ARDS: MANAGEMENT UPDATE

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The AECC Definition

Timing		Acute onset, within 48-72 hours
Oxygenation	ALI	PaO2/FiO2<300 (regardless of positive end expiratory pressure level)
	ARDS	PaO2/FiO2<200 (regardless of positive end expiratory pressure level)
Chest radiograph		Bilateral infiltration seen on frontal chest radiograph
Pulmonary artery occlusion pressure		<18mmHg when measure or no clinical evidence of left atrial hypertension

Bernard GR, et al. Report of the American European consensus conference on ARDS:definitions, mechanisms, relevant outcomes and clinical trial coordination. The Consensus Committee. Intensive Care Med 1994;20:225-232.

Berlin Definition of ARDS

Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging	Bilateral opacities-not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assesment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenetion **Mild** **Moderate** **Severe**	 200mmHg<PaO2/FiO2≤300 with PEEP or CPAP≥5cmH2O 100mmHg<PaO2/FiO2≤200 with PEEP or CPAP≥5cmH2O PaO2/FiO2≤100 with PEEP or CPAP≥5cmH2O

JAMA 2012;307:2526-33.

Acta Paediatrica ISSN 0803–5253

REGULAR ARTICLE

Incidence, management and mortality of acute hypoxemic respiratory failure and acute respiratory distress syndrome from a prospective study of Chinese paediatric intensive care network

X Hu[1], S Qian[2], F Xu[3], B Huang[4], D Zhou[5], Y Wang[6], C Li[7], X Fan[2], Z Lu[1], B Sun (bsun@dhmu.edu.cn; guang75@yahoo.com.cn)[1], Chinese Collaborative Study Group for Pediatric Respiratory Failure

Acta Paediatr 2010;99:715-21.

- In China, 26 PICUs, within 1 year period, multicenter prospective study,
- 11521 PICU patients
- **Incidence:** ALI in 4%, ARDS in 2.7%
- **Etiology:** Pneumonia in 75%, Sepsis in 14.7% of ARDS patients
- **Mortality rate:** 44% in children with ARDS
- Total mortality rate is 15%
- Mortality rate is significant high especially in children with pneumonia and sepsis.

Table 3. Organ failure and treatment characteristics in survivors, nonsurvivors, and all children infected with pandemic influenza (H1N1)

	All (n = 83)	Survivor (n = 58)	Nonsurvivor (n = 25)	[a]p
Pediatric Index of Mortality II score (mean ± standard deviation)	9.4 ± 26.5	5.9 ± 16.1	22.3 ± 34.2	<.001
Pediatric Logistic Organ Dysfunction score, median (range)	11 (0–61)	10 (0–40)	20 (2–61)	<.001
Multiple organ dysfunction, n (%)	42 of 83 (50.6)	17 of 58 (29.3)	25 of 25 (100)	<.001
Respiratory	60 of 83 (72.3)	36 of 58 (62.1)	24 of 25 (96.0)	.002
Cardiovascular	31 of 83 (37.3)	16 of 58 (27.6)	15 of 25 (60.0)	.005
Renal	14 of 83 (16.9)	6 of 58 (10.3)	8 of 25 (31.0)	.016
Hematologic	19 of 83 (22.9)	10 of 58 (17.2)	9 of 25 (36.0)	.062
Neurologic	29 of 83 (34.9)	11 of 58 (19.0)	18 of 25 (72.0)	<.001
Hepatic	21 of 83 (25.3)	8 of 58 (13.8)	13 of 25 (52.0)	<.001
Acute lung injury/acute respiratory distress syndrome, n (%)				
Po_2/Fio_2, median (range), mm Hg	220 (18–520)	250 (64–520)	179 (18–332)	.001
Acute lung injury, n (%)	23 of 83 (27.7)	20 of 58 (34.5)	3 of 25 (12.0)	.001
Acute respiratory distress syndrome, n (%)	34 of 83 (41.0)	16 of 58 (27.6)	18 of 25 (72.0)	.001
Mechanical ventilation, n (%)	51 of 83 (61.4)	27 of 58 (46.6)	24 of 25 (96.0)	<.001
Conventional mechanical ventilation	51 of 83 (61.4)	27 of 58 (46.6)	24 of 25 (96.0)	<.001
Noninvasive mechanical ventilation	6 of 83 (7.2)	2 of 58 (3.4)	4 of 25 (16.0)	
High–frequency oscillatory ventilation	3 of 83 (3.6)	0	3 of 25 (12.0)	
Inotropes/vasopressors, n (%)				
Dopamine	31 of 83 (37.3)	10 of 58 (17.2)	21 of 25 (84.0)	<.001
Dobutamine	25 of 83 (30.1)	8 of 58 (13.8)	17 of 25 (68.0)	<.001
Epinephrine	20 of 83 (24.1)	2 of 58 (3.4)	18 of 25 (872.0)	<.001
Renal replacement therapy/plasmapharesis				
Renal replacement therapies, n (%)	6 of 83 (7.2)	1 of 58 (1.7)	5 of 25 (4.0)	.009
Plasmapharesis	4 of 83 (4.8)	1 of 58 (1.7)	3 of 25 (12.0)	.079
Use of oseltamivir, day, median (range)	5 (0–20)	5 (1–20)	5 (0–11)	.075
Length of pediatric intensive care unit stay, hr, median (range)	168 (5–1296)	156 (24–720)	168 (5–1296)	.827
Nosocomial infection, n (%)				
Ventilator–associated pneumonia	11 of 83 (13.3)	6 of 58 (10.3)	5 of 25 (20)	.234
Blood stream infection	7 of 83 (8.4)	4 of 58 (6.9)	3 of 25 (12)	.443
Major features of clinical courses in nonsurvivors, n (%)				
H1N1 infection			16 of 25 (64)	
Secondary infection			4 of 25 (16)	
Primary disease progression			5 of 25 (20	

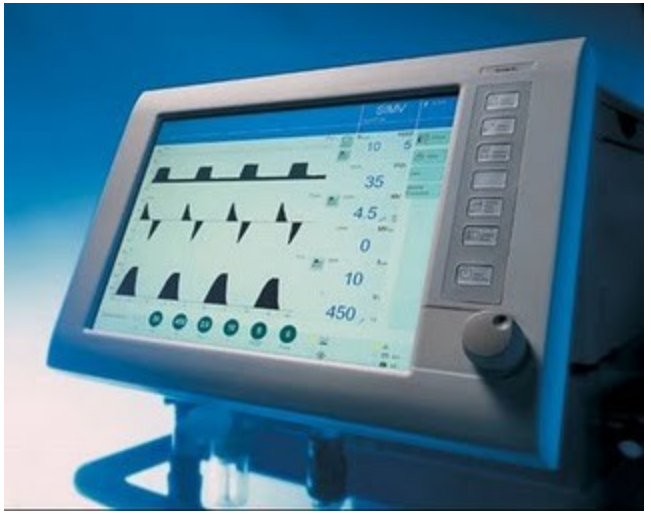
TRATMENTS in ARDS

- Mechanical Ventilation managements
- Supportive treatments
- Pharmacologic treatments

Mechanical Ventilation Treatments

Conventional MV

- Pressure Control
- Volume Control



New Methods

- APRV
- HFOV

Treatment Mains

- Reduction to O2 consumption
- Decreased to respiratory work
- O2 delivery as sufficient and non-toxic concentration
- Open to atelectatic areas in lung
- Continious open-lung strategy with ideal PEEP

Protective Lung Methods in MV

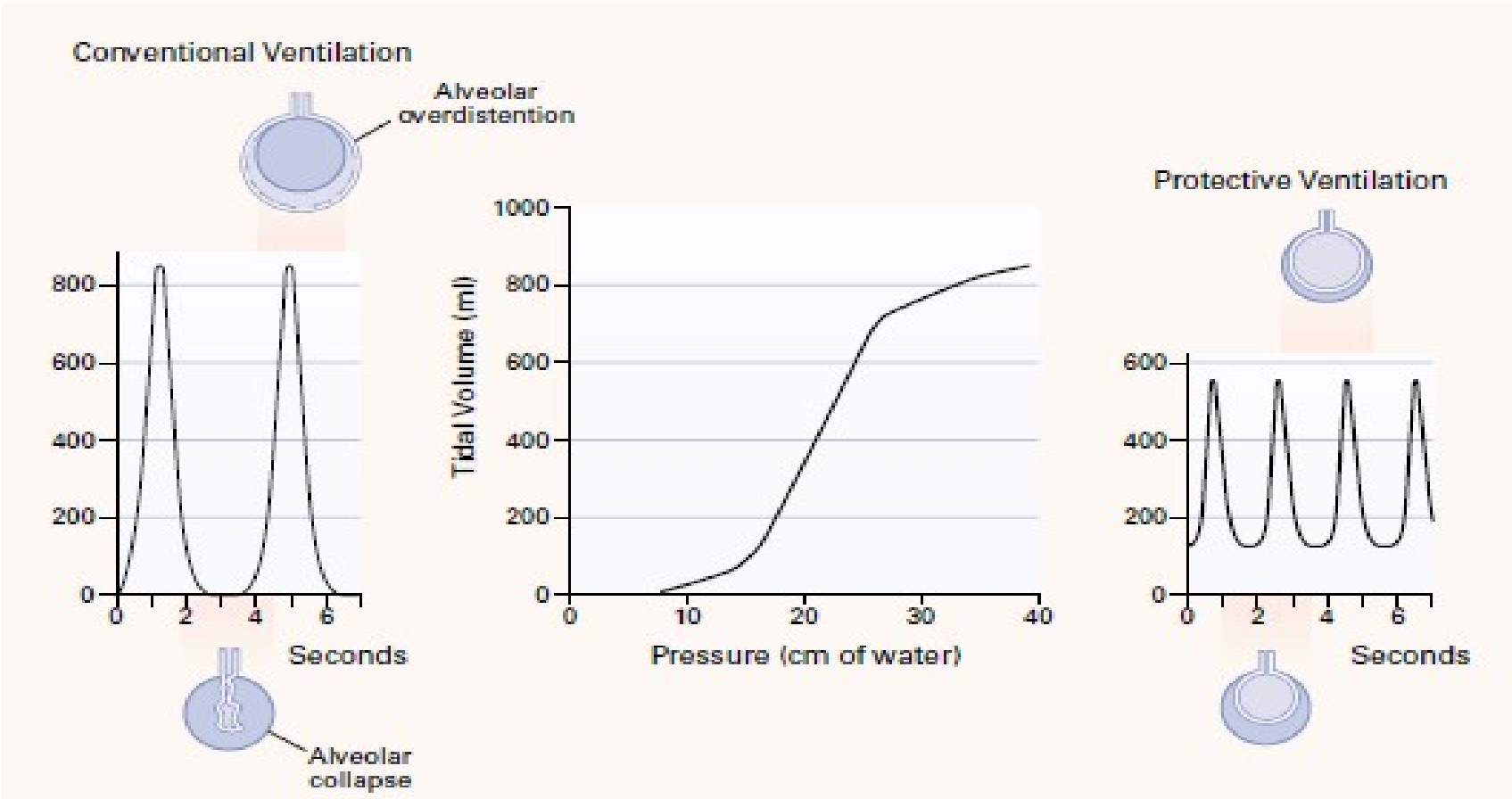
High TVs is harmful for lung (10-15 ml/kg) !!!

- High PEEP ~ 10-15 cmH_2O
- Permissive hypercapnia

  ($pH>7.25$, pCO_2 :60-80mmHg)
- Permissive hypoxia

  ($pO_2>50mmHg$, $sO_2>\%85$)

Conventional and lung protective MV

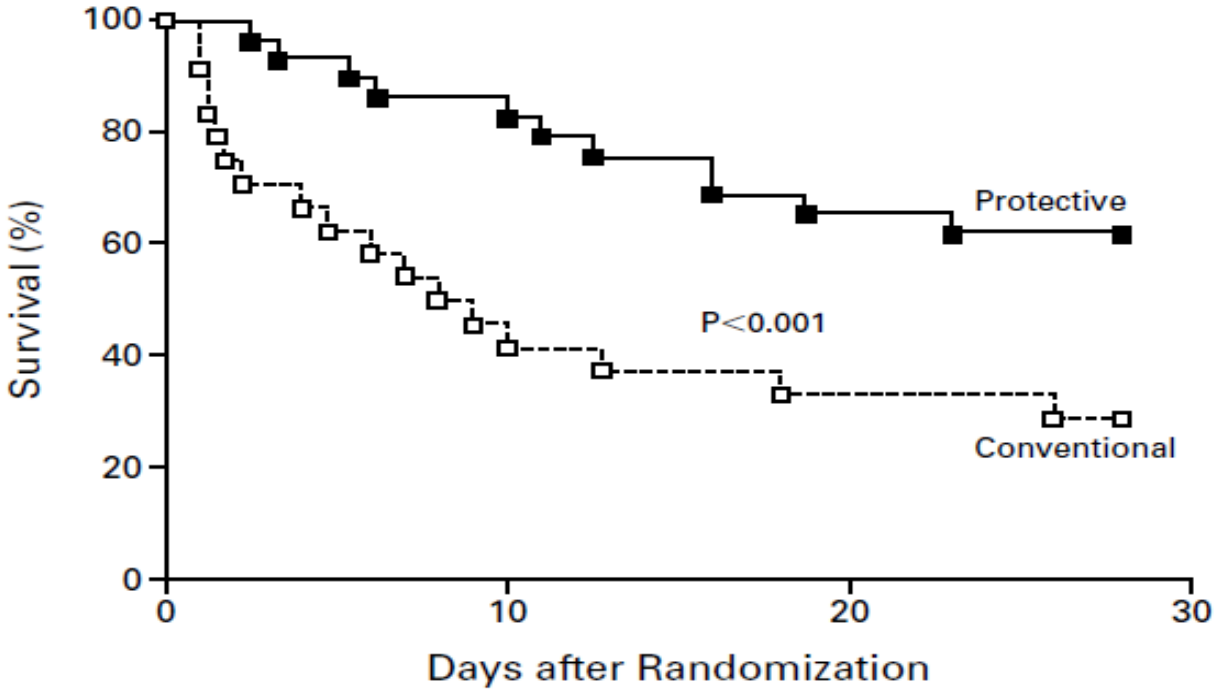


Tobin MJ. Advances in mechanical ventilation. N Eng J Med 2001;344:1986-96.

EFFECT OF A PROTECTIVE-VENTILATION STRATEGY ON MORTALITY IN THE ACUTE RESPIRATORY DISTRESS SYNDROME

MARCELO BRITTO PASSOS AMATO, M.D., CARMEN SILVIA VALENTE BARBAS, M.D., DENISE MACHADO MEDEIROS, M.D., RICARDO BORGES MAGALDI, M.D., GUILHERME DE PAULA PINTO SCHETTINO, M.D., GERALDO LORENZI-FILHO, M.D., RONALDO ADIB KAIRALLA, M.D., DANIEL DEHEINZELIN, M.D., CARLOS MUNOZ, M.D., ROSELAINE OLIVEIRA, M.D., TERESA YAE TAKAGAKI, M.D., AND CARLOS ROBERTO RIBEIRO CARVALHO, M.D.

. (N Engl J Med 1998;338:347-54.)



NO. AT RISK				
Protective	29	25	20	18
Conventional	24	11	9	7

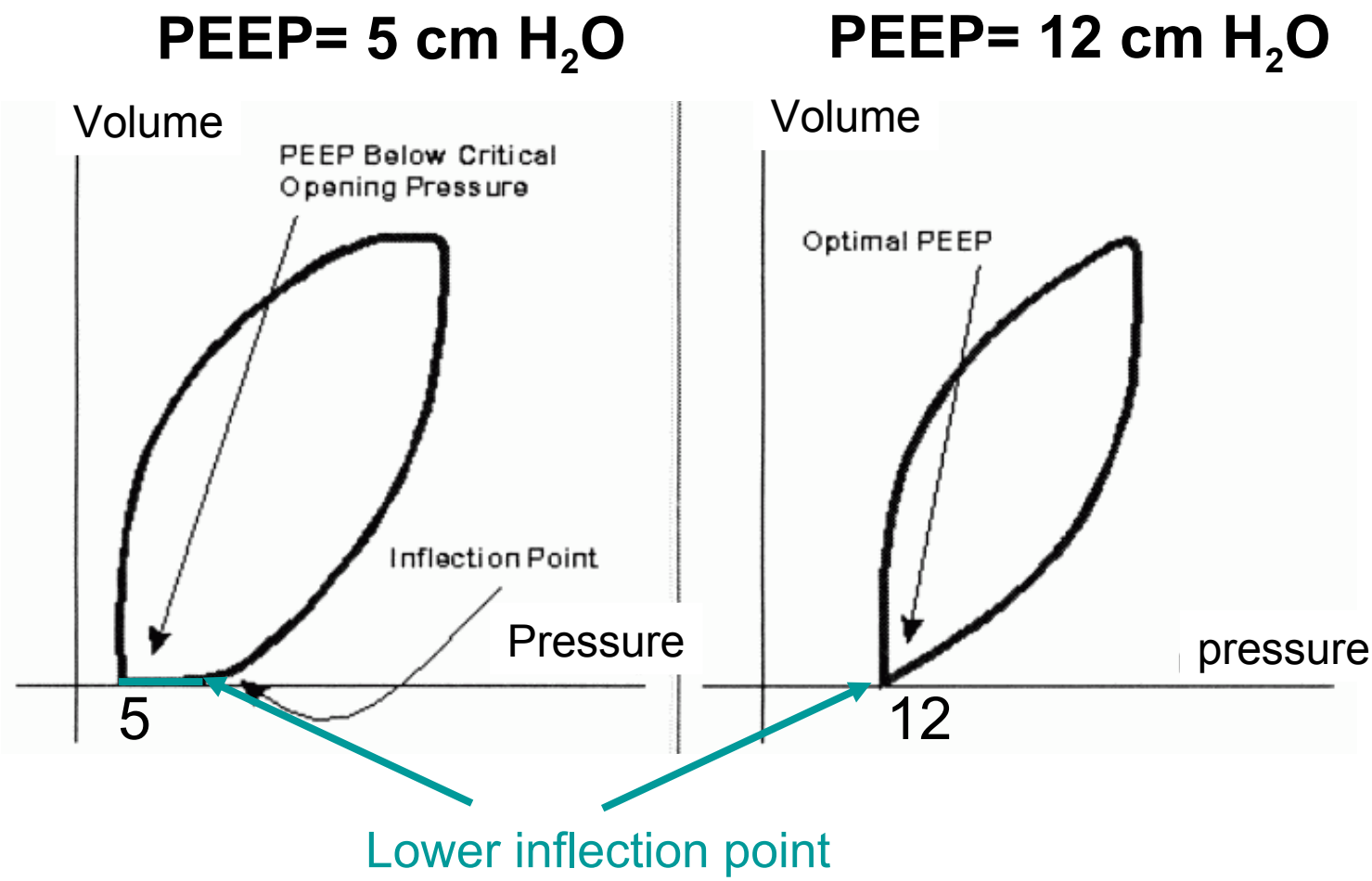
Positive end-expiratory pressure: PEEP

- M
- In
- O
- Au
- Decrease to intrapulmonary shunt
- D
- T ffect.

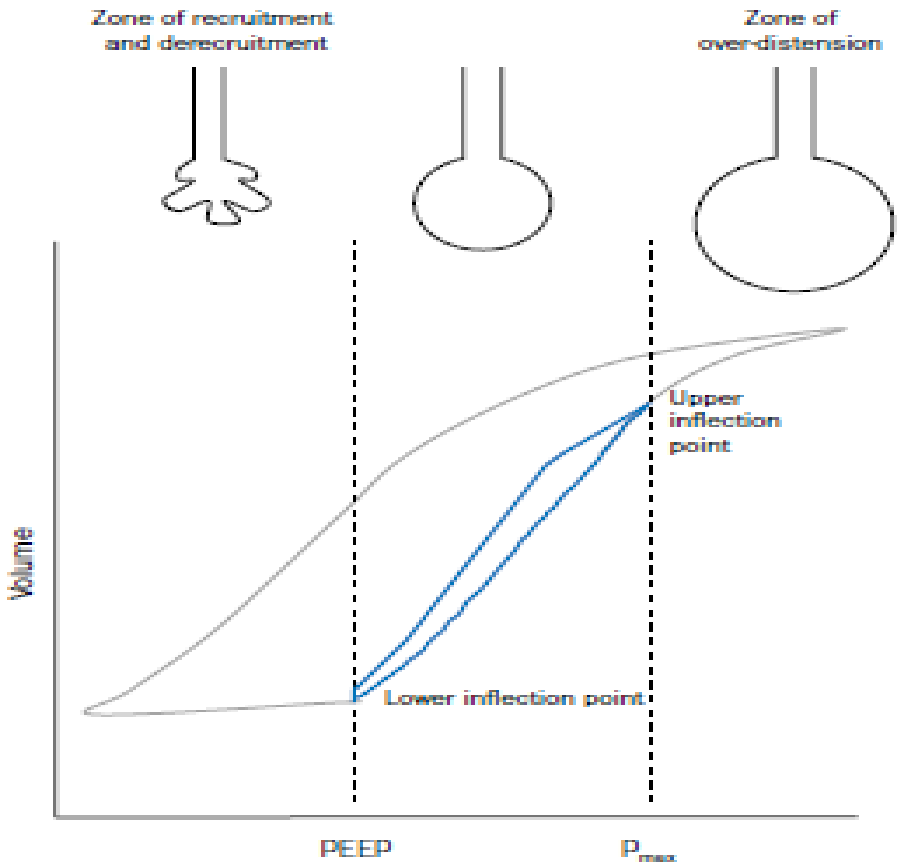
Evaluate to compliance and set to ideal PEEP at level of the best of compliance.

Ideal PEEP is over 2 cmH_2O than lower iflection point.

PEEP and Lower inflection point



The Pressure-Volume relation during MV treatment in patients with ALI



Pinhu L, et al. Ventilator-associated lung injury. Lancet 2003;361:332-340.

Ideal PEEP

- Technically, the definition of ideal PEEP is not easy.
- Our main way is one side increase to PEEP and other side decrease to FiO2

FiO_2	<0.4	0.5	0.6	0.7	0.8	0.9	1
PEEP	5	8-10	10	12-14	14	16-18	18-20

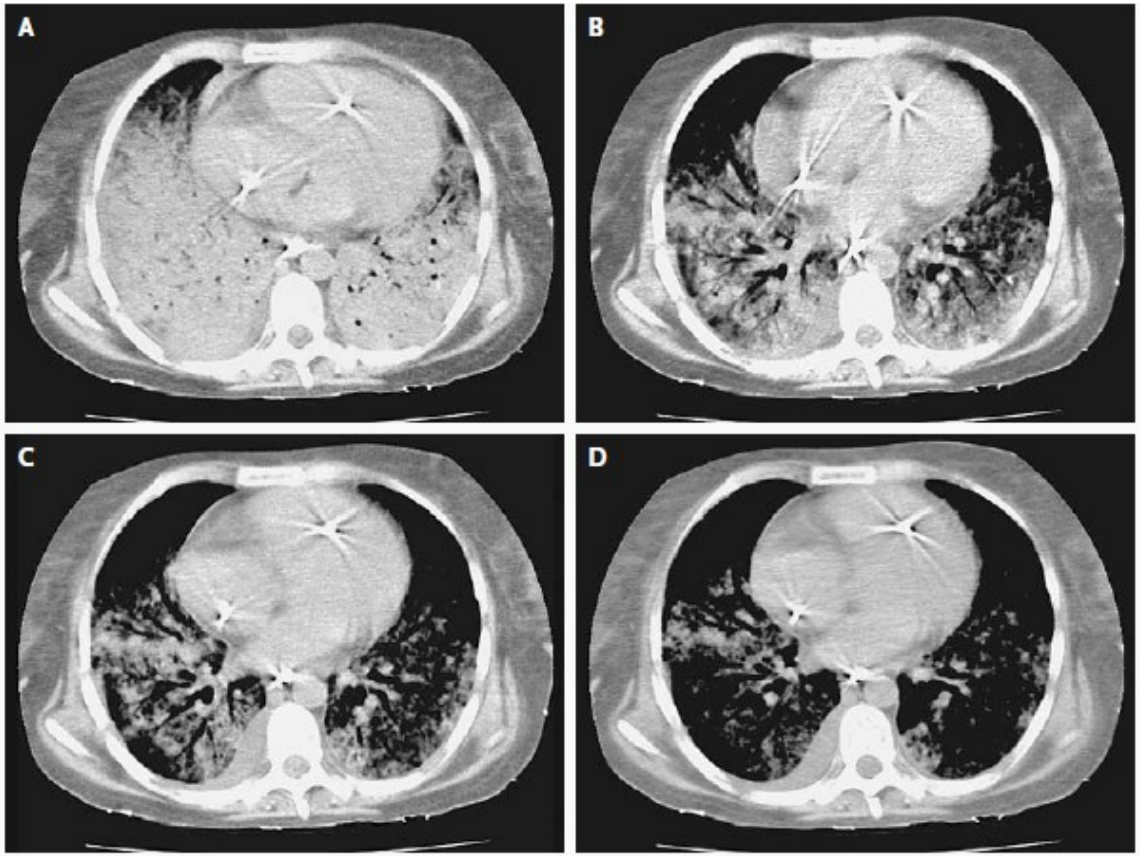


Figure 1. Computed Tomographic Images Obtained at the End-Expiratory Pause in a Patient with Pneumocystosis and the Acute Respiratory Distress Syndrome.

The images were obtained under different ventilatory conditions: a positive end-expiratory pressure (PEEP) of 5 cm of water and a plateau pressure of 20 cm of water (Panel A), a PEEP of 17 cm of water and a plateau pressure of 40 cm of water (Panel B, similar to the strategy used by Gattinoni et al.), a PEEP of 25 cm of water and a plateau pressure of 40 cm of water (Panel C), and a PEEP of 25 cm of water and a plateau pressure of 60 cm of water (Panel D). The corresponding potential for recruitment (relative to the conditions in Panel A) was 35 percent for the conditions in Panel B, 67 percent for the conditions in Panel C, and 87 percent for the conditions in Panel D. At the same plateau pressures (Panels B and C), the application of a higher PEEP (25 cm of water in Panel C) improved the efficacy of the maneuver. A further increase in inspiratory plateau pressure (Panel D) revealed the full potential for recruitment.

Kenneth P. et al. N Engl J Med 2006

Permissive Hypercapnia

- **Well accepted consequence of lung protective strategies of venilatory support.**
- **Low tidal volume and together high PEEP cause to increased dead space and caused to hypercapnia**

  (pH>7.25, pCO_2 :65-85mmHg)

For decrease to excessive CO2 produce;

- **Restrict to excessive carbonhydrate intake**
- **Control to fever**
- **Decrease to muscle activity with sedative and paralytic drugs**

Contraindications for permissive hypercapnia;

- **Increased intracranial pressure,**
- **Sickle cell disease,**
- **Pulmonary HT**
- **Severe cardiac dysfunction**

Prone Positioning

- Another way to recruit atelectatic dependent zones of the lung.
- Several mechanism have been proposed to account for this effect,
- Better Ventilation/perfusion matching
- Increase to end-expiratory lung volume
- Improve overall oxygenetion
- But there is not clearly effect on mortality and duration of MV in meta-analyses.

Priya Prabhakaran . ARDS.. Indian Pediatr 2010;47.


VIASYS
M&K

High Frequency Oscillatory Ventilation (HFOV)

- With HFOV treatment in ARDS, There is possible to provide open alveoles and prevent to excessive strenght of lung tissue with low TV (1ml/kg)

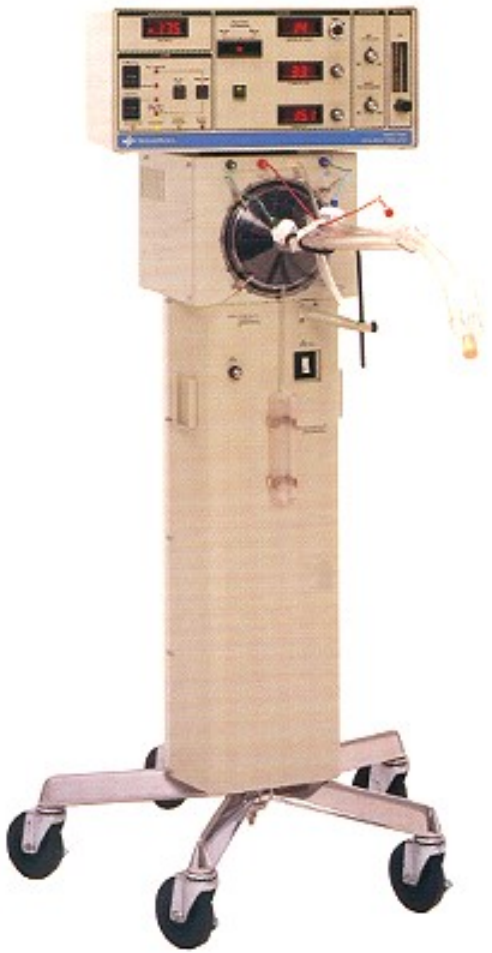
- There is additional advantage that CO2 removel by high respiratory rate (900/min) in HFOV.

HFOV

- Oxygenetion Index= OI

OI= [(MAPx FiO_2/PaO_2)x100]

- If OI > 13-15; HFOV indication



HFOV Advantages

- Improve oxygenetion in shorter time
- Decrease to risk of barotrauma than conventional MV methods
- Demonstrated to decreased changes of chronic lung diseases

ARDS in Children. Pediatric Critical Care, 3rd Edition, Brandley Fuhrrman,Jerry Zimmerman, 2011;731-740
Arnold J, Crit Care Med 1994

Clinical Use of High-Frequency Oscillatory Ventilation for Acute Respiratory Distress Syndrome

Dincer Yildizdas[1], Hacer Yapicioglu[2], Ibrahim Bayram[3], Levent Yilmaz[4] and Yasar Sertdemir[5]

Results. A total of 20 patients were enrolled. The median age of the subjects was 70 (3-168) months; 10 were male. All patients received conventional ventilation before HFOV. After initiation of HFOV, there was an immediate and sustained increase in PaO_2/FiO_2 ratio. The PaO_2/FiO_2 ratio was elevated and OI was decreased significantly after 10-20 minutes and maintained for at least 48 hours (p= 0.03, both). Thirteen of the 20 patients were successfully weaned. No significant change in the mean arterial pressure and heart rate was noted after HFOV. Overall survival rate was 65%. Of 20 patients, 11 patients suffered from extrapulmonary ARDS (ARDSexp) and 9 from pulmonary ARDS (ARDSp). When HFOV was initiated, there was significant increase in PaO_2/FiO_2 and decrease in OI in ARDSexp compared to ARDSp (p= 0.03, both). Also mortality rate was significantly lower in patients with ARDSexp (9% vs.66%), (p= 0.01).

- **Turkey**
- **In 20 children with severe ARDS,**
- **Conventional MV was switched to HFOV because of insuffiency**
- **13/20 (65%) patients survived**

Indian J Pediatr 2009

APRV: Airway Pressure Release Ventilation

- More easier to exhalation with very low PEEP and high and long PIP

Possible Effects:

- Improve to ventilation/perfusion match
- Decrease to barotrauma and hemodynamic adverse events of mechanical ventilation

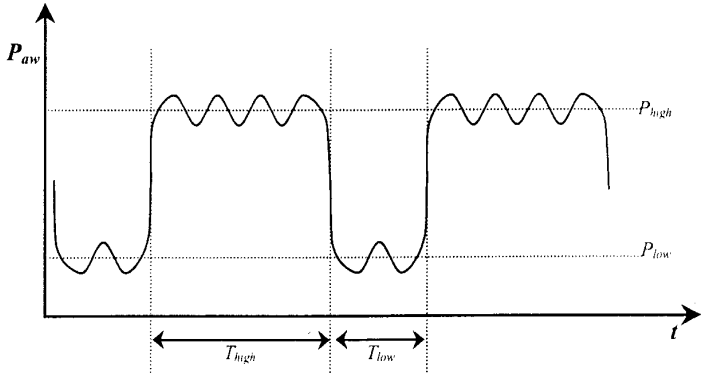


Figure 1. Diagram of pressure changes over time in airway pressure release ventilation.

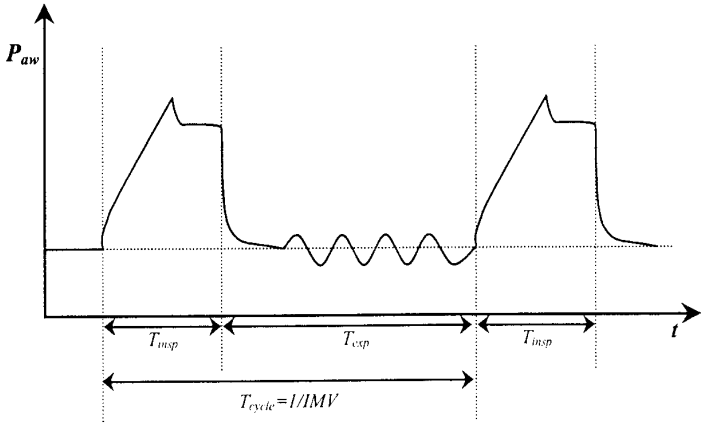


Figure 2. Diagram of pressure changes over time in volume control ventilation (synchronized intermittent mechanical ventilation).

Airway Pressure Release Ventilation: An Alternative Ventilation Mode for Pediatric Acute Hypoxemic Respiratory Failure

Demet Demirkol · Metin Karabocuoglu · Agop Citak

- 3 children with ARDS
- Switcthed to APRV because of severe hypoxemia contineued under conventional MV
- All patients survived.

Indian J Pediatr 2010;77:1322-25)

Airway Pressure Release Ventilation: A Pediatric Case Series

Jambunathan Krishnan, MD[1]* and Wynne Morrison, MD[2]

- 7 children with ARDS, Conventional MV is insuffiency and switched to APRV
- 4/7 survived.

Pediatr Pulmonol 2010;42:83-88.

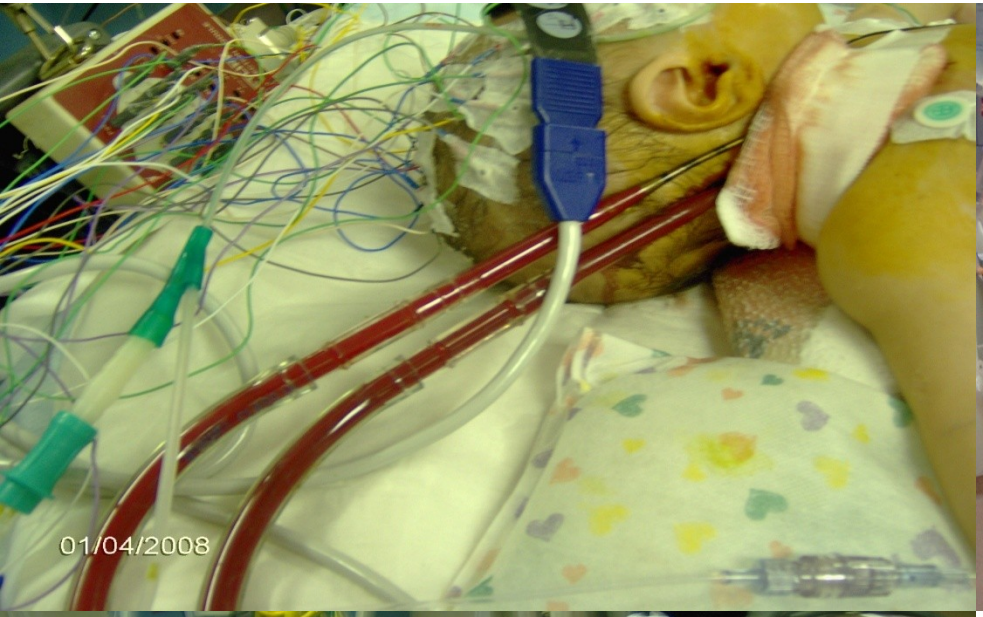
-In adults, Randomized-controlled study for compare to conventional MV (SIMV+PS) and APRV mode.

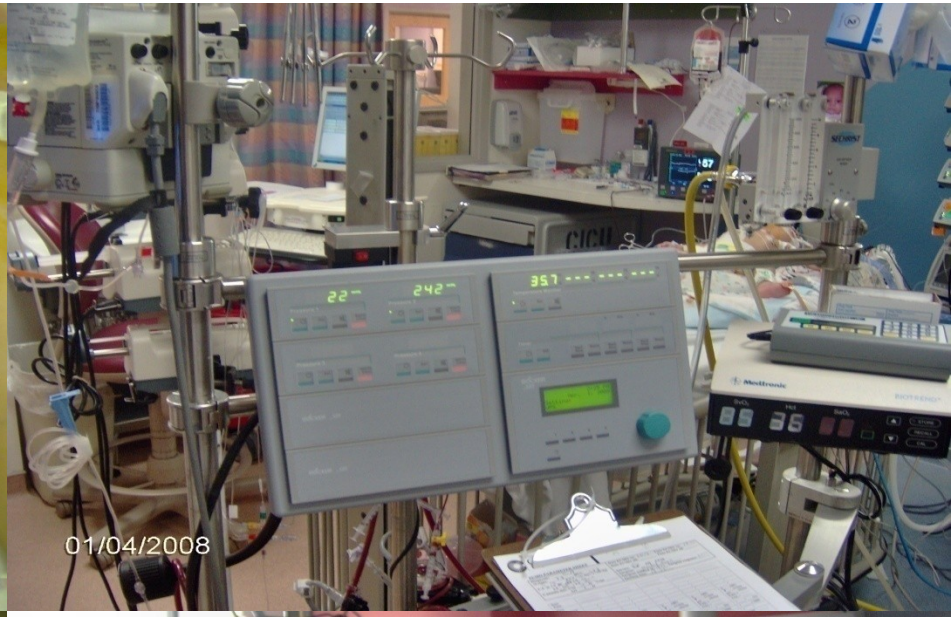
-There isn't any significant duration of MV and mortality between two modes.

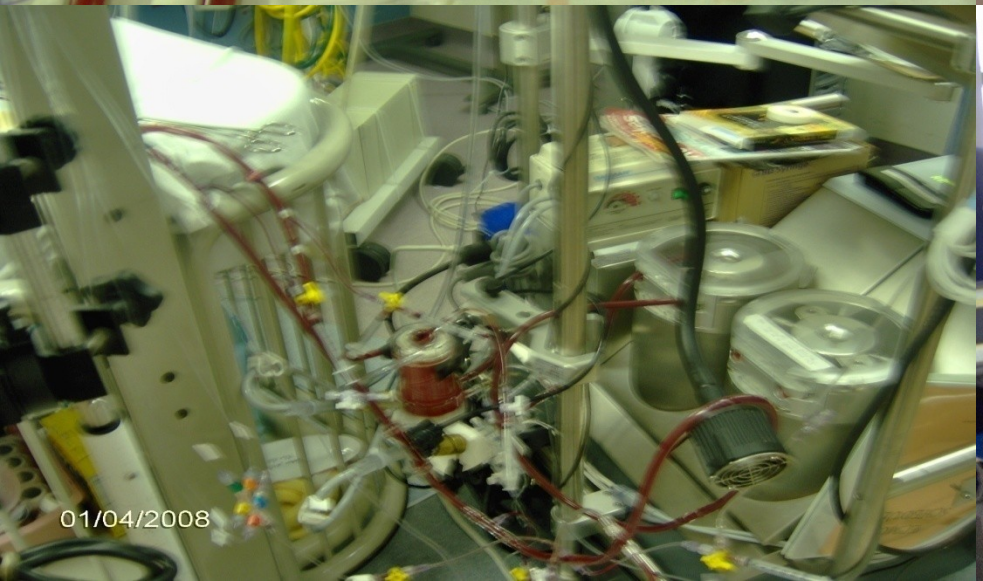
Varpula T, et al. Acta Aneasthesiol Scand 2004;48:722-31.

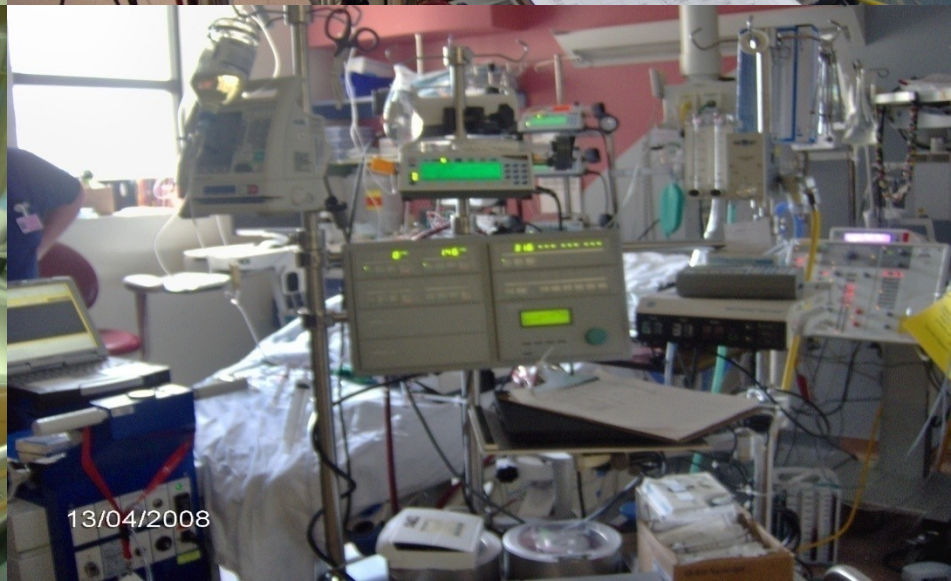
-There isn't any randomized-controlled study about the APRV mode effects in children with the ARDS

ECMO
(Extracorpereal Membran Oxygenetion)









Extracorpereal Life Support

- Provides both gas exhange and circulatory support for children with life-threatening ALI and ARDS.
- Allows the lung the rest from mechanical ventilation.
- ELCS can be provided by venoarterial or venovenous bypass techniques

JAMA®

Online article and related content current as of November 5, 2009.

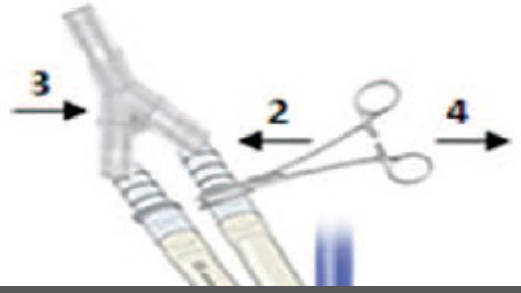
Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome

The Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators

JAMA. 2009;302(17):1888-1895 (doi:10.1001/jama.2009.1535)

- 15 adult ICUs, ECMO performed when conventional MV was insufficient,
- 68 patients with ARDS due to pandemic influenza
- At the beginning of the ECMO; PO_2/FiO_2 : 56 (48-63)
- Duration time of ECMO: 10 (7-15) days
- Mortality rate: 29%

Initial Expe … nnulation for Venove … ne Oxygenatic … ilure*



Circuit Exchange	Bleeding Complications	Survival	Cause of Death
No	Grade IV intraventricular hemorrhage	Dead	Brain herniation
No	DIC	Alive	
Yes	Pulmonary hemorrhage requiring operation	Dead	Hypoxic respiratory failure
Yes	None	Dead	Hypoxic respiratory failure
Yes	Pulmonary hemorrhage; ischemic stroke	Alive	
No	DIC	Dead	Hypoxic respiratory failure
Yes	Coagulopathy	Dead	Multisystem organ failure
No	None	Alive	
No	None	Alive	
No	None	Dead	Multisystem organ failure
Yes	None	Alive	

Supportive Tretments

1) Hemodynamic Support

- Fluid restriction? (Avoid to volume overload!!!!)
- Determine to intravascular volume(CVP follow!!!!)
- Albumin infusion?
- Inotropic support (Dobutamin ?)

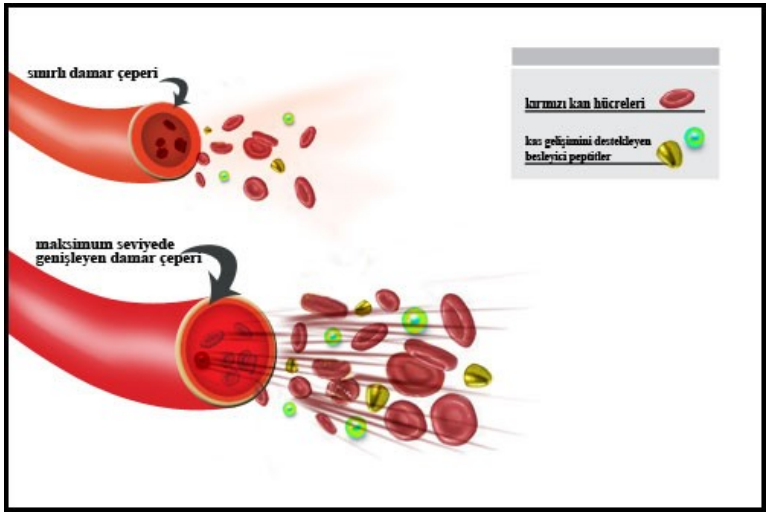
2) Feeding

- Prefer enteral feeding
- Low carbonhydrate, and high lipid involved parenteral feeding.

ARDS in Children, Pediatric Critical Care, Third Edition, Brandley Fuhrrman,Jerry Zimmerman, chapter 46, page:731-740

Pharmacologic Therapies

- Surfactant
- Steroid
- İnhaler nitric oxide
- Other agents



SURFACTANT

- Main effect ; prevent to alveol collapse
- Basic trouble in ARDS; surfactant making and functional trouble

-in USA, 21 PICUs, 153 children,
-Randomized-controlled study
-Mortality rate in Surfactant treatment group:19.4% (15/77), non-surfactant group: 36% (27/75) (p=0.03)
-Conclusion: Surfactant is beneficial in children with ARDS
-Decreased to mortality but;
-Lenght stay of PICU and duration of MV were same

Willson DF, et al. Effect of exogenous surfactant (Calfactant) in pediatric acute lung injury: a randomized controlled study.
JAMA 2005;293:470-6.

But there is contraversial opinion about this study;

- There are more immunsupressed children in non-surfactant group(22 patient in surfactant group vs 30 children in non-surfactant group)
- Unclear surfactant doses and type
- Very expensive treatment

The use of surfactant in children with acute respiratory distress syndrome: efficacy in terms of oxygenation, ventilation and mortality

Hacer Yapıcıoğlu[a,*], Dinçer Yıldızdaş[b], İbrahim Bayram[c], Yaşar Sertdemir[d], H. Levent Yılmaz[e]

Pulmonary Pharmacol & Therapeutics 2003;16:327-333.

- **Turkey, 36 children with ARDS**
- **12 children treated with surfactant,**
- **The most frequent cause is Sepsis (42%)**
- **Within 24-hour after surfactant treatment; improved oxygenetion**
- **Mortatlity rate is 42% in surfactant treated group vs 63% in non-surfactant treated group (p>0.05)**

Research

Open Acc

Surfactant therapy for acute respiratory failure in children: a systematic review and meta-analysis

Mark Duffett[1], Karen Choong[1], Vivian Ng[2], Adrienne Randolph[3] and Deborah J Cook[4]

Crit Care 2007

-6 studies, 314 children with ARDS,

-Surfactant can decrease to mortality

-Increase to without mechanical ventilation days,

-There isn't important adverse effect

Commentary

Surfactant for acute respiratory failure in children: where should it fit in our treatment algorithm?

Margrid Schindler

Crit Care 2007

- There are unresponsive a lot of questions about surfactant,
- Unclear treatment doses and time
- In surfactant treatment; we should decide, individually

STEROID

-In adult studies, steroid may beneficial

if steroid treatment is started

in late period (>7day).

-There isn't randomized-controlled study

about streoid treatment in children with ARDS.

-It is beneficial in anectodal cases.

-Steroid treatmen in ARDS; increase to

neuromuscular weakness and sepsis.

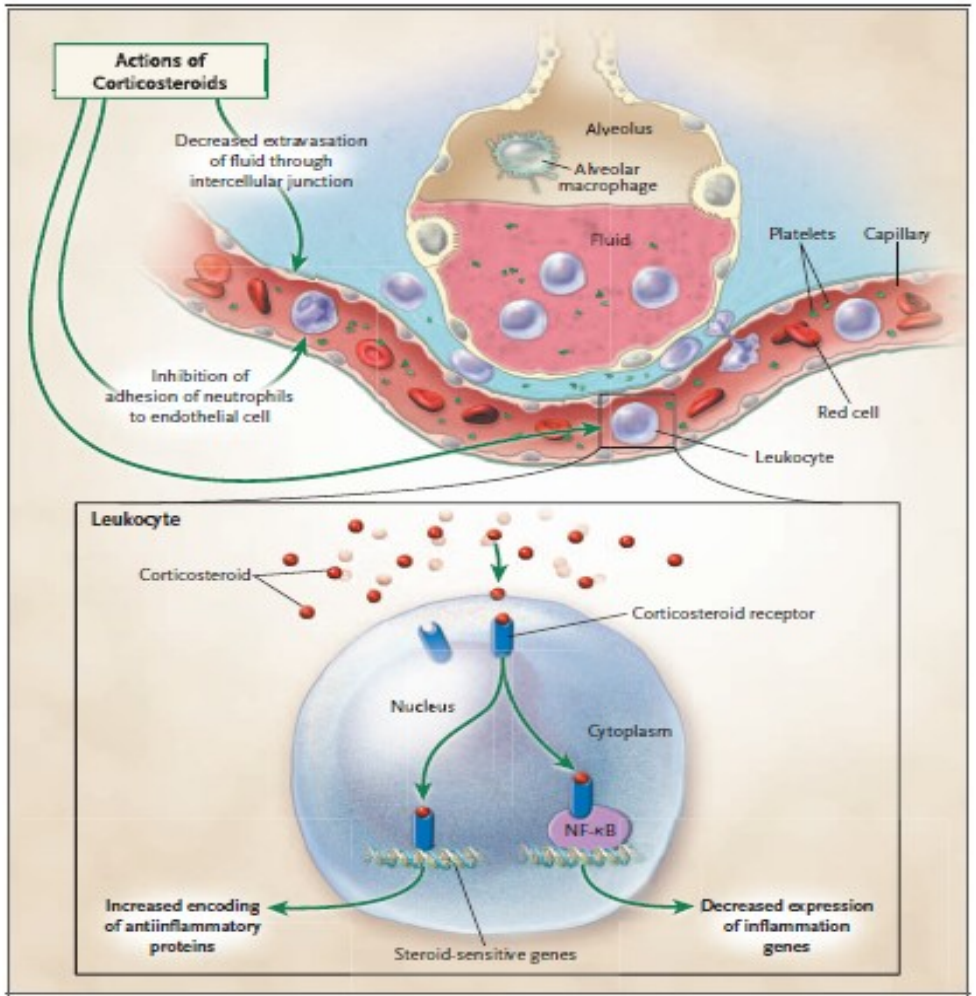


Figure 1. **Pathways of the Inhibition of Inflammation by Corticosteroids in ARDS.**

Corticosteroids can decrease the signs and symptoms of inflammation by reducing the extravasation of plasma through intercellular junctions of the capillary and inhibiting the adhesion and migration of leukocytes across the capillary wall. Corticosteroids diffuse across leukocyte cell membranes and bind to glucocorticoid receptors in the cytoplasm. The activated corticosteroid–receptor complexes translocate into the nucleus, where they bind to the promoter regions of corticosteroid-responsive genes called glucocorticosteroid-response elements, which may encode antiinflammatory proteins. Activated nuclear corticosteroid receptors also inhibit, or switch off, inflammation genes, thereby blocking the transcription of inflammatory proteins by nuclear factor-κB (NF-κB) and activator protein 1.[4,5]

Efficacy and Safety of Corticosteroids for Persistent Acute Respiratory Distress Syndrome

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

N Engl J Med 2006;354;1671-84.

- 180 adult patients wit ARDS longer than 7 days,
- Randomized-controlled study,
- 91 patients received placebo, 89 patients received methyl prednisolon (2mg/kg)
- There isn't significant difference mortality rates at 60th day (28,6% and 29.2%) between 2 groups.
- In steroid treated group; oxygenetion, without ventilator days and blood pressure are better
- It isn't effect on infection risk.
- Increased to neuromuscular weakness.

iNO

- iNO selective pulmonary vasodilatator and minimal systemic effect
- Improve oxygenetion but can not be decreased mortality rate.
- If OI>25 must be consider iNO treatment.
- Its effects can be increased together with HFOV.

DobynsEL, et al. Multicenter randomized controlled trial of inhaled nitric oxide therapy on gas exchange in children with acute hypoxic respiratory failure. J Pediatr 1999;4:406-412.

IMMUNODEFIENCY/ ARDS / MORTALITY

- **ARDS developed in 43 children after BMT,**
- **BMT indications: Solid tumors (30%), leukemia (44%), Primary immunodefincies (19%), and aplastic anemia (7%).**
- **The most frequent cause of ARDS: pneumonia (43%)**
- **Mortality rate is 88%**

  Bojko T, et al. Acute hypoxemic respiratory failure in children following bone marrow transplantation: An outcome and pathologic study. Crit Care Med 1995;23:755-59.

-MV indications after BMT in children

-Mortality rate is 81%

Keenan Ht, et al. Outcome of childre who required mechanically ventilatory support after bone marrow tranplantation.
Crit Care Med 2000;28;830-35.

-In 5 children with SCID and ARDS developed at follow; mortality rate is 100%.

Kendirli T, Doğu F, İkincioğulları A, Aytekin C, Yıldıran A, Yüksek M, İnce E. Fatal acute respiratory distress syndrome in children with combined immunedeficiencies. Asthma Allergy Immunol 2009;7:180-188.

PROGNOSIS

- Mortality rate is decreasing in ALI and ARDS.
- Mortality rate is 20-30%
- ***The causes of Mortality:***

The most frequent cause of mortality in children with ARDS; Sepsis and MODS

- Neurologic deficit
- Prolongation of mechanical ventilation
- Critical illness polymyoneuropathy
- Pneumothorax, pneumomediastinum

Incidence and Outcomes of Pediatric Acute Lung Injury

Jerry J. Zimmerman, Saadia R. Akhtar, Ellen Caldwell and Gordon D. Rubenfeld
Pediatrics 2009;124;87-95
DOI: 10.1542/peds.2007-2462

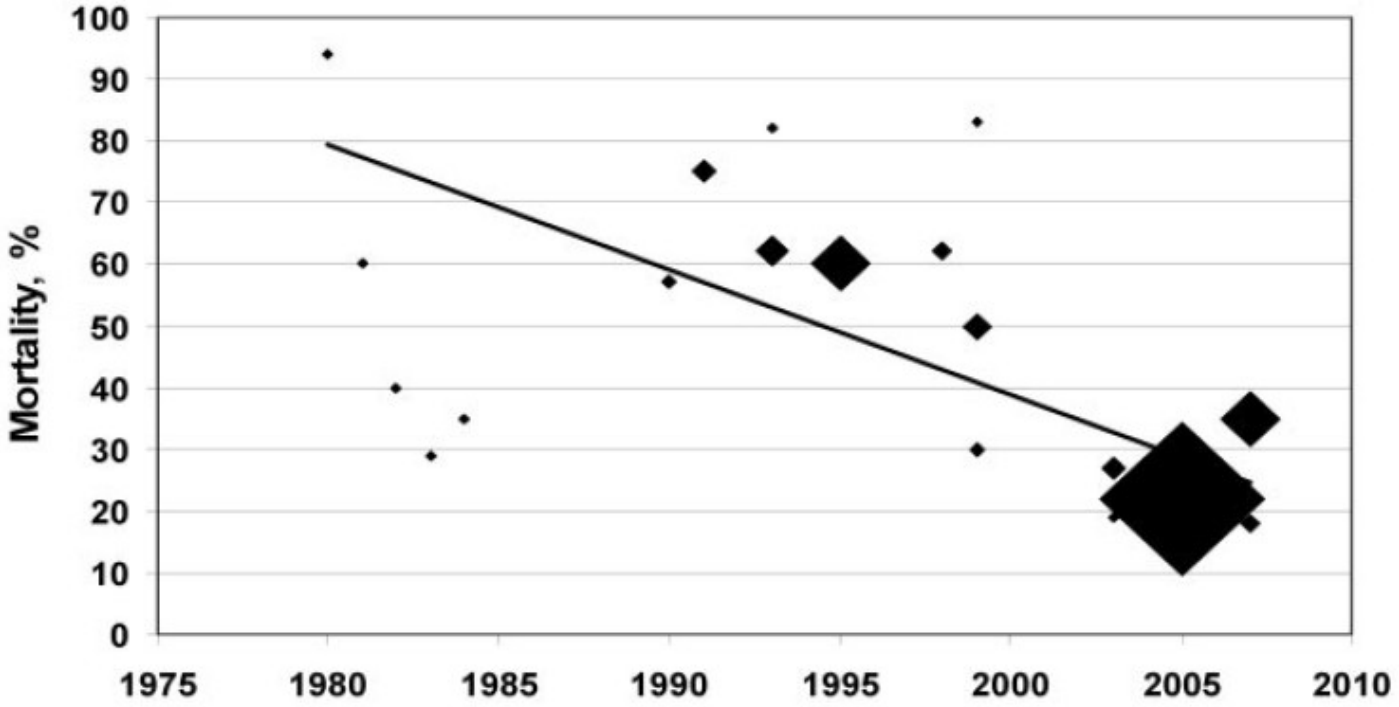


FIGURE 1

Pediatric ALI mortality rates reported since 1980. Each data point represents one of the studies summarized in Table 4, with appropriate weighting on the basis of the number of cases reported to generate the trend line (total $N = 978$; Pearson's correlation coefficient $= -0.750$).

THANKS