34TH ANNUAL MEETING OF THE NCSRC SYMPOSIUM 2012

CURRENT SYNOPSIS OF THE PRONE POSITION *IN* ACUTE RESPIRATORY DISTRESS SYNDROME

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What You Should Get:

Provide improved medical care to ARDS patients.

Review of current literature regarding physiologic effects, support devices, complications and management of prone positioning.

Show scientific evidence pertinent to this case sort; provide potential practice paradigm for future improvement in patient care. Take away more from the bedside of your proned patients.

Be able to discuss risks and benefit of proning to family members, nursing staff, and other practitioners.

Recognize variation in practitioners' comfort levels with this modality and be able to have evidence based discourse regarding outcomes.

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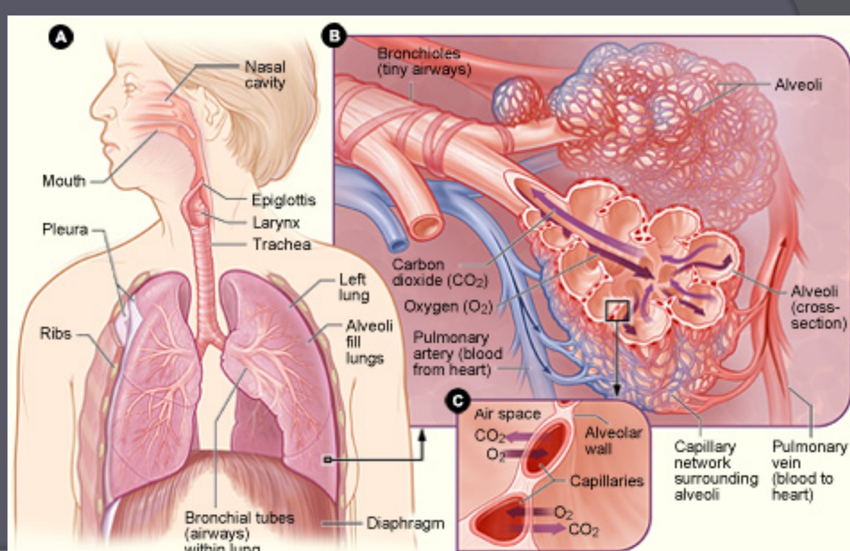
THE LUNG IS A *UNIT* CREATED OF:

- GAS
  - Inspired
  - Expired
- CONDUITS
  - Anatomic dead spaces
  - Nares to terminal bronchioles
- PARENCHYMA
  - Supportive
  - Interface: Alveolar surface area
- BLOOD
  - Supportive, bronchial flow
  - Gas exchange, pulmonary flow

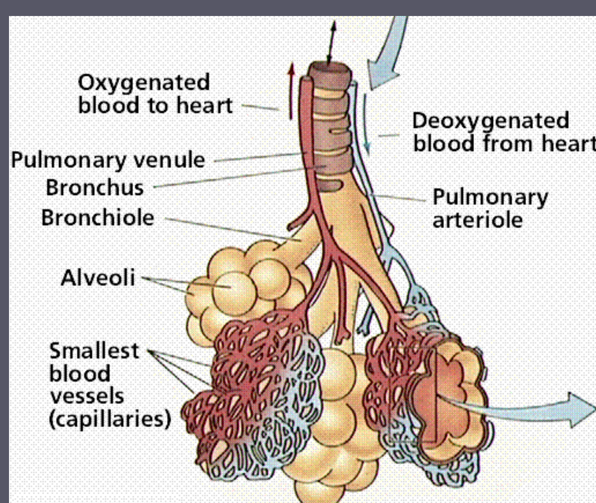
Lung Anatomy



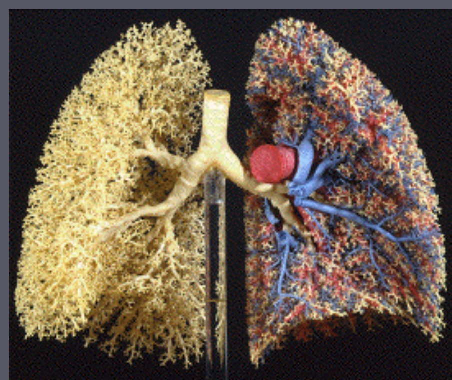
Or Is It?

- "The Lung" is a myriad of decremental functional units.
- Its "average" function as we note by typical physiologic testing or observations during mechanical ventilation is therefore a clinical pitfall.
- There is a potential continuum of VQ within *any* theoretical subunit, even to neighboring alveoli.

Countless Interface Combinations



Complex Interface of Ventilation and Perfusion



Review of Positional Forces

- The lung is a complicated interface!
- Variable transpleural forces apex to base affecting alveolar gas volumes
- Variable blood volume/pressure apex to base
- There is a gravitational component as well as an anatomic component to this

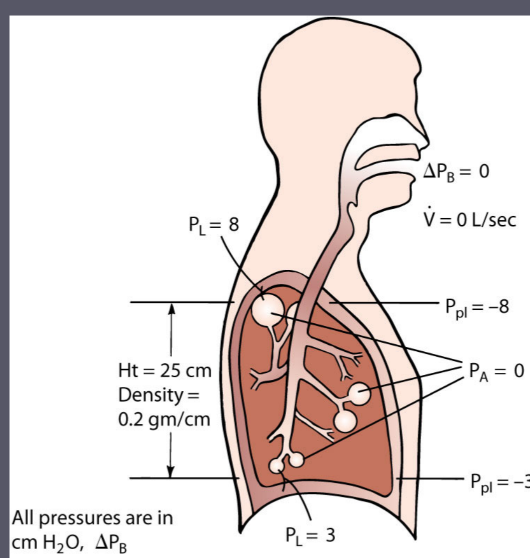
Potential Physiologic Benefits of Prone Ventilation

- Optimization of ventilation/perfusion match
  - Gravity effects
  - Shape of lungs, larger surface area posterior
- Pleural gradient changes
  - Recruitment of alternate/dorsal alveolar regions
  - Cardiac mass contribution
- Abdomen position
  - Decrease pressure on vena cava when abdomen is in the dependent position (RV preload?)
  - Recruitment of caudal/basal alveolar units
- Mobilization of secretions

Pelosi, 2002, J European Resp Soc, 20(4)

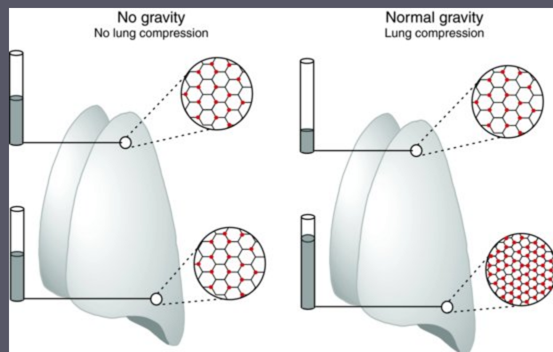
ANATOMIC and GRAVITATIONAL FORCES on VENTILATION

Increasing Alveolar Diameter



Increasing Contribution to FRC

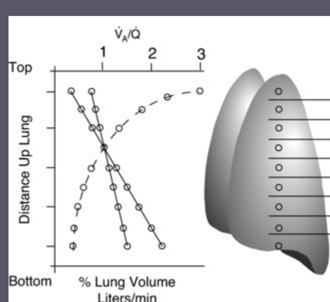
ANATOMIC and GRAVITATIONAL FORCES on ALVEOLAR SIZE



The lung compresses under its own weight. Because of gravity, alveoli are smaller, there are more vessels per unit volume, and the hydrostatic pressure is greater at the lung base

N Gjorevski *et al. Compr Physiol* 2011 DOI: 10.1002/cphy.c090002

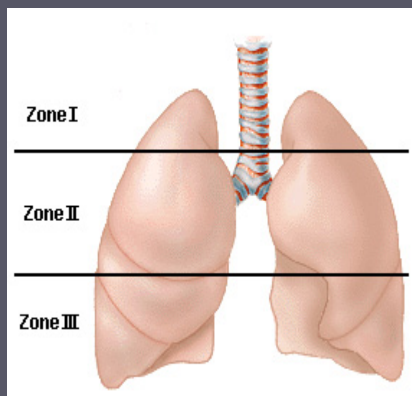
Effect of Gravity on Ventilation and Perfusion Matching

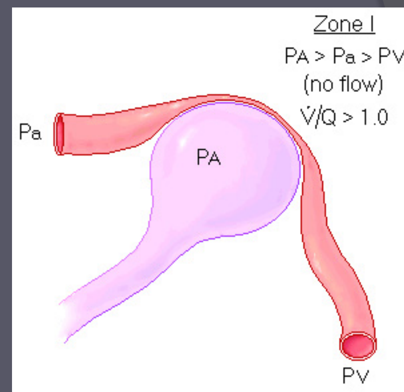


Vol. %	P_A l/min	Q l/min	P_{AP}/Q	P_{O2} mmHg	P_{CO2} mmHg
7	0.24	0.07	3.3	132	28
8	0.33	0.19	1.8	121	34
10	0.42	0.33	1.3	114	37
11	0.52	0.50	1.0	108	39
12	0.59	0.66	0.90	102	40
13	0.67	0.83	0.80	98	41
13	0.72	0.98	0.73	95	41
13	0.78	1.15	0.68	92	42
13	0.82	1.29	0.63	89	42
Mixed Arterial				97	40
A-a O_2 difference				4	1

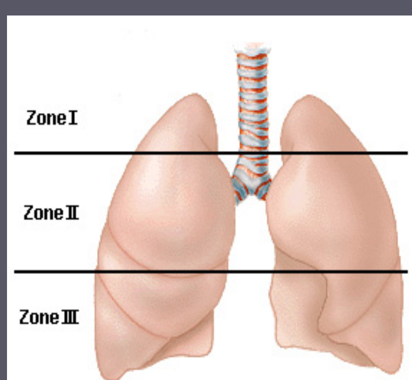
Gravity imposes a vertical gradient on both ventilation and perfusion (left) grossly matching ventilation and perfusion. However, the vertical gradient of perfusion is relatively larger resulting in some ventilation to perfusion inequality at the top and bottom of lung. West and colleagues proposed that this V/Q heterogeneity down the lung accounted for the observed A-aO2 difference in the normal lung.

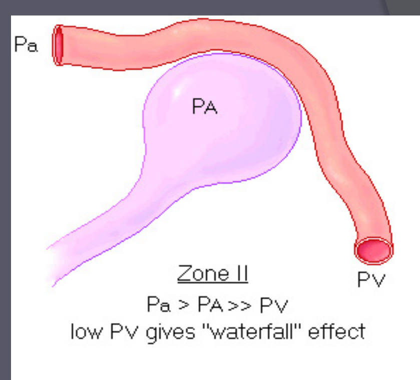
Zone of West I



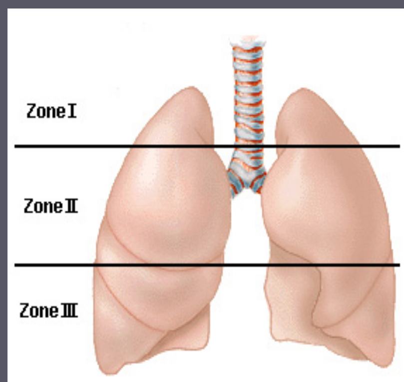


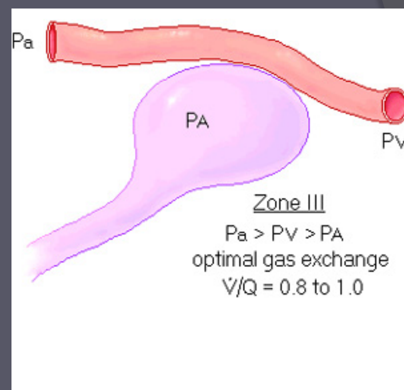
Zone of West II



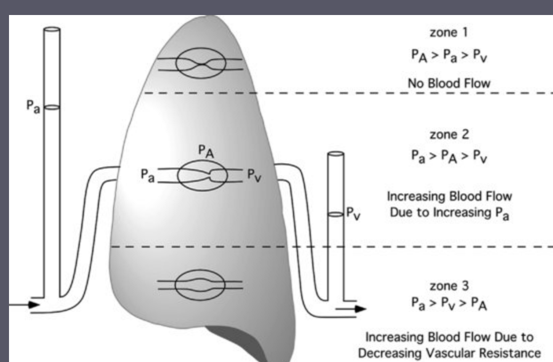


Zone of West III



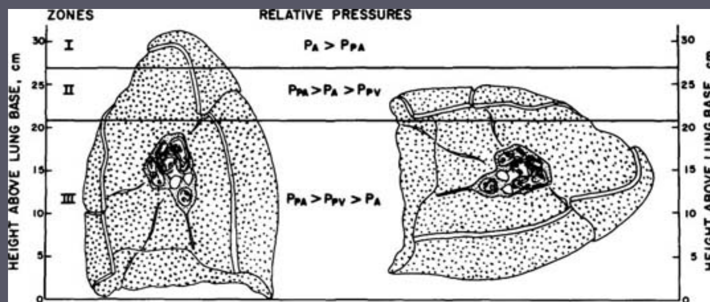


Zones of West



The relationships between Pa, Pv, and PA create regional differences in pulmonary perfusion. The zones have been traditionally vertically stacked on top of each other. However, recent observations that perfusion is heterogeneous within isogravitational planes demonstrates that zonal conditions may also vary within horizontal planes. The numbers of different zones within each plane likely shifts with increasing hydrostatic pressure down the lung from predominantly zones 1 and 2 at the top of the lung to all zone 3 conditions in the dependant lung regions.

Zone Changes on the Horizontal



Essentially rotating the lung about the axis of the root, showing the distance above respected base (caudal vs. dorsal). The distribution of Zone I becomes more theoretic based on the decrease in lung mass below in supine position, as well as the shortened distance above the pulmonary artery to the apex (cephalad to ventral).

Schematic of Contribution of Blood Flow Apex to Base

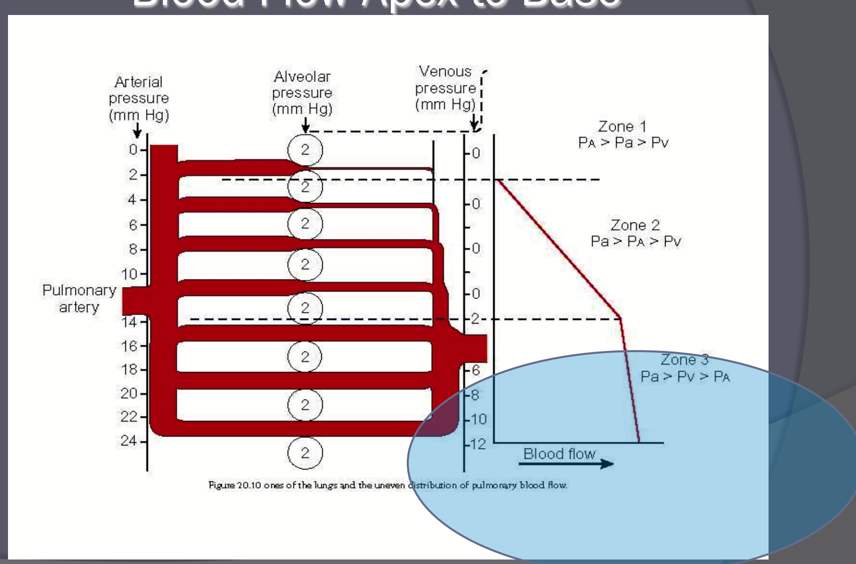
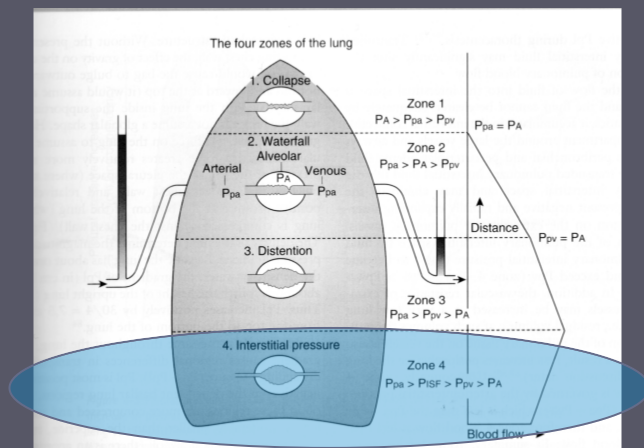


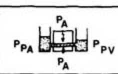
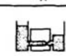
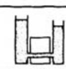
Figure 20.10 ones of the lungs and the uneven distribution of pulmonary blood flow.

Another Complexity Arises in the Deep Bases



The downward increase in lung perfusion reverses in the lower third, thus giving rise to a zone of reduced basal perfusion (zone 4). The flow in zone 4 is regulated by the relative increased resistance in extra-alveolar vessels, the diameter of which is determined by lung volume, perivascular interstitial pressure, and vasomotor tone.

The Four Lung Zones

PRESSURES IN ZONES		ALVEOLAR CAPILLARY FLOW	FLOW DEPENDS ON:
I $P_A > P_{PA} > P_{PV}$		NONE TO LOW	PULSATILITY (FLOW CONTINUES THROUGH CORNER VESSELS)
II $P_{PA} > P_A > P_{PV}$		INTERMEDIATE	$P_{PA} - P_A$ (STARLING RESISTOR)
III $P_{PA} > P_{PV} > P_A$		HIGH	$P_{PA} - P_{PV}$
IV $P_{PA} > P_{PV} > P_A$ $P_{INTERSTITIAL}$		INTERMEDIATE	RESISTANCE IN EXTRA-ALVEOLAR VESSELS

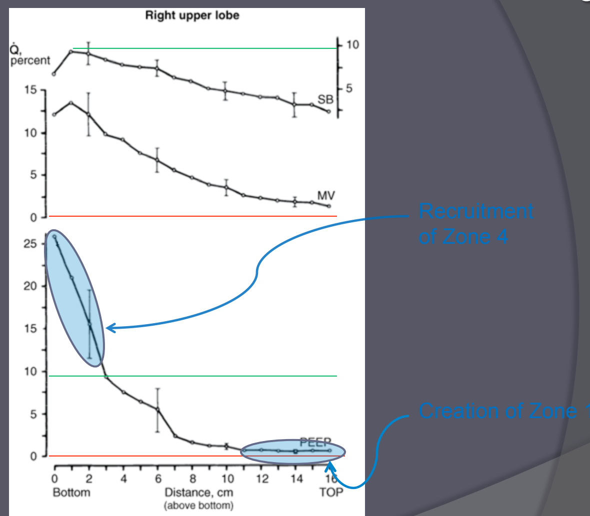
Potential Physiology of “Zone 4”:

1. increase in interstitial pressure at lung bases
2. closure of small airways at low lung volumes
3. increased extra-alveolar vascular resistance

With the relative increase in Pa there is creation either zone 1 or zone 2 conditions

The Effects of Mechanical Ventilation and Increased Alveolar Pressure on the Vertical Distribution of Blood Flow in the Lung.

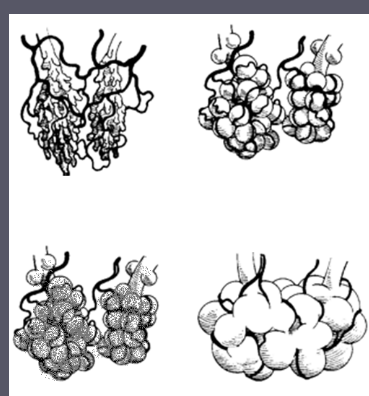
Positive alveolar pressures are largely the cause of the vertical gradient of perfusion more-so than the hydrostatic pressure within the blood vessels.



1. Spontaneous breathing (SB), there is a very small vertical gradient of perfusion.
2. Mechanical ventilation increases this gradient
3. PEEP of 20 cmH_2O further increases the vertical distribution.

N Gjorevski *et al. Compr Physiol* 2011
DOI: 10.1002/cphy.c090002

SHUNT to DEADSPACE



De-recruited Alveoli (or potentially Zone 4) VQ << optimal VQ matching

Balanced recruitment of alveoli to vascularity (Zone 3)

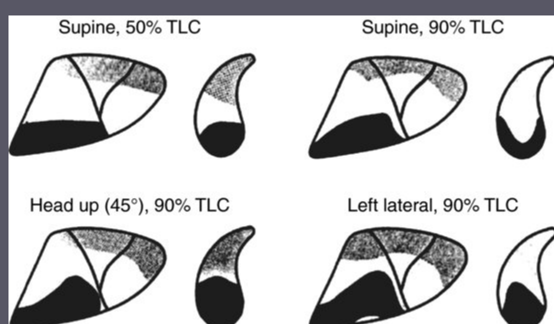
Filled Alveoli, (ARDS) with open vasculature (creation of SHUNT)

Overdistended alveoli, (PEEP) with vascular resistance (Zone 1 to frank DEAD SPACE)

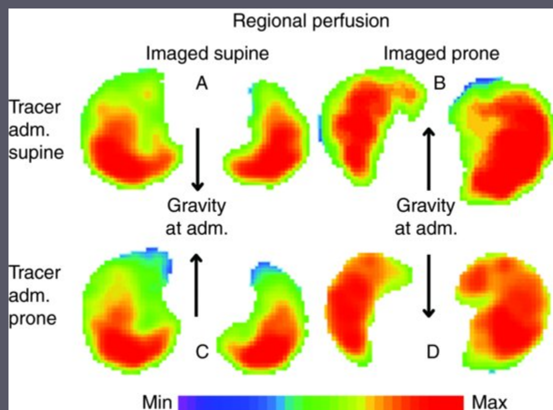
Adapted from Pierce

Theory vs. Practicality

ALVEOLAR CONTINUUM	VQ	RESULT
***COMPLETE* OVERDISTENTION**	∞	***DEAD SPACE***
ZONE1	>>1	Inefficient Gas Exchange
ZONE2	>0.8	Non-optimal Gas Exchange in favor of ventilation
ZONE3	0.8	Optimal Exchange
ZONE4	<0.8	Non-optimal Gas Exchange in Favor of perfusion
***COMPLETE* FILLING**	0	***SHUNT***

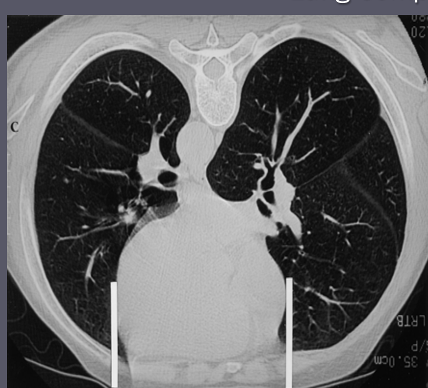


Diagrammatic representation of anatomic locations of lung regions with 25% highest (dark area) and 25% lowest (light shaded areas) vascular conductances. The areas of high conductance remain high and the low-conductance areas remain low regardless of posture or lung volume.



N Gjorevski *et al. Compr Physiol* 2011 DOI: 10.1002/cphy.c090002

Prone Positioning Relieves Lung Compression by the Heart



Prone

Supine

% of total lung volume under heart when supine: 7% (subcarinal) to 42% (basal section)

% of total lung volume under heart when prone: 1% to 4% for same sections

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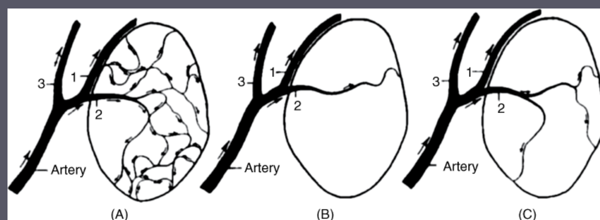
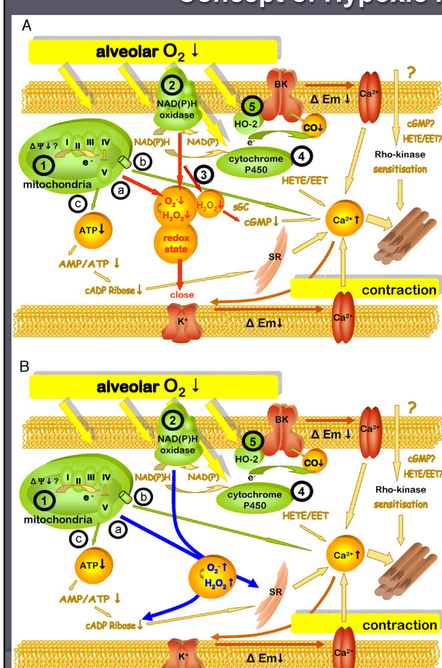
Vascular Control Mechanisms in VQ



Alveolar capillary pathways as drawn from observations through the pleural surface of a laboratory animal. Wearn et al. noted that alveolar capillaries open and close over time without an apparent change in the driving pressures in the feeding artery. They also demonstrated that capillaries could be recruited by increasing cardiac output.

N Gjorevski *et al. Compr Physiol* 2011 DOI: 10.1002/cphy.c090002

Concept of Hypoxic Pulmonary Vasoconstriction.

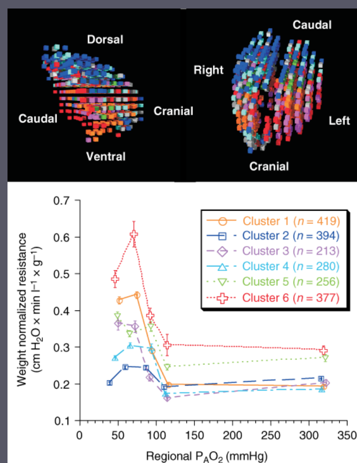


Hypoxic pulmonary vasoconstriction is a physiological response of the lung to alveolar hypoxia, which redistributes pulmonary blood flow from areas of low oxygen partial pressure to areas of high oxygen availability. This mechanism thus optimizes gas exchange and helps to prevent arterial hypoxemia.

Impairment of HPV under pathophysiological conditions, including acute respiratory distress syndrome or hepato-pulmonary syndrome, or during anesthesia, may result in poor arterial blood oxygenation by allowance of VQ mismatching.

Weissmann N et al. Cardiovasc Res 2006;71:620-629

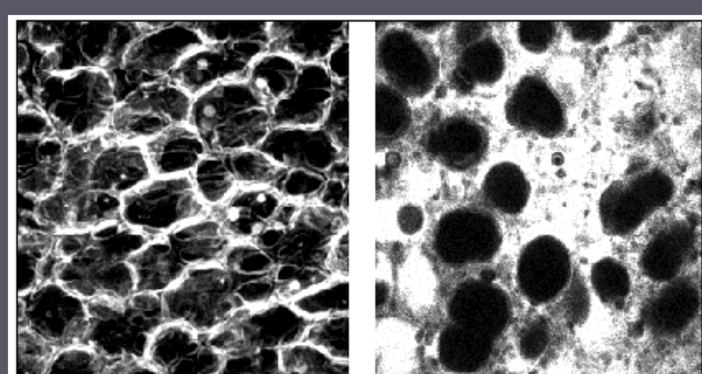
Hypoxic Pulmonary Vasomotor Tone



The hypoxic pulmonary vasoconstriction (HPV) response to global hypoxia varies within regions of the lung. In this study by Lamm et al., nearly 2000 lung pieces (~2 cm^3 in volume) were clustered into groups defined by changes in the vascular resistance to each piece with gradated hypoxia. The clusters are color coded and then represented in their spatial location above. Note that piece with a similar HPV response are grouped together.

While the distribution of perfusion is largely due to passive determinants such as vascular geometry and hydrostatic pressures, active mechanisms such as vasoconstriction induced by local hypoxia can also redistribute blood flow.

N Gjorevski *et al. Compr Physiol* 2011. DOI: 10.1002/cphy.c090002



British Journal of Anaesthesia 98 (4): 420–8 (2007)
doi:10.1093/bja/aem036 Advance Access publication March 8, 2007

BJA

REVIEW ARTICLES

Distribution of blood flow and ventilation in the lung: gravity is not the only factor

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Current textbooks in anaesthesia describe how gravity affects the regional distribution of ventilation and blood flow in the lung, in terms of vertical gradients of pleural pressure and pulmonary vascular pressures. This concept fails to explain some of the clinical features of disturbed lung function. Evidence now suggests that gravity has a less important role in the variation of regional distribution than structural features of the airways and blood vessels. We review more recent studies that used a variety of methods: external radioactive counters, measurements using inhaled and injected particles, and computer tomography scans. These give a higher spatial resolution of regional blood flow and ventilation. The matching between ventilation and blood flow in these small units of lung is considered; the effects of microgravity, increased gravity, and different postures are reviewed, and the application of these findings to conditions such as acute lung injury is discussed. Down to the scale of the acinus, there is considerable heterogeneity in the distribution of both ventilation and blood flow. However, the matching of blood flow with ventilation is well maintained and may result from a common pattern of asymmetric branching of the airways and blood vessels. Disruption of this pattern may explain impaired gas exchange after acute lung injury and explain how the prone position improves gas exchange.

Br J Anaesth 2007; **98**: 420–8

Keywords: fractals; gravity; model, structural; ventilation, perfusion

American-European Consensus Conference on ARDS

- Acute Lung Injury
  - PaO_2/FiO_2 <300 regardless of PEEP
  - Bilateral Infiltrates on a Frontal Chest Radiograph
  - Pulmonary Artery Wedge <18 mmHg

- Acute Respiratory Distress Syndrome
  - PaO_2/FiO_2 <200 regardless of PEEP
  - Bilateral Infiltrates on a Frontal Chest Radiograph
  - Pulmonary Artery Wedge <18 mmHg

Bernard GR, et. al., *Am J Respir Crit Care Med* 1994;149(3):818-824.

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ARDS
Non-cardiogenic

Absence of left atrial hypertension

- Classically defined as PCWP < 18
- Diminished use of right heart catheters: surrogate absence of LAE/Left HF

Intensive Care Med (2000) 26: 1215–1227

ORIGINAL

L. Puybasset
P. Gusman
J.-C. Muller
P. Cluzel
P. Coriat
J.-J. Rouby
and the CT Scan ARDS Study Group

Regional distribution of gas and tissue in acute respiratory distress syndrome. III. Consequences for the effects of positive end-expiratory pressure

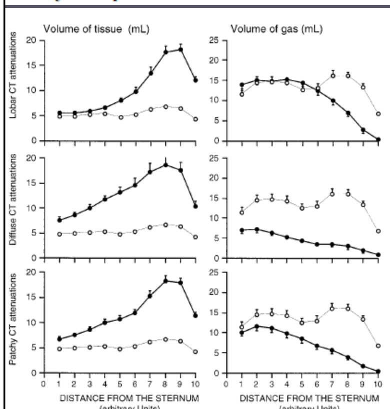
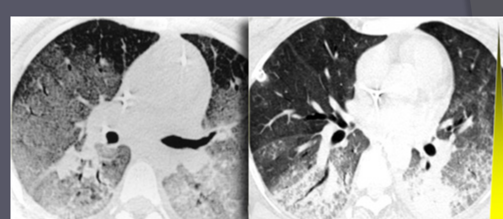


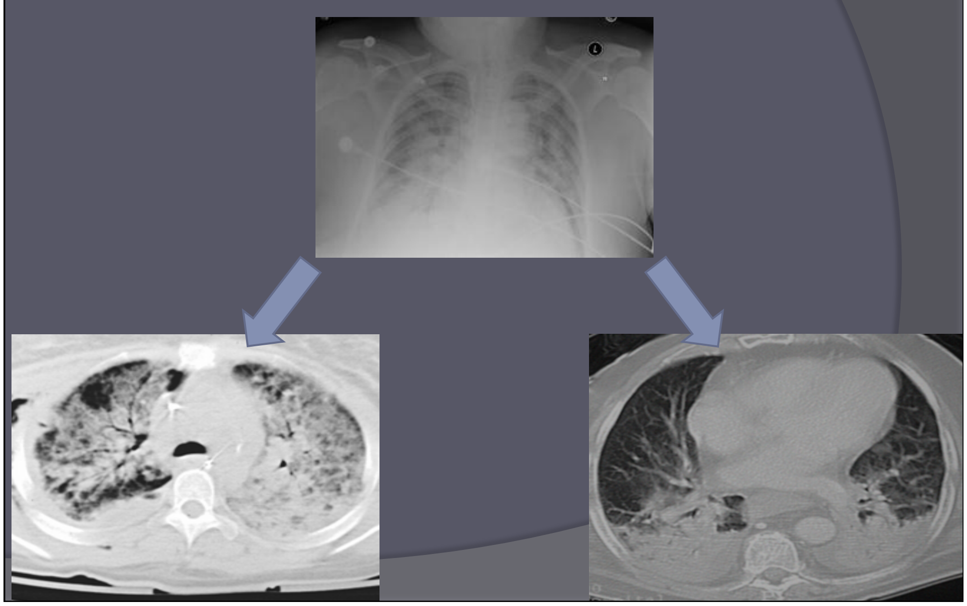
Fig. 7 Anteroposterior distribution of tissue (*left*) and gas (*right*) in patients with lobar CT attenuations (*upper*), diffuse CT attenuations (*middle*), patchy CT attenuations (*lower*) in ZEEP conditions. *X-axis* The distance from the anterior chest wall. Each unit is one-tenth of the total distance between the anterior chest wall and the vertebra (arbitrary units). *Open circles* Healthy volunteers; *filled circles* patients with ARDS



Radiographically, who will prone "well"?

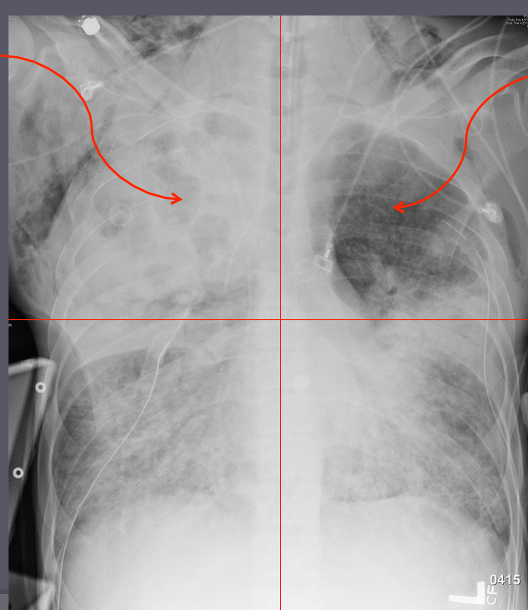
- AP films without any ability to view lateral are a pitfall!
- The diffuse appearance of a 2D film may infact be a largely posterior infiltrate.
- The clear domes of AP imaged diaphragms can well hide a dense infiltrate in the tail of the lung
- CT is best modality, but clinically or fiscally not feasible as routine evaluation for ARDS patients.

Matching CXR to potential VQ is not always easy….



Anticipate basilar infiltrates and VQ mismatch based on natural history of the disease.

LATERAL POSITION DEPENDENCE



Mechanical Ventilation in ARDS*

A State-of-the-Art Review

Timothy D. Girard, MD; and Gordon R. Bernard, MD, FCCP

Mechanical ventilation is an essential component of the care of patients with ARDS, and a large number of randomized controlled clinical trials have now been conducted evaluating the efficacy and safety of various methods of mechanical ventilation for the treatment of ARDS. Low tidal volume ventilation (≤ 6 mL/kg predicted body weight) should be utilized in all patients with ARDS as it is the only method of mechanical ventilation that, to date, has been shown to improve survival. High positive end-expiratory pressure, alveolar recruitment maneuvers, and prone positioning may each be useful as rescue therapy in a patient with severe hypoxemia, but these methods of ventilation do not improve survival for the wide population of patients with ARDS. Although not specific to the treatment of ARDS, protocol-driven weaning that utilizes a daily spontaneous breathing trial and ventilation in the semirecumbent position have proven benefits and should be used in the management of ARDS patients. ***(CHEST 2007; 131:921–929)***

Key words: acute lung injury; ARDS; mechanical ventilation; positive end-expiratory pressure; prone position; tidal volumes

Abbreviations: ALI = acute lung injury; ALVEOLI = Assessment of Low Tidal Volume and Elevated End-Expiratory Pressure To Obviate Lung Injury; APACHE = acute physiology and chronic health evaluation; APRV = airway pressure release ventilation; ARMA = Respiratory Management in Acute Lung Injury/Acute Respiratory Distress Syndrome; CI = confidence interval; FIO_2 = fraction of inspired oxygen; IL = interleukin; IRV = inverse ratio ventilation; PEEP = positive end-expiratory pressure; Pflex = lower inflection point on the pressure-volume curve of the respiratory system

Table 1—*Randomized Controlled Trials Evaluating Strategies of Mechanical Ventilation for the Treatment of ARDS**

Study	Patients, No.	Intervention	Mortality Rates†	p Value
Amato et al[10]	53	≤ 6 mL/kg ABW; VT; < 20 cm H_2O Pdriving	38% vs 71%‡	0.001
Stewart et al[11]	120	≤ 8mL/kg IBW; VT; ≤ 30 cm H_2O Pplat	50% vs 47%	0.72
Brochard et al[12]	116	6–10 mL/kg IBW; VT; 25–30 cm H_2O Pplat	47% vs 38%§	0.38
Brower et al[13]	52	≤ 8 mL/kg PBW; VT; ≤ 30 cm H_2O Pplat	50% vs 46%	0.61
ARMA[14]	861	≤ 6mL/kg PBW; VT; ≤ 30 cm H_2O Pplat	31% vs 40%	0.007
Derdak et al[32]	148	HFOV	37% vs 52%‖	0.10
Bollen et al[33]	61	HFOV	43% vs 33%‖	0.59
ALVEOLI[35]	549	High-PEEP protocol	28% vs 25%	0.48
Villar et al[36]	103	5–8 mL/kg PBW; VT; PEEP of Pflex + 2 cm H_2O	34% vs 56%	0.04
Gattinoni et al[49]	304	Prone position 6 h/d for 10 d	63% vs 59%¶	0.65
Guerin et al[50]	791	Prone position 8 h/d	32% vs 32%‡	0.77
Mancebo et al[51]	136	Prone position 20 h/d	50% vs 62%	0.22

*ABW = actual body weight; VT = tidal volume; Pdriving = driving pressure; IBW = ideal body weight; Pplat = plateau pressure; PBW = predicted body weight; HFOV = high-frequency oscillatory ventilation.
†Values are given as the in-hospital mortality rates of intervention vs control group, unless otherwise noted.
‡28-day mortality rate.
§60-day mortality rate.
‖30-day mortality rate.
¶180-day mortality rate.

www.chestpubs.org CHEST / 137 / 6 / JUNE, 2010 1437

CHEST Postgraduate Education Corner

CONTEMPORARY REVIEWS IN CRITICAL CARE MEDICINE

Severe Hypoxemic Respiratory Failure

Part 2—Nonventilatory Strategies

Suhail Raoof, MD, FCCP; Keith Goulet, MD; Adebayo Esan, MD; Dean R. Hess, PhD, RRT, FCCP; and Curtis N. Sessler, MD, FCCP

Table 1—*Summary of Four Randomized Trials on Prone Position*

	Gattinoni et al[68]	Guerin et al[69]	Mancebo et al[70]	Taccone et al[71]
No. of patients	304	791	136	343
Prone	152	413	76	168
Supine	152	378	60	174
Enrollment criteria	ALI	ALI	ARDS	ARDS
	$PaO_2/FIO_2 < 300$	$PaO_2/FIO_2 < 300$	$PaO_2/FIO_2 < 200$	$PaO_2/FIO_2 < 200$
Daily proning				
Planned	> 6 h/d	> 8 h/d	20 h/d	20 h/d
Actual	7 h/d	8 h/d	13 h/d	18-20 h/d
Number of days	10 d	4 d	10 d	28 d
Oxygenation	Improved	Improved	Improved	Improved
VAP	Not assessed	Reduced	Not reduced	Not assessed
Primary end point	10-d mortality	28-d mortality	ICU mortality	28-d mortality
Prone vs supine	21.1% vs 25%	32.4% vs 31.5%	43% vs 58%	31.0% vs 32.8%
	RR, 0.84	RR, 0.97	RR, 0.74	RR, 0.97
	95% CI, 0.56-1.27	95% CI, 0.79-1.19	95% CI, 0.53-1.04	95% CI, 0.84-1.13
	P = .50	*P* = .77	*P* = .12	*P* = .72

ALI = acute lung injury; RR = relative risk; VAP = ventilator-associated pneumonia.

In a *post hoc* analysis of the patients with ARDS, Gattinoni et al[68] found a significantly lower 10-day mortality rate in the patients in the quartile with the lowest PaO_2/FIO_2 ratio (≤88 mm Hg; 23.1% vs 47.2%; relative risk of death 0.49; 95% CI, 0.25-0.95) ventilated in the prone position as compared with the supine position. When pooled with similar results by Mancebo et al,[70] mortality was reduced in patients

Prone positioning has been associated with complications that include pressure sores, endotracheal tube obstruction, unplanned extubation, loss of central venous access, and increased use of sedation.[68,71] Despite these limitations, Girard and Bernard[61] concluded that prone positioning may be considered a reasonable short-term therapy for patients with ARDS requiring high FIO_2 (>0.6) or elevated plateau pressure (>30 cm H_2O). In light of recent findings,[68,70,71] we recommend that prone positioning be considered in the subgroup of patients with severe refractory hypoxemia.

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REVIEW

Positive end-expiratory pressure, prone positioning, and activated protein C: a critical review of meta-analyses

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ABSTRACT

The results of meta-analyses on the effectiveness of high positive end-expiratory pressure (PEEP) and prone positioning in acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) are not consistent. In addition, the meta-analyses on the activated protein C in patients with sepsis combine trials with discordant results. Therefore, the aim of this paper was to give a critical review of these meta-analyses. All relevant meta-analyses were identified by a computerized search of PubMed using combinations of the following terms: acute lung injury, acute respiratory distress syndrome, positive end-expiratory pressure, mechanical ventilation, prone position, drotrecogin, activated protein C, sepsis, and septic patients. A high level of PEEP and prone ventilation was shown to reduce the mortality in patients with severe acute hypoxemic respiratory failure. Although the evidence for the efficacy of activated protein C is not conclusive, it should be considered in patients that are at a high risk for death without any contraindications related to bleeding risk. Meta-analysis models can be very useful for clinical decisions if they include all of the similar papers on a medical topic and are correct from the methodological point of view: however, these results must be checked by a careful and well-informed reader. *(Minerva Anestesiol 2010;76:929-36)*

Key words: Positive End-Expiratory Pressure - Activated protein C - Meta-analysis [Publication Type].

In summary, the conclusions from this paper on prone position agree with the following statement by Sud *et al.*:[38] "Prone ventilation significantly reduced mortality in patients with severe acute hypoxemic respiratory failure and improved oxygenation, but also increased the risk of adverse events".

Stronger evidence for this conclusion has been recently obtained by Gattinoni *et al.*[41] by displaying survival curves for the patients enrolled in four large randomized trials according to the severity of their hypoxemic status. A statistically significant result (P=0.03), which was in favor of the prone position, was only observed for 486 severely hypoxemic patients (226 randomized to the prone position and 260 to the supine position, respectively).

Thus, the prone position must be considered a rescue maneuver, and it should be reserved only for patients with severe acute hypoxemic respiratory failure, such as a PaO_2/FiO_2 ratio that is <100 mmHg in the early phase of the disease. The prone position can also be associated with adverse effects.

Decrease in $Paco_2$ with prone position is predictive of improved outcome in acute respiratory distress syndrome*

Luciano Gattinoni, MD, FRCP; Federica Vagginelli, MD; Eleonora Carlesso, MSC; Paolo Taccone, MD; Valeria Conte, MD; Davide Chiumello, MD; Franco Valenza, MD; Pietro Caironi, MD; Antonio Pesenti, MD; for the Prone-Supine Study Group

Crit Care Med 2003 Vol. 31, No. 12 2727

Objective: To determine whether gas exchange improvement in response to the prone position is associated with an improved outcome in acute lung injury (ALI)/acute respiratory distress syndrome (ARDS).

Design: Retrospective analysis of patients in the pronation arm of a controlled randomized trial on prone positioning and patients enrolled in a previous pilot study of the prone position.

Setting: Twenty-eight Italian and two Swiss intensive care units.

Patients: We studied 225 patients meeting the criteria for ALI or ARDS.

Interventions: Patients were in prone position for 10 days for 6 hrs/day if they met ALI/ARDS criteria when assessed each morning. Respiratory variables were recorded before and after 6 hrs of pronation with unchanged ventilatory settings.

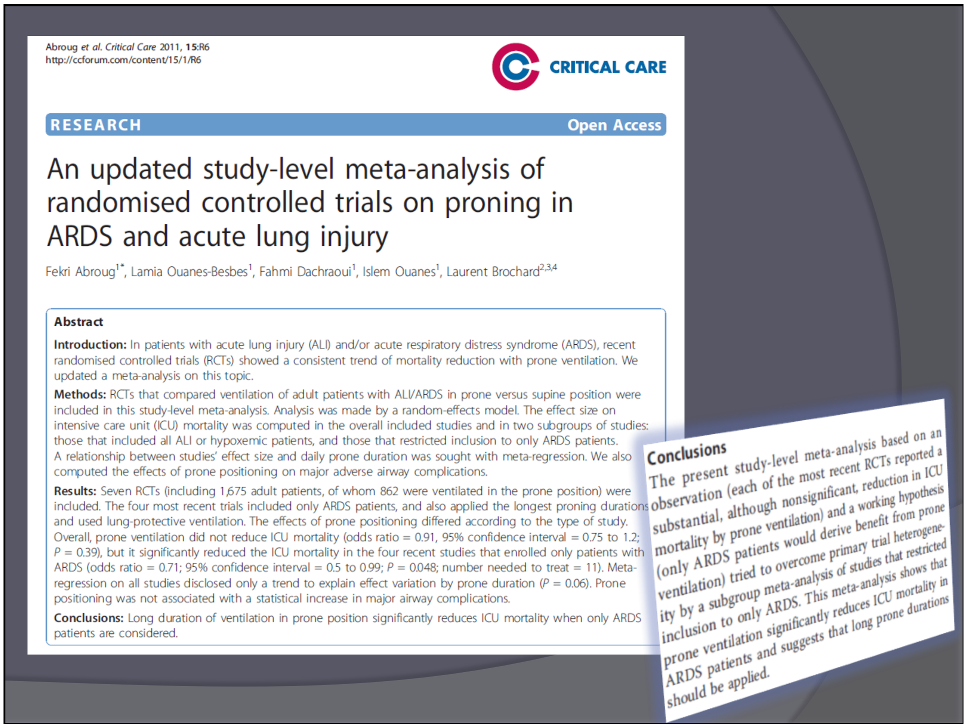
Measurements and Main Results: We measured arterial blood gas alterations to the first pronation and the 28-day mortality rate. The independent risk factors for death in the general population were the Pao_2/Fio_2 ratio (odds ratio, 0.992; confidence interval, 0.986–0.998), the minute ventilation/$Paco_2$ ratio (odds ratio, 1.003; confidence interval, 1.000–1.006), and the concentration of plasma creatinine (odds ratio, 1.385; confidence interval, 1.116–1.720). Pao_2 responders (defined as the patients who increased their Pao_2/Fio_2 by ≥20 mm Hg, 150 patients, mean increase of 100.6 ± 61.6 mm Hg [13.4 ± 8.2 kPa]) had an outcome similar to the nonresponders (59 patients, mean decrease −6.3 ± 23.7 mm Hg [−0.8 ± 3.2 kPa]; mortality rate 44% and 46%, respectively; relative risk, 1.04; confidence interval, 0.74–1.45, p = .65). The $Paco_2$ responders (defined as patients whose $Paco_2$ decreased by ≥1 mm Hg, 94 patients, mean decrease −6.0 ± … ± 0.8 kPa]) had an improved survival when … nonresponders (115 patients, mean increase 6 ± … 0.8 kPa]; mortality rate 35.1% and 52.2%, respe… risk, 1.48; confidence interval, 1.07–2.05, p = .0…

Conclusion: ALI/ARDS patients who respond to … ing with reduction of their $Paco_2$ show an increase… days. Improved efficiency of alveolar ventilati… physiologic deadspace ratio) is an important … tients who will survive acute respiratory failure. … 2003; 31:2727–2733)

Key Words: acute lung injury; acute respiratory … drome; prone position; carbon dioxide exchange

CONCLUSIONS

This study has several limitations. It is retrospective, a number of physiologic variables were not collected (because to ensure that a multiple-center trial is feasible we have to keep variables to a minimum), and a control group at 6 hrs is not available. However, a single fact remains true: Independently of the ventilator setting, which was maintained unmodified, the patients who reacted to prone positioning with a decrease in $Paco_2$ had a better outcome than the patients who did not. The $Paco_2$ change *per se* does not seem to influence the outcome. However, the change during prone positioning probably indicates some difference in the underlying pathology: a lower potential for recruitment in $Paco_2$ nonresponders and a higher potential in responders.



Abroug et al. Critical Care 2011, 15:R6
http://ccforum.com/content/15/1/R6

CRITICAL CARE

RESEARCH Open Access

An updated study-level meta-analysis of randomised controlled trials on proning in ARDS and acute lung injury

Fekri Abroug[1*], Lamia Ouanes-Besbes[1], Fahmi Dachraoui[1], Islem Ouanes[1], Laurent Brochard[2,3,4]

Abstract

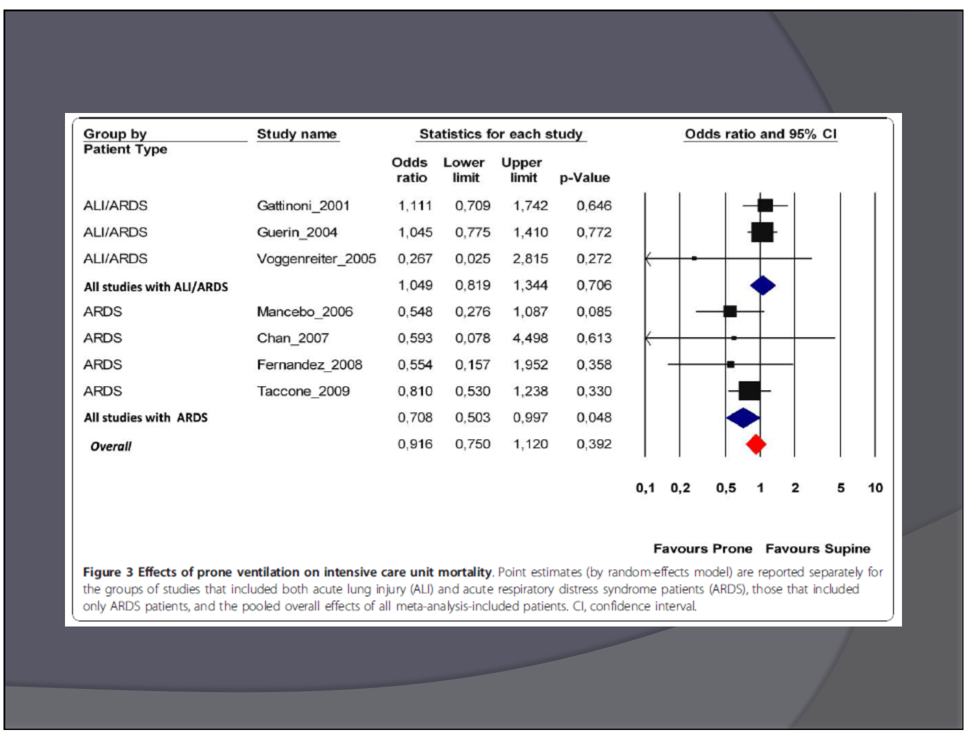
Introduction: In patients with acute lung injury (ALI) and/or acute respiratory distress syndrome (ARDS), recent randomised controlled trials (RCTs) showed a consistent trend of mortality reduction with prone ventilation. We updated a meta-analysis on this topic.

Methods: RCTs that compared ventilation of adult patients with ALI/ARDS in prone versus supine position were included in this study-level meta-analysis. Analysis was made by a random-effects model. The effect size on intensive care unit (ICU) mortality was computed in the overall included studies and in two subgroups of studies: those that included all ALI or hypoxemic patients, and those that restricted inclusion to only ARDS patients. A relationship between studies' effect size and daily prone duration was sought with meta-regression. We also computed the effects of prone positioning on major adverse airway complications.

Results: Seven RCTs (including 1,675 adult patients, of whom 862 were ventilated in the prone position) were included. The four most recent trials included only ARDS patients, and also applied the longest proning durations and used lung-protective ventilation. The effects of prone positioning differed according to the type of study. Overall, prone ventilation did not reduce ICU mortality (odds ratio = 0.91, 95% confidence interval = 0.75 to 1.2; P = 0.39), but it significantly reduced the ICU mortality in the four recent studies that enrolled only patients with ARDS (odds ratio = 0.71; 95% confidence interval = 0.5 to 0.99; P = 0.048; number needed to treat = 11). Meta-regression on all studies disclosed only a trend to explain effect variation by prone duration (P = 0.06). Prone positioning was not associated with a statistical increase in major airway complications.

Conclusions: Long duration of ventilation in prone position significantly reduces ICU mortality when only ARDS patients are considered.

Conclusions
The present study-level meta-analysis based on an observation (each of the most recent RCTs reported a substantial, although nonsignificant, reduction in ICU mortality by prone ventilation) and a working hypothesis (only ARDS patients would derive benefit from prone ventilation) tried to overcome primary trial heterogeneity by a subgroup meta-analysis of studies that restricted inclusion to only ARDS. This meta-analysis shows that prone ventilation significantly reduces ICU mortality in ARDS patients and suggests that long prone durations should be applied.



Group by Patient Type	Study name	Odds ratio	Lower limit	Upper limit	p-Value
ALI/ARDS	Gattinoni_2001	1,111	0,709	1,742	0,646
ALI/ARDS	Guerin_2004	1,045	0,775	1,410	0,772
ALI/ARDS	Voggenreiter_2005	0,267	0,025	2,815	0,272
All studies with ALI/ARDS		1,049	0,819	1,344	0,706
ARDS	Mancebo_2006	0,548	0,276	1,087	0,085
ARDS	Chan_2007	0,593	0,078	4,498	0,613
ARDS	Fernandez_2008	0,554	0,157	1,952	0,358
ARDS	Taccone_2009	0,810	0,530	1,238	0,330
All studies with ARDS		0,708	0,503	0,997	0,048
Overall		0,916	0,750	1,120	0,392

Figure 3 Effects of prone ventilation on intensive care unit mortality. Point estimates (by random-effects model) are reported separately for the groups of studies that included both acute lung injury (ALI) and acute respiratory distress syndrome patients (ARDS), those that included only ARDS patients, and the pooled overall effects of all meta-analysis-included patients. CI, confidence interval.

Study name	Statistics for each study				Complications / Total	
	Odds ratio	Lower limit	Upper limit	p-Value	Prone	Supine
Gattinoni_2001	0,783	0,354	1,733	0,546	12 / 152	15 / 152
Guerin_2004	0,970	0,634	1,484	0,889	50 / 413	47 / 378
Voggenreiter_2005	0,900	0,052	15,466	0,942	1 / 21	1 / 19
Mancebo_2006	5,057	0,592	43,205	0,139	6 / 76	1 / 60
Chan_2007	0,304	0,011	8,319	0,481	0 / 11	1 / 11
Fernandez_2008	0,900	0,052	15,466	0,942	1 / 21	1 / 19
Taccone_2009	2,490	1,052	5,894	0,038	18 / 168	8 / 174
	1,160	0,753	1,784	0,501		

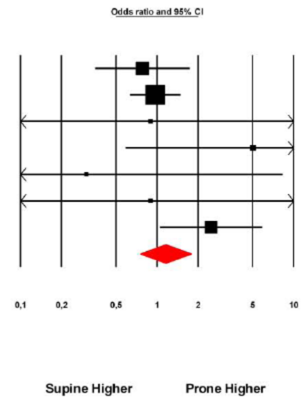


Figure 5 Incidence of major airway complications. CI, confidence interval.

Key messages

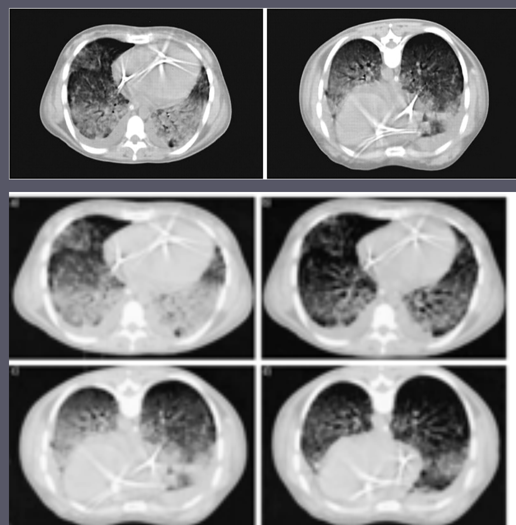
• The use of prone positioning during ARDS ventilation has a robust scientific ground.

• Available RCTs that were frequently underpowered failed to document an impact on mortality mainly because they included patients with a wide spectrum of disease (ALI and ARDS) and applied variable length of prone positioning.

• Study-level meta-analyses published so far only suggested beneficial effects on mortality.

• Meta-analyses of individual patient data have recently shown that prone positioning could reduce ICU mortality in the subgroup of the most severe patients (PaO_2/FiO_2 ratio <100 mmHg).

• Using a subgroup analysis focusing on trials that restricted inclusion to only ARDS patients, our study-level meta-analysis shows that prone positioning reduces ICU mortality in patients with ARDS.

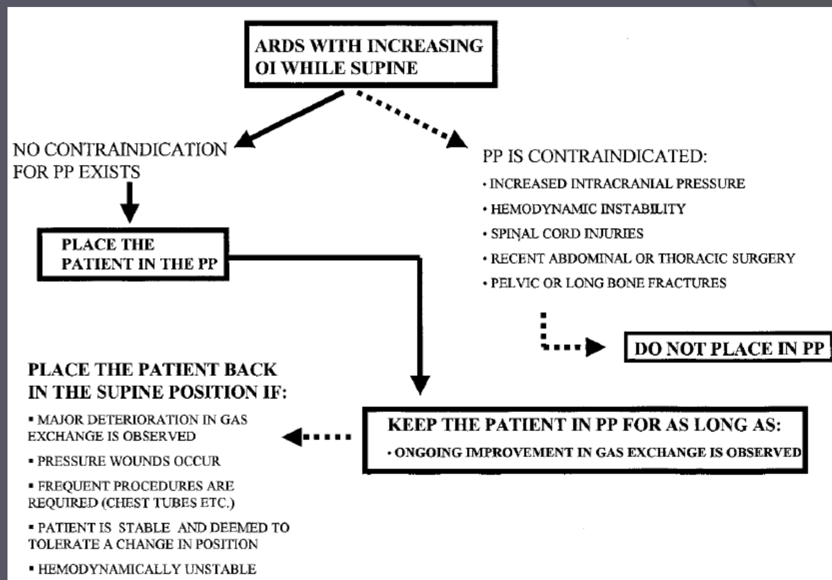


General Principles for Effective Prone Positioning in ALI/ARDS

Conditions for which prone positioning could be beneficial:

- Moderate to severe ALI/ARDS and no contraindications
- When high values for ventilatory pressure, positive end-expiratory pressure (PEEP), and FiO_2 are needed to maintain adequate arterial oxygen pressure
  - >10 cm H_2O PEEP at FiO_2 of >0.6 to maintain oxygen saturation at >90%
  - Tidal thoracic compliance (tidal volume/[plateau pressure – total PEEP]) of <0.040 L/cm H_2O [1]
- Patients with a P/F <140 [2]

1. Marini J, et al. Ventilatory management of acute respiratory distress syndrome: a consensus of two. *Crit Care Med*, 2004; 32(1): 250-255
2. Sud S, et al. Effect of mechanical ventilation in the prone position on clinical outcomes in patients with acute hypoxemic respiratory failure: a systematic review and meta-analysis. *CMAJ*, 2008; 178(9): 1153-1161



A Meta-analysis: Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia

Objective

- To determine effects of prone versus supine ventilation in AHRF (acute hypoxemic respiratory failure) and severe hypoxemia [partial pressure of arterial oxygen (PaO(2))/inspired fraction of oxygen (FiO(2)) <100 mmHg] compared with moderate hypoxemia (100 mmHg </= PaO(2)/FiO(2) </= 300 mmHg).

Methods

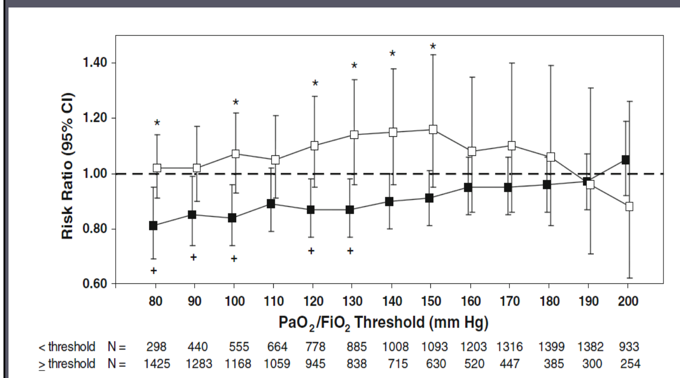
- Systematic review and meta-analysis.
- Electronic databases (to Nov 2009) and conference proceedings searched.
- Ten trials (N = 1,867 patients) met inclusion criteria; most patients had acute lung injury.

Results

- Post hoc analysis demonstrated statistically significant improved mortality in the more hypoxemic subgroup and significant differences between subgroups using a range of PaO2/FiO2 thresholds up to approximately 140 mmHg.

Sud S, et al. Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. *Intensive Care Med*, 2010; 36: 585-599

A Meta-analysis: Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia



- 10 randomized clinical trials were utilized in this meta-analysis
- No evidence of statistical heterogeneity was found for all mortality analyses (*I 2 = 0%)*
- Although there was a trend towards improved survival in less hypoxemic patients (P/F >140 mmHg), it wasn't statistically significant

Error bars indicate width of 95% confidence interval of relative risk in the severe (black squares) and moderate (white squares) baseline hypoxemic subgroups. * Treatment effects differed significantly in subgroups ($p<0.05$). + Prone ventilation significantly decreased mortality in associated subgroups ($p<0.05$)

Prone positioning increased the risk of: 1. Pressure ulcers ($p<0.00001$); 7 trials 2. Endotracheal tube obstruction ($p = 0.0002$); 7 trials 3. Inadvertent chest tube removal ($p = 0.05$); 8 trials of which only 2 reported any events

Sud S, et al. Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. *Intensive Care Med*, 2010; 36: 585-599

Prone Positioning

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Features of the RotoProne™ Therapy System

- Rotation programmable in 1° increments
  - Allows customization of therapy
- Acclimation mode
  - Slow increase in degree of turn allows unstable patients to gradually become accustomed to therapy
- Pause and Hold functions
  - Facilitates nursing care
- Tube management system
  - Helps prevent line and tube dislodgement
- Electronically monitored buckles
  - Ceases rotation and alarms if buckles are not secured
- Ergonomically designed head positioning system
  - Adjustable for size and shape of patient
- CPR
  - Returns patient from prone to supine in < 40 seconds in the event of a code

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ORIGINAL

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Routine prone positioning in patients with severe ARDS: feasibility and impact on prognosis

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Abstract *Purpose:* Since 1997, we have routinely used prone positioning (PP) in patients who have a PaO_2/FiO_2 below 100 mmHg after 24–48 h of mechanical ventilation and who are ventilated using a low stretch ventilation strategy. We report here the characteristics and prognosis of this subgroup of patients with severe lung injury to illustrate the feasibility, role, and impact of routine PP in acute respiratory distress syndrome (ARDS). *Results:* A total of 218 patients were admitted because of ARDS between 1997 and 2009. Of these patients, 57 (26%) were positioned prone because of a PaO_2/FiO_2 below 100 mmHg after 24–48 h of mechanical ventilation. Age was 51 ± 16 years, PaO_2/FiO_2 74 ± 19, and $PaCO_2$ 54 ± 10 mmHg. The lung injury score was 3.13 ± 0.15. Tidal volume was 7 ± 2 mL/kg, PEEP 5.6 ± 1.2 cmH_2O, and plateau pressure 27 ± 3 cmH_2O. Prone sessions lasted 18 h/day and 3.4 ± 1.1 sessions were required to obtain an FiO_2 below 60%. The 60-day mortality was 19% and death occurred after 12 ± 5 days. The ratio between observed and predicted mortality was 0.43. In patients with a PaO_2/FiO_2 below 60 mmHg, the 60-day mortality was 28%. Logistic regression analysis showed that among the 218 patients, PP appeared to be protective with an odds ratio of 0.35 [0.16–0.79]. *Conclusion:* We demonstrate the clinical feasibility of routine PP in patients with a PaO_2/FiO_2 below 100 mmHg after 24–48 h and suggest that, when combined with a low stretch ventilation strategy, it is protective with a high survival rate.

Keywords ARDS · Prone position · Survival

Complications

- Other
  - Compartment syndrome, Rhabdomyolysis
  - Venous air embolism
  - Visceral ischemia: pancreatitis
  - Undiagnosed space occupying lesions

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Chart 2 - Main side effects related to the prone position

Facial edema
Airway obstruction
Skin lesions
Difficulties with enteral feeding
Transitory decrease in oxygen saturation
Hypotension
Arrhythmias
Loss of venous accesses and probes
Loss of dialysis drains and catheters
Accidental extubation
Apical atelectasis due to incorrect positioning of the tracheal tube
Increased need for sedation

Injuries: Brachial Plexus

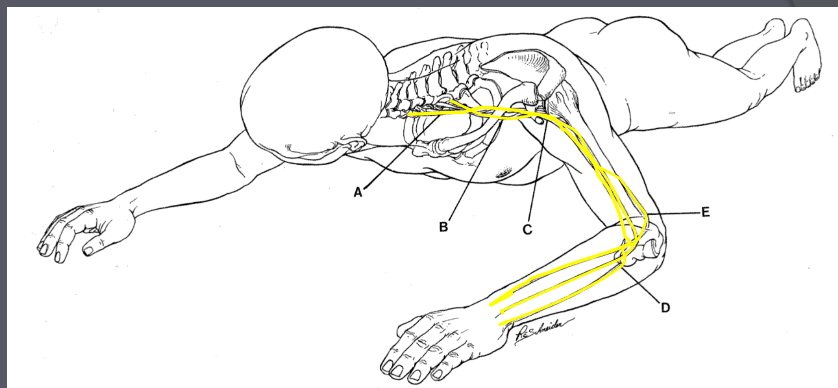

Figure 10–29

Sources of potential injury to the brachial plexus and its peripheral components in a pronated patient. Head position stretching plexus against anchors in shoulder (A). Closure of retroclavicular space by chest support with arms at side; neurovascular bundle trapped against first rib (B). Head of humerus thrust into neurovascular bundle if arm and axilla are not relaxed (C). Compression of ulnar nerve in cubital tunnel (D). Area of vulnerability of radial nerve to compression above elbow (E).

[9] Martin JT and Warner MA (eds). Positioning in Anesthesia and Surgery (3rd edition) . WB Saunders, PA 1997.

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Complications

- Airway
  - Accidental extubation
  - Obstruction of ETT bloody secretions/ sputum plugs
  - Facial, Airway edema
    - Prolonged head low position, ↑ crystalloid infusion
    - Problems with extubation

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Be Careful!

- Watch lines
- Watch for breakdown
- Watch cervical angles
- Wacth for plexus injuries
- Monitor pulmonary toilet

- THANK YOU!!