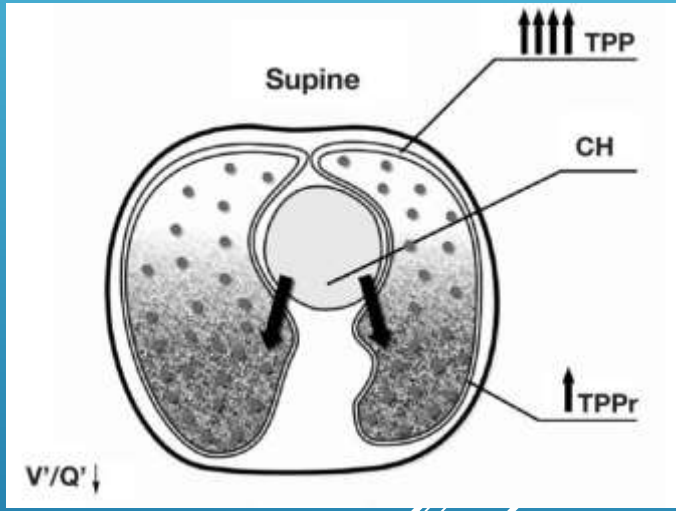
PRONE VENTILATION IN ARDS

Dr Dominic So
ICU, PMH

PHYSIOLOGY - SUPINE

- In ARDS, the **dorsal/dependent regions** of lungs are more susceptible to **decruitment** in supine position :
  - Pressure exerted by the heart
  - Pressure by lung mass itself
  - Accumulation of fluid in pleural space
  - Pressure exerted by abdominal contents (in patients who have lost diaphragmatic tone)
  - High lung compliance in nondependent region

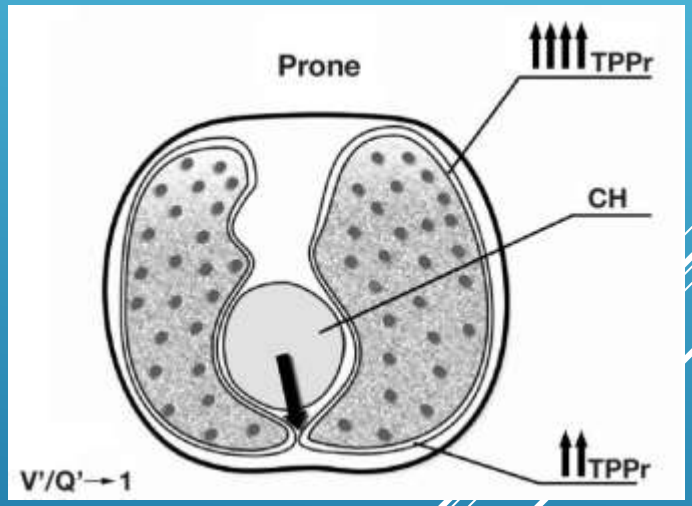
- The consequence is uneven alveolar filling with **VQ mismatch**



Arch Bronconeumol. 2009;45(6):291-296

PHYSIOLOGY - PRONE

- Prone position results in **more even alveolar ventilation** :
  - Infiltrates redistribution
  - Reduced compression of the lungs by the heart and lung
  - Decreased lung compliance in nondependent region
  - Less pressure from abdominal contents
  - Facilitates drainage of secretions
- Blood flow pattern does not change significantly.
- **VQ matching** therefore **improves**.



Arch Bronconeumol. 2009;**45(6)**:291-296

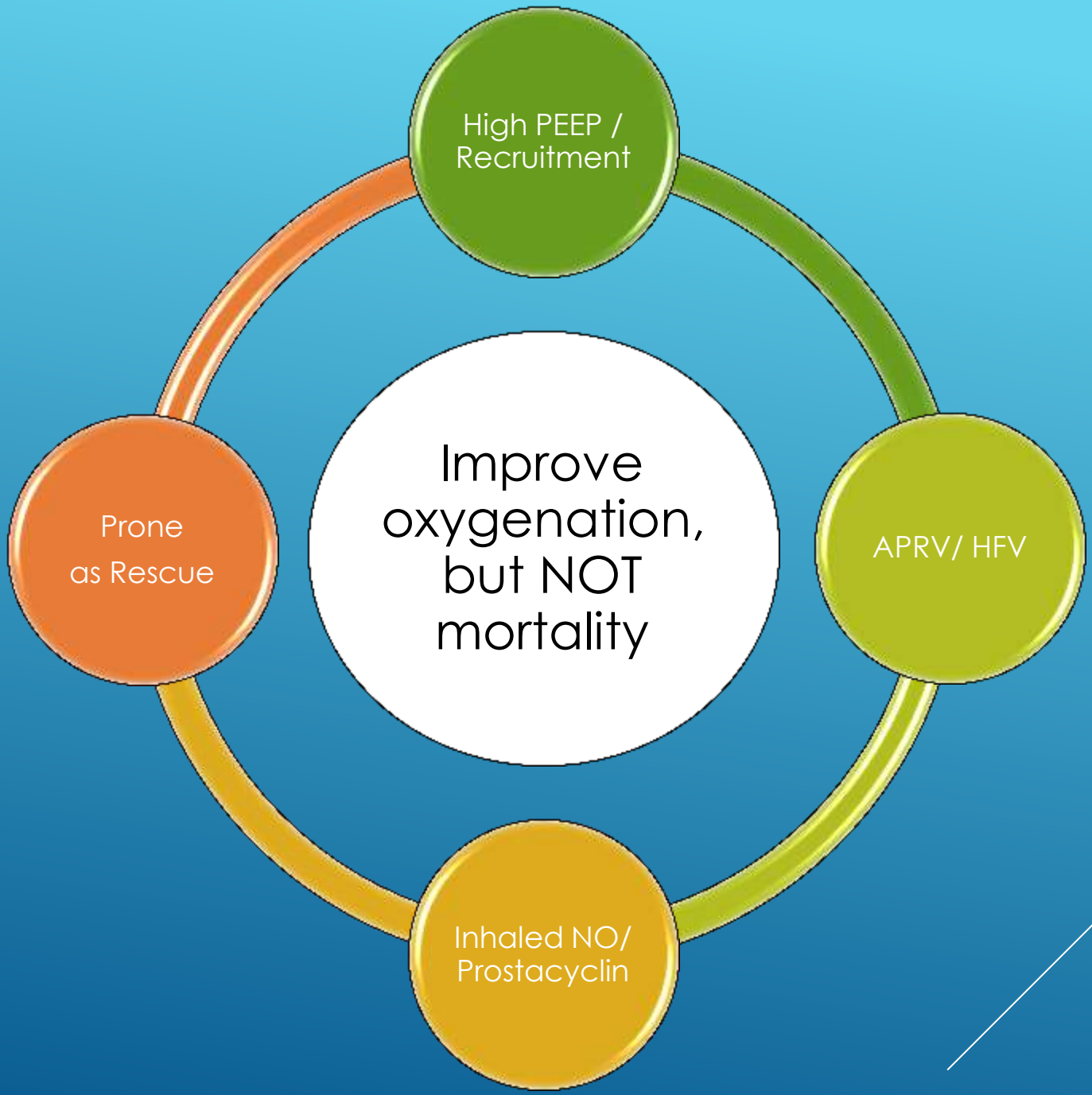
EFFECT OF PRONE ON OXYGENATION

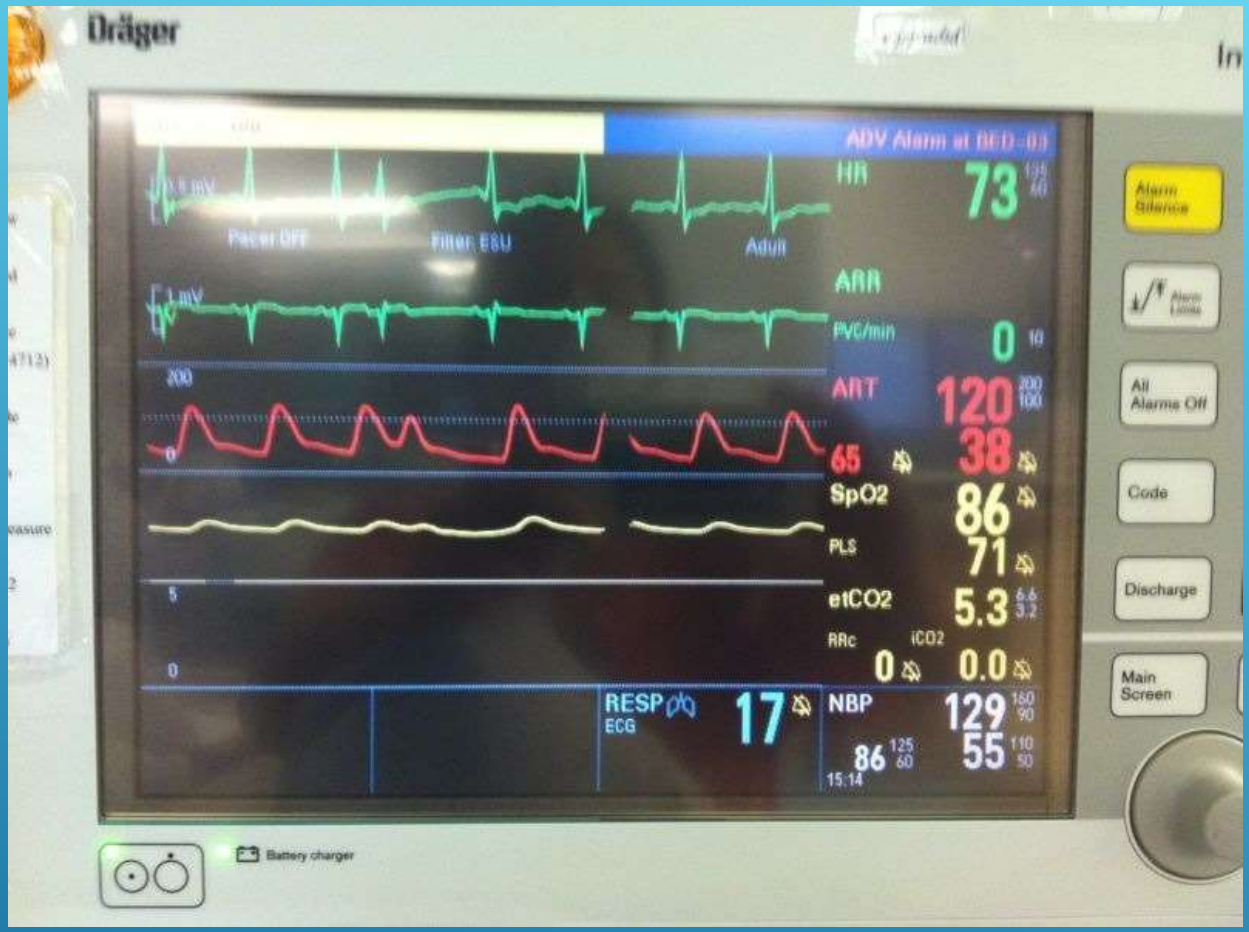
6 randomized controlled trials prior to 2013

- **All demonstrated improvements in oxygenation** with prone.
- But **none showed statistical difference in mortality**.

Found :

- Response time short.
- Improvements in oxygenation usually persistent.
- Most likely to respond: increased IAP, lower lung compliance in prone, dependent alveolar collapse, extrapulmonary ARDS.


High PEEP / Recruitment
APRV/ HFV
Inhaled NO/ Prostacyclin
Prone as Rescue
Improve oxygenation, but NOT mortality



NOT HYPOXAEMIA KILLING PATIENTS PER SE

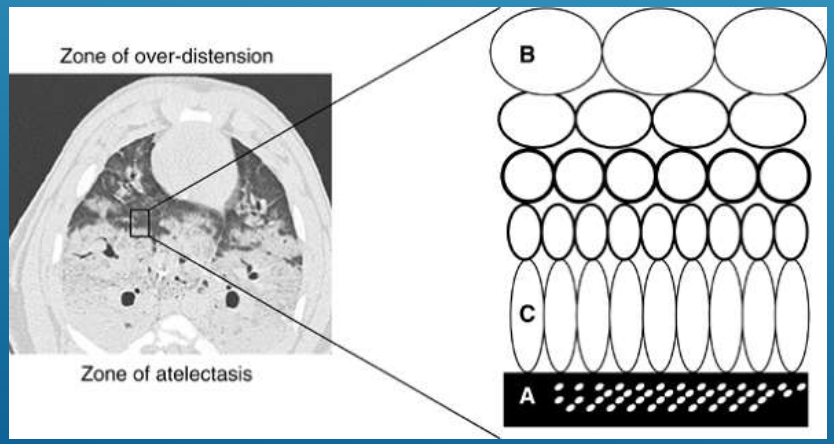
VENTILATOR ASSOCIATED LUNG INJURY (VALI)

- **Lung injury** from:
  - Overdistension/shear -> physical injury
  - Mechanotransduction -> "biotrauma"
  - Repetitive opening/closing
  - Shear at open/collapsed lung interface

Volutrauma

Atelectrauma

- Systemic inflammation and death from:
  - Systemic release of cytokines, endotoxin, bacteria, proteases



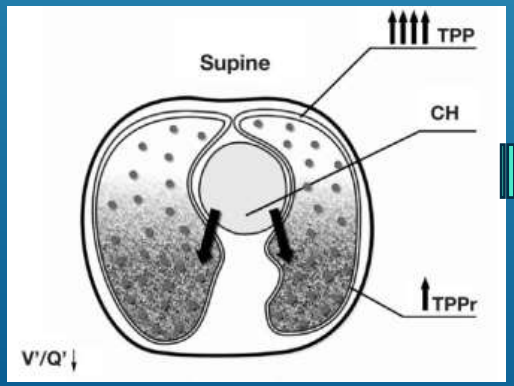
- **Therapy must be directed towards preventing VALI** rather than purely improving oxygenation.

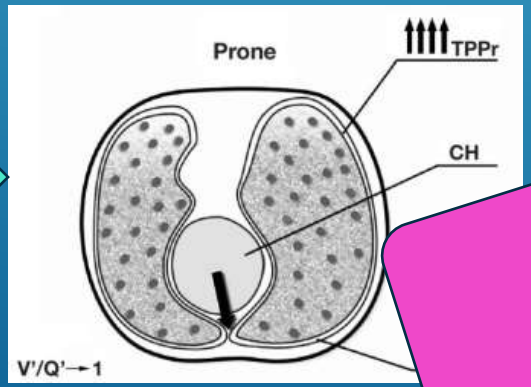
- That way, when primary pathology (e.g. pneumonia) is reversed, the patients can be rapidly weaned off from the ventilator because the lungs have not been further damaged by VALI.

PRONE VENTILATION IN PREVENTING VALI

- **Lung injury** from:
  - Overdistension/shear -> physical injury
  - Mechanotransduction -> "biotrauma"
  - Repetitive opening/closing
  - Shear at open/collapsed lung interface

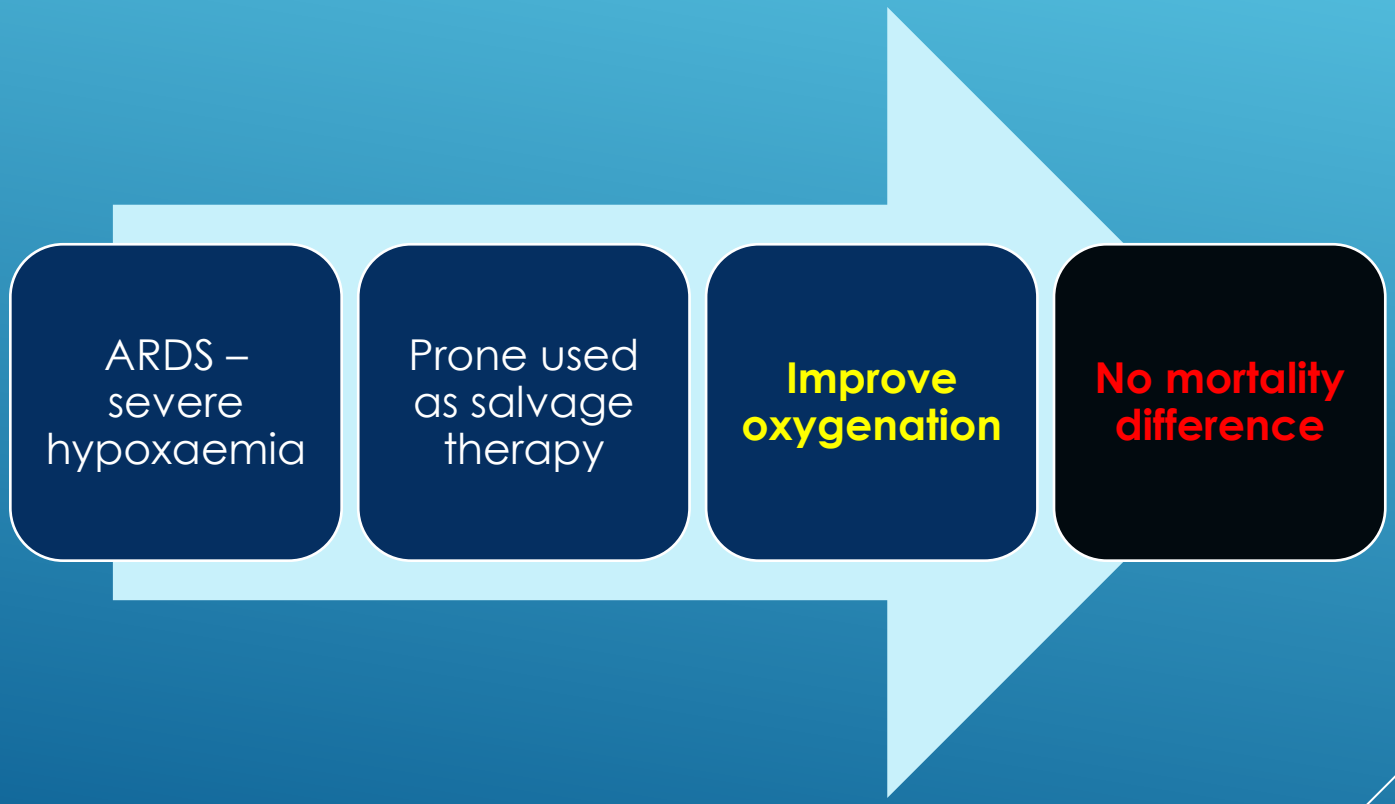
- Systemic inflamm and death from:
  - Systemic releas ytokines, endotoxin, bacteria, proteases





More homogenous ventilation

EARLIER TRIALS ON PRONE VENTILATION



EARLIER TRIALS OF PRONE

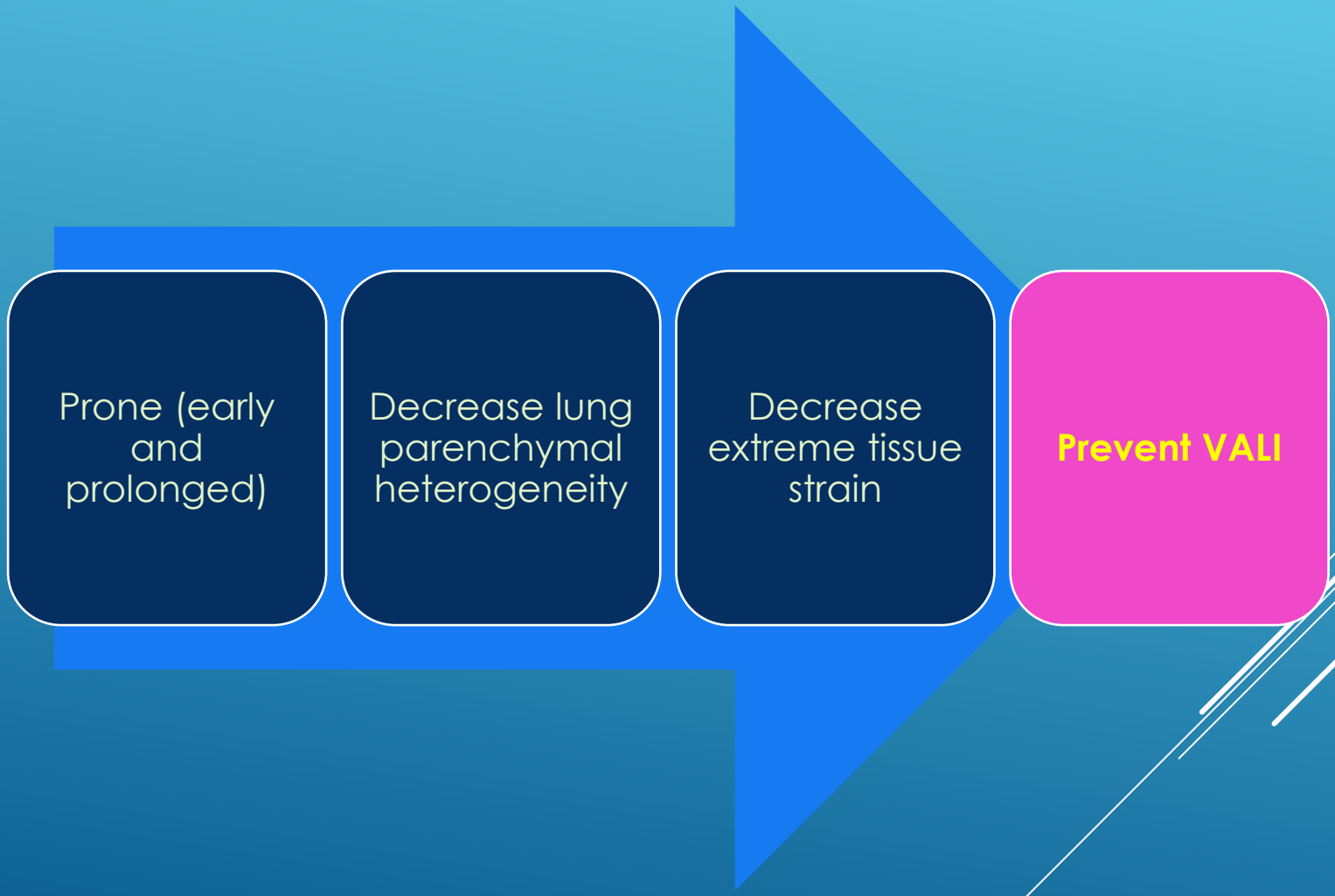
Selected baseline characteristics, within trial mechanical ventilation parameters and mortality of included trials investigating prone positioning

First author (reference), year	Patients, n		PaO_2/FiO_2 at baseline*, mmHg		Tidal volume during trial*, mL/kg		PEEP during trial*, cmH_2O		Duration of prone*,	Mortality†, %		P for mortality†
	P	S	P	S	P	S	P	S	h	P	S	
Gattinoni (29), 2001	152	152	85.7±24.6	88.3±25.9	10.3±2.7	10.3±2.9	9.7±2.9	9.6±3.2	7	21.1	25.0	NS
Guérin (18), 2004	413	378	150±59	155± 59	8.1±2.0	8.1±1.9	7.9± 3.4	7.5± 3.2	8	31.5	32.4	NS
Mancebo (17), 2006	76	60	107±65	126±94	8.3 ±1.7	8.6±1.6	12.4 ±1.9	12.3±2.4	17	43	58	NS
Chan (19), 2007	11	11	111±62	107±81	7.8±1.0	7.6±1.2	13.1±1.5	13.6±2.3	72	36.4	36.4	NS
Fernandez (20), 2008	21	19	113±43	122±40	8.6±2.1	9.2±2.2	11.1±4.1	11.4±3.8	NR	38.0	53.0	NS
Taccone (16), 2009	168	174	113±39‡	–	8.0±1.7	–	10±3	–	18	31	32.8	NS

Problems : ***not use in a way to reduce VALI!***

- Use **large tidal volumes** -> amplify lung strain in both groups
- Duration **too short** (hours per day, total no of days) -> not enough to mitigate VALI
- Used **too late** -> VALI already established

EFFECT OF PRONE ON MORTALITY



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ESTABLISHED IN 1812 JUNE 6, 2013 VOL. 368 NO. 23

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 – **EARLY, PROLONGED**

Indications :

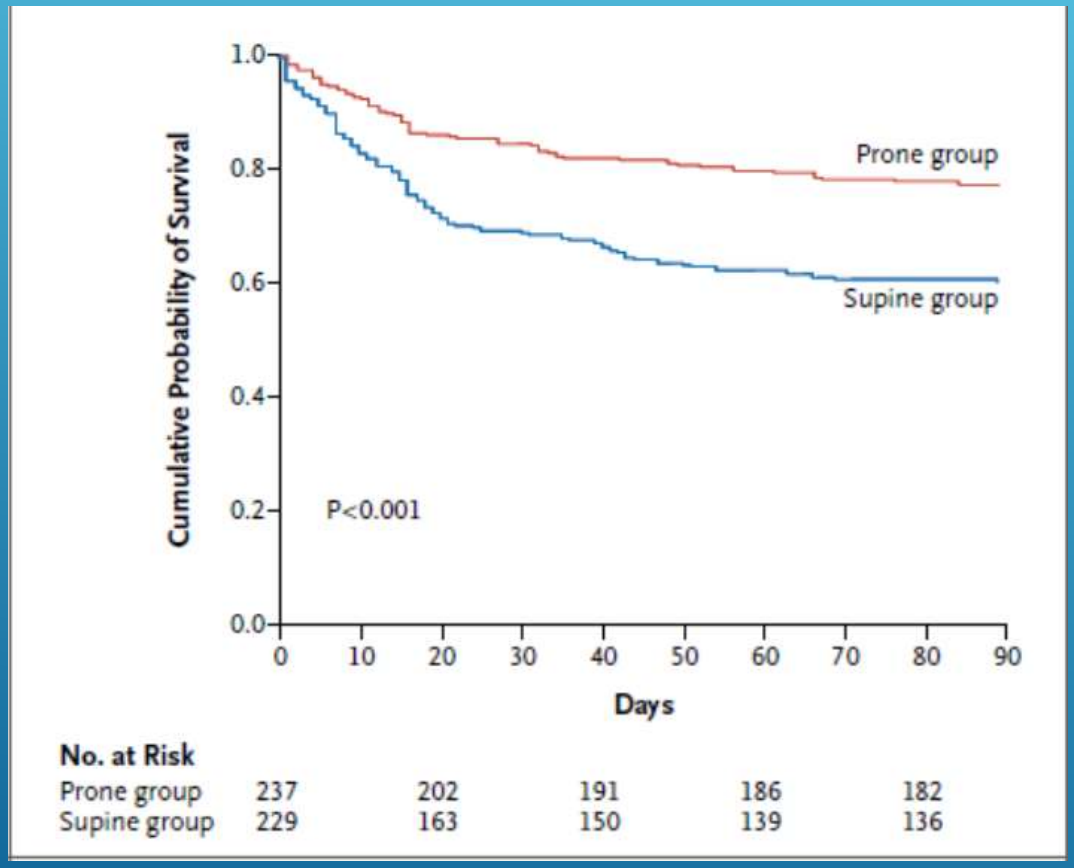
Patients with severe ARDS, defined as

- **PaO_2:FiO_2 ratio of <150** mmHg (20 kPa) with **FiO_2 of ≥0.6**, **PEEP of ≥5**

Prone protocol :

- At least **16 hours per day**
- **Continue daily** until improvement (PaO_2:FiO_2 ≥150 mmHg, with PEEP of ≤10 and FiO_2 of ≤0.6, 4 hours after supine)

PROSEVA



Mortality 32.8% -> 16%

COMPARED WITH EARLIER TRIALS

Selected baseline characteristics, within trial mechanical ventilation parameters and mortality of included trials investigating prone positioning

First author (reference), year	Patients, n		PaO_2/FiO_2 at baseline*, mmHg		Tidal volume during trial*, mL/kg		PEEP during trial*, cmH_2O		Duration of prone*, h	Mortality†, %		P for mortality†
	P	S	P	S	P	S	P	S		P	S	
Gattinoni (29), 2001	152	152	85.7±24.6	88.3±25.9	10.3±2.7	10.3±2.9	9.7±2.9	9.6±3.2	7	21.1	25.0	NS
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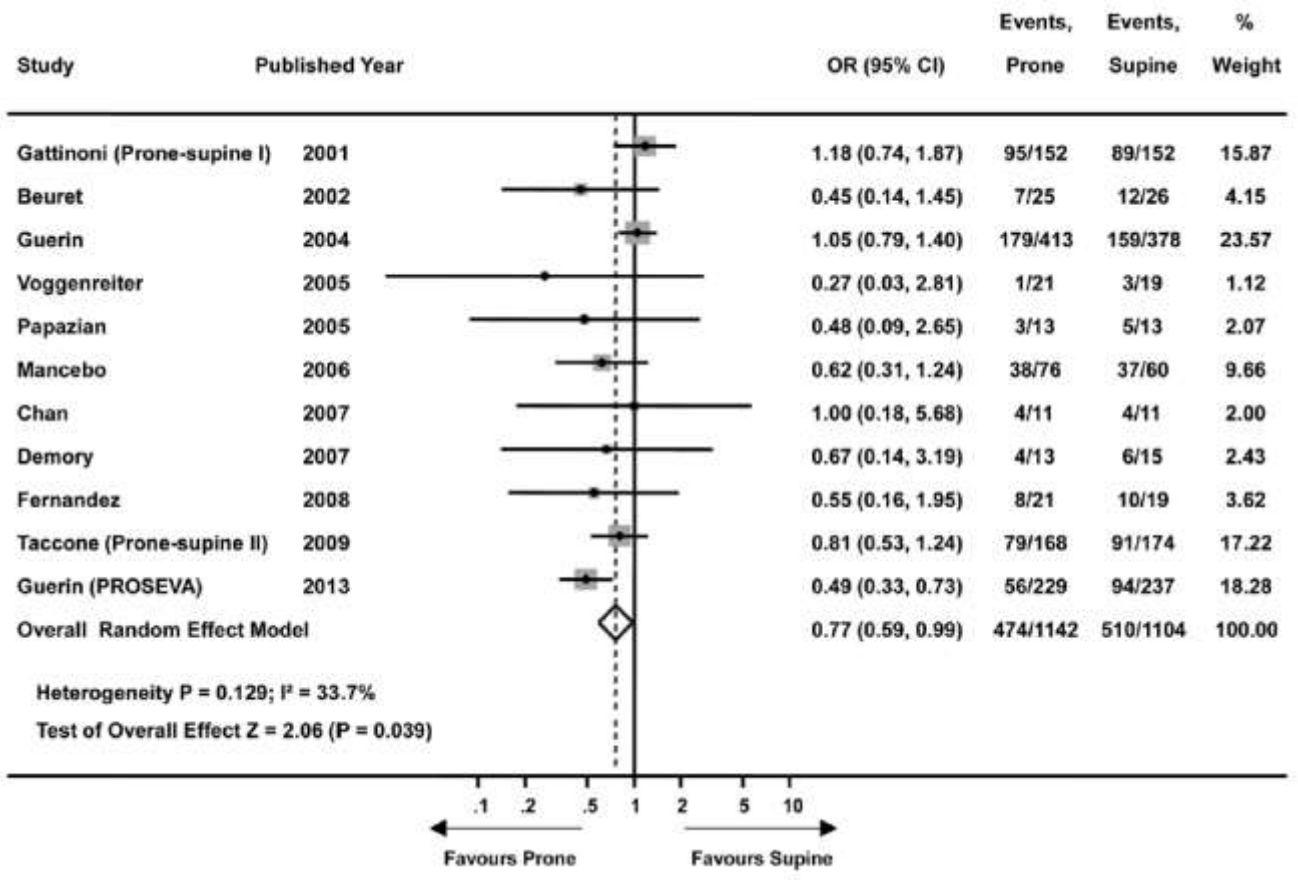
Taccone (16), 2009	168	174	113±39‡	–	8.0±1.7	–	10±3	–	18	31	32.8	NS
Guérin (30), 2013	237	229	100±30	100±20	6.1±0.6	6.1±0.6	10±3	10±4	17	16	32.8	<0.001

**All values reported separately for prone (P) and supine (S) groups, and as mean ± SD where data were available. Where separate group values are not shown, values reflect the mean of both P and S groups; †Mortality rates and P values reported for primary outcome measure in each study; ‡Values not reported separately for P and S groups. FiO_2 Fraction of inspired oxygen; NR Not reported; NS Not significant; PaO_2 Partial pressure of oxygen; PEEP Positive end-expiratory pressure*

The Efficacy and Safety of Prone Positional Ventilation in Acute Respiratory Distress Syndrome: Updated Study-Level Meta-Analysis of 11 Randomized Controlled Trials*

Joo Myung Lee, MD, MPH[1]; Won Bae, MD[2]; Yeon Joo Lee, MD[2]; Young-Jae Cho, MD, MPH[2]

CCM 2014; 42:1252-1262



- Included 11 RCT
- Prone ventilation significantly reduced mortality (odds ratio, 0.77; 95% CI, 0.59–0.99; *p* = 0.039).

	No. of Trials	No. of Patients	Odds Ratio (95% CI) for Mortality	Interaction P
Statistical Model				
Fixed effects	11	2,246	0.82 (0.69-0.97)	
Radom Effects	11	2,246	0.77 (0.59-0.99)	
Lung Protective Ventilation				**0.015**
Yes	8	1,100	0.62 (0.48-0.79)	
No	3	1,146	1.04 (0.80-1.36)	
Duration of Prone Positioning				**0.015**
≥ 10 hours/session	8	1,100	0.62 (0.48-0.79)	
< 10 hours/session	3	1,146	1.04 (0.80-1.36)	
Patient Population				**0.021**
ARDS only	7	1,060	0.62 (0.48-0.80)	
ALI/ARDS	4	1,186	1.02 (0.76-1.36)	
Severe ARDS population (PaO2/FiO2 ratio)				0.635
≤ 150 mmHg	8	1,364	0.72 (0.55-0.95)	
> 150 mmHg	3	882	0.77 (0.38-1.55)	
HFOV were used with positioning				0.661
Yes	2	54	0.57 (0.18-1.82)	
No	9	2,192	0.77 (0.58-1.02)	
Adequate concealment of allocation				0.764
Yes	10	2,224	0.76 (0.58-0.99)	
No/unclear	1	22	1.00 (0.18-5.68)	

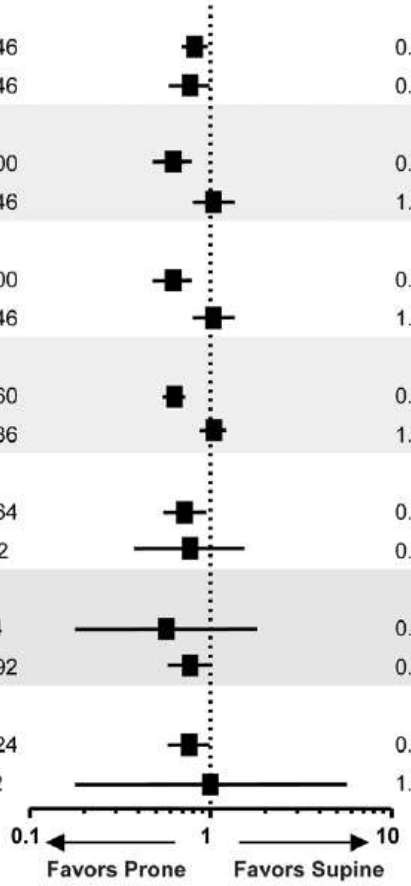
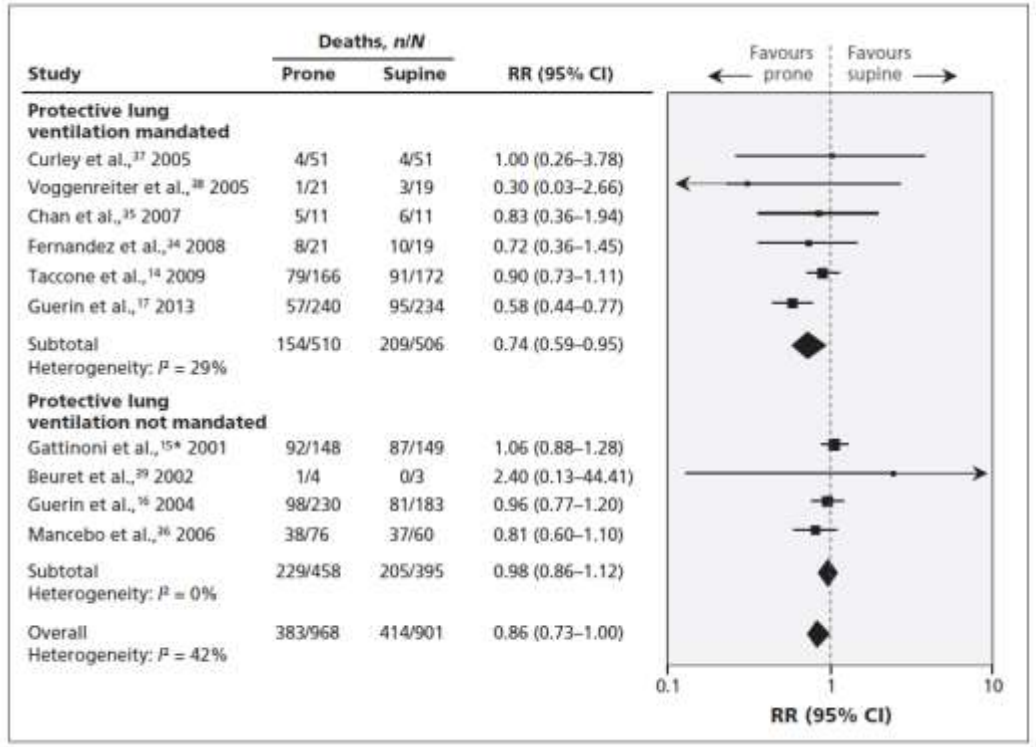


Figure 4. Stratified subgroup analyses according to the study protocols. The forest plot shows odds ratios (by random-effects model) for overall mortality associated with prone versus supine positioning with studies stratified according to 1) lung protective ventilation, 2) actual duration of prone positioning, 3) disease severity of patients, 4) Pao_2/Fio_2 ratio, 5) high-frequency oscillatory ventilation as a concomitant maneuver, and 6) adequacy of allocation concealment. The *squares* and the *horizontal lines* indicate the odd ratios (ORs) (by random-effects model) and the 95% CI for each trial included. The *dotted line* indicates the point of neutral effect for overall mortality (i.e., the point of random-effects model OR of 1.0). ARDS = acute respiratory distress syndrome, ALI = acute lung injury, HFOV = high-frequency oscillatory ventilation.

Effect of prone positioning during mechanical ventilation on mortality among patients with acute respiratory distress syndrome: a systematic review and meta-analysis

Sachin Sud MD MSc, Jan O. Friedrich MD DPhil, Neill K. J. Adhikari MDCM MSc, Paolo Taccone MD, Jordi Mancebo MD, Federico Polli MD, Roberto Latini MD, Antonio Pesenti MD, Martha A.Q. Curley RN PhD, Rafael Fernandez MD, Ming-Cheng Chan MD, Pascal Beuret MD, Gregor Voggenreiter MD, Maneesh Sud MD, Gianni Tognoni MD, Luciano Gattinoni MD, Claude Guérin MD PhD *CMAJ* 2014. DOI:10.1503



Study	Deaths, *n*/*N* Prone	Supine	RR (95% CI)
Protective lung ventilation mandated			
Curley et al.,[37] 2005	4/51	4/51	1.00 (0.26–3.78)
Voggenreiter et al.,[38] 2005	1/21	3/19	0.30 (0.03–2.66)
Chan et al.,[35] 2007	5/11	6/11	0.83 (0.36–1.94)
Fernandez et al.,[34] 2008	8/21	10/19	0.72 (0.36–1.45)
Taccone et al.,[14] 2009	79/166	91/172	0.90 (0.73–1.11)
Guerin et al.,[17] 2013	57/240	95/234	0.58 (0.44–0.77)
Subtotal Heterogeneity: I^2 = 29%	154/510	209/506	0.74 (0.59–0.95)
Protective lung ventilation not mandated			
Gattinoni et al.,[15*] 2001	92/148	87/149	1.06 (0.88–1.28)
Beuret et al.,[39] 2002	1/4	0/3	2.40 (0.13–44.41)
Guerin et al.,[16] 2004	98/230	81/183	0.96 (0.77–1.20)
Mancebo et al.,[36] 2006	38/76	37/60	0.81 (0.60–1.10)
Subtotal Heterogeneity: I^2 = 0%	229/458	205/395	0.98 (0.86–1.12)
Overall Heterogeneity: I^2 = 42%	383/968	414/901	0.86 (0.73–1.00)

Figure 2: Effect of prone positioning during mechanical ventilation on all-cause mortality among patients with acute respiratory distress syndrome in trials that used protective lung ventilation (tidal volume < 8 mL/kg) and in trials that did not mandate protective ventilation. Risk ratios less than 1.0 indicate a decreased risk of death with prone positioning. *Mortality data differed from the original publication after verification by the primary investigator. The test for subgroup interaction is statistically significant (p = 0.05). CI = confidence interval, RR = risk ratio.

Variable	No. of trials	Deaths, *n*/*N*		RR (95% CI)	I^2 value, %
		Prone	Supine		
Protective lung ventilation					
Mandated	6	154/510	209/506	0.74 (CI 0.59–0.95)	29
Not mandated	4	229/458	205/395	0.98 (CI 0.86–1.12)	0
Duration of prone positioning					
≥ 16 h/d	6	191/565	243/547	0.77(CI 0.64–0.92)	21
< 16 h/d	4	192/403	171/354	1.02 (CI 0.88–1.17)	0
Level of hypoxemia*					
Severe	6	75/210	102/209	0.76 (CI 0.61–0.94)	0
Moderate	6	75/274	102/268	0.74 (CI 0.48–1.16)	42
Mild	4	3/22	3/23	0.98 (CI 0.18–5.24)	0

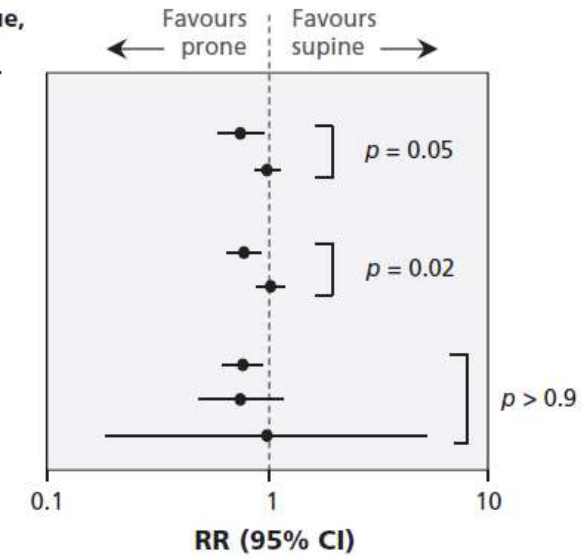
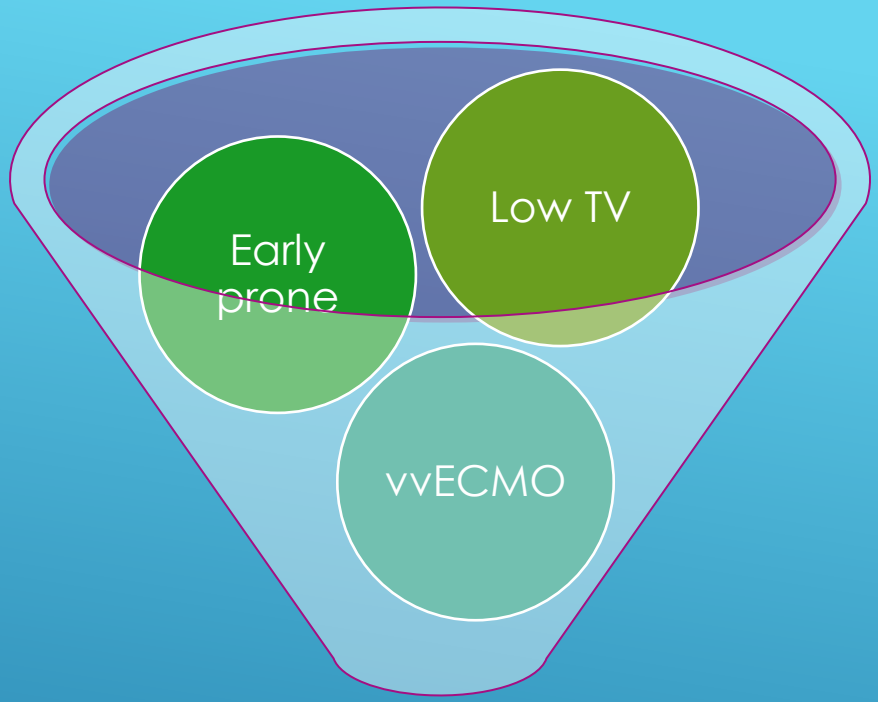


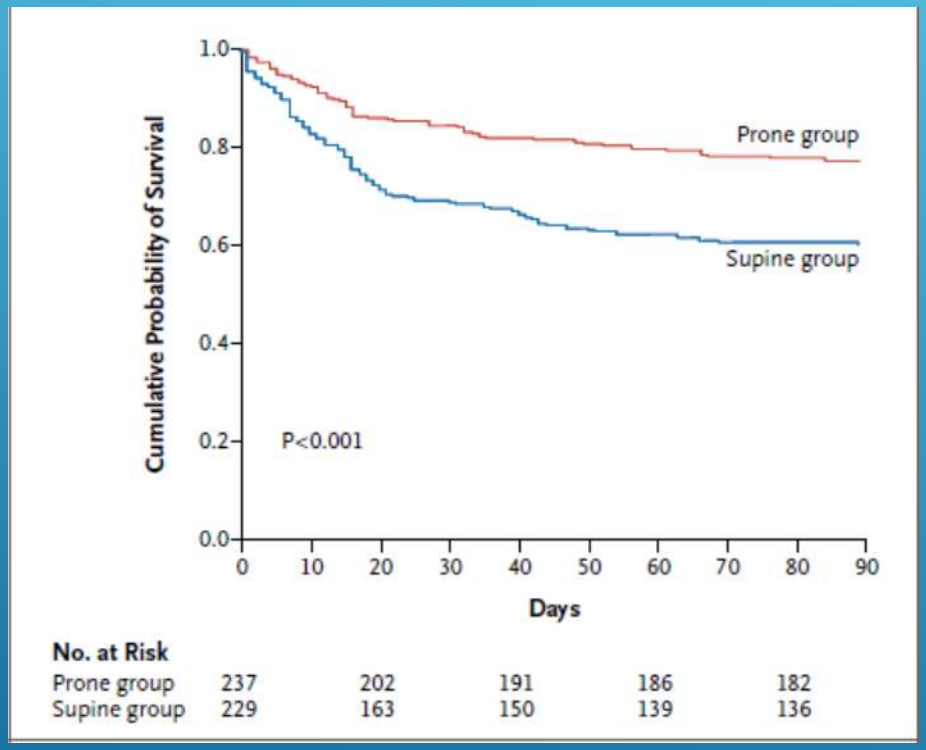
Figure 3: Effect of prone positioning during mechanical ventilation on all-cause mortality according to prespecified patient-level and trial-level subgroups. Risk ratios less than 1.0 indicate a decreased risk of death with prone positioning. *Severe hypoxemia = ratio of partial pressure of arterial oxygen to fraction of inspired oxygen (Pao_2/Fio_2) < 100 mm Hg; moderate = Pao_2/Fio_2 ratio 100–199 mm Hg; mild = Pao_2/Fio_2 ratio 200–299 mm Hg. CI = 95% confidence interval, RR = risk ratio. Baseline Pao_2/Fio_2 ratios were unavailable for 10 patients in 3 trials.[17,34,35]



Prevent VALI

Improve mortality

WHEN ECMO?



Mortality 32.8% -> 16%

Can ECMO produce a mortality < 16% in these patients?

Many of these patients don't need ECMO

Which patients should be put on ECMO?

PRONE FAILURE / PRONE RESPONSIVENESS

Prone Position in Mechanically Ventilated Patients with Severe Acute Respiratory Failure

GÉRARD CHATTE, JEAN-MICHEL SAB, JEAN-MARC DUBOIS, MICHEL SIRODOT, PHILIPPE GAUSSORGUES, and DOMINIQUE ROBERT

Service de Réanimation Médicale et Assistance Respiratoire, Hôpital de la Croix Rousse, Lyon, France

AM J RESPIR CRIT CARE MED 1997;155:473–478.

- Looks at **prone responsiveness**
- Prone criteria : PaO_2:FiO_2 <150 with FiO_2 of > 0.5

After ***1 hour of prone ventilation***, patients are classified as

Nonresponders

- patients without a PaO_2:FiO_2 improvement > 20mmHg (2.7 kPa)

Responders

- patients with a PaO_2:FiO_2 response > 20 mmHg
- further subdivided into "**nonpersistent**" and "**persistent**" improvement according to stability of the positive effect of the prone position for 1 h after returning to supine

Mortality in PROSEVA control : 32%

TABLE 2

MEAN AND STATISTICAL ANALYSIS OF THE PATIENT CHARACTERISTICS ACCORDING TO TYPES OF Pa_{O_2}/Fi_{O_2} RESPONSE

	Age	Wt (*kg*)	SAPS	LIS	MVbf	Vt (*ml/kg*)	PEEP	Fi_{O_2}	Mortality
Total (n = 32)	56 ± 16	68 ± 14	13 ± 4	2.6 ± 0.8	7 ± 10	10 ± 3	9 ± 5	0.75 ± 0.17	18/32 (56%)
Nonresponder: NR (n = 7)	55 ± 22	59 ± 12	14 ± 5	3.1 ± 0.8	6 ± 8	9 ± 3	13 ± 5	0.93 ± 0.10	5/7 (71%)
All responder: R (n = 25)	56 ± 15	71 ± 14	12 ± 4	2.5 ± 0.7	8 ± 10	10 ± 3	8 ± 4	0.71 ± 0.16	13/25 (52%)
Responder nonpersistent subgroup: RNP (n = 10)	53 ± 13	70 ± 18	12 ± 4	2.5 ± 0.7	7 ± 11	11 ± 2	7 ± 5	0.73 ± 0.14	6/10 (60%)
Responder persistent subgroup: RP (n = 13)	57 ± 16	72 ± 10	12 ± 5	2.5 ± 0.8	9 ± 10	10 ± 3	9 ± 4	0.66 ± 0.15	5/13 (38%)
Groups	Comparisons Between Different Responses								
NR/R	NS	$p < 0.08$	NS	NS	$p < 0.05$	NS	$p < 0.05$	$p < 0.01$	NS
NR/RNP/RP	NS	NS	NS	NS	NS	NS	NS	$p < 0.05$	NS

Definition of abbreviations: SAPS = simplified acute physiologic score; LIS = lung injury score; MVbf = duration of mechanical ventilation before the first 4 h prone trial (day); NR/R are between nonresponder and responder; NR/RNP/RP, AOV are between the three types of response.

- Mostly responders
- Responsiveness highly predictive of outcome/mortality (over-estimated due to high TV used and much shorter duration of prone ventilation)

	Estimated Mortality	Decision for vvECMO
Nonresponders	*~40%*	**Proceed to vvECMO** if indications for vvECMO met
Responder nonpersistent	*~30%*	**Consider for vvECMO** weighing the benefits and risks e.g. age, days of MV, viral vs bacterial, bleeding risks
Responder persistent	*<16%*	**No need for ECMO**

- Start **ECMO early** if prone fails (**aim to limit VALI**)
  Most responders have improvement in gas exchange within 1 hour

OUR STRATEGY IN PMH

- Difficult oxygenation/ventilation
- **Early prone ventilation**
  - PROVESA: P/F<150, FiO2>0.6, PEEP>5
- **Early ECMO**
  - For **nonresponder**
  - Things to consider : viral vs bacterial
    age
    days of MV
    SOFA score

PRONE VENTILATION PROTOCOL

Prone Ventilation Protocol

***Indications* [1]:**

Patients with severe ARDS, defined as

a **PaO_2:FiO_2 ratio of <150** mmHg (20 kPa) with an **FiO_2 of ≥0.6**, a **PEEP of ≥5** cm of water and a tidal volume of about 6 ml per kg of predicted body weight

***Contraindications* :**

Absolute :	Spinal instability
	Unmonitored increased ICP
Relative :	Open abdominal wounds
	Multiple trauma with unstabilized fractures
	Pregnancy
	Severe hemodynamic instability
	High dependency on airway and vascular access

Prone protocol (aim for **early prone ventilation** for **extended periods**) :

1. Place patient in a completely prone position for **at least 16 consecutive hours per day**. Prone ventilation should be resumed at any time before the planned assessment at 4 hours in the supine position if oxygenation cannot be maintained.
2. **Continue daily** prone ventilation until improvement in gas exchange.

***Ventilator Setting* :**

Tidal volume targeted at 6 ml per kg of predicted body weight with high PEEP level adjusted according to individual unit's practice.

The goal is to maintain Pplat of no more than 30 cm of water and an arterial pH of 7.20 to 7.45.

After 1 hour of prone ventilation, patients are classified as

Nonresponders

- patients without a PaO_2:FiO_2 improvement greater than 20mmHg (2.7 kPa)
- more likely in patients with lower PaO_2:FiO_2, higher PEEP, longer duration mechanical ventilation prior to proning

Responders

- patients with a PaO_2:FiO_2 response greater than 20 mmHg (2.7 kPa)
- further subdivided into "**nonpersistent**" and "**persistent**" improvement according to stability of the positive effect of the prone position for 1 h after returning to supine

	* Estimated Mortality [4]	Decision for vvECMO
Nonresponders	71% *(~80%)*	Proceed to vvECMO if indications for vvECMO met
Responder nonpersistent	60% *(~70%)*	Consider for vvECMO weighing the benefits and risks e.g. age, days of mechanical ventilation, viral vs bacterial, bleeding risks
Responder persistent	38% *(~16%)*	No need for ECMO

(*Estimated mortality likely over-estimated due to high tidal volume and much shorter prone duration used in trial, see attached table, figures in brackets are estimates based on current data)

Proceed to **ECMO early** if prone ventilation fails.

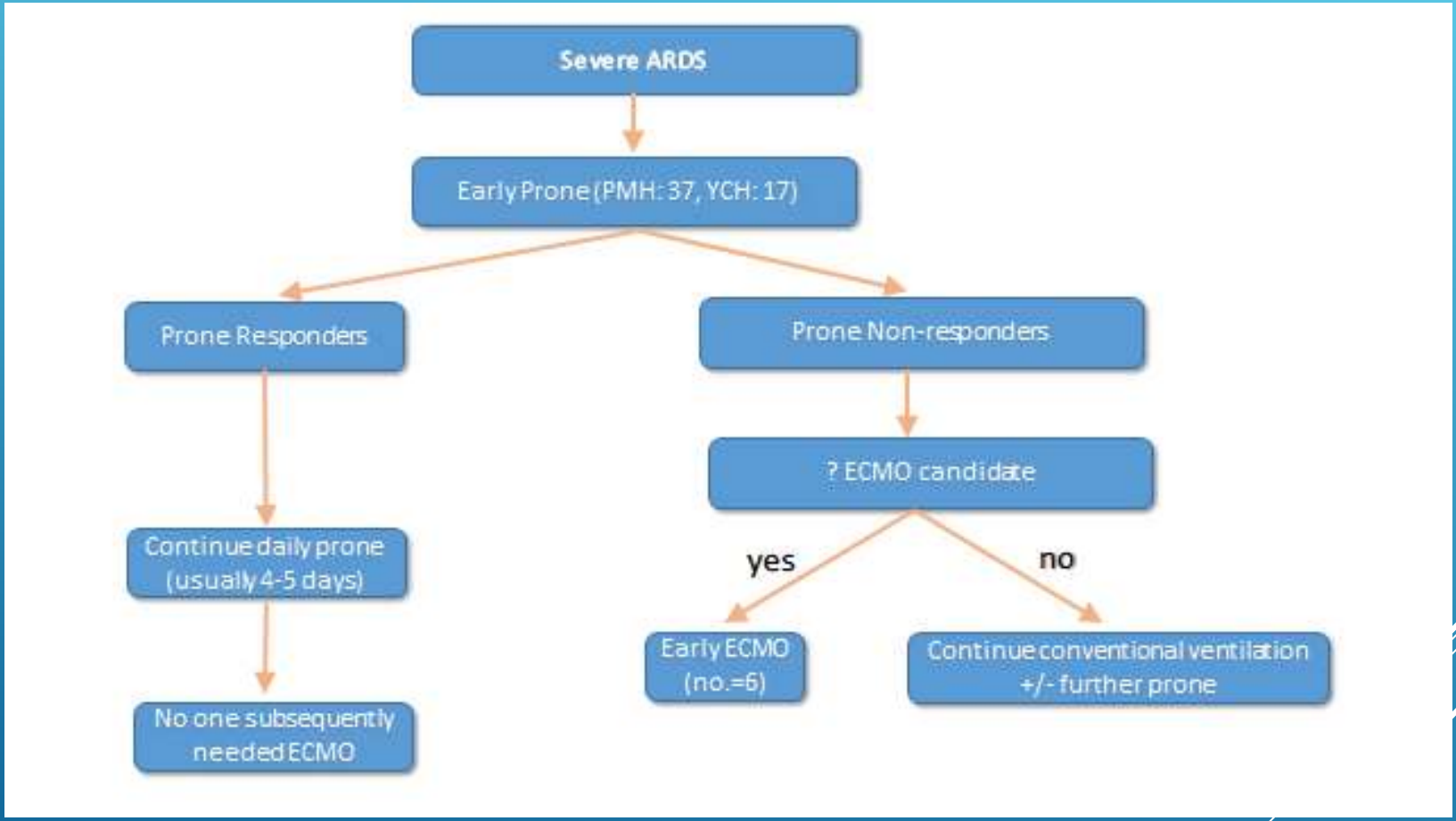
Criteria for stopping prone treatment:

- Improvement in oxygenation (defined as a PaO_2:FiO_2 ratio of ≥150 mmHg (20 kPa), with a PEEP of ≤10 cm of water and an FiO_2 of ≤0.6; these criteria have to be met in the supine position at least 4 hours after the end of the last prone session);
- A decrease in the PaO_2:FiO_2 ratio of more than 20%, relative to the ratio in the supine position;
- Or serious complications related to prone positioning.

Reference:

1. *Prone Positioning in Severe Acute Respiratory Distress Syndrome (PROSEVA study). C Guérin et al. N Engl J Med. 2013 Jun 6;368(23):2159-68.*
2. *Prone positioning reduces mortality from acute respiratory distress syndrome in the low tidal volume era: a meta-analysi Bellier et al. Intensive Care Medicine, ISSN 0342-4642, 03/2014, Volume 40, Issue 3, pp. 332–341.*
3. *Prone Position in Acute Respiratory Distress Syndrome. Rationale, Indications, and Limits J. Gattinoni et al. Am J Respir Crit Care Med Vol 188, Iss. 11, pp 1286–1293, Dec 1, 2013.*
4. *Prone Position in Mechanically Ventilated Patients with Severe Acute Respiratory Failure. G Chatte, J Sab, J Dubois, M Strodot, P Gaussorgues, and D Robert. AM J RESPIR CRIT CARE MED 1997;155:473-478.*

PMHYCH ICU CASES SINCE AUG 2013



OUR 6 ECMO CASES

Case	1	2	3	4	5	6
ICU Admission time	7/9/13 11:54	21/1/14 15:40	18/2/14 15:33	19/3/14 00:300	26/11/14 16:50	25/12/14 10:13
Hospital	YCH	YCH	PMH	PMH	YCH	*Referral from other ICU*
Start prone after ICU admission	5 hrs (17:00-10:00)	2.5 hrs (18:00-10:00)	0.5 hrs (16:00-19:00)	3.5 hrs (04:00-09:00)	9 hrs (02:00-11:00)	*24 hrs (for 10 hrs)*
Start ECMO after ICU admission	22 hrs	24 hrs	3 hrs	13 hrs	21 hrs	*7 days*

TRAINING:
PRACTICE SESSIONS……

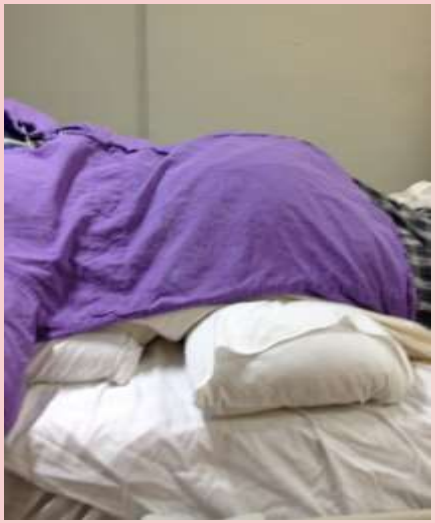
1 2

Turning steps

4 3

Use "C" shape donut or silicon

Place ***3*** transverse pillows



HEAD SUPPORT

PUT INTO ACTION……

COMPLICATIONS

- Unplanned extubation
- Selective intubation into main bronchus
- Endotracheal tube obstruction
- Loss of venous or arterial access
- Facial and airway edema *
- Pressure ulcers *
- Thoracotomy tube dislodgement or kinking
- Hypotension and arrhythmias

No difference in adverse events in PROSEVA trial, complications likely related to a lack of familiarity /experience with the procedure

PRESSURE ULCERS

CONCLUSION

- Prone ventilation improves mortality by protecting the lungs from VALI.
- Must be done early and for prolonged periods rather than using it as salvage therapy.
- Complication rates are low with proper training and familiarity of procedure.
- Should be used as part of bundle therapy in severe ARDS to prevent VALI: low TV -> early prone -> early ECMO.

THANK YOU