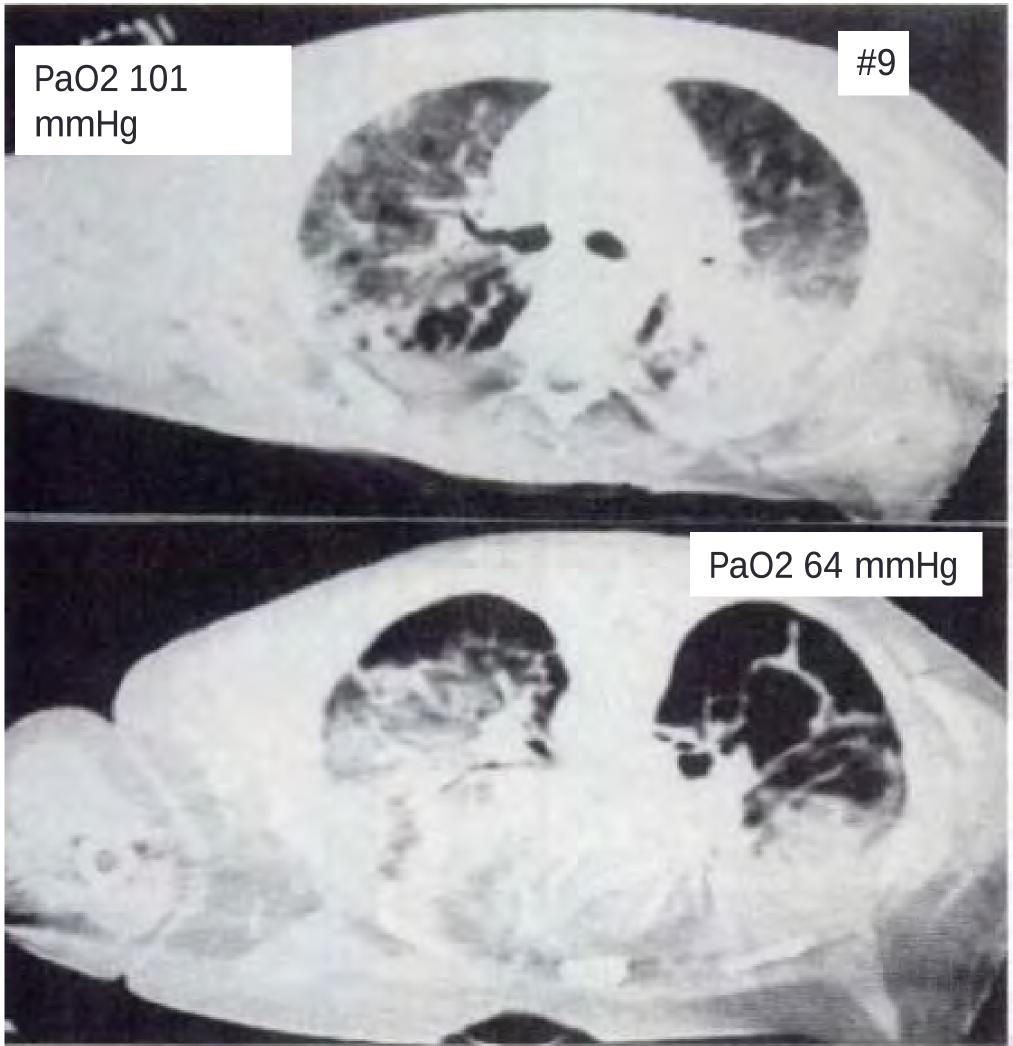
Sud et al. ICM 2010



1	Bacterial pneumonia						
2	Sepsis, pulmonary embolism (?)						
3	Aspiration pneumonia						
4	Viral pneumonia						
5	Bacterial pneumonia						
6	Blunt chest trauma, pneumonia						
7	Sepsis, aspiration pneumonia						
8	Blunt chest trauma						
9	Viral pneumonia						
10	Sepsis, restrictive lung disease						
11	Blunt chest trauma						
12	Bacterial pneumonia						
13	Viral pneumonia						

					VE, L/min	RR, L/min	FIO_2, %
					7.0	15	50
					11.0	15	50
					1.7	5	50*
4	23	450	28	10	7.5	17	60
5	59	1400	28	10	12.7	15	40
6	41	1500	47	10	10.5	16	60
7	26	653	32	10	7.8	16	60
8	13	525	45	20	1.1	5	90*
9	29	750	38	10	10.8	16	60
10	16	363	35	10	10.5	16	60
11	52	1060	26	12	13.0	16	80
12	42	1000	23	8	11.7	19	65
13	22	320	64	24	3.7	5	100*

Langer Chest 1988



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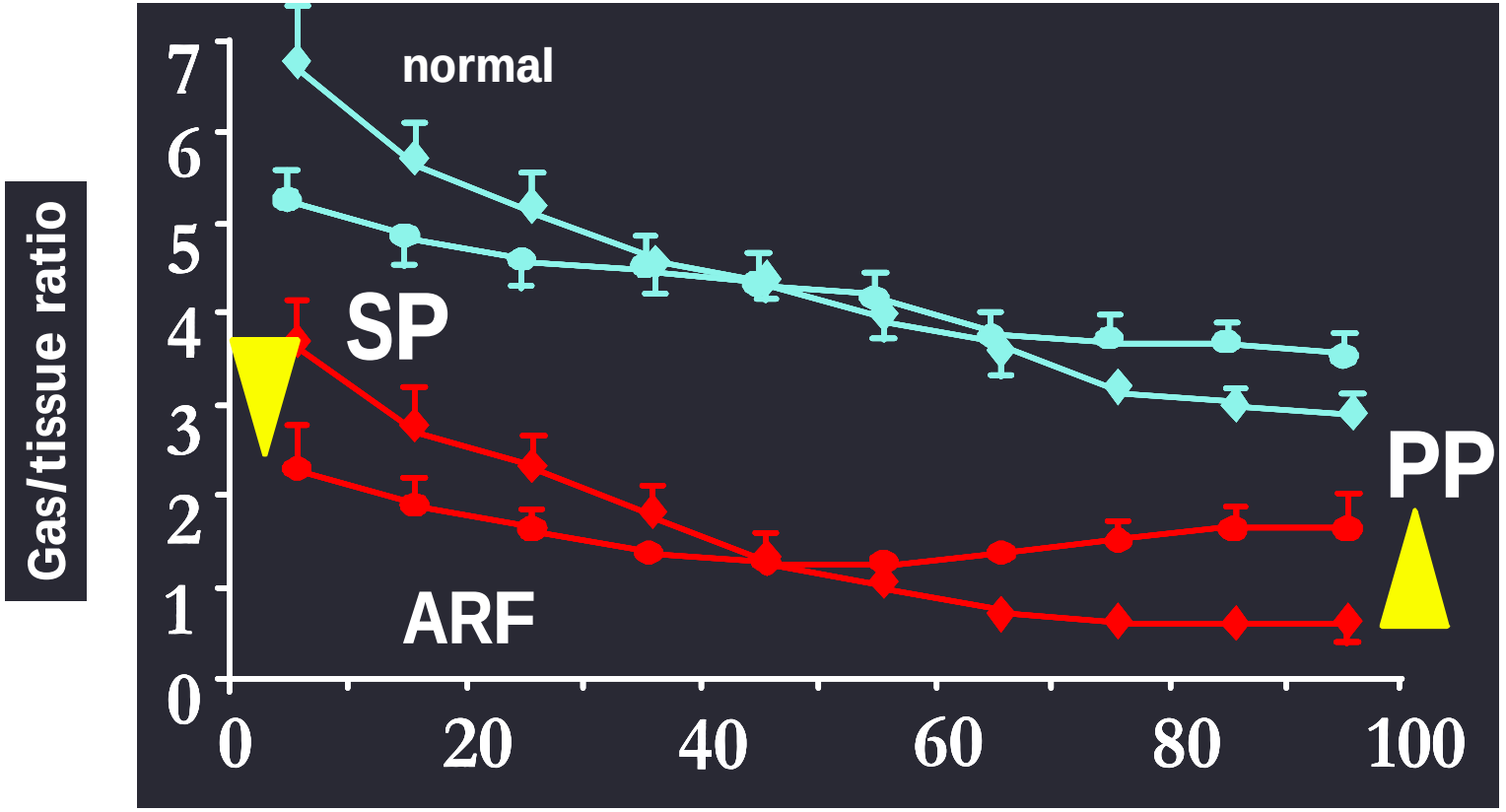
Langer Chest 1988

With prone, reduction in density in dorsal lung regions (increase in G/T ratio) is offset by increase in lung density in the ventral now dependent lung regions (decrease in G/T ratio).



10 patients with ARF
VT 10 ml/kg MBW, PEEP 11 cm H2O, FIO2 0.58

Gattinoni Anesthesiology 1991

Improvement in oxygenation with prone position in ARDS

Dorsal recruitment > ventral derecruitment

+

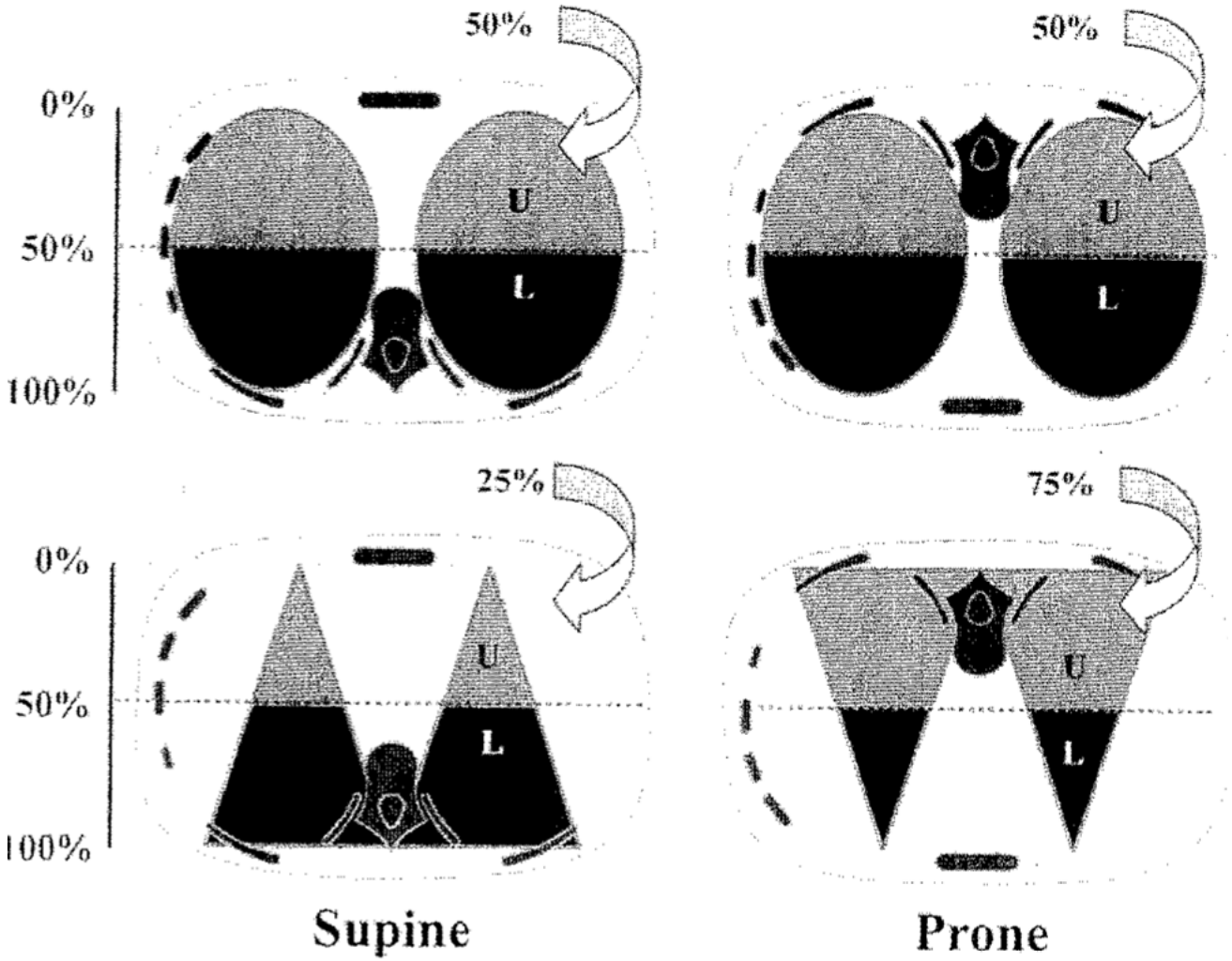
Lung perfusion still prevalent in the dorsal regions

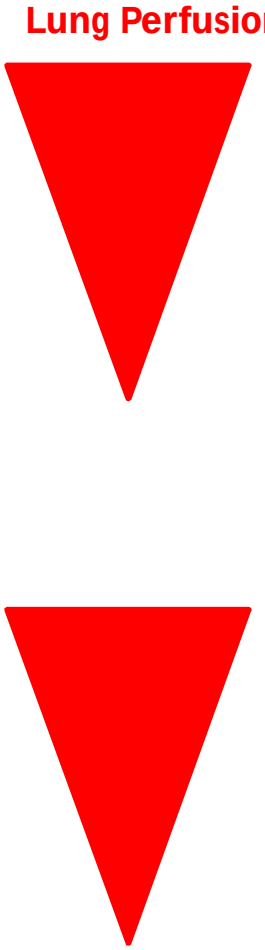
More ventilation in perfused lung areas

Intra-pulmonary shunt

The triangular shape of the lung into the thorax should promote prevalence of Dorsal recruitment over ventral derecruitment

From Gattinoni et al.



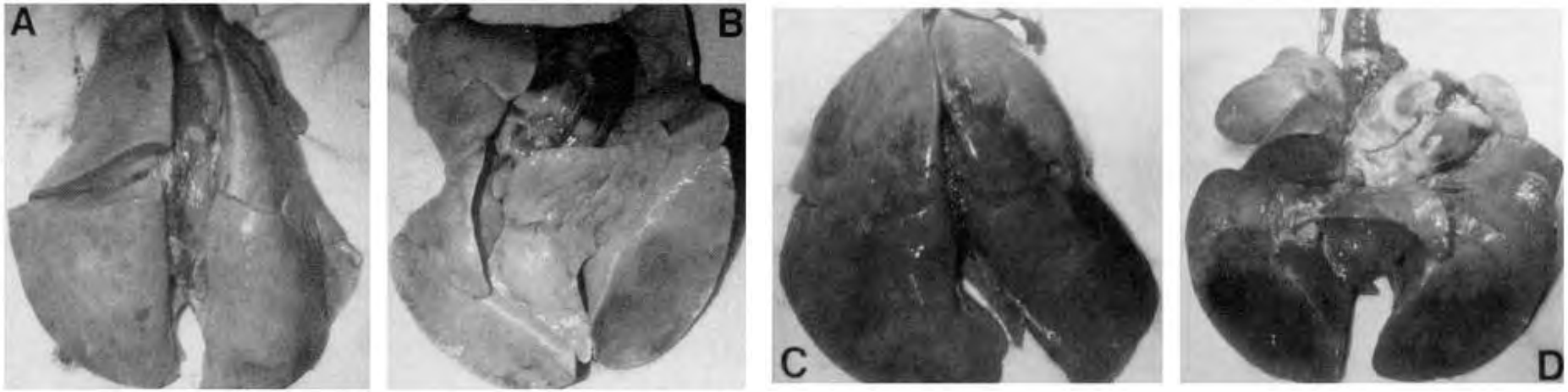


WHAT IS THE RATIONALE ?

2. Reduction in Ventilator-Induced Lung Injury

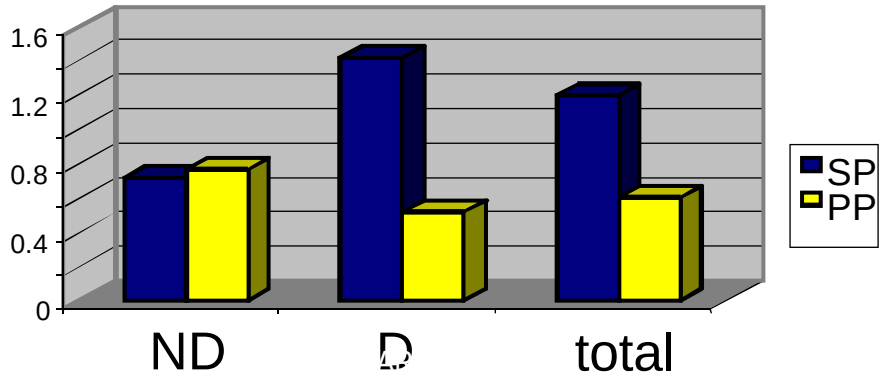
- Direct evidence in normal dogs ***(Broccard 2000)***

Normal dogs, V_T = 77 ml/kg, Pplat,L = 35 cm H_2O



Prone 6 hours

Supine 6 hours



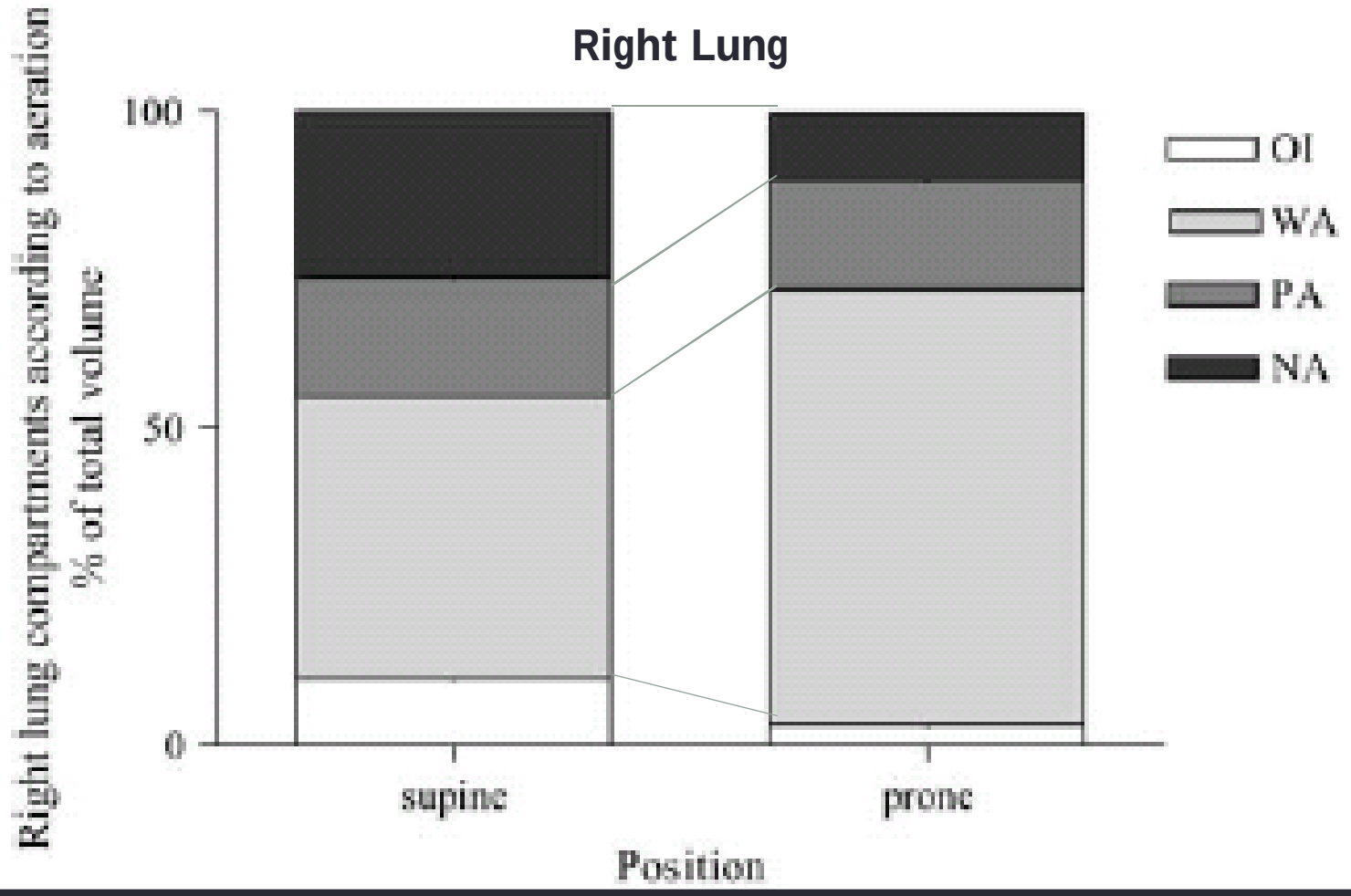
Broccard et al.
CCM 2000

WHAT IS THE RATIONALE ?

2. Reduction in Ventilator-Induced Lung Injury

- Prone position makes the followings more homogeneously distributed: lung density (Gattinoni Anesthesiology 1991), lung ventilation (Richard 2008), intra-pulmonary shunt (Richter 2005) and trans-pulmonary pressure (Mutoh 1992)
- Therefore, applied to an homogeneous lung the distribution of the lung stress and strain due to mechanical ventilation is also more homogeneously distributed
- Furthermore, global stress and strain are reduced in prone position (Mentzelopoulos 2005, Galiastou 2006, Cornejo 2013)

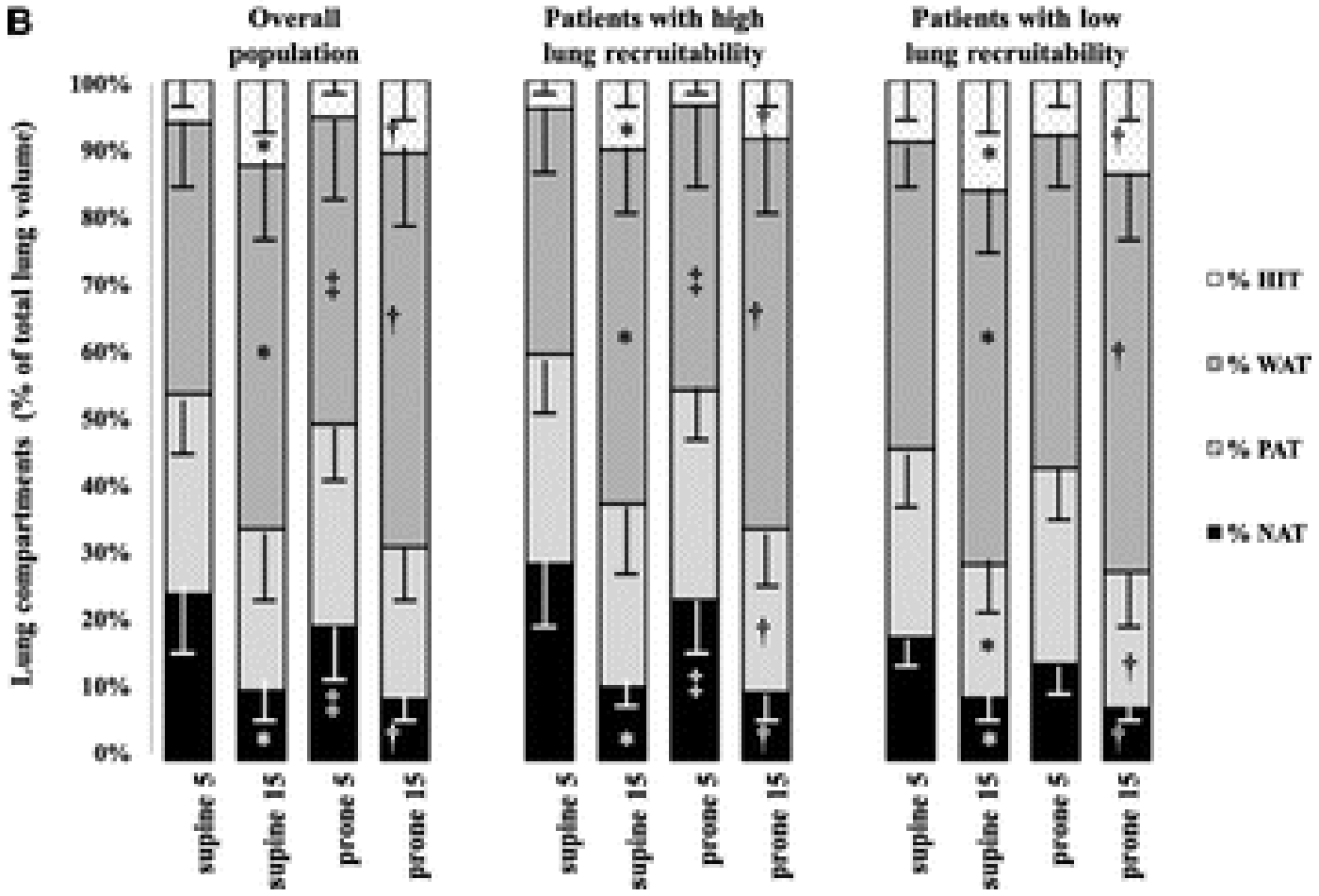
Alveolar recruitment + less hyperinflation



Mostly in LOBAR ARDS as compared to DIFFUSE ARDS

Galiastou AJRCCM 2006

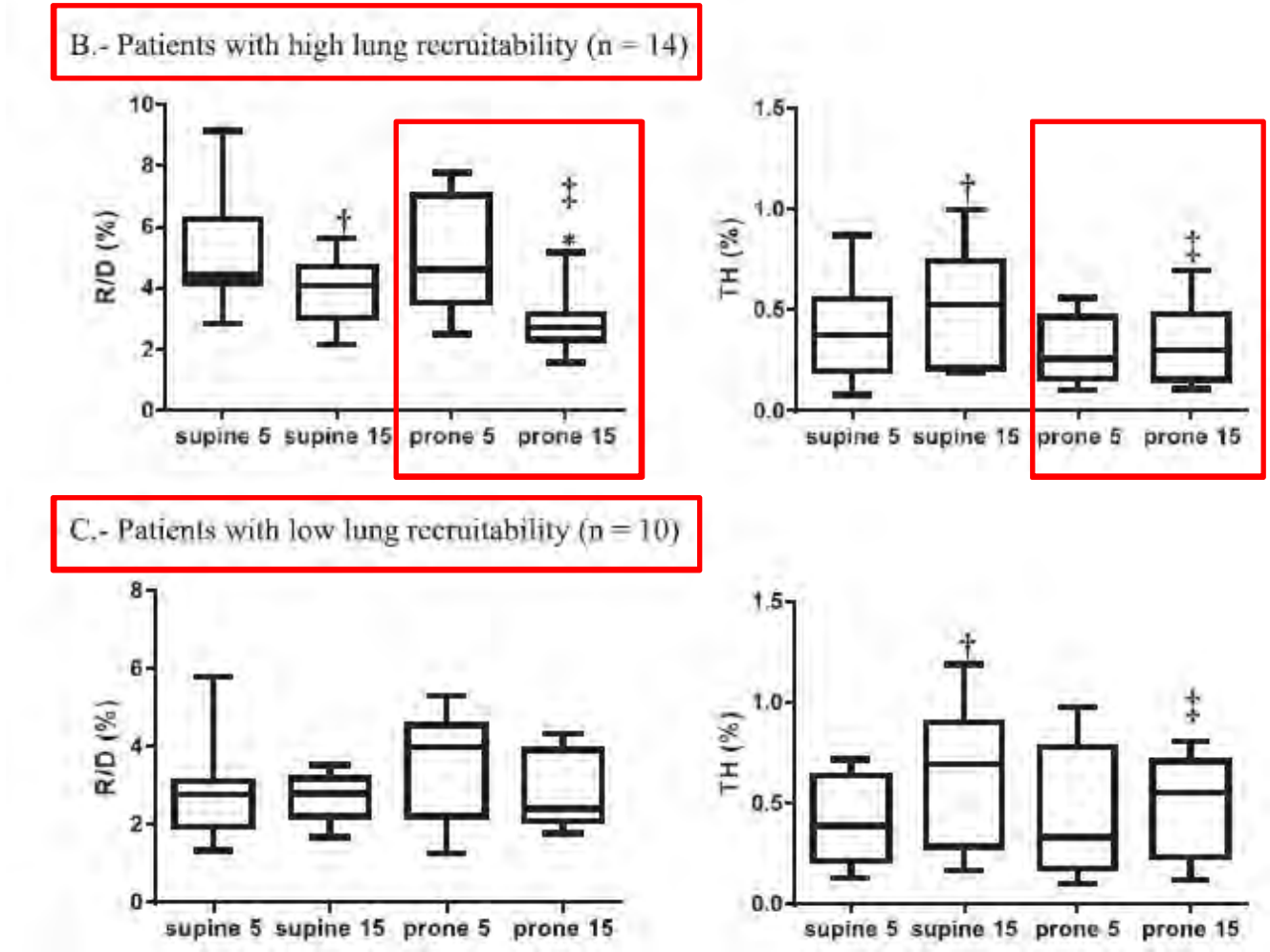
Alveolar recruitment + less hyperinflation



In both low and high recruiters

Cornejo et al. AJRCCM 2013

Recruitement/derecruitment + tidal hyperinflation



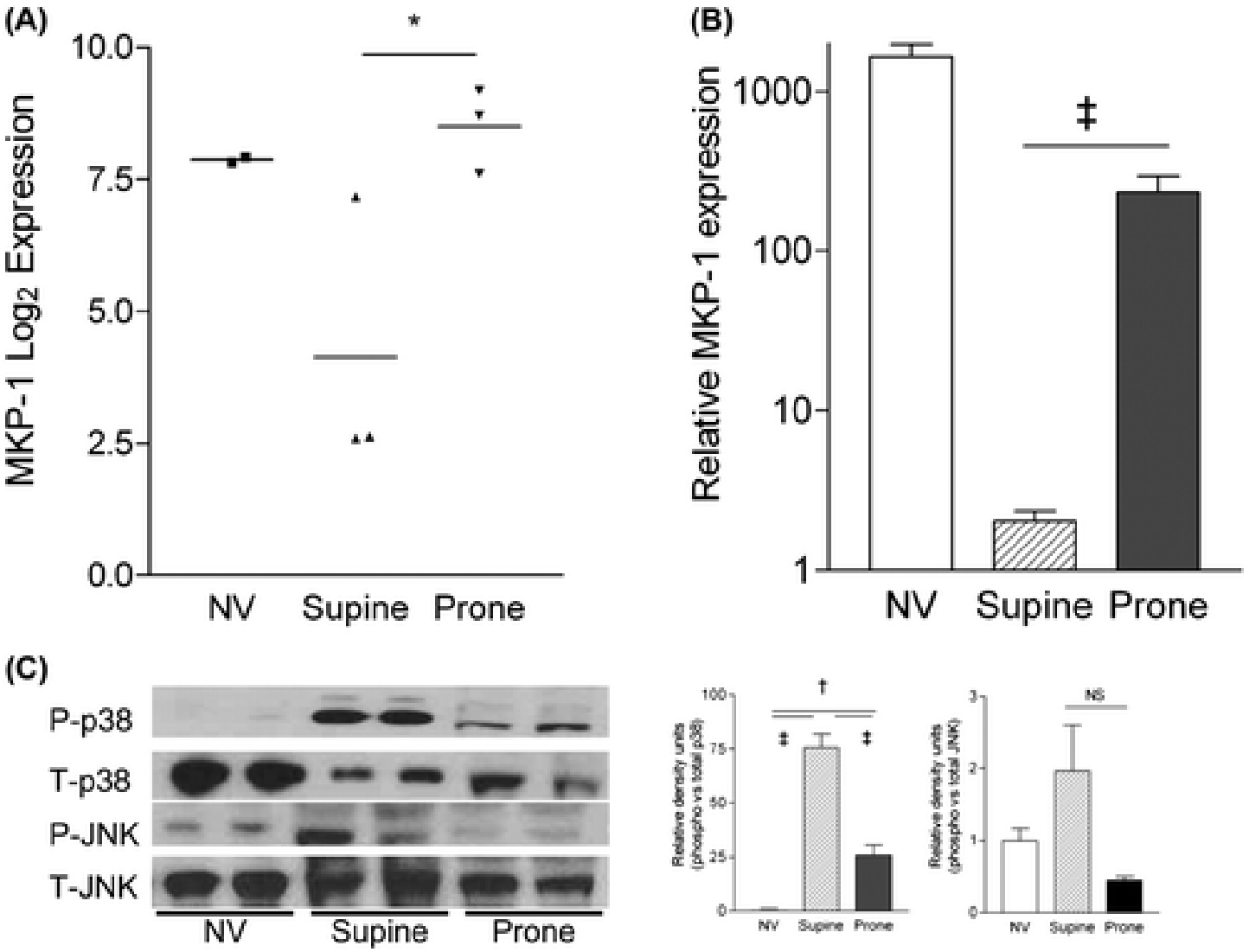
In RECRUITERS at High PEEP not in NON RECRUITERS

Cornejo et al. AJRCCM 2013

WHAT IS THE RATIONALE ?

2. Reduction in Ventilator-Induced Lung Injury

- Biotrauma is reduced (Papazian 2005)

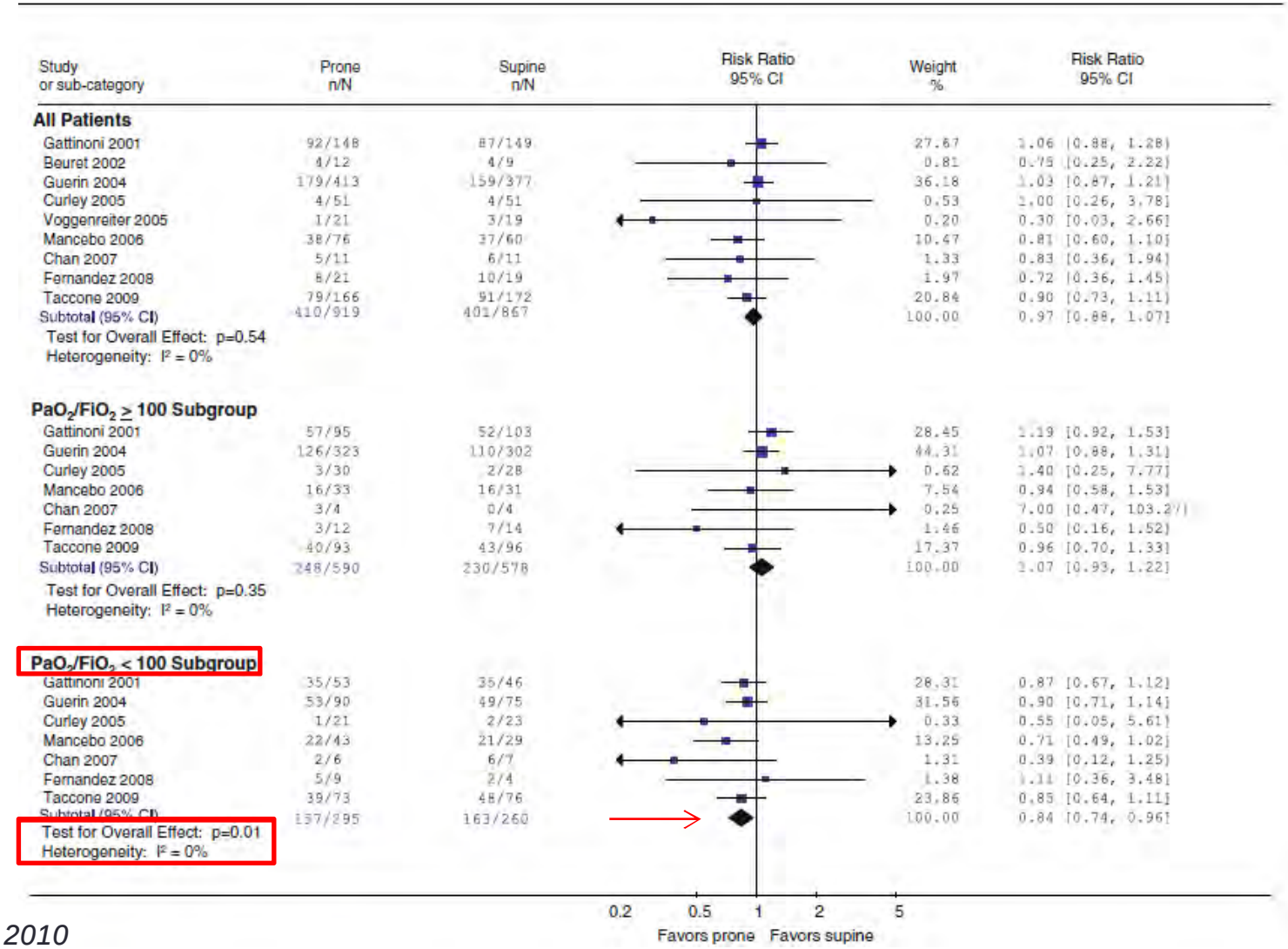


Park et al. AJRCCM 2012

Prone ventilation modulates the expression of Mitogen Activated protein kinase phosphatase 1 in rats subjected to high VT (18 ml/kg PEEP 0) and reduces kinase activation.

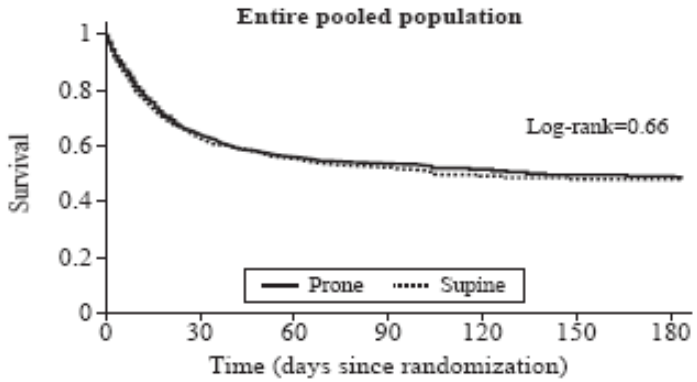
WHAT IS THE EVIDENCE ?

Meta-analysis on grouped data



Sud ICM 2010

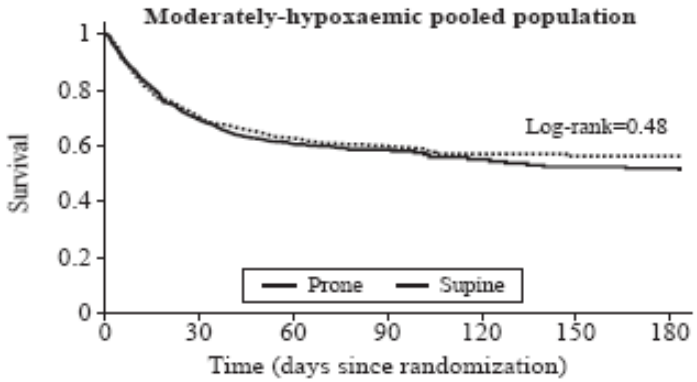
Individual data meta-analysis



No. at risk

Prone	764	467	399	368	148	143	143
Supine	809	501	421	394	155	149	148

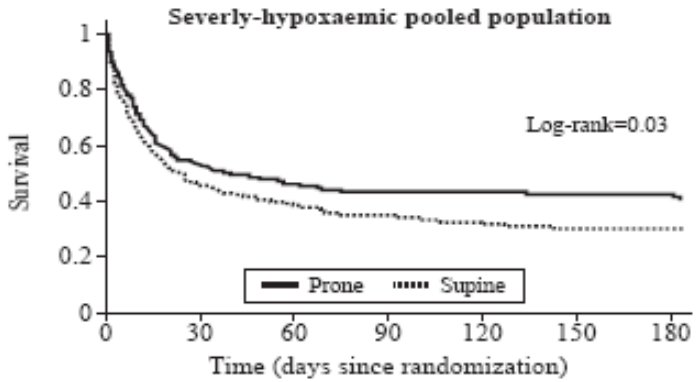
A



No. at risk

Prone	538	369	319	297	106	104	104
Supine	549	373	317	301	100	95	94

B



No. at risk

Prone	226	98	80	71	41	40	40
Supine	260	128	140	93	55	54	54

C

Gattinoni et al. Minerva Anesthesiologica 2010

Figure 3.—Kaplan-Meier estimates of survival rates at the latest follow-up of the prone (magenta line) and supine (green line) patients from the studies included in the pooled analysis of the four largest existing trials [15, 16, 18, 20] investigating the effects of prone positioning: entire pooled population (A), moderately hypoxemic patients (B) and severely hypoxemic patients (C) from the same pooled population.

The NEW ENGLAND JOURNAL of MEDICINE **2013, June 6th**

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*

Specific Features

1. ARDS criteria **confirmed** after 12-24 hours
2. ARDS with **severity criteria**

   PaO2/FiO2 < 150 mmHg FIO2 ≥ 0.6 + PEEP ≥ 5 cm H2O + VT 6 ml/kg PBW
3. Several **non inclusion criteria**
4. Strict **Lung Protective mechanical ventilation** in both groups
5. First session started **within the hour** after randomization
6. Proning sessions of **at least 16 consecutive hours**
7. Predetermined **stopping criteria** of proning
8. **Cross over not allowed** except as life saving procedure
9. **Neuromuscular blockade** in both groups
10. Centers with **expertise** in proning for many years

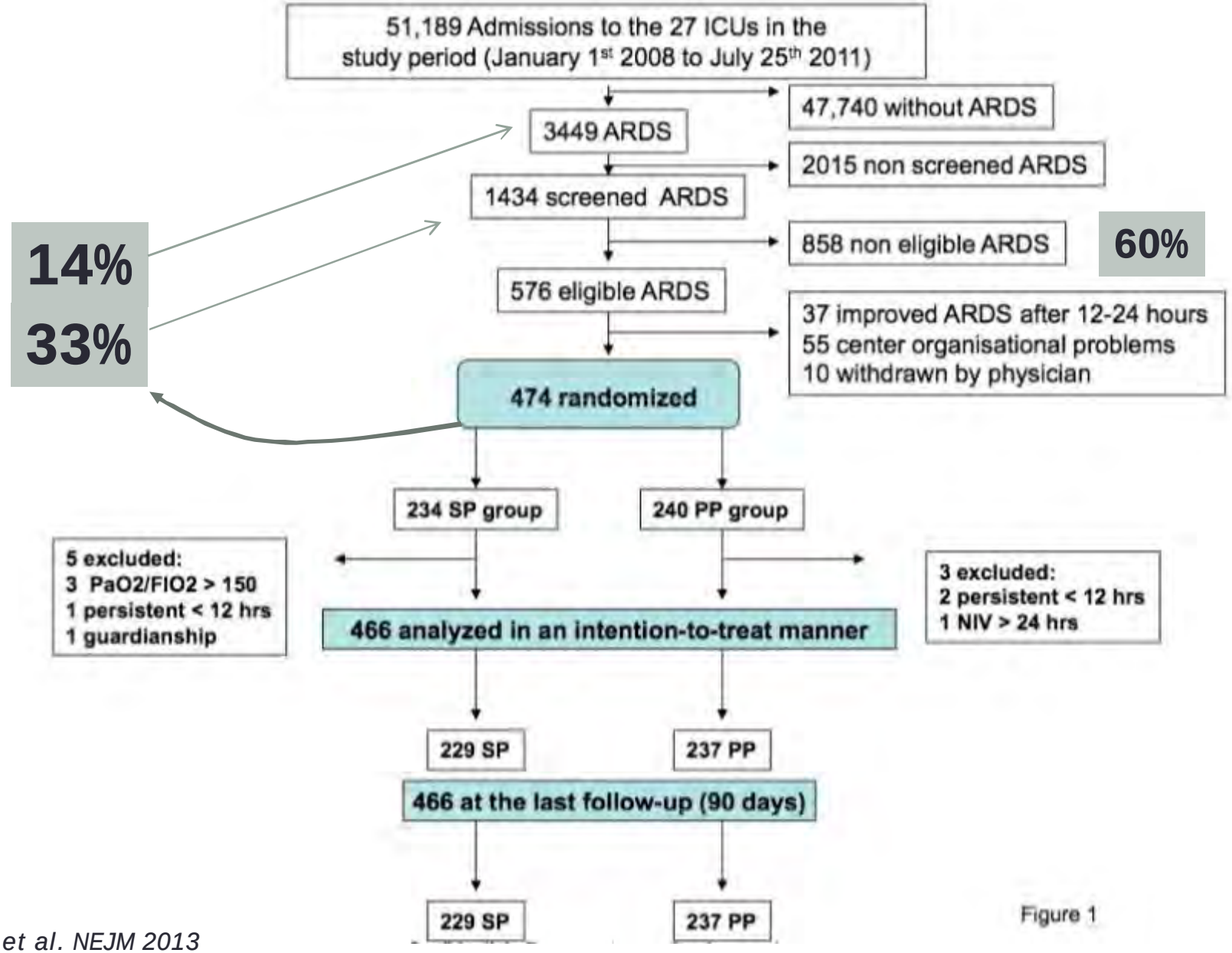


Figure 1

Guérin et al. NEJM 2013

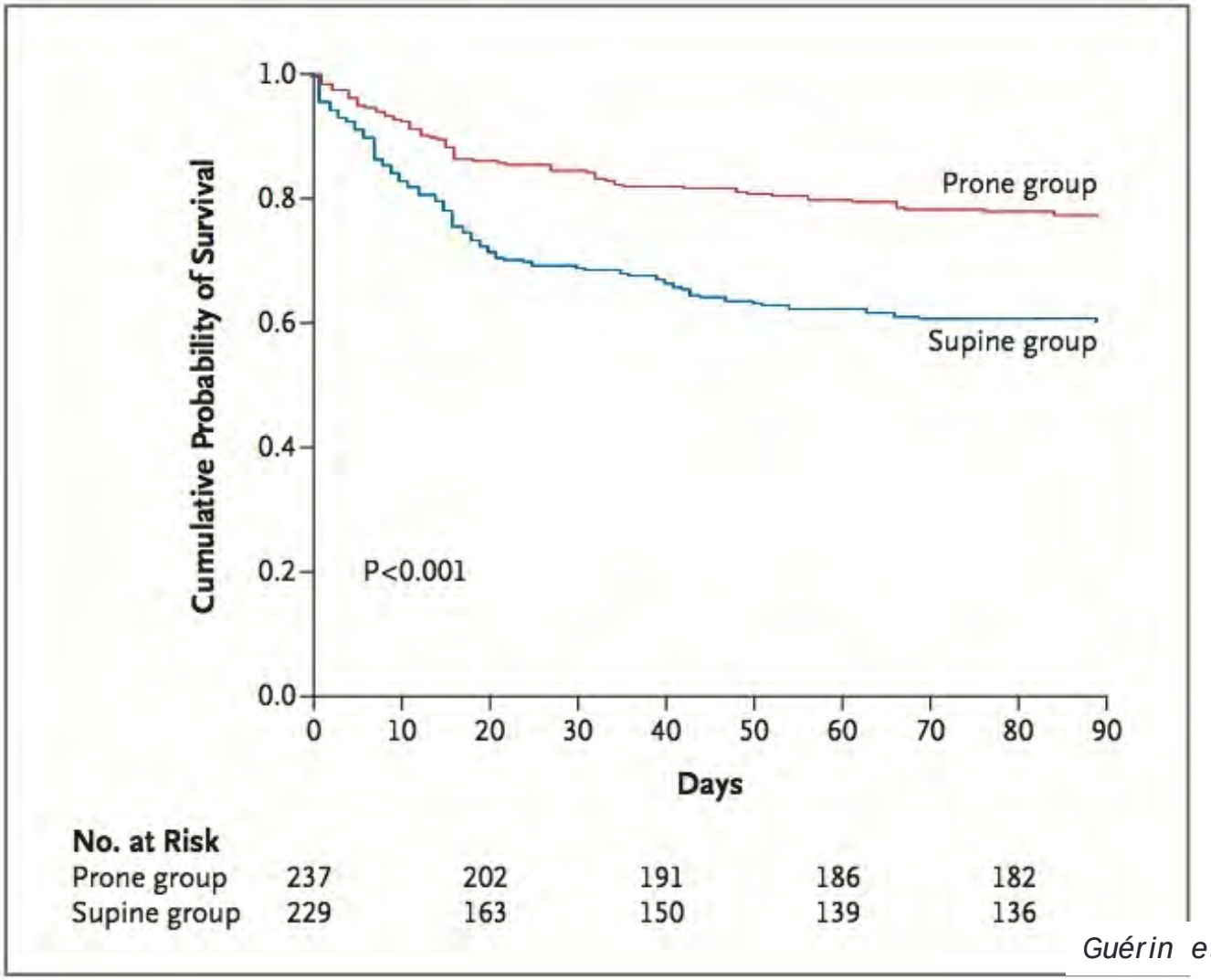
Major outcome

Table 3. Primary and Secondary Outcomes According to Study Group.*

Outcome	Supine Group (N=229)	Prone Group (N=237)	Hazard Ratio or Odds Ratio with the Prone Position (95% CI)	P Value
Mortality — no. (% [95% CI])				
At day 28				
Not adjusted	75 (32.8 [26.4–38.6])	38 (16.0 [11.3–20.7])	0.39 (0.25–0.63)	<0.001
Adjusted for SOFA score†			0.42 (0.26–0.66)	<0.001
At day 90				
Not adjusted	94 (41.0 [34.6–47.4])	56 (23.6 [18.2–29.0])	0.44 (0.29–0.67)	<0.001
Adjusted for SOFA score†			0.48 (0.32–0.72)	<0.001
Successful extubation at day 90 — no./total no. (% [95% CI])	145/223 (65.0 [58.7–71.3])	186/231 (80.5 [75.4–85.6])	0.45 (0.29–0.70)	<0.001

Guérin et al. NEJM 2013

Major outcome



Guérin et al. NEJM 2013

Complications

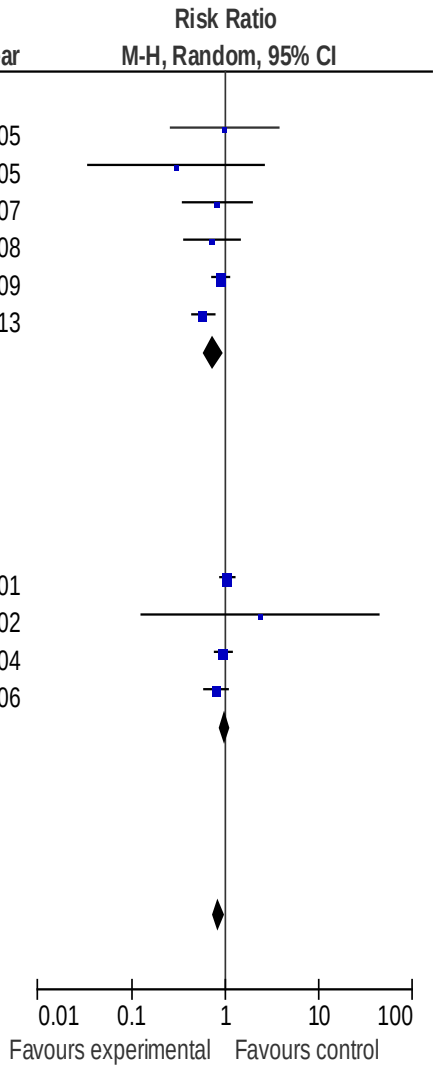
N° (%)	SP group (n=229)	PP group (n=237)	P value
Unscheduled extubation	25 (10.9)	31 (13.1)	0.473
Main stem bronchus intubation	5 (2.2)	6 (2.5)	0.804
Endotracheal tube obstruction	5 (2.2)	11 (4.9)	0.141
Hemoptysis	12 (5.2)	6 (2.5)	0.129
Pneumothorax requiring chest tube	13 (5.7)	15 (6.3)	0.767
Cardiac arrest	31 (13.5)	16 (6.8)	0.015
SpO2<85% or PaO2<55mmHg (< 7,3 kPa) > 5 minutes	164 (71.6)	155 (65.4)	0.149
Heart Rate<30/min>1 minute	27 (11.8)	26 (11.0)	0.780
SBP < 60 mmHg>5 minutes	48 (21.0)	35 (14.8)	0.081

CONCLUSIONS of our trial

- Prone positioning reduced mortality
  - In patients with confirmed ARDS + with severity criteria
  - (Who were highly selected by study design)
  - For long sessions
  - In centers with the expertise for the procedure

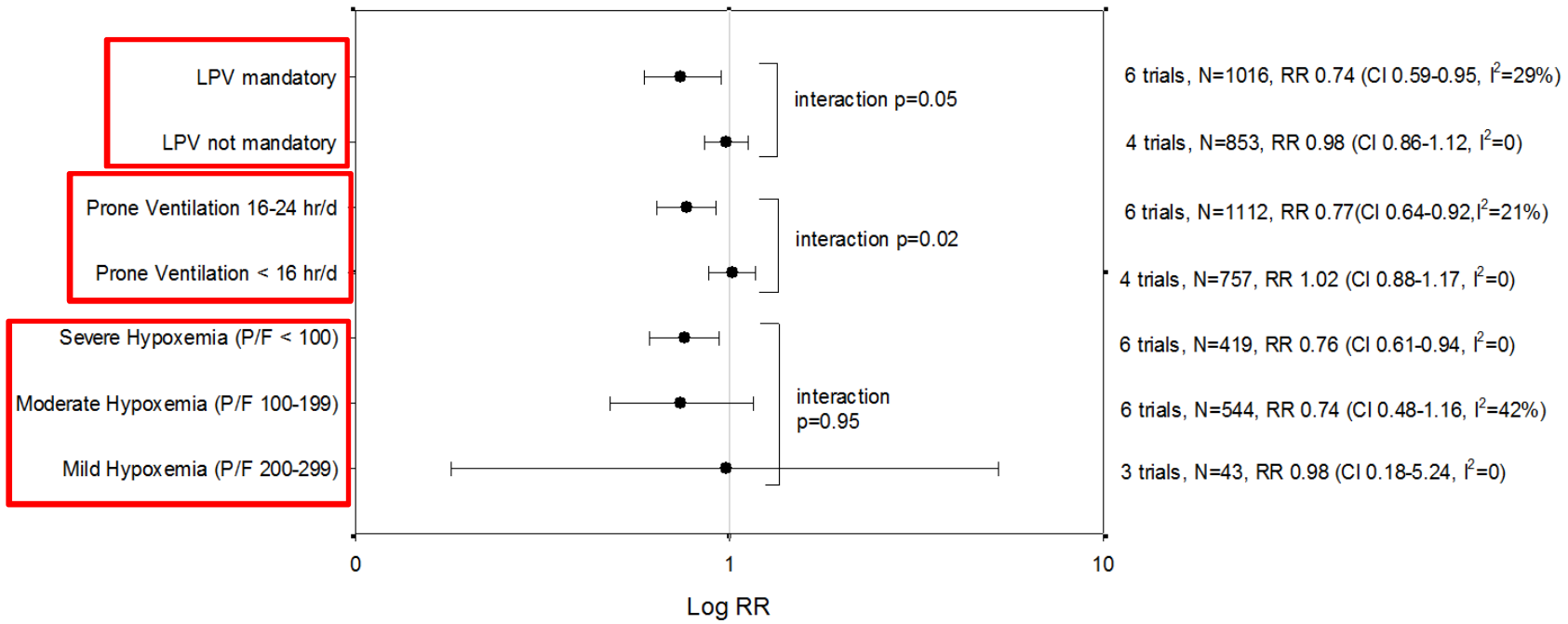
Post-proseva Meta-analysis

Study or Subgroup	Prone Events	Prone Total	Supine Events	Supine Total	Weight	Risk Ratio M-H, Random, 95% CI	Year	Risk Ratio M-H, Random, 95% CI
2.27.1 used Lung Protective Ventilation								
Curley 2005	4	51	4	51	1.4%	1.00 [0.26, 3.78]	2005	
Voggenreiter 2005	1	21	3	19	0.5%	0.30 [0.03, 2.66]	2005	
Chan 2007	5	11	6	11	3.2%	0.83 [0.36, 1.94]	2007	
Fernandez 2008	8	21	10	19	4.5%	0.72 [0.36, 1.45]	2008	
Taccone 2009	79	166	91	172	19.5%	0.90 [0.73, 1.11]	2009	
Guerin 2013	57	240	95	234	15.8%	0.58 [0.44, 0.77]	2013	
Subtotal (95% CI)		**510**		**506**	**44.9%**	**0.74 [0.59, 0.95]**		
Total events	154		209					
Heterogeneity: Tau² = 0.02; Chi² = 7.01, df = 5 (P = 0.22); I² = 29%								
Test for overall effect: Z = 2.40 (P = 0.02)								
2.27.2 did not use Lung Protective Ventilation								
Gattinoni 2001	92	148	87	149	21.4%	1.06 [0.88, 1.28]	2001	
Beuret 2002	1	4	0	3	0.3%	2.40 [0.13, 44.41]	2002	
Guerin 2004	98	230	81	183	19.0%	0.96 [0.77, 1.20]	2004	
Mancebo 2006	38	76	37	60	14.5%	0.81 [0.60, 1.10]	2006	
Subtotal (95% CI)		**458**		**395**	**55.1%**	**0.98 [0.86, 1.12]**		
Total events	229		205					
Heterogeneity: Tau² = 0.00; Chi² = 2.69, df = 3 (P = 0.44); I² = 0%								
Test for overall effect: Z = 0.29 (P = 0.77)								
Total (95% CI)		**968**		**901**	**100.0%**	**0.86 [0.73, 1.00]**		
Total events	383		414					
Heterogeneity: Tau² = 0.02; Chi² = 15.65, df = 9 (P = 0.07); I² = 42%								
Test for overall effect: Z = 1.90 (P = 0.06)								
Test for subgroup differences: Chi² = 3.93, df = 1 (P = 0.05), I² = 74.6%								



Sud S et al. JAMA submitted

Post-proseva Meta-analysis



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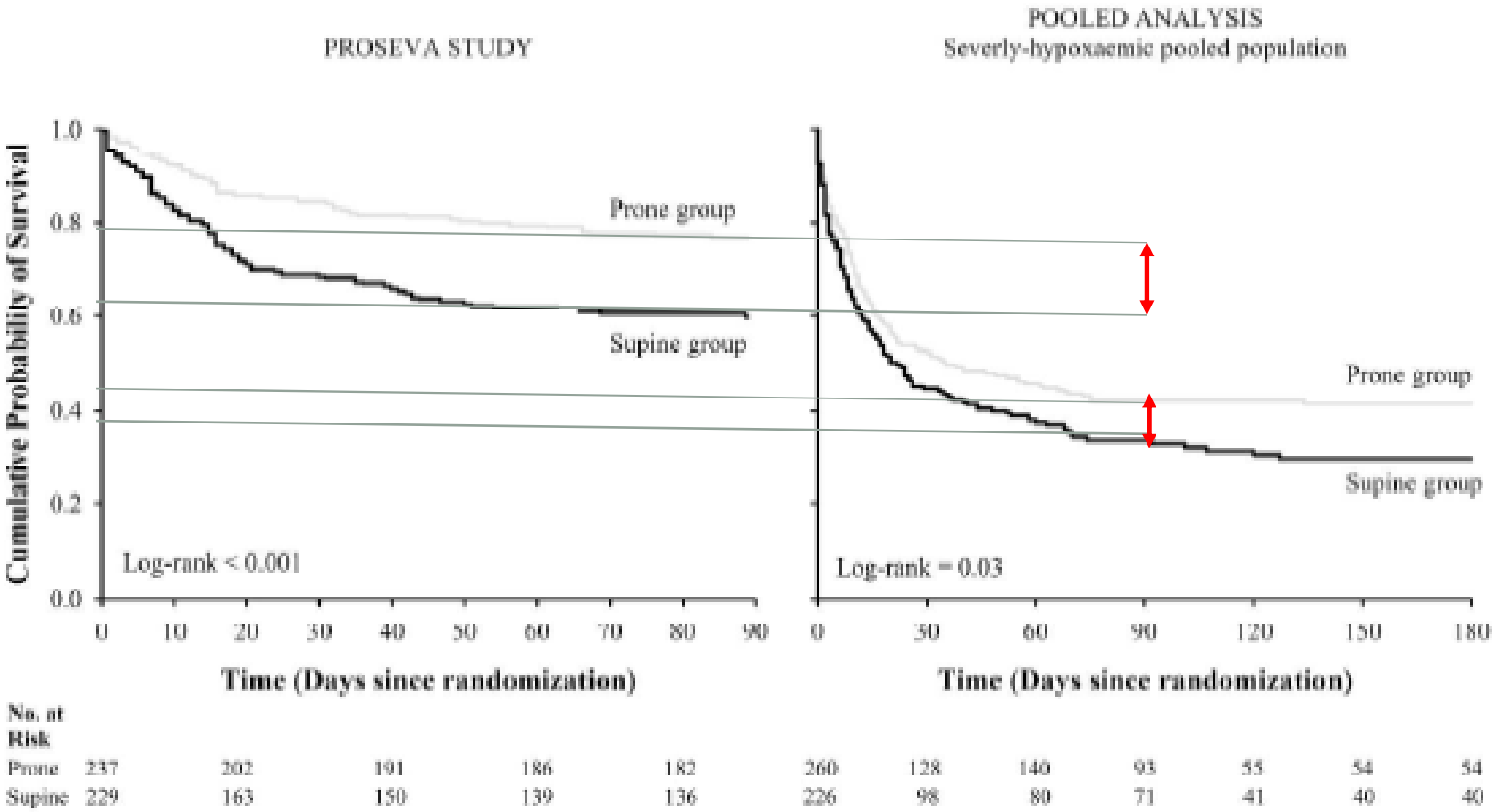
Post-Proseva meta-analysis



Gattinoni AJRCCM 2013

Conclusions

- Prone position should be recommended in severe ARDS as a first line therapy


Thank you very much for the
Invitation !