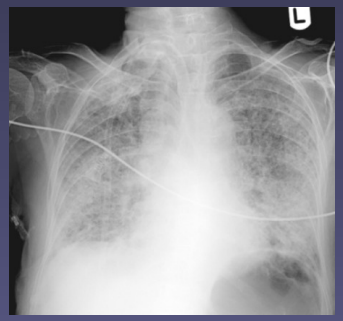
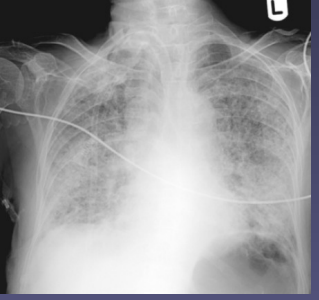


ARDS
Acute Respiratory Distress Syndrom

Jan Maláska

Klinika anesteziologie, resuscitace a intenzivní medicíny
Fakultní nemocnice Brno a Lékařská fakulta Masarykovy univerzity Brno



- 1821 – R.T.H. Laennec
- První publikovaný vědecký popis
- Popis idiopatické anasarky plic
- Plicní edém bez známek srdečního selhání

Thorax, 1981, **36**, 81–90

R T H Laënnec 1781–1826
His life and work: a bicentenary appreciation

ALEX SAKULA

From Redhill General Hospital, Redhill, Surrey

ABSTRACT René Théophile Hyacinthe Laënnec was born on 17 February 1781 in Quimper and spent much of his youth in Nantes, where his uncle Guillaume was Dean of the Faculty of Medicine. He was considerably influenced by his uncle and went to study medicine in Paris where he qualified in 1804. Among his teachers were Corvisart and Bayle who stimulated his interest in the clinical diagnosis of diseases of the chest and especially tuberculosis, from which Laënnec himself suffered. His clinical experience and morbid anatomical dissections at the Necker Hospital culminated in his invention of the stethoscope (1816) and the writing of his masterpiece *De l'Auscultation Médiate* (1819) which may be regarded as the pioneer treatise from which modern chest medicine has evolved. Despite his great success in Paris, Laënnec always retained a great love for his native Brittany. When his health finally broke down, he returned to his home Kerlouarnec, near Quimper, and died there on 13 August 1826, aged 45 years. On the occasion of the bicentenary of his birth we pay homage to the memory of this great French physician.

"People will not look forward to posterity who never look backward to their ancestors."

Edmund Burke: Reflections on the Revolution in France

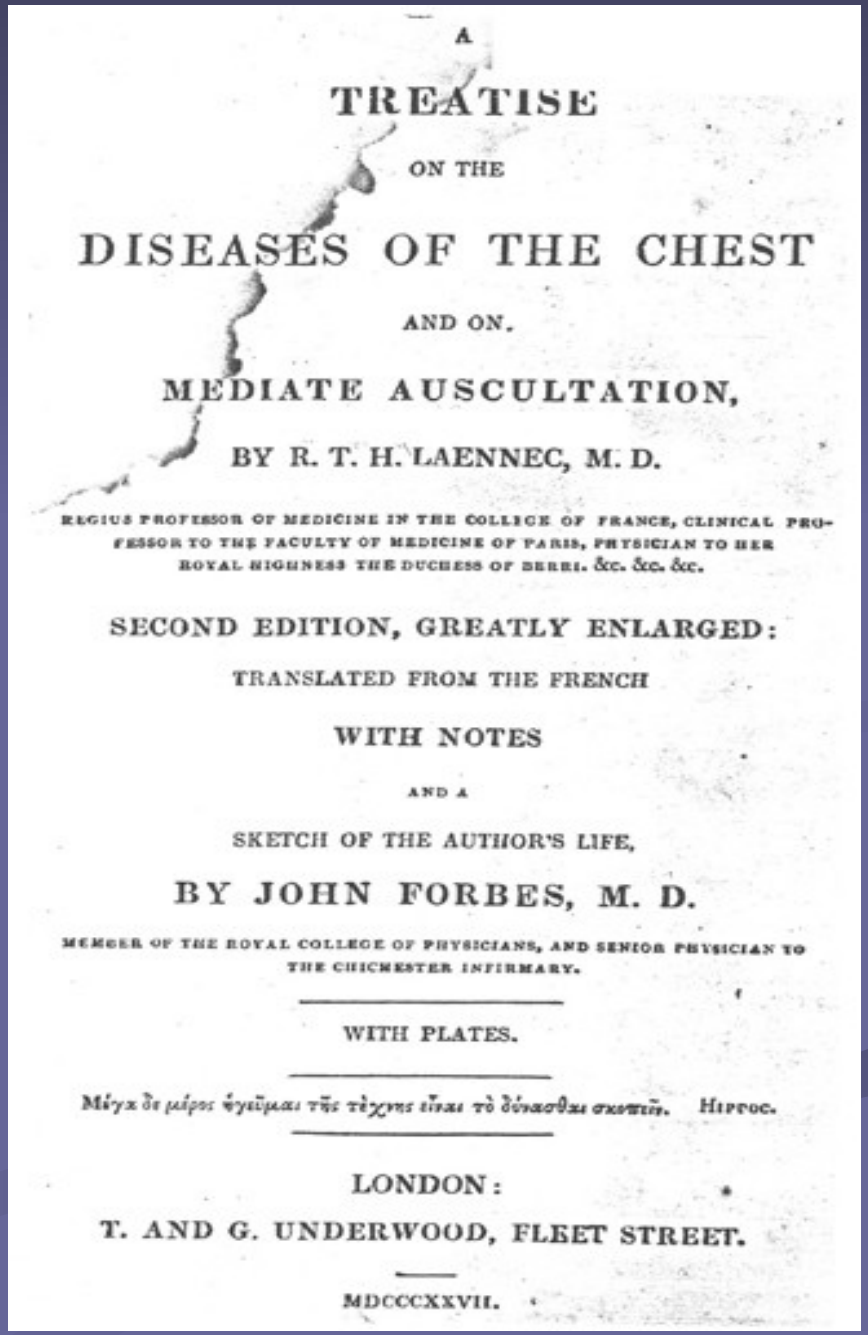
Two hundred years have elapsed since the birth of the great French physician, René Théophile Hyacinthe Laënnec, who, by his invention of the stethoscope, bequeathed to us the first tool to aid clinical diagnosis, as well as providing the symbol by which, more than any other, the physician is at present recognised. Moreover, in his great treatise, *De l'Auscultation Médiate*, Laënnec's rational clinico-pathological approach may be said to have laid the foundations of modern clinical medicine and especially our understanding of cardiorespiratory disease.

Birth and early years in Quimper

Laënnec (fig 1) was born on 17 February 1781 at 2 rue du Quai, Quimper, in Southern Brittany, France. Quimper, at the junction of the rivers Odet and Steir, is the capital of the county of Cornouaille, in the *département* of Finisterre. It was, and is, a charming old walled city, with its

Address for reprint requests: Dr A Sakula, Redhill General Hospital, Earlswood Common, Redhill, Surrey RH1 6LA.

Fig 1 *RTH Laënnec. From coloured engraving, reproduced by courtesy of the Wellcome Trustees.*



A

TREATISE

ON THE

DISEASES OF THE CHEST

AND ON

MEDIATE AUSCULTATION,

BY R. T. H. LAENNEC, M. D.

REGIUS PROFESSOR OF MEDICINE IN THE COLLEGE OF FRANCE, CLINICAL PROFESSOR TO THE FACULTY OF MEDICINE OF PARIS, PHYSICIAN TO HER ROYAL HIGHNESS THE DUCHESS OF BERRI. &c. &c. &c.

SECOND EDITION, GREATLY ENLARGED:

TRANSLATED FROM THE FRENCH

WITH NOTES

AND A

SKETCH OF THE AUTHOR'S LIFE,

BY JOHN FORBES, M. D.

MEMBER OF THE ROYAL COLLEGE OF PHYSICIANS, AND SENIOR PHYSICIAN TO THE CHICHESTER INFIRMARY.

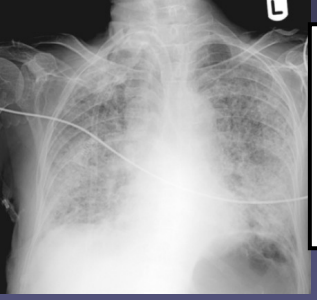
WITH PLATES.

Μέγα δε μέρος ὑγιεῖμαι τῆς τέχνης εἶναι τὸ δύνασθαι σκοπεῖν. HIPPOC.

LONDON:

T. AND G. UNDERWOOD, FLEET STREET.

MDCCCXXVII.



Acute respiratory distress in adults. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Lancet. 1967 Aug 2;2(7511):319-23.

- Těžká dyspnoe
- Tachypnoe
- Cyanóza refrakterní na O2
- Snížená compliance (Cst, rs)
- Difůzní alveolární infiltáty na RTG
- Atelaktázy, vyskulární kongesce, hemoragie, plicní edém a hyalinní membrány při autopsii

ACUTE RESPIRATORY DISTRESS IN ADULTS

DAVID G. ASHBAUGH
M.D. Ohio State
ASSISTANT PROFESSOR OF SURGERY

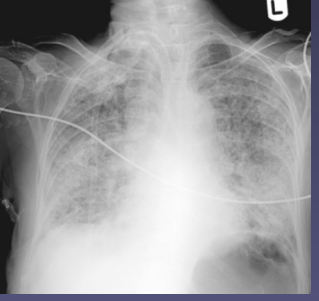
D. BOYD BIGELOW
M.D. Colorado
ASSISTANT IN MEDICINE AND AMERICAN THORACIC SOCIETY-NATIONAL TUBERCULOSIS ASSOCIATION FELLOW IN PULMONARY DISEASE

THOMAS L. PETTY
M.D. Colorado
ASSISTANT PROFESSOR OF MEDICINE

BERNARD E. LEVINE
M.D. Michigan
AMERICAN THORACIC SOCIETY-NATIONAL TUBERCULOSIS ASSOCIATION FELLOW IN PULMONARY DISEASE*

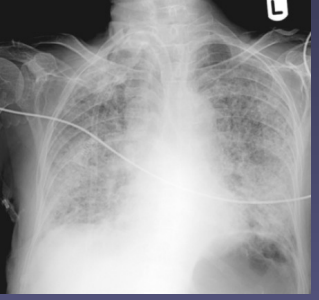
From the Departments of Surgery and Medicine, University of Colorado Medical Center, Denver, Colorado, U.S.A.

Summary The respiratory-distress syndrome in 12 patients was manifested by acute onset of tachypnœa, hypoxæmia, and loss of compliance after a variety of stimuli; the syndrome did not respond to usual and ordinary methods of respiratory therapy. The clinical and pathological features closely resembled those seen in infants with respiratory distress and to conditions in congestive atelectasis and postperfusion lung. The theoretical relationship of this syndrome to alveolar surface active agent is postulated. Positive end-expiratory pressure was most helpful in combating atelectasis and hypoxæmia. Corticosteroids appeared to have value in the treatmcnt of patients with fat-cmbolism and possibly viral pneumonia.



ARDS- synonyma

- DaNang lung
- Šoková plíce
- Post-traumatická plíce
- Syndrom hyalinních membrán
- 1971 Petty a Ashbaugh –"adult respiratory distress syndrom" – odlišení od IRDS



AMERICAN JOURNAL OF
Respiratory and
Critical Care Medicine®
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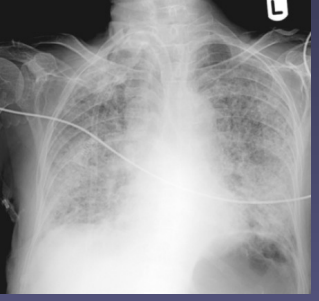
Am. J. Respir. Crit. Care Med., Vol 149, No. 3, Mar 1994, 818-824.
The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination
GR Bernard, A Artigas, KL Brigham, J Carlet, K Falke, L Hudson, M Lamy, JR Legall, A Morris and R Spragg
Vanderbilt University, Nashville, Tennessee.

- ALI (Acute Lung Injury)
  Pao2/Fio2 <300 mm Hg
- ARDS (Acute Respiratory Distress Syndrom)
  Pao2/Fio2 <200 mm Hg
- „syndrome of inflammation and increased permeability that is associated with a constellation of clinical, radiologic, and physiologic abnormalities that cannot be explained by, but may coexist with, left atrial or pulmonary capillary hypertension."



AMERICAN JOURNAL OF
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The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination

GR Bernard, A Artigas, KL Brigham, J Carlet, K Falke, L Hudson, M Lamy, JR Legall, A Morris and R Spragg
Vanderbilt University, Nashville, Tennessee.

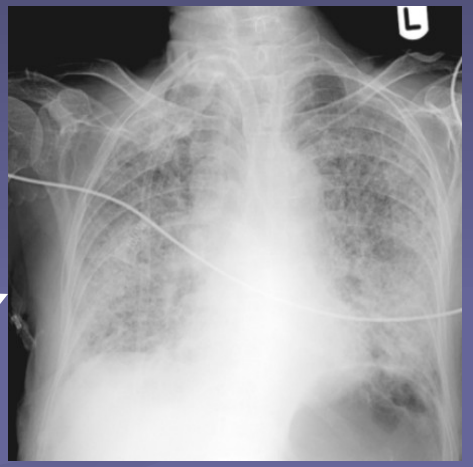
ALI/ARDS

- Akutní začátek
- Oxygenace:PaO2/FIO2

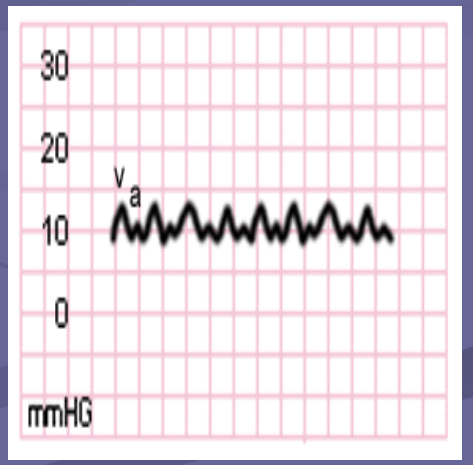
< 300 mm per Hg pro ALI

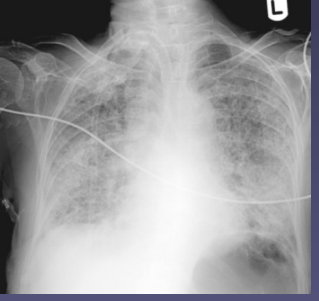
< 200 mm per Hg for ARDS (nezávisle na PEEP)

- RTG plic – bilaterální infiltráty
- PAWP < 18 mmHg nebo nepřítomnost známek AHF



PAWP





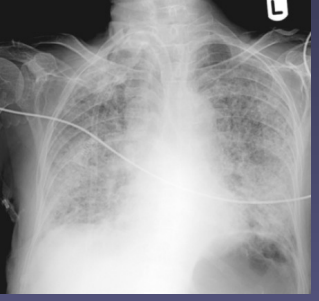
Validita kritérií PaO2/FiO2 + RTG

Oxygenační index (Horowitz): nespecifický pro ARDS

RTG kritéria: vágní, častá neshoda rentgenologů (*Meade, AJRCCM 2000*)

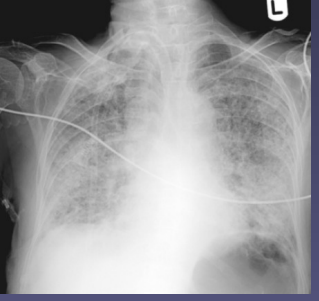
Diff.dg.:

- Intersticiální procesy
- Idiopatická pulmonální fibróza
- Lymfangoitis carcinomatosa
- Plicní veno-okluzivní choroba
- Zvýšený hydrostatický tlak

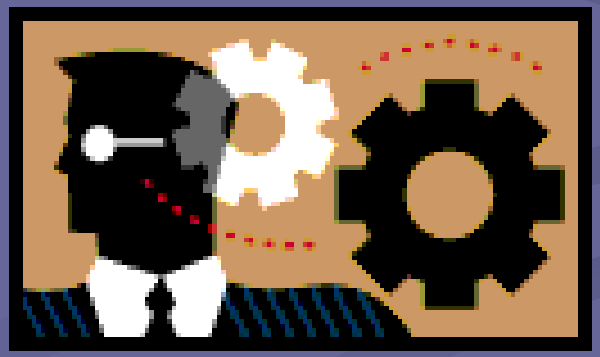


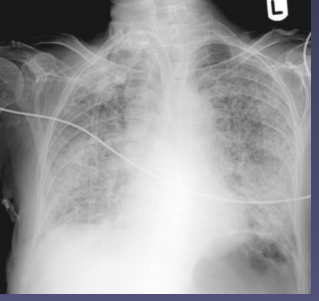
Validita kritérií PAOP

- PAOP > 18 (19) mm Hg nevylučuje ALI/ARDS, koexistence diagnóz
- PAOP < 18 (19) mm Hg neznamená též dg. ALI/ARDS - tvorba edémové tekutiny na základě sníženého COP (koloidně-osmotického tlaku) – např. při hypoAlb.



ARDS je syndrom společný pro různé nozologické jednotky!

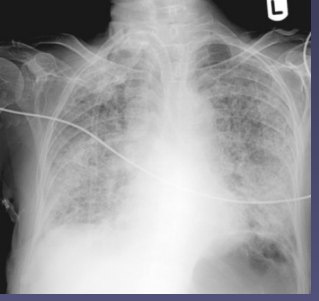




Epidemiologie a incidence

- Od roku 1972 bylo mnoho studií na incidenci ALI/ARDS
- Různé metodologie, doba sledování, ARDS definice
- Těžké srovnání jednotlivých dat
- Dnešní data:

20–50 případů/10^5 obyvatel/rok



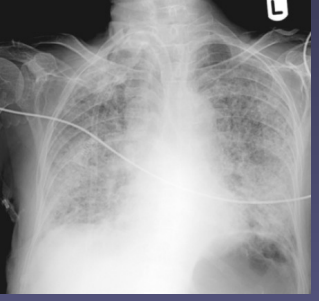
Incidence

Table 2. Selected incidence studies for acute lung injury (ALI) and acute respiratory distress syndrome (ARDS)

Study Location (Sample Time of Study) (Reference)	Definition	Incidence
Grand Canaria (1983–1985) (51)	1. Risk 2. Pao_2 <55 on FIo_2 >0.5 with PEEP 5 and no improvement in 24 hrs and also Pao_2/FIo_2 <150 3. Bilateral infiltrates 4. No clinical left atrial hypertension	1.5 per 10^5 person-years for Pao_2/FIo_2 <110 3.5 per 10^5 person-years for Pao_2/FIo_2 <50 10.6 per 10^5 person-years for acute respiratory failure
Utah (12 mos, 1989–1990) (52)	1. Pao_2/Pao_2 ≤0.2 2. Bilateral infiltrates 3. No clinical evidence of left atrial hypertension 4. Static thoracic compliance <50 mL/cm H_2O	4.8–8.3 per 10^5 person-years for ARDS
Berlin (8 wks in 1991) (19)	Severe lung injury: Murray-Matthay score >2.5	3.0 per 10^5 person-years for severe lung injury 88.6 per 10^5 person-years for acute respiratory failure
Sweden, Denmark, Iceland (8 wks in 1997) (18)	AECC criteria	17.9 per 10^5 person-years for ALI 13.5 per 10^5 person-years for ARDS 76.8 per 10^5 person-years for acute respiratory failure
Australia (8 wks in 1999) (10)	AECC criteria	34 per 10^5 person-years for ALI 28 per 10^5 person-years for ALI
United States (38)	Extrapolation from ARDS Network screening data using AECC criteria	22–87 per 10^5 person-years for ALI
United States (50)	ICD-9 codes and mortality rates	17–26 per 10^5 person-years for ARDS

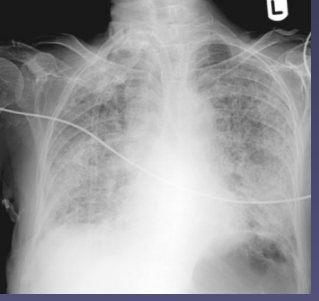
PEEP, positive end-expiratory pressure; AECC, American-European Consensus Conference; ICD, International Classification of Disease.

Crit Care Med 2003; 31[Suppl.]:S276 –S284



Mortalita

- Mortalita je klesající
- Nyní 32 až 45 procent
- V 80´ letech 53 až 68 procent
- Rasové rozdíly v mortalitě
- Muži mají také větší mortalitu
- Mortalita je srovnatelná s HIV infekcí, s nádorem prsu a astma.



Although the annual acute respiratory distress syndrome mortality rate is slowly declining in the United States, significant race and gender differences in acute respiratory distress syndrome mortality exist.

Race and gender differences in acute respiratory distress syndrome deaths in the United States: An analysis of multiple-cause mortality data (1979–1996)*

Marc Moss, MD; David M. Mannino, MD

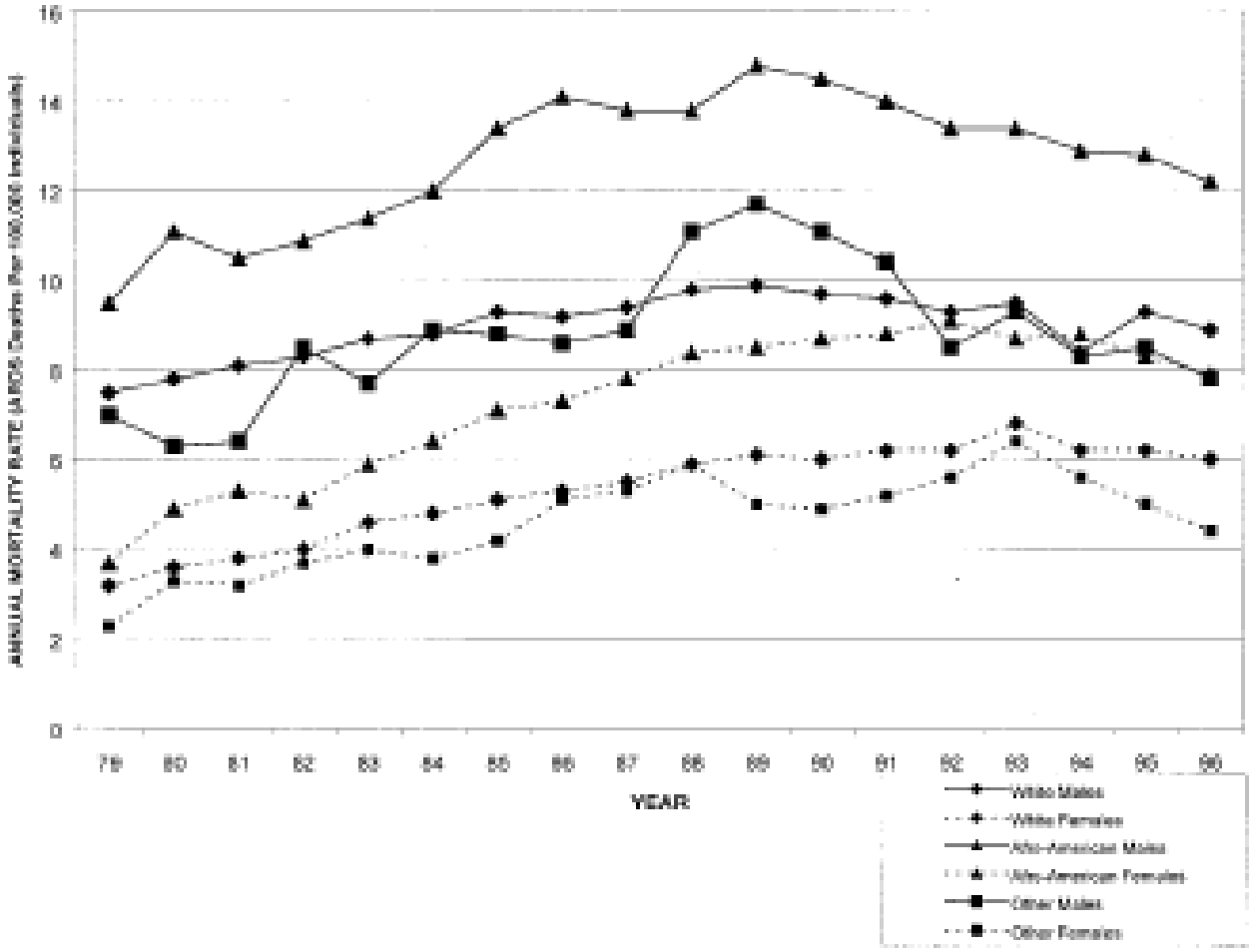
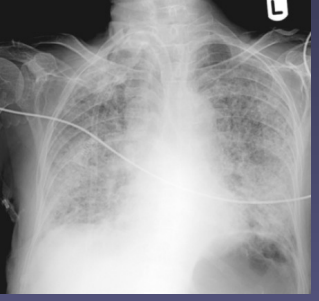


Figure 4. Annual acute respiratory distress syndrome (*ARDS*) mortality rate from 1979 to 1996 stratified by race and gender. Data are age adjusted to the 1980 U.S. population.

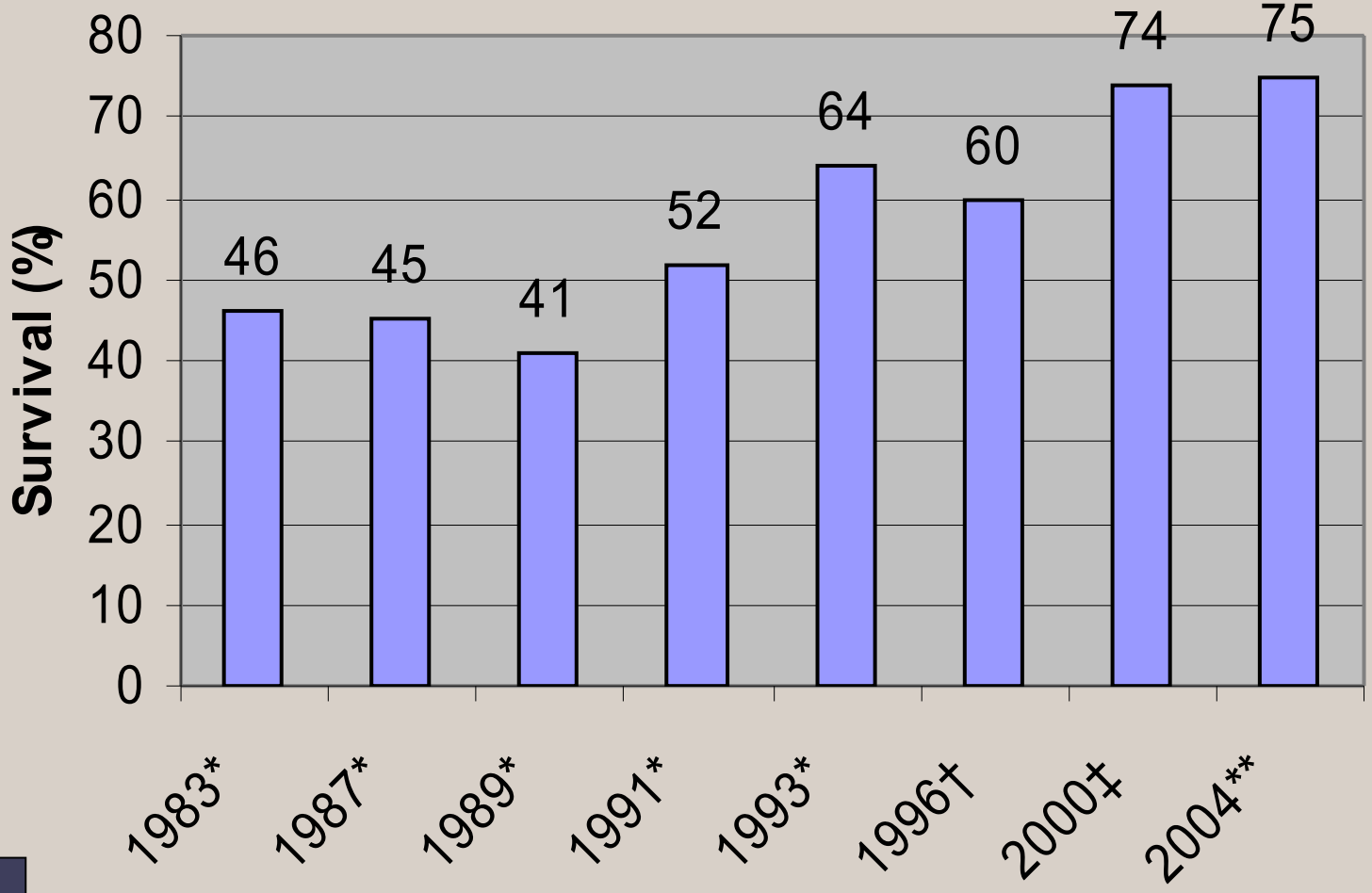


* Mildberg, 1995

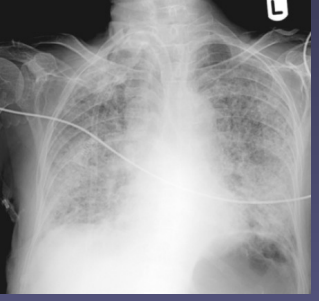
† Weidemann – surfactant

‡ ARDS net – low tidal volume

** ARDS net - ALVEOLI



Bernard, RCCM 2005; 172:798-806.

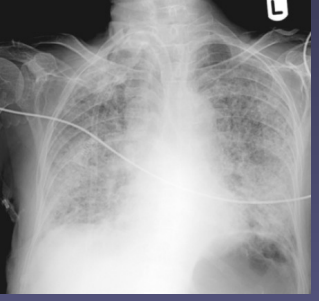


Dlouhodobá morbidita

PROBLÉM: přeživší pacienti s ARDS

1. Dlouhodobý pobyt na ICU
2. Významné funkční omezení

- 70-80´ léta - hlavní obava - dlouhodobé postižení plicních funkcí
- Studie z 90´ let však ukázaly vyznamné zlepšení po 6 a 12 měsících (efekt protektivní ventilace?)
- Aktuální zaměření spíše na neuro-psychiatrické problémy, únavu a svalovou slabost



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 20, 2003 VOL. 348 NO. 8

One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome

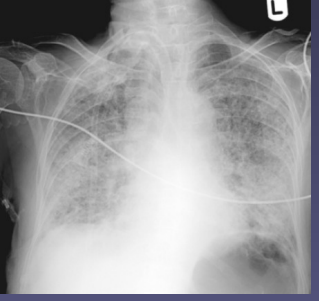
Margaret S. Herridge, M.D., M.P.H., Angela M. Cheung, M.D., Ph.D., Catherine M. Tansey, M.Sc., Andrea Matte-Martyn, B.Sc., Natalia Diaz-Granados, B.Sc., Fatma Al-Saidi, M.D., Andrew B. Cooper, M.D., Cameron B. Guest, M.D., C. David Mazer, M.D., Sangeeta Mehta, M.D., Thomas E. Stewart, M.D., Aiala Barr, Ph.D., Deborah Cook, M.D., and Arthur S. Slutsky, M.D., for the Canadian Critical Care Trials Group

Table 2. Recovery of Pulmonary Function among Patients with the Acute Respiratory Distress Syndrome during the First 12 Months after Discharge from the ICU.

Variable	3 Mo (N=71)*	6 Mo (N=77)†	12 Mo (N=80)‡
	median (interquartile range)		
Forced vital capacity (% of predicted)	72 (57–86)	80 (68–94)	85 (71–98)
Forced expiratory volume in one second (% of predicted)	75 (58–92)	85 (69–98)	
Total lung capacity (% of predicted)§	92 (77–97)	92 (83–101	
Residual volume (% of predicted)§	107 (87–121)	97 (82–117	
Carbon monoxide diffusion capacity (% of predicted)§¶	63 (54–77)	70 (58–82)	

Table 3. Ability to Exercise and Return to Work and Health-Related Quality of Life among Patients with the Acute Respiratory Distress Syndrome during the First 12 Months after Discharge from the ICU.

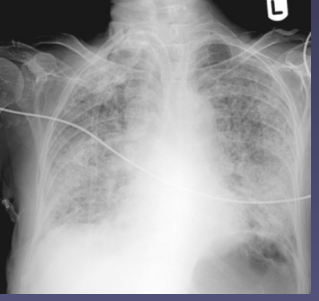
Outcome	3 Months	6 Months	12 Months
Distance walked in 6 min			
No. evaluated	80*	78†	81‡
Median — m	281	396	422
Interquartile range — m	55–454	244–500	277–510
Percentage of predicted value§	49	64	66
Returned to work — no./total no. (%)¶	13/83 (16)	26/82 (32)	40/82 (49)‖
Returned to original work — no./total no. (%)	10/13 (77)	23/26 (88)	31/40 (78)



ARDS
Pulmonální X extrapulmonální

I. Pulmonální – primární- ARDS:

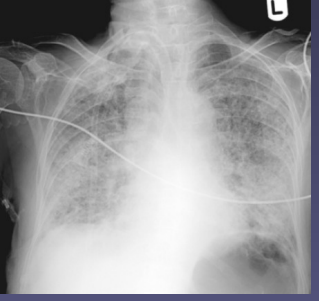
- Aspirace žaludečního obsahu
- Pneumonie
- Inhalační trauma
- Plicní kontuze
- Tonutí
- Tuková embolie
- Reperfuzní poranění po transplantaci plic



ARDS
Pulmonální X extrapulmonální

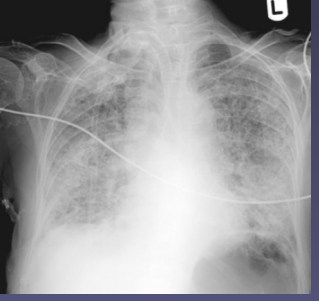
II. Extrapulmonální – sekundární - ARDS:

- Težká sepse/septický šok
- Trauma – hypovolemický šok
- Pankreatitida (SIRS)
- Vícečetné transfůze (TRALI)
- Intoxikace léky



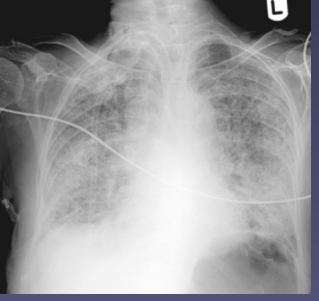
Patofyziologie - rozdělení

1. Akutní fáze - exudativní
2. Subakutní fáze - reparační
3. Pozdní fáze - fibroproliferativní

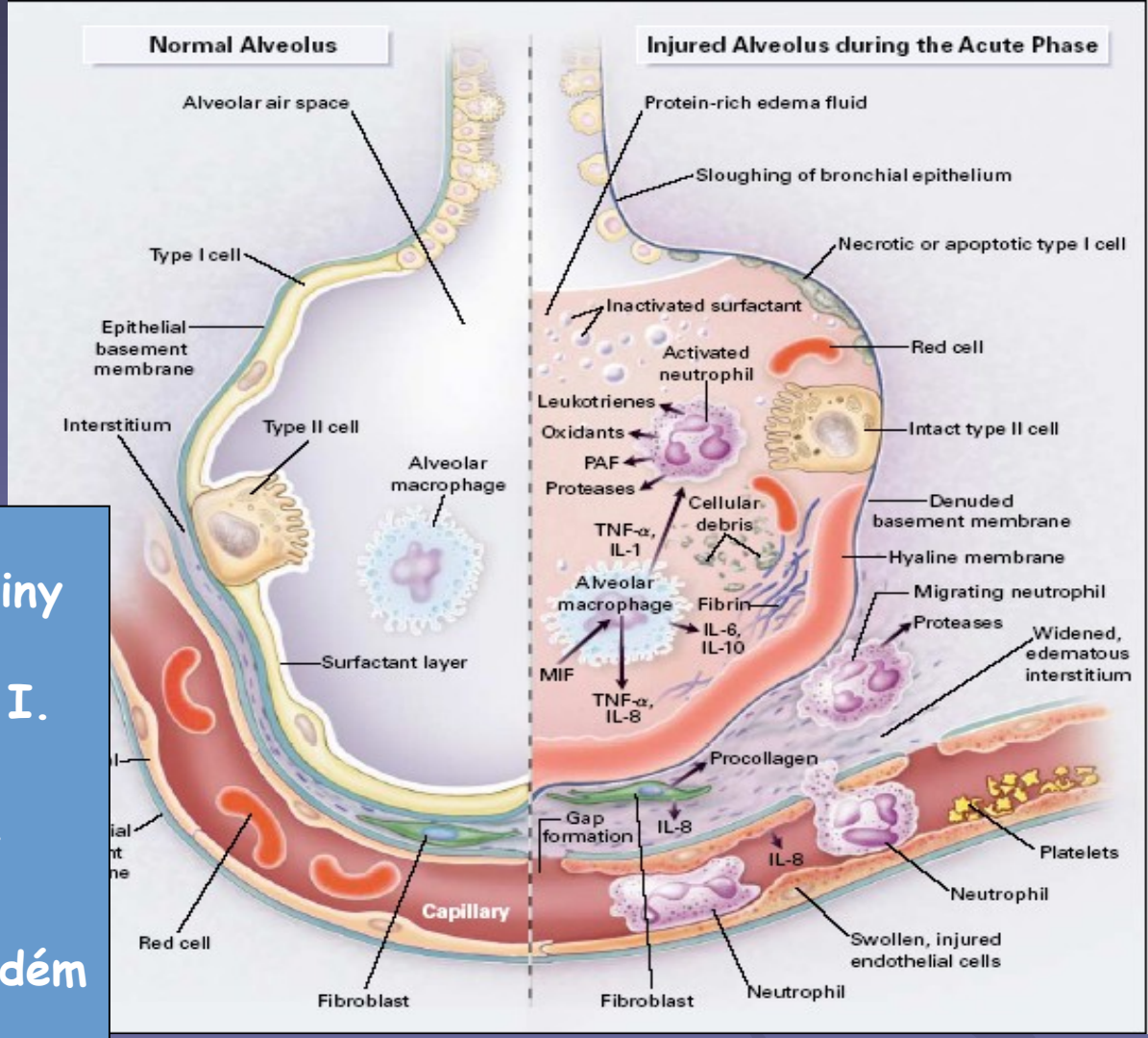


Akutní fáze – exudativní I.

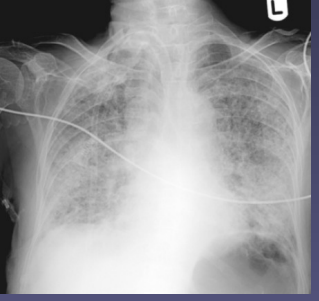
- Centrální role aktivovaných neutrofilů – aktivace přes NF-κB => TNF, p38, PI3-K, IL-1, 8,
- Zvýšení oxidativního stresu a aktivity proteáz => snížení tvorby a destrukce surfaktantu => atelektázy
- Proteázy destruují plicní parenchym
- Postižení alveolárních bb. i endotelií => edém alveolů, snížení clearance BAF (broncho-alveolar fluid)
- Aktivace trombocytů - mikrotrombotizace
- Aktivace koagulace – snížení proteinu C, S => zvýšení TF a PAI
- Snížená permeabilita alveolokapilární membrány – DAD – diffuse alveolar damage



- Infiltrace neutrofily
- Tekutina se serovými proteiny
- Porucha BM
- Destrukce alveolárních bb. I. +II.
- Inaktivace surfaktantu
- Zvýšení povrchového napětí
- Atelektázy
- Intersticiální a alevolární edém
- Mikrovaskulární trombózy
- Rekruitment mezenchymálních bb s produkcí procolagenu
- Maximum v oblasti dependetních partií



Ware NEJM 2000

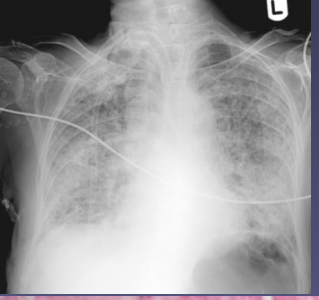


Pozdní fáze - fibroproliferativní

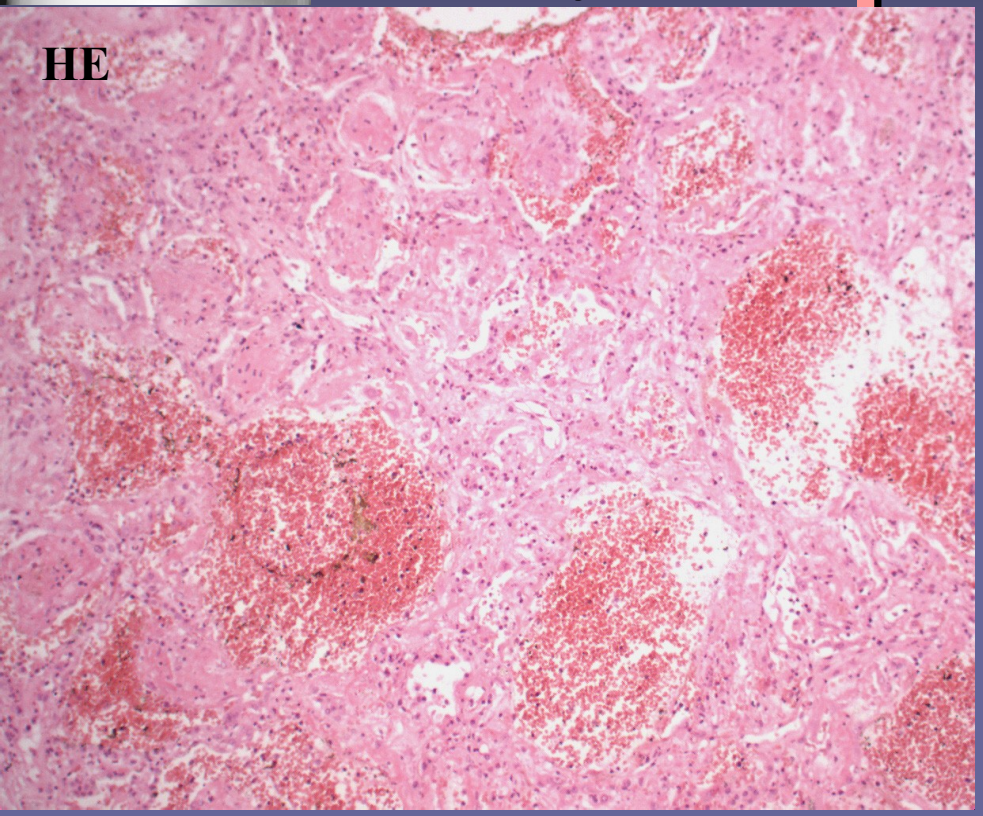
- Pokračující chronický zánět
- Fibróza
- Neovaskularizace

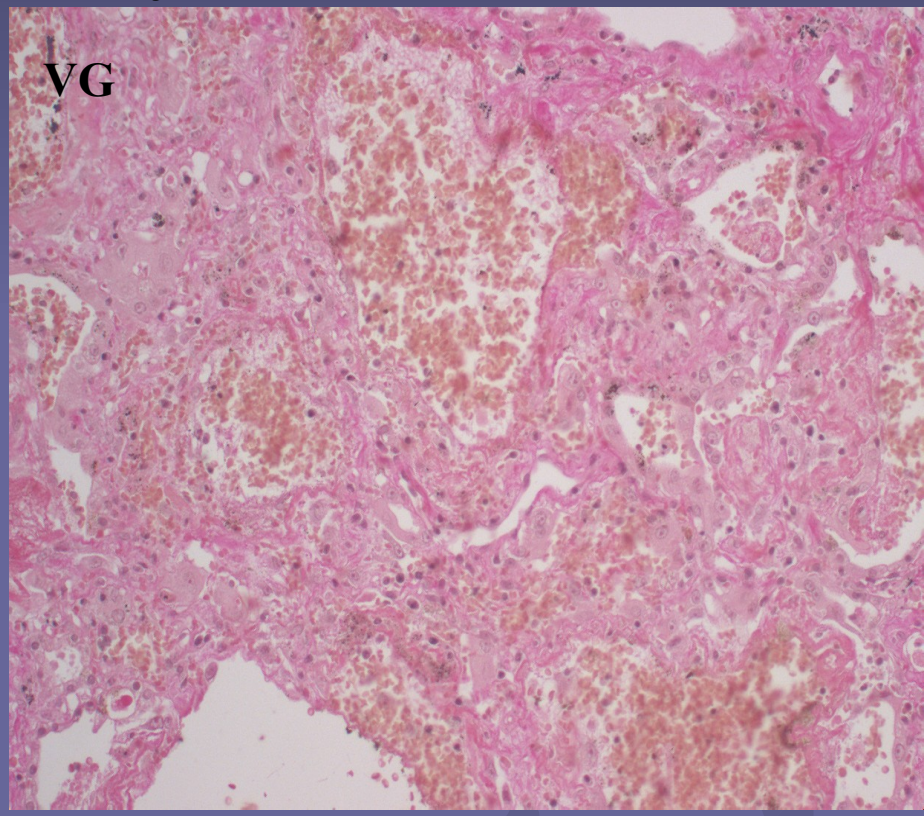
Rozlišení fází?

Jedině plicní biopsie, její význam není zatím jasně stanoven.

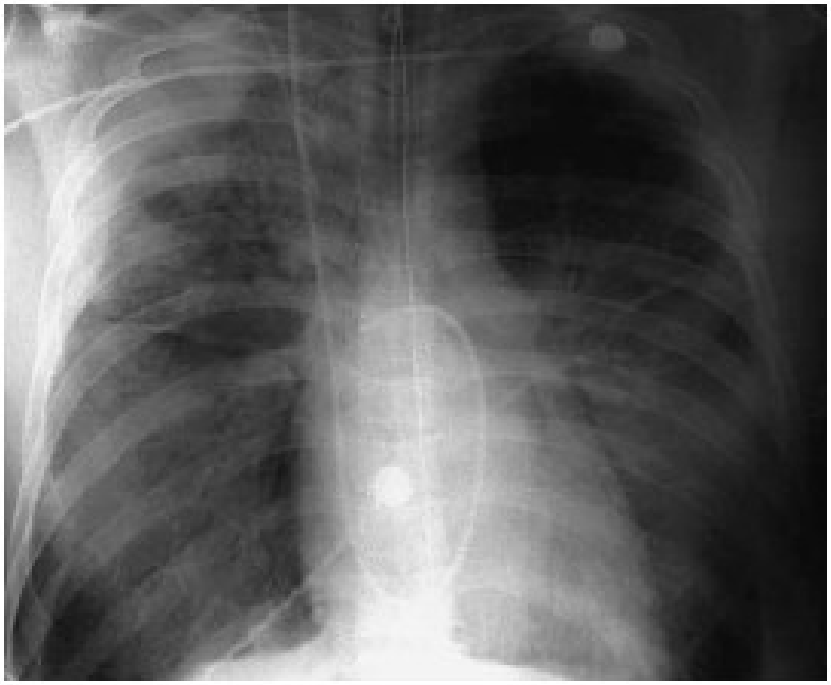


Pozdní fáze - fibroproliferativní

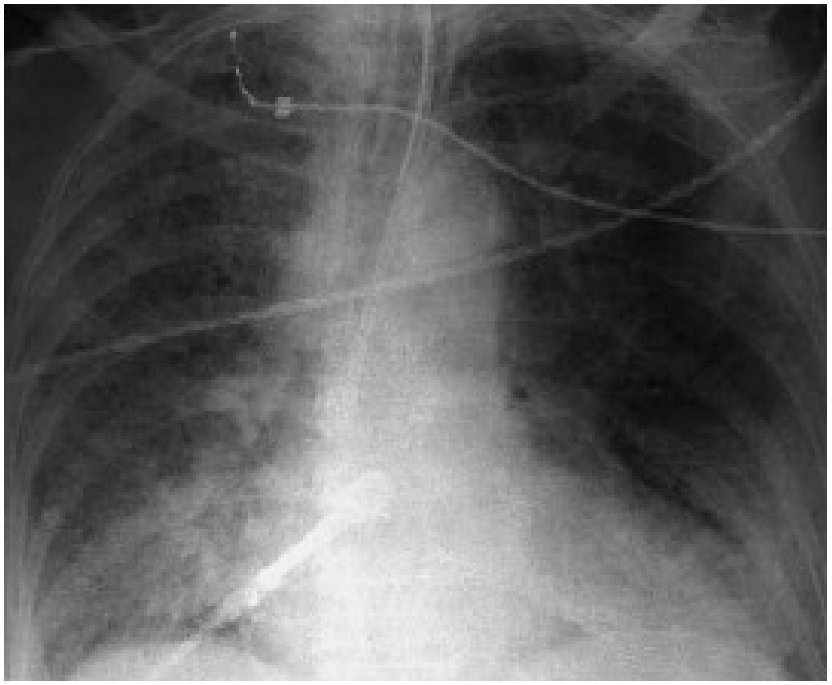




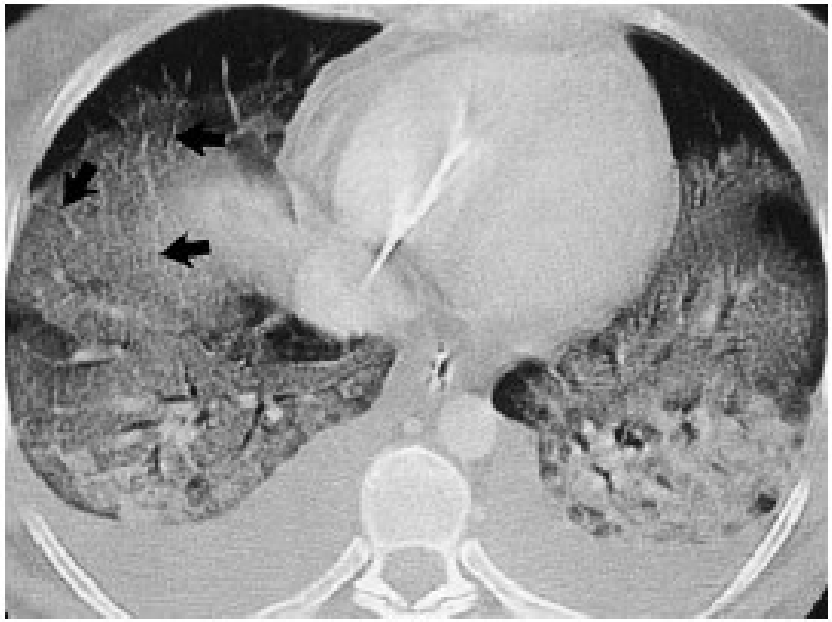
V přehledném barvení hematoxylin-eosin je zřetelná difuzní intersticiální plicní fibróza s řídkou chronickou zánětlivou celulizací, regionálně přítomna i organizovaná bronchioloalveolitida, dále jsou patrné hyalinní membrány na stěnách alveolů a také pneumoragie. Speciální barvení na kolagen (van Gieson) jen potvrzuje přítomnost fibrózy.

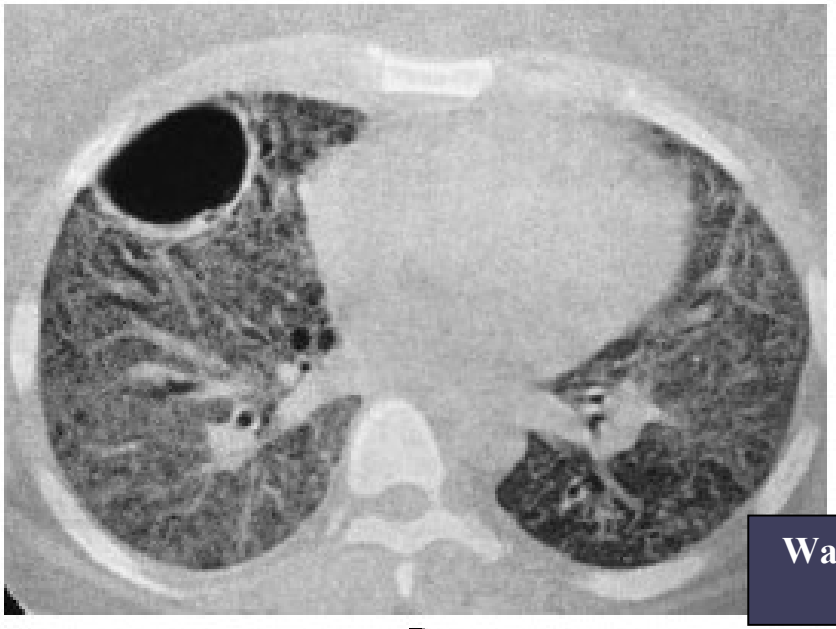


A

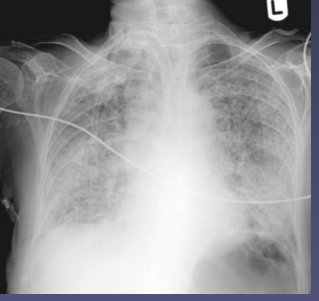


B



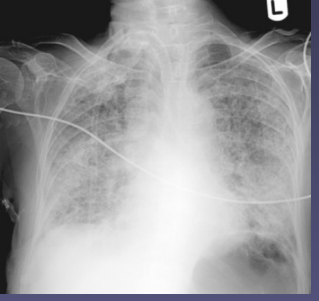


Ware NEJM 2000



Změny plicní mechaniky

- Maximum v oblasti dependetních partií
- Snížení plicní compliance - C_L
- Intrapulmonální shunty
- Porucha V/Q
- Zvýšení Vd
- Zvýšení WOB (dechové práce)
- Nehomogenita – okrsky hyperinflace, atelektatické (CT plic)
- Pacienti s ARDS umírají mnohem častěji na MODS než na nekorigovatelnou hypoxémii
- Ventilujeme plíci cca 5-6 letého dítěte



3 kompartmenty ARDS plic

I. Uninvolved regions – zdravé jednotky

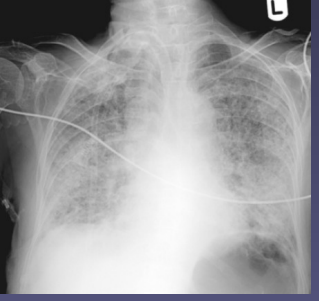
Normální compliance a vzdušnost, funkčně normální

II. Non-recruitable regions

bezpečný IP neprovzdušní

III. Recruitable regions

Zkolabované, vyplněné tekutinou, ale bezpečné IP mohou opět provzdušnit



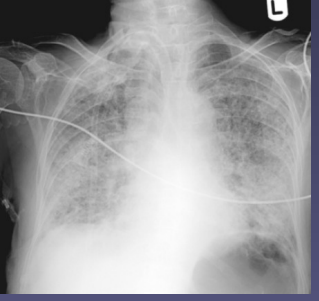
TERAPIE ARDS

I. NEFARMAKOLOGICKÁ

1. UPV – Vt, PEEP, FiO2
2. Pronační poloha
3. Tekutinový režim „suchá plíce“

II. FAMAKOLOGICKÁ


MAGIC
BULLET?



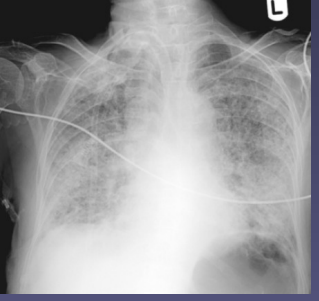
Protektivní plicní ventilace

- Tradiční Vt do 70-90´ let byly až 10-15ml/kg
- Vycházela z doporučení z 60´let, kdy se tyto Vt používaly při nutnosti pooperační ventilace
- Používány ale u „zdravých" plic.
- Průlom:

1. K. G. Hickling1, S. J. Henderson and R. Jackson

Low mortality associated with low volume pressure limited ventilation with permissive hypercapnia in severe adult respiratory distress syndrome. ICM 1990

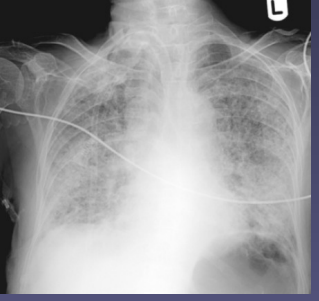
2. Studie na zvířatech



VILI (VALI)

- VOLUTRAUMA – nadměrné rozepnutí alveolu a kapilár – závislé na Vt a EILV
- ATELEKTRAUMA – působení tzv. „shear forces" střižných sil na rozhraní ventilovaných a neventilovaných regionů – závislé na EELV
- Mechanické bronchiální trauma při kolapsu malých DC
- Vysoký transkapilární tlak – lokálně zvýšený intravaskulární tlak na rozhraní ventilovaných a neventilovaných regionů

Největší riziko VILI je u ARDS plíce

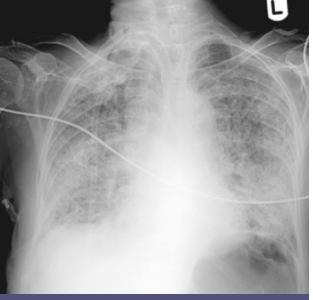


Studie stran Vt u ARDS

TABLE 1. NUMBER OF PATIENTS, TIDAL VOLUMES STUDIED, AND MORTALITY RATES IN FIVE RANDOMIZED CLINICAL TRIALS

Author (Ref.)	Number of Patients		Tidal Volume		Mortality Rate		Reported Mortality Difference (*p Value*)
	Low Tidal Volume	Control	Low Tidal Volume* (*ml/kg*)	Control* (*ml/kg*)	Low Tidal Volume (%)	Control (%)	
Amato and coworkers (3)	29	24	6.1 ± 0.2†‡	11.9 ± 0.5†‡	38	71	< 0.001
Stewart and coworkers (5)	60	60	7.2 ± 0.8§	10.6 ± 0.2§	50	47	0.72
Brochard and coworkers (6)	58	58	7.2 ± 0.2‖	10.4 ± 0.2‖	47	38	0.38
Brower and coworkers (7)	26	26	7.3 ± 0.1¶	10.2 ± 0.1¶	50	46	0.60
ARDSNet (4)	432	429	6.3 ± 0.1¶	11.7 ± 0.1¶	31	40	0.007

Am J Respir Crit Care Med Vol 166. pp 1510–1514, 2002



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.

- 53 patients
- Stanovení P/V křivky

Konvenční ventilace
- lowPEEP/high Vt

Protektivní ventilace
- highPEEP/low Vt
- Použití recruitment manévru v případě potřeby

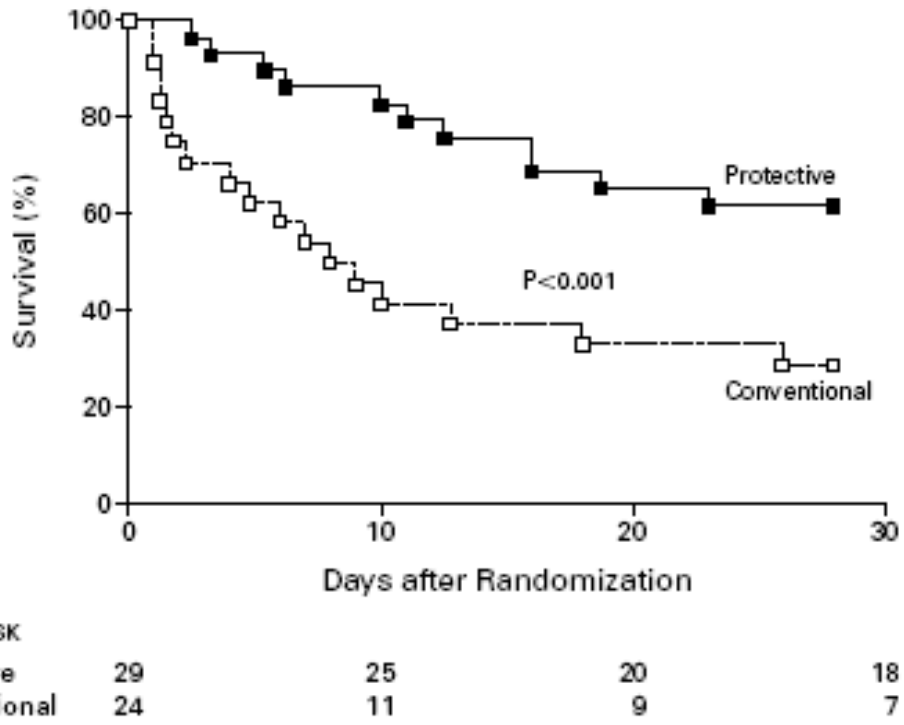
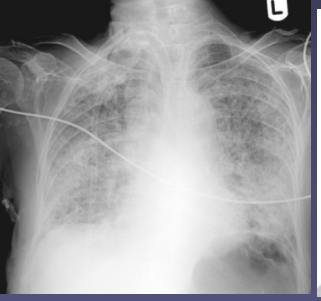


Figure 1. Actuarial 28-Day Survival among 53 Patients with the Acute Respiratory Distress Syndrome Assigned to Protective or Conventional Mechanical Ventilation.

The data are based on an intention-to-treat analysis. The P value indicates the effect of ventilatory treatment as estimated by the Cox regression model, with the risk of death associated with the adjusted base-line score on APACHE II included as a covariate.

Kritika: vysoká mortalita v kontrolní skupině



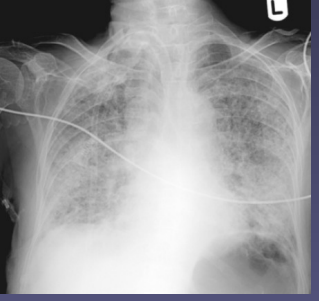
ARDSNET

Založena v roce 1994

www.ardsnet.org

Nejvýznamější studie:

- ARMA- Lower Tidal Volume vs. Higher Tidal Volume Ventilation for Treatment of ALI/ARDS….Jediná průkazná
- ALVEOLI- Higher End-expiratory Lung Volume/Lower FiO2 vs. Lower End-expiratory Lung Volume/Higher FiO2 Ventilation in Acute Lung Injury and Acute Respiratory Distress Syndrome
- LaSRS- LATE STERIOD RESCUE STUDY
- Fluid and Catheter Treatment Trial (FACTT)
- KARMA- Ketoconazole in ALI/ARDS
- LARMA- Lisofylline in ALI/ARDS



ARMA Trial

The New England Journal of Medicine

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VOLUME 342 MAY 4, 2000 NUMBER 18

VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

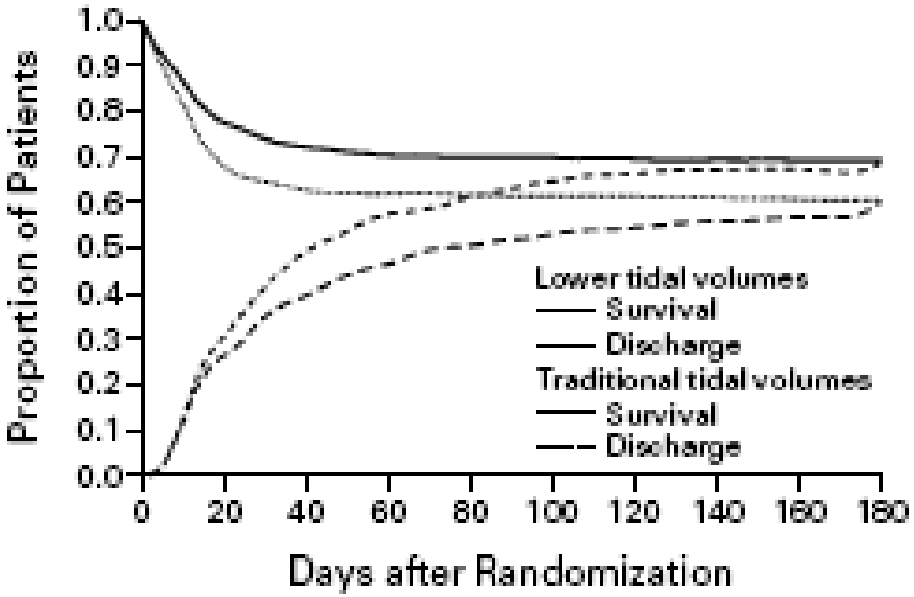
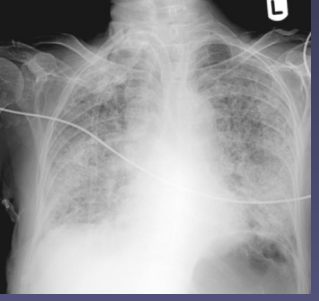


Figure 1. Probability of Survival and of Being Discharged Home and Breathing without Assistance during the First 180 Days after Randomization in Patients with Acute Lung Injury and the Acute Respiratory Distress Syndrome.

Ventilator mode	Volume assist-control
Tidal volume	≤ 6 mL/kg predicted body weight†
Plateau pressure	≤ 30 cm H_2O
Ventilation set rate/ pH goal	6–35/min, adjusted to achieve arterial pH ≥ 7.30 if possible
Inspiratory flow, I:E	Adjust flow to achieve I:E of 1:1–1:3
Oxygenation goal	55 ≤ Pa_{O_2} ≤ mm Hg or 88 ≤ Sp_{O_2} ≤ 95%
F_{IO_2}/PEEP (mm Hg) combinations‡	0.3/5, 0.4/5, 0.4/8, 0.5/8, 0.5/10, 0.6/10, 0.7/10, 0.7/12, 0.7/14, 0.8/14, 0.9/14, 0.9/16, 0.9/18, 1.0/18, 1.0/22, 1.0/24
Weaning	Attempts to wean by pressure support required when F_{IO_2}/PEEP ≤ .40/8

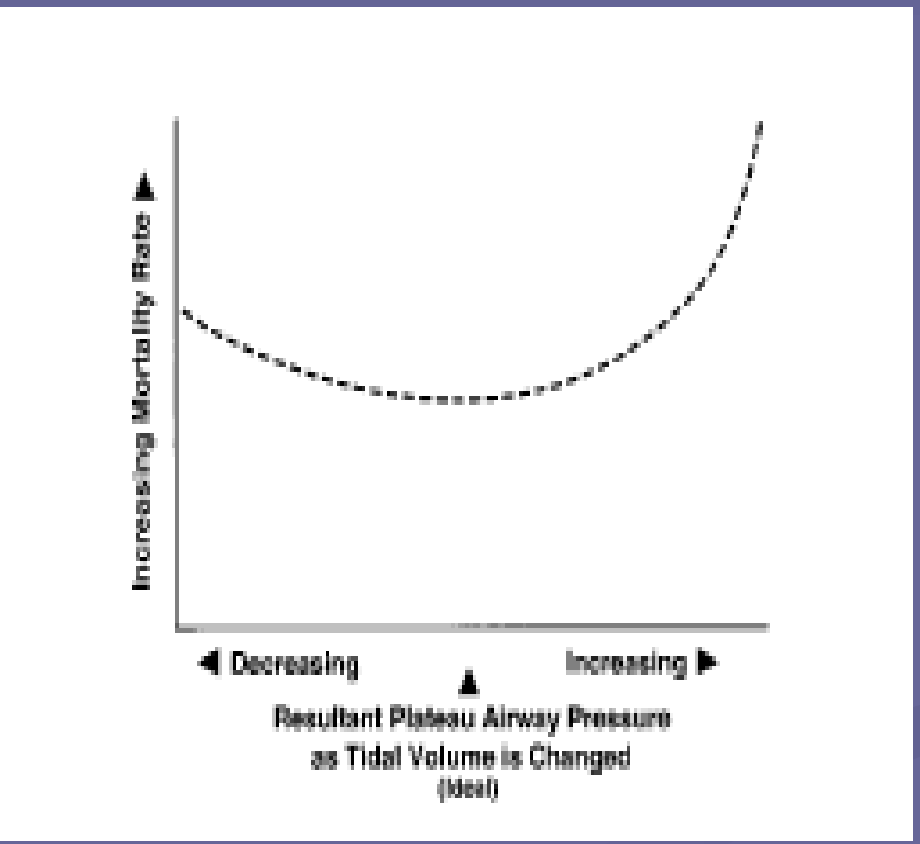


Critical Care Perspective

Meta-Analysis of Acute Lung Injury and Acute Respiratory Distress Syndrome Trials Testing Low Tidal Volumes

Peter Q. Eichacker, Eric P. Gerstenberger, Steven M. Banks, Xizhong Cui, and Charles Natanson

Critical Care Medicine Department, Clinical Center, National Institutes of Health, Bethesda, Maryland

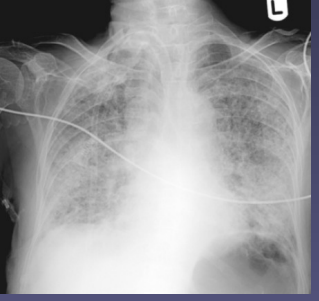


Kritika:

- Zásadní rozdíl v použitém PEEP v pozitivních studiích (AmatoxARDSnet)
- Problémy s kontrolními skupinami

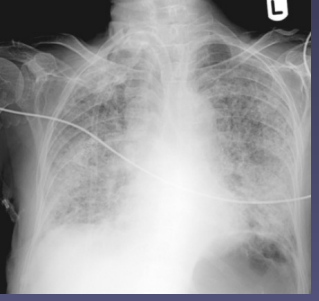
Vztah velikosti Vt a mortality:

1. Závislost má tvar J křivky
2. Mortalita je spojena s velmi vysokými ale také s velmi nízkými objemy
3. Nejlepších výsledků dosaženo při použití intermediárních objemů, (tj.7-10 ml/IBW)



PEEP

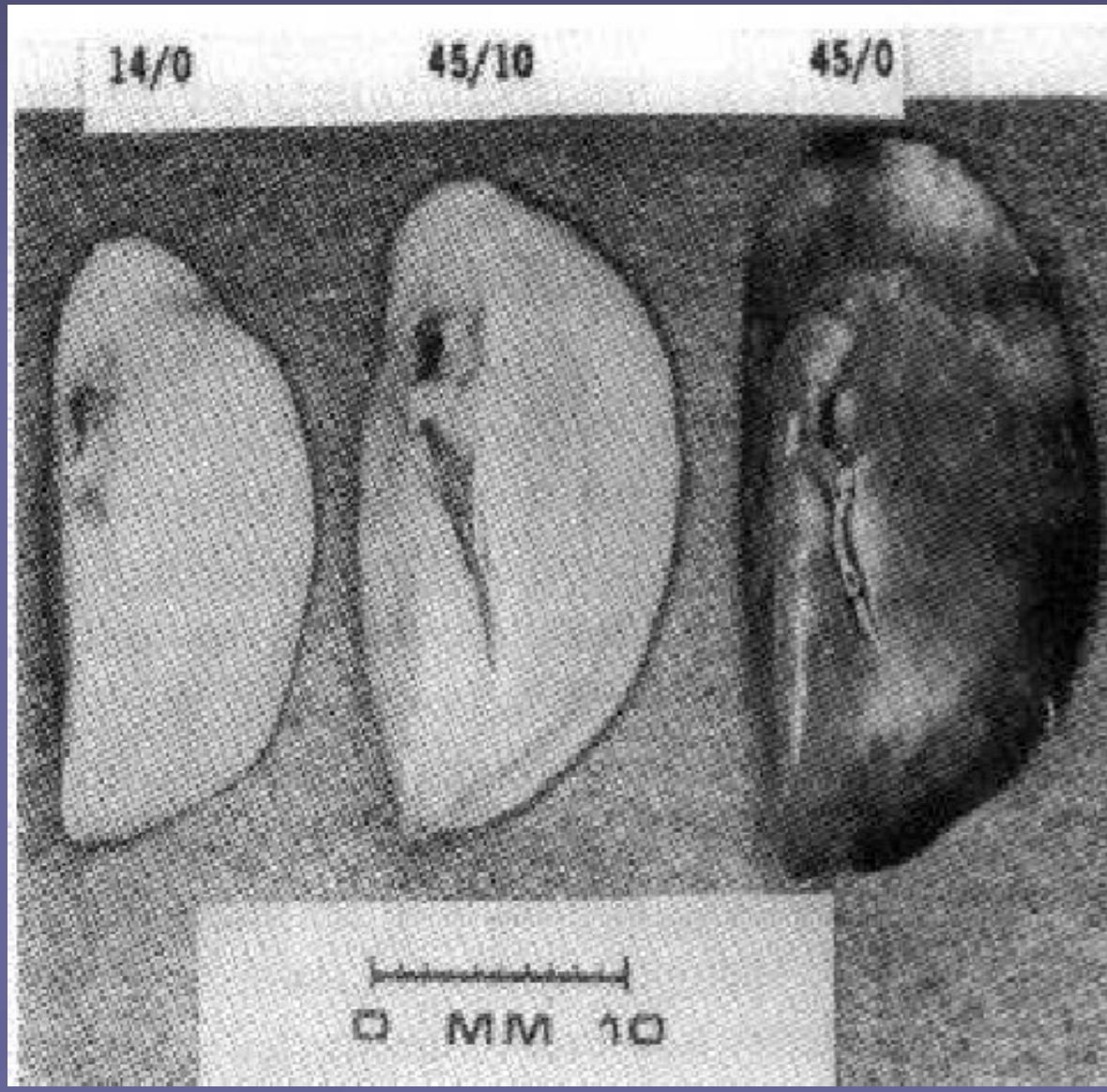
- Zlepšení oxygenace
- Recruitment atelektatických partií plic
- Zlepšení mechanických vlastností plic (compliance)
- Prevence atelektraumatu (shear forces)
- Důležitý zejéma u malých Vt

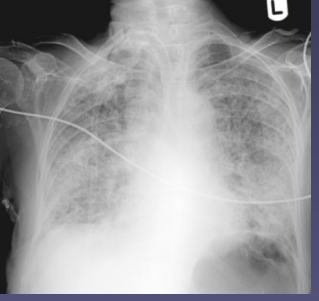


PEEP

Webb a Tierne, 1977

PIP	PEEP
14	0
45	10
45	0





The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 22, 2004 VOL. 351 NO. 4

Higher versus Lower Positive End-Expiratory Pressures in Patients with the Acute Respiratory Distress Syndrome

The National Heart, Lung, and Blood Institute ARDS Clinical Trials Network*

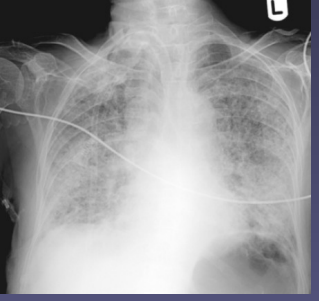
ALVEOLI Trial

Table 1. Summary of Ventilator Procedures in the Lower- and Higher-PEEP Groups.*

Procedure	Value
Ventilator mode	Volume assist/control
Tidal-volume goal	6 ml/kg of predicted body weight
Plateau-pressure goal	≤30 cm of water
Ventilator rate and pH goal	6–35, adjusted to achieve arterial pH ≥7.30 if possible
Inspiration:expiration time	1:1–1:3
Oxygenation goal	
PaO_2	55–80 mm Hg
SpO_2	88–95%
Weaning	Weaning attempted by means of pressure support when level of arterial oxygenation acceptable with PEEP ≤8 cm of water and FiO_2 ≤0.40

Allowable combinations of PEEP and FiO_2†

Lower-PEEP group														
FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18–24
Higher-PEEP group (before protocol changed to use higher levels of PEEP)														
FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0	
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22–24	
Higher-PEEP group (after protocol changed to use higher levels of PEEP)														
FiO_2	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0				
PEEP	12	14	14	16	16	18	20	22	22	22–24				

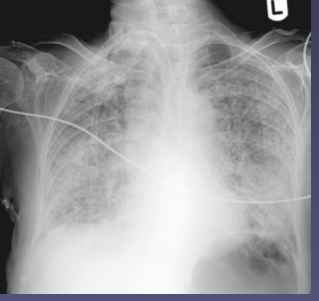


ALVEOLI study- výsledky

- PEEP 8.3±3.2 cm H20 v low-PEEP skupině
- PEEP 13.2±3.5 cm H20 v high-PEEP skupině (P<0.001).
- Mortalita před propuštěním byla 24.9 percent a 27.5 percent
- Klinický výsledek se neliší v závislosti na hodnotě PEEP při použití protektivní ventilační strategie

Table 3. Respiratory Values during the First Seven Days of Treatment.*

Variable	Day 1		Day 3		Day 7	
	Lower-PEEP Group	Higher-PEEP Group	Lower-PEEP Group	Higher-PEEP Group	Lower-PEEP Group	Higher-PEEP Group
Tidal volume (ml/kg of predicted body weight)	6.1±0.8	6.0±0.9†	6.1±1.1	5.8±1.0†	6.2±1.3	5.8±1.2
No. of patients	236	258	171	160	83	97
Plateau pressure (cm of water)	24±7	27±6†	24±6	26±7†	26±8	26±6
No. of patients	230	252	165	155	78	96
Mean airway pressure (cm of water)	15±5	20±5†	15±5	18±5†	15±7	19±6†
No. of patients	233	261	167	164	82	94
Respiratory rate (breaths/min)	29±7	29±7	30±7	30±7	28±7	30±7
No. of patients	248	263	180	173	98	102
Minute ventilation (liters/min)	12±4	12±3	12±4	12±3	12±4	12±3
No. of patients	247	264	178	171	96	104
FiO_2	0.54±0.18	0.44±0.17†	0.52±0.18	0.40±0.14†	0.52±0.20	0.40±0.11†
No. of patients	249	264	179	173	98	103
PEEP (cm of water)						
All patients	8.9±3.5	14.7±3.5†	8.5±3.7	12.9±4.5†	8.4±4.3	12.9±4.0†

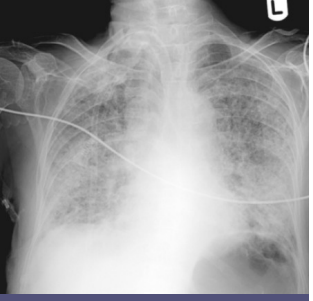


Pronační poloha

- 1976 Piehn a Brown - PP zlepšuje oxygenaci

- **Další studie:**

1. zvýšení funkční residuální kapacity => redukce uzavírání ventilovaných okrsků v endexpiriu, zejména v dorsálních partiích, které jsou perfundovány nejvíce ve všech polohách.
2. dorso-ventrální orientace hlavních DC umožňuje lepší drenáž sekretů
3. ventilace a V/Q poměry v jednotlivých regionech více uniformní. Zlepšení výměny plynů vlivem anatomických poměrů bránice, v elastanci hrudní stěny v PP a v menším mechanickém ovlivnění plic ze strany srdce, bránice a mediastina v PP.
4. efekt rekruitment manévrů v PP je větší a prolongovanější
5. redukce VILI

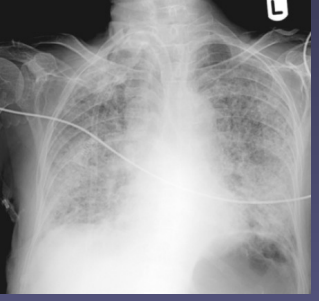


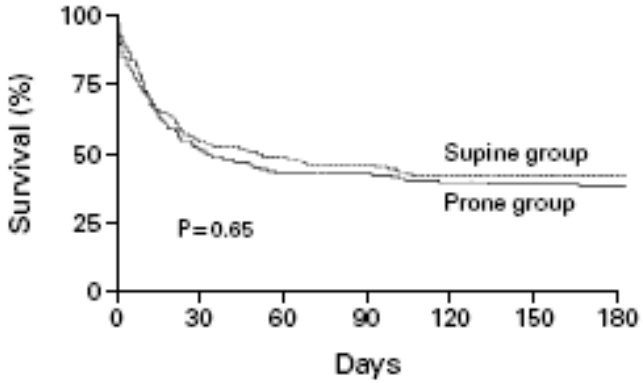
The New England Journal of Medicine

EFFECT OF PRONE POSITIONING ON THE SURVIVAL OF PATIENTS WITH ACUTE RESPIRATORY FAILURE

Luciano Gattinoni, M.D., Gianni Tognoni, M.D., Antonio Pesenti, M.D., Paolo Taccone, M.D., Daniele Mascheroni, M.D., Violeta Labarta, M.S., Roberto Malacrida, M.D., Paola Di Giulio, R.N., M.S.C., Roberto Fumagalli, M.D., Paolo Pelosi, M.D., Luca Brazzi, M.D., and Roberto Latini, M.D., for the Prone–Supine Study Group*

- Multicentrická, randomizovaná studie
- Srovnání ventilace ARDS v supinní poloze a v pronační poloze
- Pronační poloha nejméně 6 hodin a více
- Po dobu 10 dnů
- Zahrnuto 304 pacientů





No. at Risk							
Supine group	152	82	72	68	62	62	62
Prone group	152	78	63	63	58	57	56

Figure 1. Kaplan–Meier Estimates of Survival at Six Months.

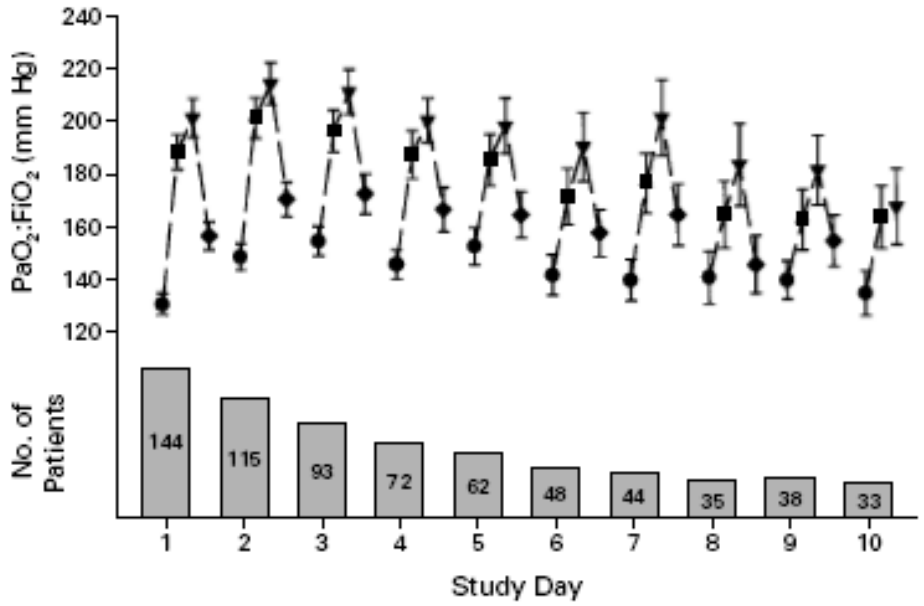
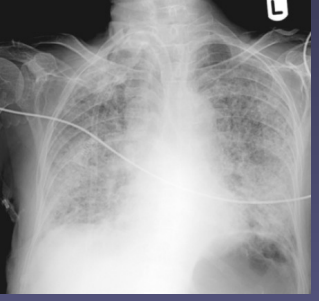


Figure 2. Mean (±SE) Ratios of the Partial Pressure of Arterial Oxygen (PaO_2) to the Fraction of Inspired Oxygen (FiO_2) Immediately before Prone Positioning (Circles), after One Hour (Squares), at the End of the Period of Pronation (Triangles), and on the Morning of the Following Day (Diamonds) during the 10-Day Study Period.

Each calculation includes only data from patients for whom values for all four measurements were available. The bars show the number of patients who were placed in the prone position each day and for whom values for all four measurements were available.

Although placing patients with acute respiratory failure in a prone position improves their oxygenation, it does not improve survival.



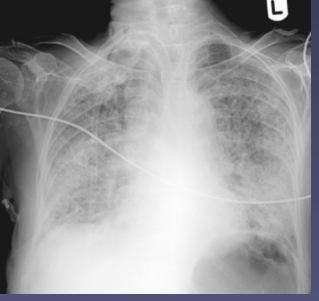
Gattinoni – analýza

Slutsky:

- Pacienti byli v PP v průměru 7 hodin/den – omezená doba
- Jako mortlaitní studie měla málo pacientů – byla předčasně ukončena pro záměr provádění PP v kontrolní skupině
- Nebyl zde záměr zařazovat pacienty v časném stádiu ARDS (20% pacientů mělo poruchu integrity kůže)
- 8% pacientů z kontrolní skupiny (!) bylo 43 krát v PP pro těžkou hypoxemii. Oproti tomu 27% v pronační skupině nemělo 91 naplánovaných pronací v důsledku „staffing limitations"
- Intervence byla jen 10 dní

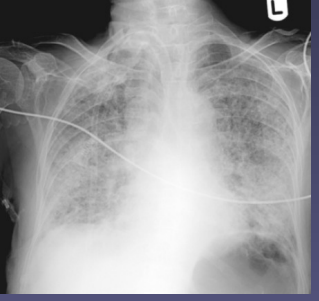
Post hoc analýza:

Mortalita byla významně redukována (47 vs 23%) ve skupině s nejhorším oxygenačním indexem (PaO2/FIO2 8) a se SAPS II více jak 49 (19 vs 49%)



Tekutinová terapie u ARDS

- Porucha mikrocirkulace v plicích
- Dochází k akumulaci tekutiny => EVLW
- Zvířecí model: redukcí edémové tekutiny => zlepšení oxygenace a compliance plic – c_L
- Humánní studie:
  - Simmons RS, Berdine GG, Seidenfeld JJ, et al. Fluid balance and the adult respiratory distress syndrome. Am Rev Respir Dis 1987;135:924-9.
  - Humphrey H, Hall J, Sznajder I, Silverstein M, Wood L. Improved survival in ARDS patients associated with a reduction in pulmonary capillary wedge pressure. Chest 1990;97:1176-80.
  - Mitchell JP, Schuller D, Calandrino FS, Schuster DP. Improved outcome based on fluid management in critically ill patients requiring pulmonary artery catheterization. Am Rev Respir Dis 1992;145:990-8.



FACTT Study - fluids and catheters treatment trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 25, 2006 VOL. 354 NO. 21

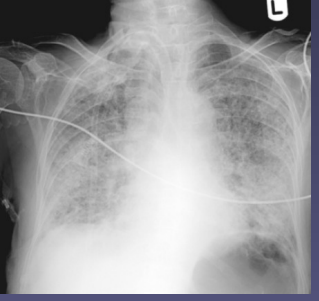
Pulmonary-Artery versus Central Venous Catheter to Guide Treatment of Acute Lung Injury

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

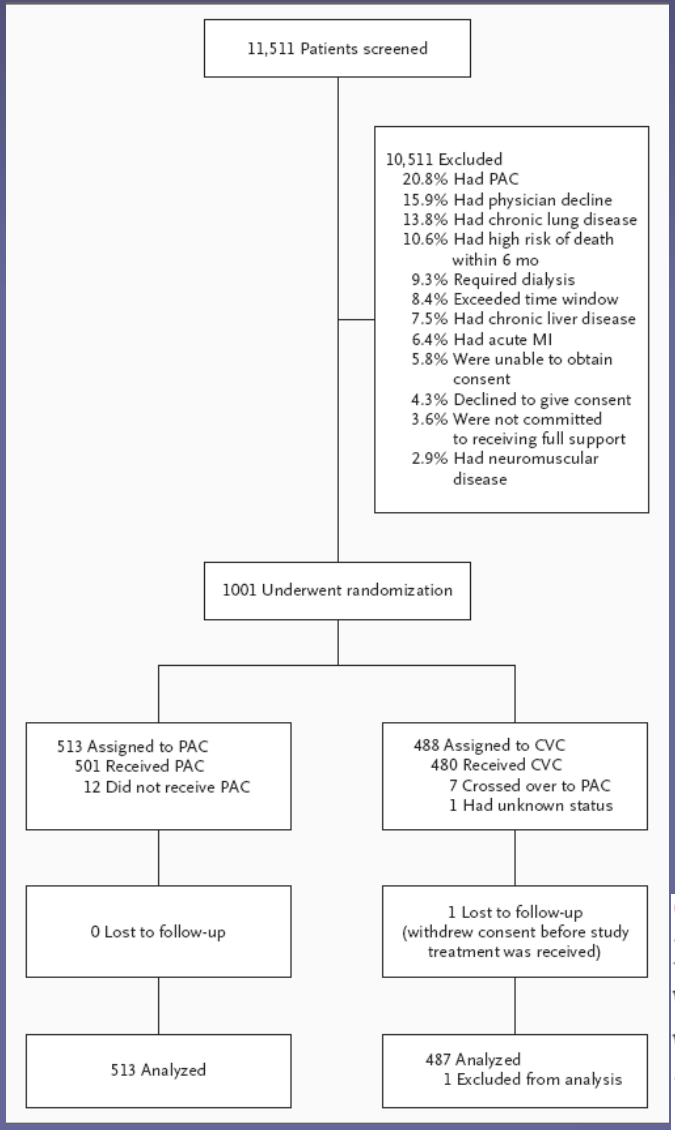
ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

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



Pulmonary-Artery versus Central Venous Catheter to Guide Treatment of Acute Lung Injury



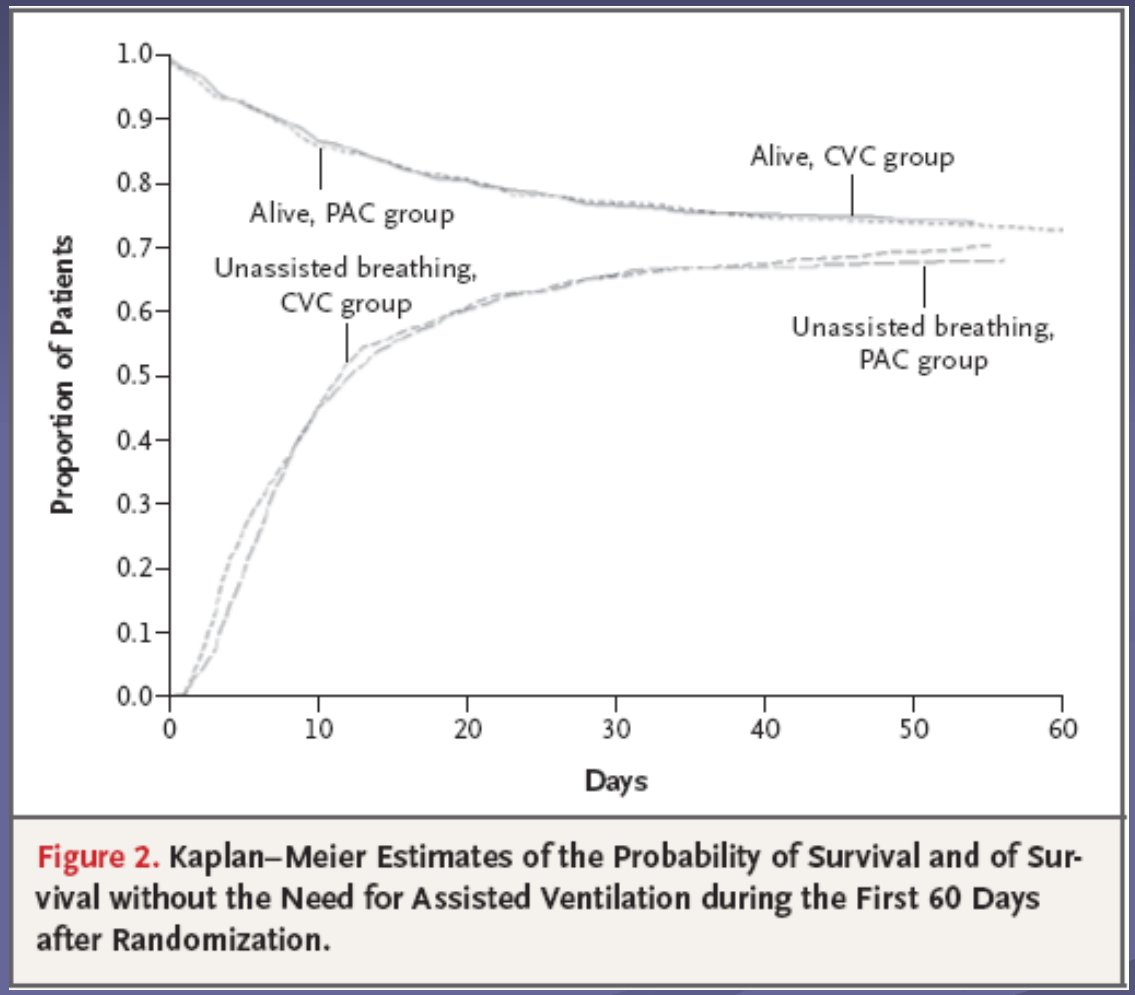
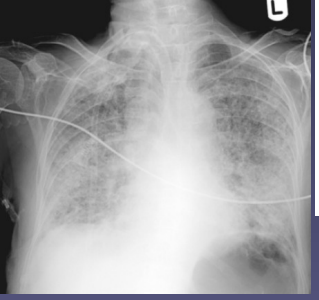


Figure 2. Kaplan–Meier Estimates of the Probability of Survival and of Survival without the Need for Assisted Ventilation during the First 60 Days after Randomization.

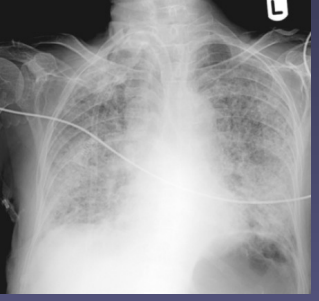
CONCLUSIONS

PAC-guided therapy did not improve survival or organ function but was associated with more complications than CVC-guided therapy. These results, when considered with those of previous studies, suggest that the PAC should not be routinely used for the management of acute lung injury. (ClinicalTrials.gov number, NCT00281268.)



Comparison of Two Fluid-Management Strategies in Acute Lung Injury

Measured intravascular pressure (mm Hg)				MAP <60 mm Hg or a need for any vasopressor (except dopamine ≤5 μg/kg/min); consider correctable causes of shock first	MAP ≥60 mm Hg without vasopressors (except dopamine ≤5 μg/kg/min)			
CVP		PAOP[G]			Average urinary output <0.5 ml/kg/hr		Average urinary output ≥0.5 ml/kg/hr	
Conservative strategy	Liberal strategy	Conservative strategy	Liberal strategy		**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation	**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation
Range 1				1 Vasopressor[F] Fluid bolus[F]	3 KVO IV Dobutamine[A] Furosemide[B,1,2,4]	7 KVO IV Furosemide[B,1,2,4]	11 KVO IV Dobutamine[A] Furosemide[B,1,3,4]	15 KVO IV Furosemide[B,1,3,4]
>13	>18	>18	>24					
Range 2					4 KVO IV Dobutamine[A]	8 KVO IV Furosemide[B,1,2,4]	12 KVO IV Dobutamine[A]	16 KVO IV Furosemide[B,1,3,4]
9–13	15–18	13–18	19–24					
Range 3				2 Fluid bolus[F] Vasopressor[F]	5 Fluid bolus[C]	9 Fluid bolus[C]	13 Fluid bolus[C]	17 Liberal KVO IV
4–8	10–14	8–12	14–18					18 Conservative Furosemide[B,1,3,4]
Range 4					6 Fluid bolus[C]	10 Fluid bolus[C]	14 Fluid bolus[C]	19 Liberal fluid bolus
<4	<10	<8	<14					20 Conservative KVO IV



CONCLUSIONS

Although there was no significant difference in the primary outcome of 60-day mortality, the conservative strategy of fluid management improved lung function and shortened the duration of mechanical ventilation and intensive care without increasing nonpulmonary-organ failures. These results support the use of a conservative strategy of fluid management in patients with acute lung injury. (ClinicalTrials.gov number, NCT00281268.)

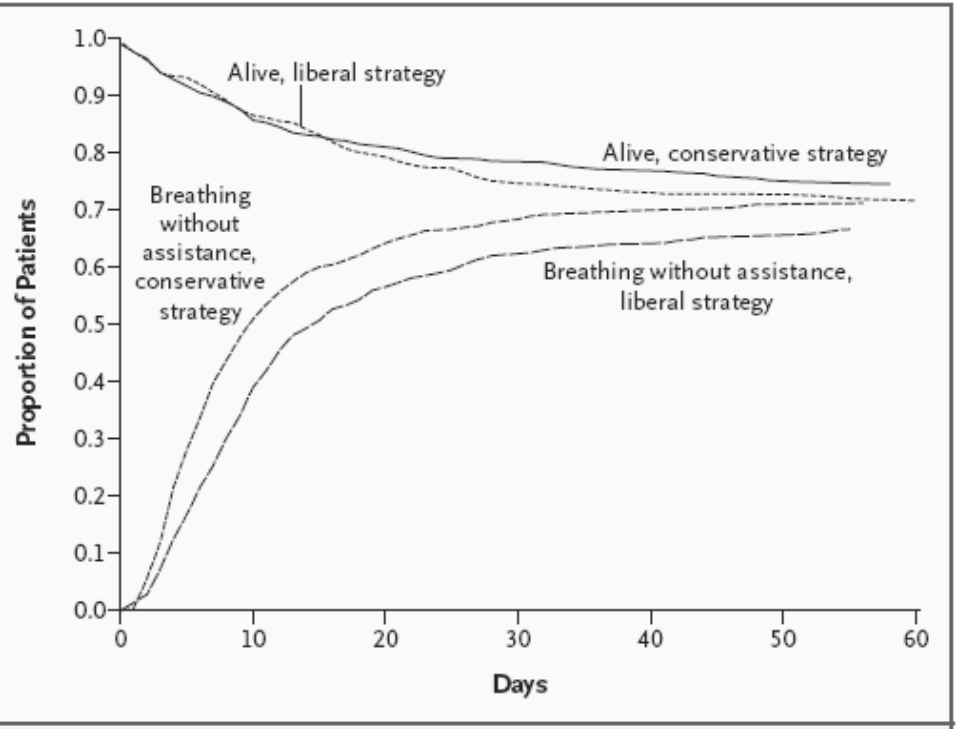
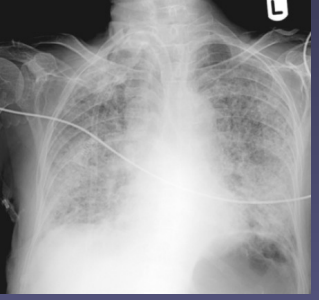


Figure 3. Probability of Survival to Hospital Discharge and of Breathing without Assistance during the First 60 Days after Randomization.

Table 2. Furosemide Dose, Fluid Intake, Fluid Output, and Fluid Balance on Each Day during the Study.*

Day	Furosemide		Fluid Intake		Fluid Output		Fluid Balance	
	Liberal	Conservative	Liberal	Conservative	Liberal	Conservative	Liberal	Conservative
	mg/24 hr (no. of patients)		*ml/24 hr (no. of patients)*		*ml/24 hr (no. of patients)*		*ml/24 hr (no. of patients)*	
1	74.27±7.48 (133)	148.94±8.52 (312)	5029.8±132.98 (485)	4230.5±120.03 (491)	2501.9±73.23 (485)	3043.8±93.90 (491)	2529.5±148.99 (484)	1186.7±151.01 (491)
2	72.46±6.65 (146)	157.35±8.91 (304)	4467.4±136.11 (479)	3590.6±98.45 (480)	2824.5±101.44 (479)	3966.7±115.57 (480)	1642.9±151.71 (479)	−376.1±161.08 (480)
3	65.28±6.49 (140)	166.90±10.01 (269)	3997.1±103.40 (465)	3390.4±85.30 (464)	3060.9±103.23 (465)	3797.3±110.48 (465)	936.12±115.32 (465)	−408.5±135.90 (464)
4	80.74±10.23 (129)	154.25±10.61 (228)	3752.0±102.07 (444)	3430.8±96.49 (437)	3188.1±109.19 (444)	3606.1±113.38 (434)	563.88±100.98 (444)	−165.5±119.92 (434)
5	73.06±8.41 (119)	164.71±12.06 (197)	3825.3±110.62 (424)	3201.1±87.23 (411)	3358.7±115.49 (421)	3444.8±108.98 (408)	483.03±109.98 (421)	−226.3±115.22 (408)
6	58.20±6.68 (106)	158.87±13.45 (165)	3782.8±104.28 (411)	3159.4±88.12 (382)	3334.4±123.99 (411)	3316.9±103.81 (379)	508.04±111.75 (410)	−144.9±110.25 (378)
7	51.03±4.31 (87)	127.86±11.61 (137)	3639.7±93.96 (390)	3226.9±108.18 (355)	3216.8±98.36 (385)	3143.9±100.16 (346)	458.95±106.85 (385)	130.08±118.47 (346)

* Plus–minus values are means ±SE. Numbers in parentheses indicate the number of patients receiving at least one dose of furosemide on that day or the number of patients with a fluid measurement. P<0.001 for all comparisons except for fluid intake on day 4 (P=0.02) and day 7 (P=0.004); fluid output on day 4 (P=0.008), day 5 (P=0.58), day 6 (P=0.94), and day 7 (P=0.61); and fluid balance on day 7 (P=0.04). Negative fluid balance means that fluid output exceeded fluid intake.

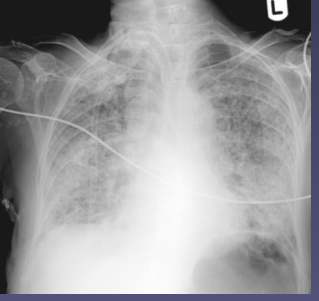


A randomized, controlled trial of furosemide with or without albumin in hypoproteinemic patients with acute lung injury*

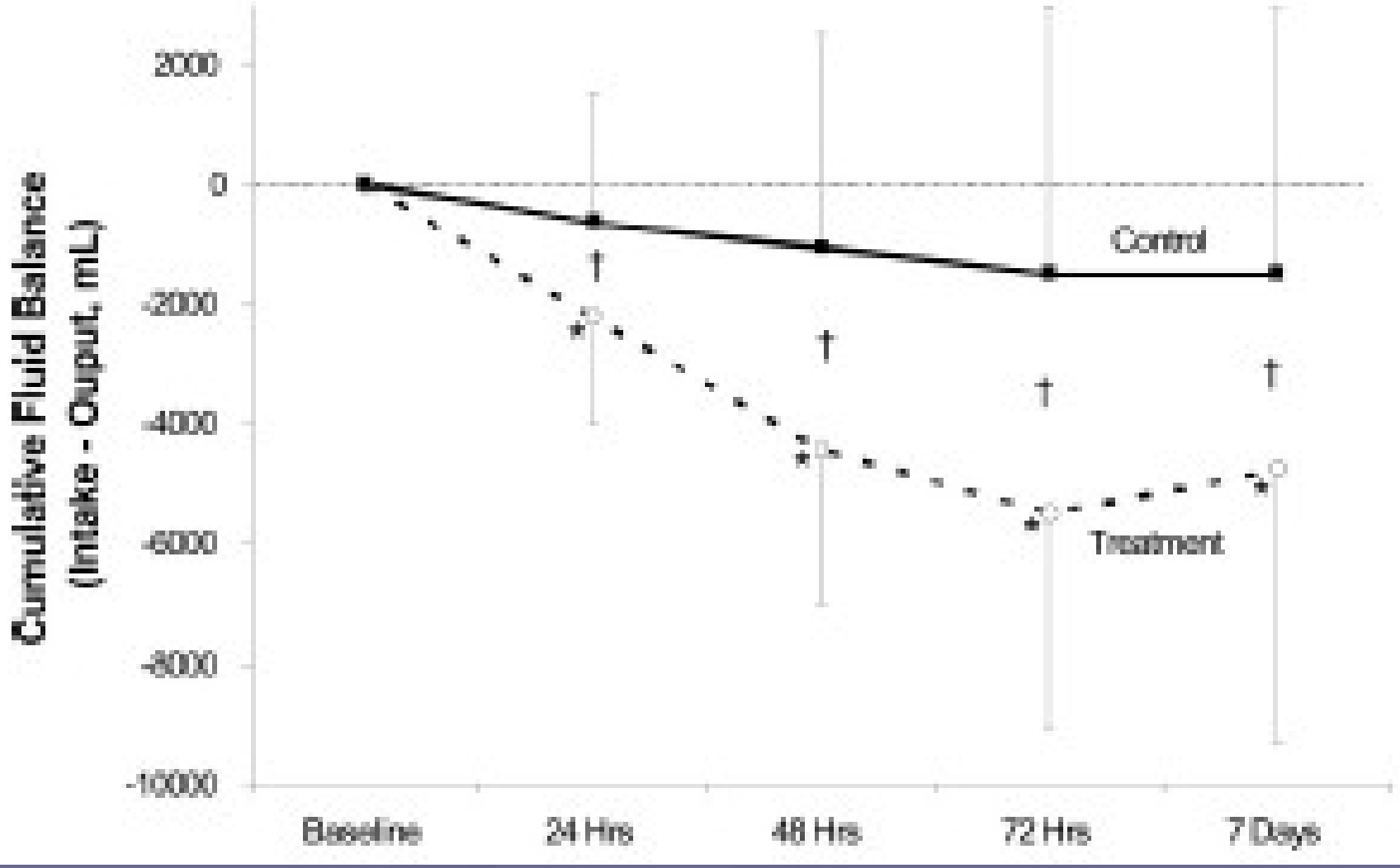
Greg S. Martin, MD, MSc; Marc Moss, MD; Arthur P. Wheeler, MD; Meredith Mealer, RN; John A. Morris, MD; Gordon R. Bernard, MD

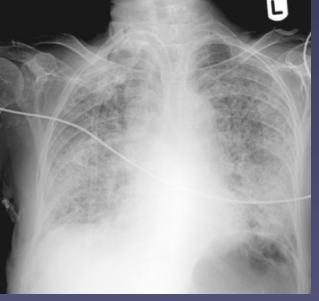
Crit Care Med
2005; 33:1681–1687

- 40 pacientů s ARDS
- CB < 60 g/l
- Randomizováni: furosemid s albuminem nebo furosemid s placebem po dobu 72 hod.
- Titrace dle bilance tekutin anebo normalizace CB
- Primární cíl: změna oxygenace

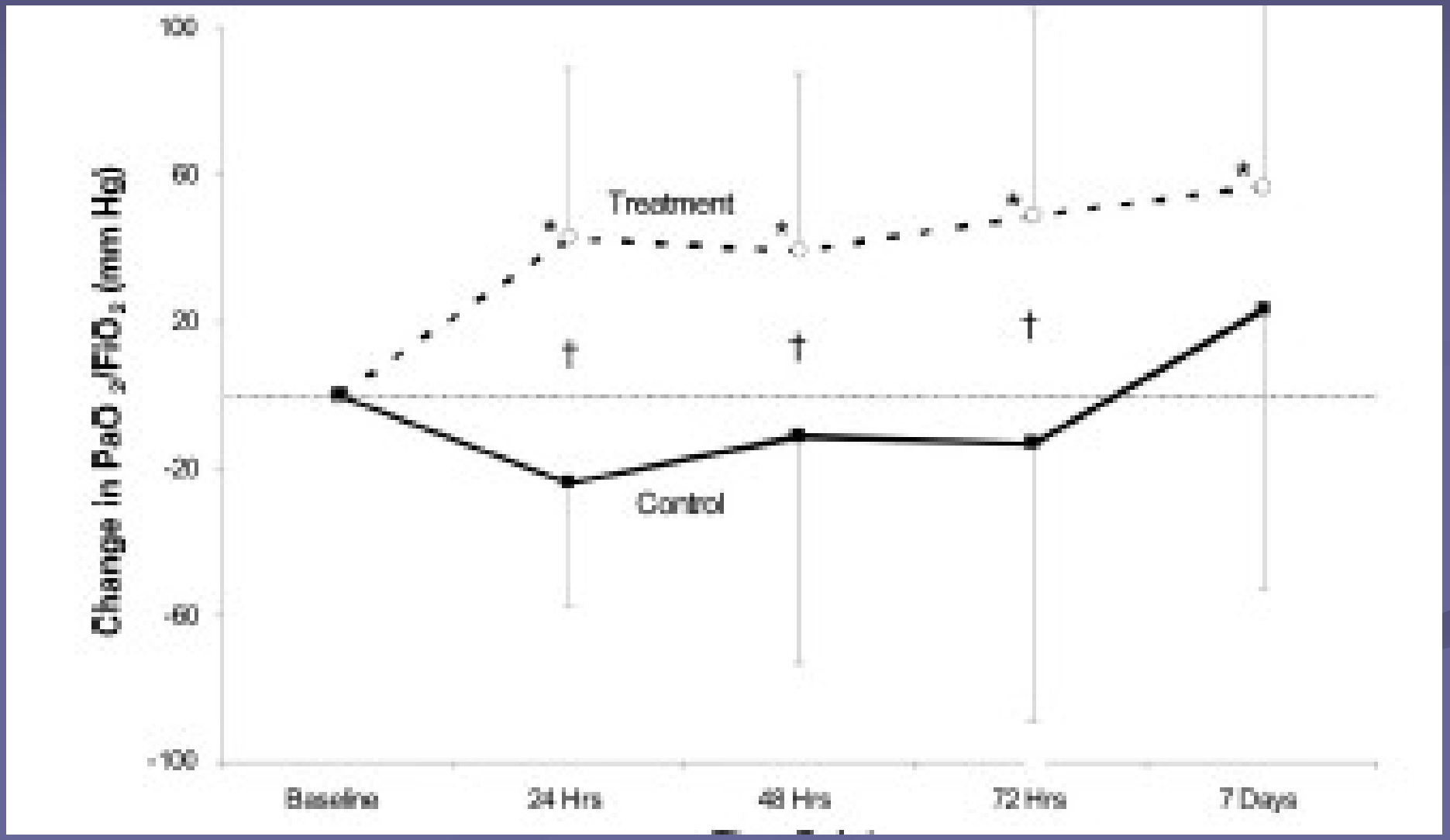


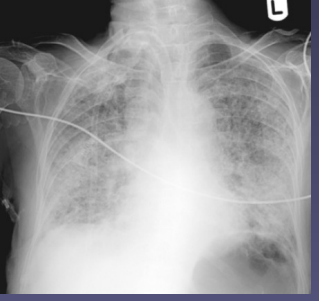
Kumulativní tekutinová bilance





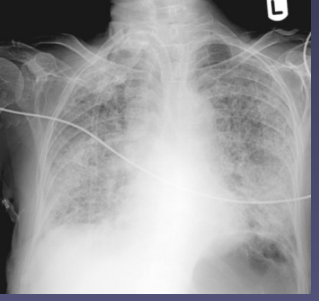
Změna oxygenace





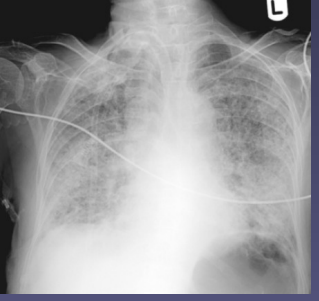
Ventilační strategie

1. Protektivní plicní ventilace s omezením Vt – ARDSnet skupina
2. Open lung approach - Amato
3. Open Lung Aproach - Lachman



Open Lung Aproach - Lachman

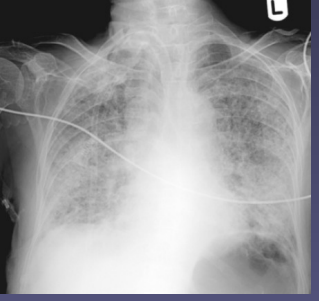
1. Krok – recruitment manévr – otevření plíce
2. Krok – hledání „uzavíracího tlaku“
3. Krok – opět recruitment
4. Krok – ventilace nad úrovní „uzavíracího tlaku“



Provedení recruitment manévru

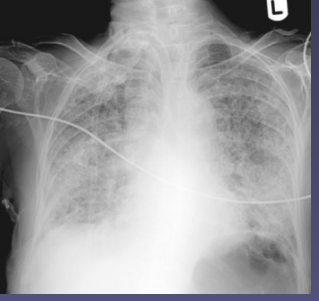
1. **CPAP** – klasická teze „40 over 40“
2. zvyšování **PIP** – při vysokém PEEP(kolem 20-25 cm H20) je postupně zvyšován PIP až na hodnoty kolem 60 cmH20. Sníží se PIP na hodnoty, které zaručí plánovaný Vt, poté klesáme s PEEP až na hodnotu tzv. *uzavíracího tlaku*
3. postupným zvyšováním **PEEP**

Hledáme nejlepší hodnotu paO2 a plicní compliance



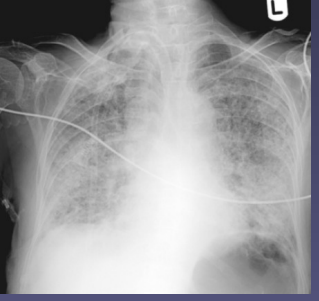
AACP 2000 - doporučení

- Omezení Vt a P_{pl}
- Tolerance hyperkapnie a RAC
- Dostatečný PEEP
- Zvážit použití pronační polohy
- Vhodný management sedace



Gattinoni: „How to ventilate ARDS patients?"

- Objasnit příčinu ARDS (primární vs sekundární)
- Stanovit potenciál recruitmentu: CT plic s PEEP 5 a15 cmH20 + sledování oxygenace, PaO2, PaCO2 + C_L (důležitá změna PaCO2)
- Vt nízké, ale ne podle IBW ale dle poměru Vt/EELV (EELV měřené heliem)
- Měřit transpulmonální tlak.



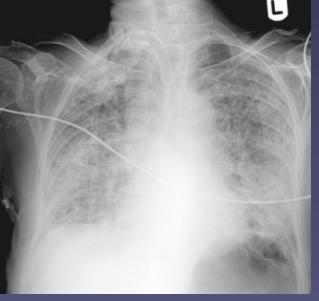
TERAPIE

I. NEFARMAKOLOGICKÁ

II. FAMAKOLOGICKÁ

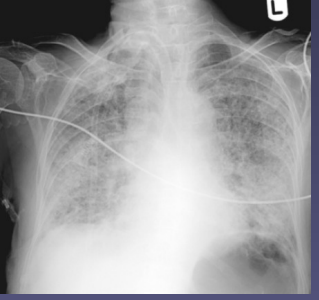
1. Kortikoidy
2. Surfaktant
3. NO
4. Prostaglandin E1
5. Experimentální a ostatní
6. Neprokázané postupy

III. Podpůrná



Kortikoidy

- Asi nejvíce kontroverzní terapie!
  - Ano či ne?
  - Kdy?
  - Dávka?
- 70´ léta
  - velké dávky – hypotéza – antiedémový a antiinflamatorní efekt
  - V časné fázi



Studie –early phase ARDS

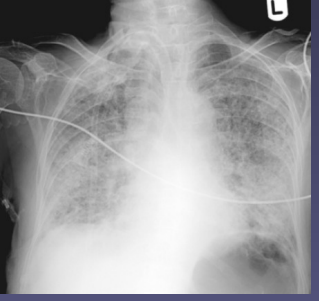
1: Luce JM, Montgomery AB, Marks JD, Turner J, Metz CA, Murray JF. Ineffectiveness of high-dose methylprednisolone in preventing parenchymal lung injury and improving mortality in patients with septic shock. Am Rev Respir Dis. 1988 Jul;138(1):62-8.

2: Bernard GR, Luce JM, Sprung CL, Rinaldo JE, Tate RM, Sibbald WJ, Kariman K, Higgins S, Bradley R, Metz CA, et al. High-dose corticosteroids in patients with the adult respiratory distress syndrome. N Engl J Med. 1987 Dec 17;317(25):1565-70.

3: Bone RC, Fisher CJ Jr, Clemmer TP, Slotman GJ, Metz CA. Early methylprednisolone treatment for septic syndrome and the adult respiratory distress syndrome. Chest. 1987 Dec;92(6):1032-6. Erratum in: Chest 1988 Aug;94(2):448.

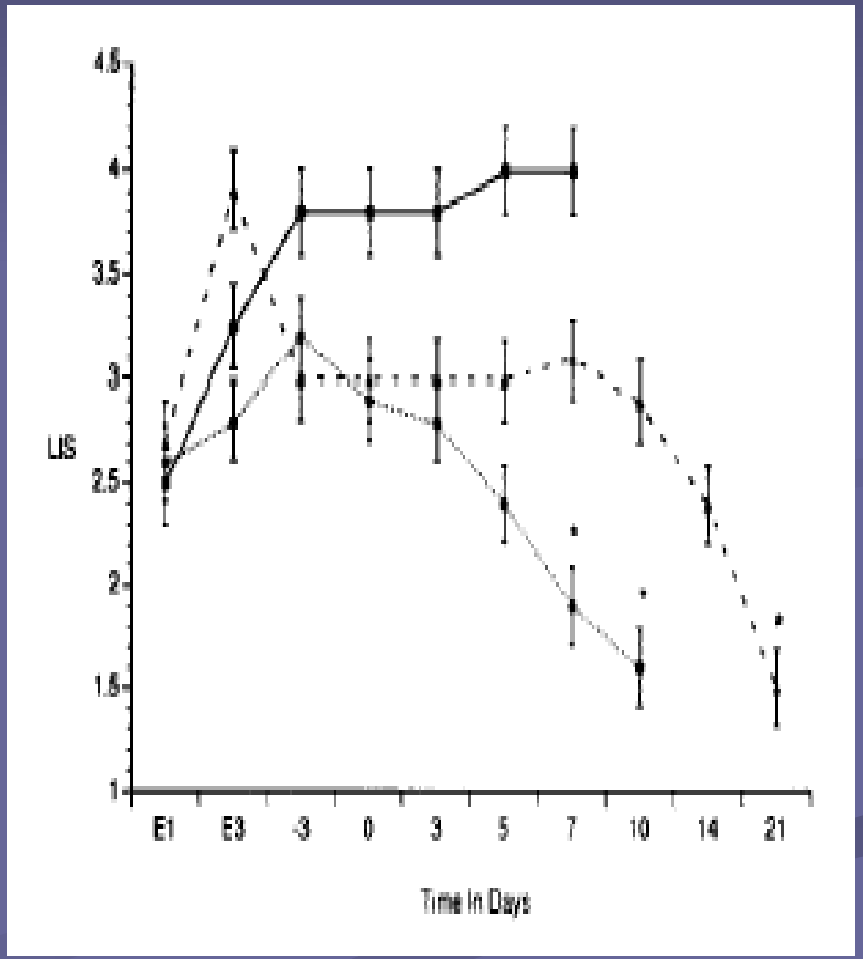
4: Sprung CL, Caralis PV, Marcial EH, Pierce M, Gelbard MA, Long WM, Duncan RC, Tendler MD, Karpf M. The effects of high-dose corticosteroids in patients with septic shock. A prospective, controlled study. N Engl J Med. 1984 Nov 1;311(18):1137-43.

5: Weigelt JA, Norcross JF, Borman KR, Snyder WH 3rd. Early steroid therapy for respiratory failure. Arch Surg. 1985 May;120(5):536-40.

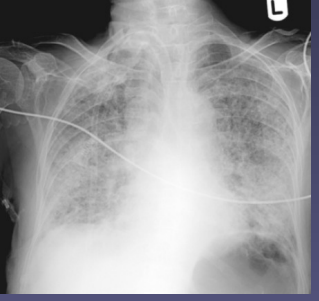


Effect of prolonged methylprednisolone therapy in unresolving acute respiratory distress syndrome: a randomized controlled trial.
Meduri GU, Headley AS, Golden E, Carson SJ, Umberger RA, Kelso T, Tolley EA

- Prospektivní randomizovaná studie
- Inclusion: perzistující ARDS více jak 7 dní
- 8 pacientů randomizováno do ramene s placebem
- 16 pacientů do skupiny s MP 2 mg/kg
- Výsledky:
  - Zlepšení LIS a MODS scóre
  - Snížení mortality: 2 (12%) of 16 vs 5 (62%) of 8 (P=.03)



JAMA. 1998 Jul 8;280(2):159-65.



Plasma and BAL Cytokine Response to Corticosteroid Rescue Treatment in Late ARDS*

G. Umberto Meduri, MD, FCCP; Stacey Headley, MD; Elizabeth Tolley, PhD; Melissa Shelby, RN, BSN; Frankie Stentz, PhD; and Arnold Postlethwaite, MD

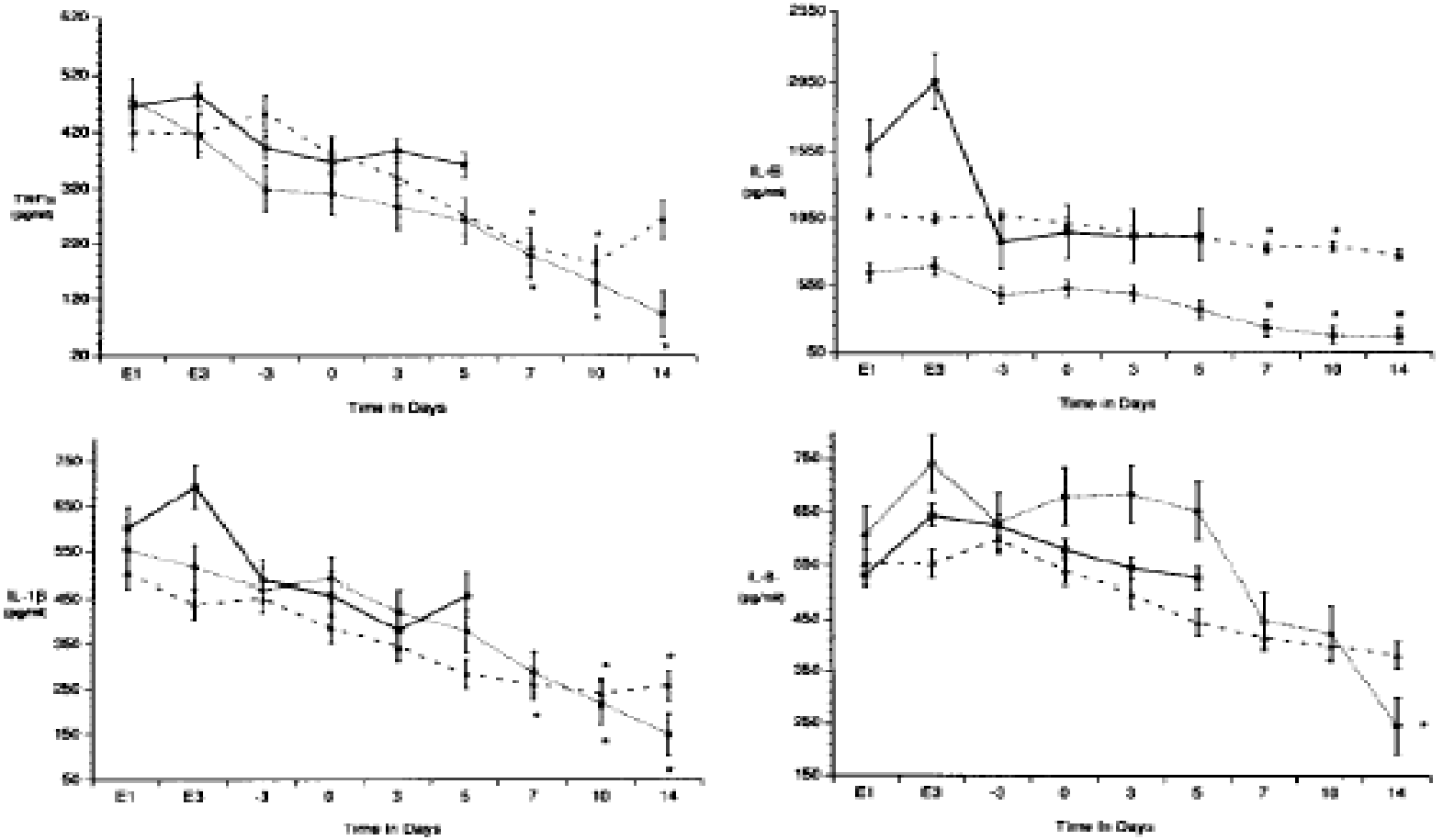
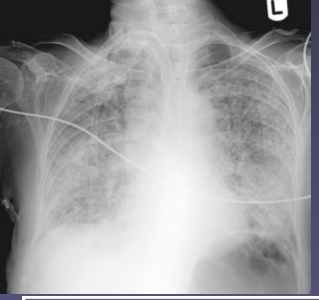


FIGURE 2. Mean changes in plasma TNF-α, IL-1β, IL-6, and IL-8 levels before and during treatment with CS in patients with rapid, delayed, and absent physiologic response. See Figure 1 legend for symbol explanation. The patient with AIDS is not included (see text).

Chest. 1995

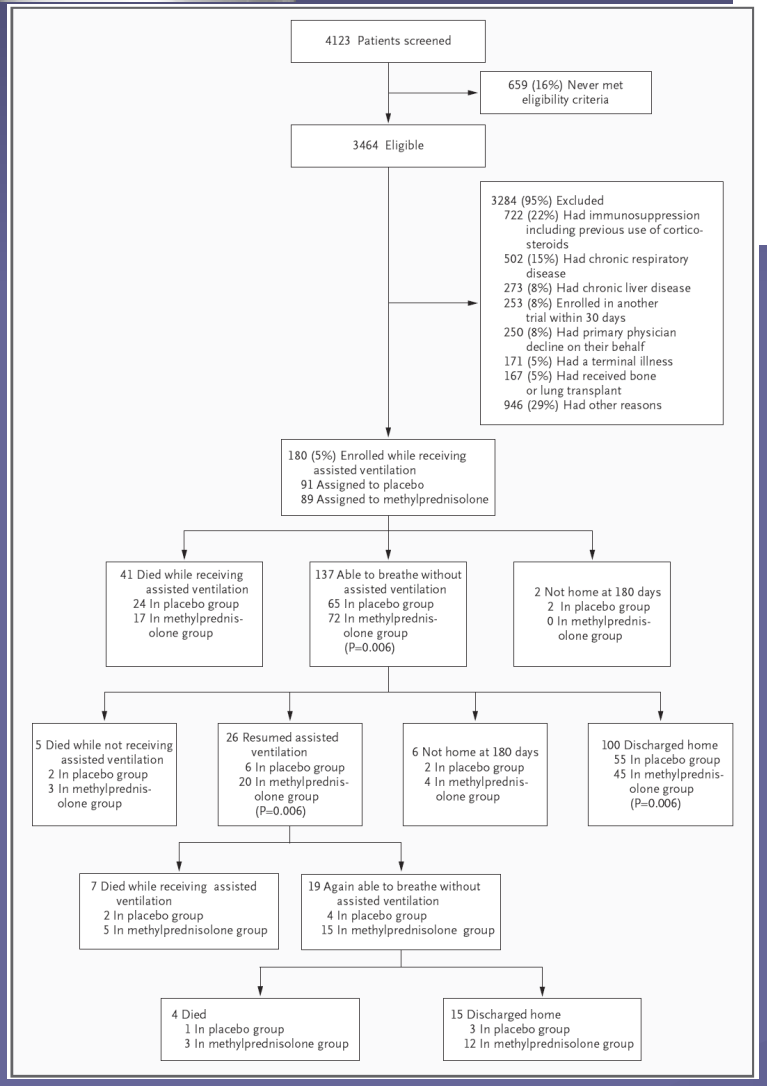


The NEW ENGLAND JOURNAL of MEDICINE

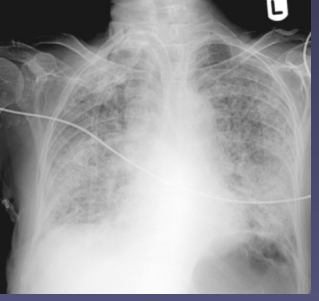
ESTABLISHED IN 1812 APRIL 20, 2006 VOL. 354 NO. 16

Efficacy and Safety of Corticosteroids for Persistent Acute Respiratory Distress Syndrome

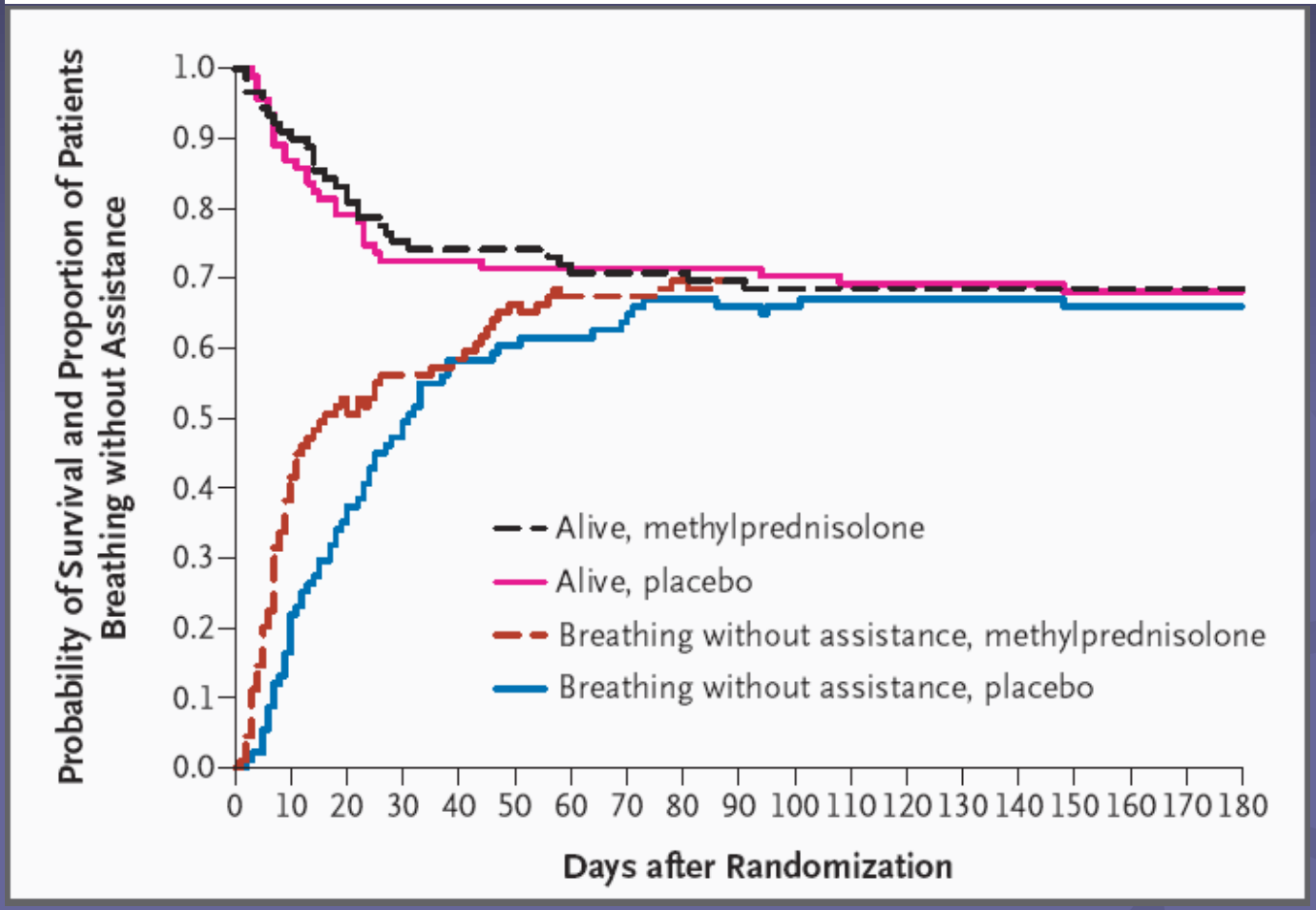
The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*



- double-blinded trial
- Randomizace methylprednisolone X placebo
- Inclusion: perzistující ARDS po 7 dnech
- End-point: redukce mortality či morbidity
- Odběr markerů inflamace z BAF a ze séra

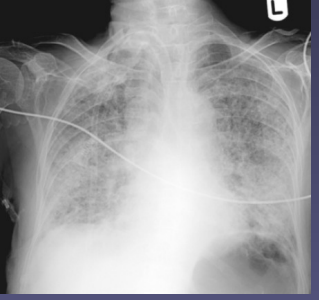


Efficacy and Safety of Corticosteroids for Persistent Acute Respiratory Distress Syndrome



CONCLUSIONS

These results do not support the routine use of methylprednisolone for persistent ARDS despite the improvement in cardiopulmonary physiology. In addition, starting methylprednisolone therapy more than two weeks after the onset of ARDS may increase the risk of death. (ClinicalTrials.gov number, NCT00295269.)

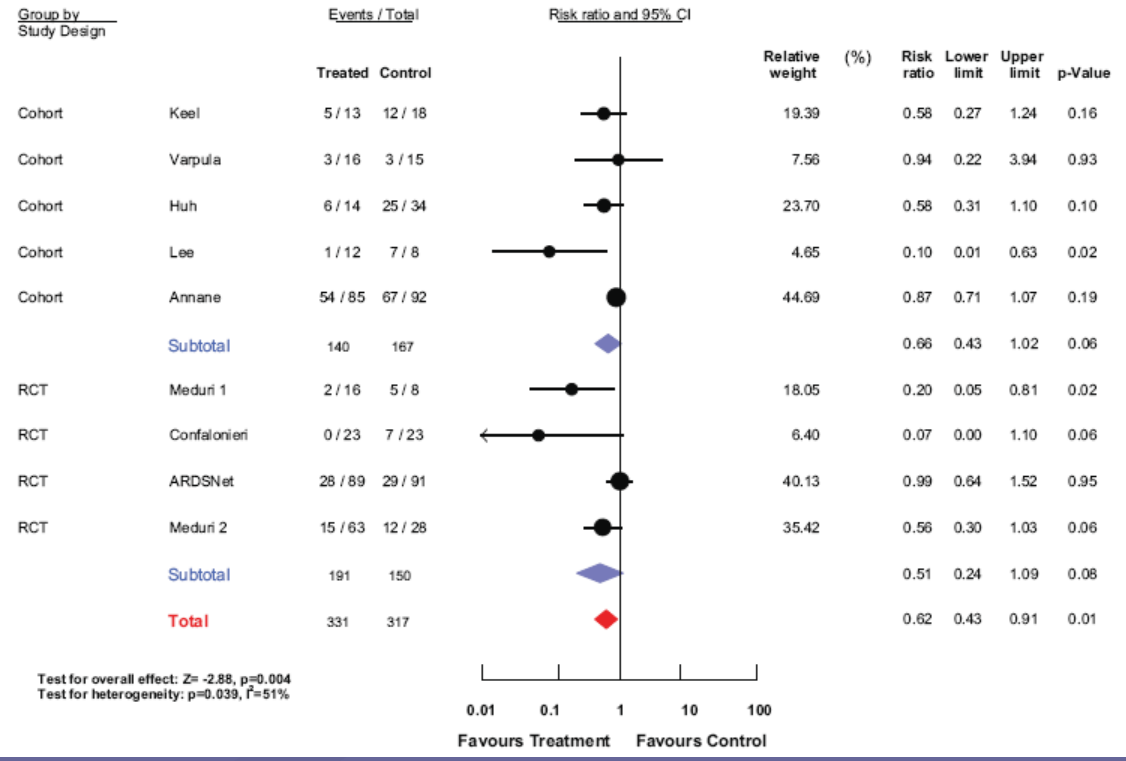


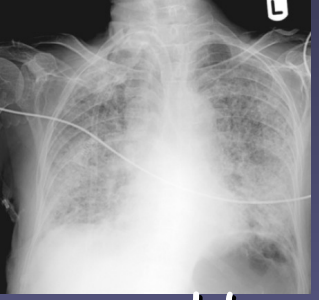
Use of corticosteroids in acute lung injury and acute respiratory distress syndrome: A systematic review and meta-analysis*

Benjamin M. P. Tang, PhD; Jonathan C. Craig, PhD; Guy D. Eslick, PhD; Ian Seppelt, MBBS; Anthony S. McLean, MBBS

	Keel et al (31)	Varpula et al (32)	Huh et al (33)	Lee et al (34)	Annane et al (35)	Meduri et al (9)	Confalonieri et al (20)	ARDSNet (11)	Meduri et al (10)
Study design	Cohort	Cohort	Cohort	Cohort	Cohort	RCT (crossover design)	RCT	RCT	RCT (crossover design)
Year of study	1995	1998	1998	2003	1999	1996	2003	2003	2002
Country	Switzerland	Finland	South Korea	South Korea	France	USA	Italy	USA	USA
Total (n)	31	31	48	20	177	24	46	180	91
Mean age (yrs)	50	43	61	67	60	48	63	49	51
Subjects	Nontrauma patients with ARDS	Patients with primary ALI	Patients with ARDS	Post-thoracic surgery patients	Septic shock patients with ARDS	Patients with severe ARDS	Patients with severe pneumonia with Pao_2/Fio_2 <250	Patients with persistent ARDS	Patients with severe early ARDS
Dose equivalent (methylprednisolone)	100–250 mg/d	120 mg/d	140 mg/d	140 mg/d	40 mg/d	140 mg/d	48 mg/d	140 mg/d	70 mg/d
Days of ALI/ARDS (d)[a]	15.0	9.7	8.0	4.4	0.0	9.2	0.0	11.3	3.0
Length of treatment (d)	8.0	27.0	7.0	9.5	7.0	32.0	7.0	25	28
Tapering of therapy	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes
Mortality of treatment vs. control groups[b]	38% vs. 67%	19% vs. 20% (30 d)	43% vs. 74%	8% vs. 88%	53% vs. 75% (28 d)	12% vs. 62%	0.0% vs. 30%	29% vs. 29% (60 d)	24% vs. 43%

Conclusion: **The use of low-dose corticosteroids was associated with improved mortality and morbidity outcomes without increased adverse reactions. The consistency of results in both study designs and all outcomes suggests that they are an effective treatment for ALI or ARDS. The mortality benefits in early ARDS should be confirmed by an adequately powered randomized trial.(Crit Care Med 2009; 37:1594–1603)**

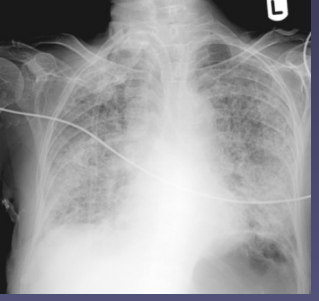




Surfaktant

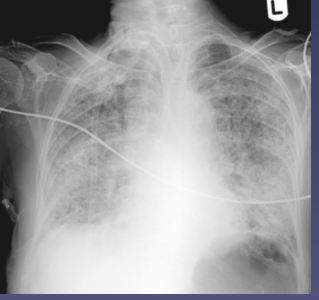
- Hypotéza: deficit surfaktantu významnou součástí ARDS (jako u IRDS)
- 9 malých studií, některé vykazuje přechodné zlepšení oxygenace, ale bez ovlivnění mortality
- ALE:
  - Chybí mortalitní studie
  - Dávka? (pokud vůbec měřena)
  - Kdy?
  - Způsob podávání? (aerosol X tracheální instilace)
  - Preparát?
    - Syntetický surfaktant s fosfolipidy
    - Syntetický surfaktant s fosfolipidy a proteiny
    - Hovězí surfaktant
    - Prasečí surfaktant

Aktuálně není možné doporučit surfaktant v léčbě ALI/ARDS



NO

- Silný vasodilatátor
- Rychle inaktivován => působí v místě podání či vzniku
- Inhalace NO => dilatuje plicní cévy perfundující ventilované regiony => snížení plicních zkratů, zlepšení oxygenace, plicní hypertenze
- Studie na zvířatech prokázaly benefit stran oxygenace a plicní hypertenze



NO - studie

1.Taylor RW, Zimmerman JL, Dellinger RP, Straube RC, Criner GJ, Davis K Jr, Kelly KM, Smith TC, Small RJ; Inhaled Nitric Oxide in ARDS Study Group. Low-dose inhaled nitric oxide in patients with acute lung injury: a randomized controlled trial. JAMA. 2004 Apr 7;291(13):1603-9.

2. Dellinger RP, Zimmerman JL, Taylor RW, Straube RC, Hauser DL, Criner GJ, Davis K Jr, Hyers TM, Papadakos P. Effects of inhaled nitric oxide in patients with acute respiratory distress syndrome: results of a randomized phase II trial. Inhaled Nitric Oxide in ARDS Study Group. Crit Care Med. 1998 Jan;26(1):15-23.

3. Rossaint R, Falke KJ, Lopez F, Slama K, Pison U, Zapol WM. Inhaled nitric oxide for the adult respiratory distress syndrome. N Engl J Med. 1993 Feb 11;328(6):399-405.

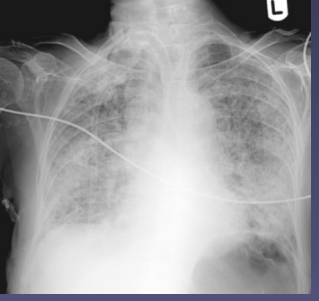
4. Payen D., Vallet B., Group G. Result of French prospective multicentric randomized double-blind placebo-controlled trial on onhaled nitric oxide in ARDS. ICM 1999; 25:S166.

- Zelpšení oxygenace
- Snížení shuntování
- Snížení plicní hypertenze

X

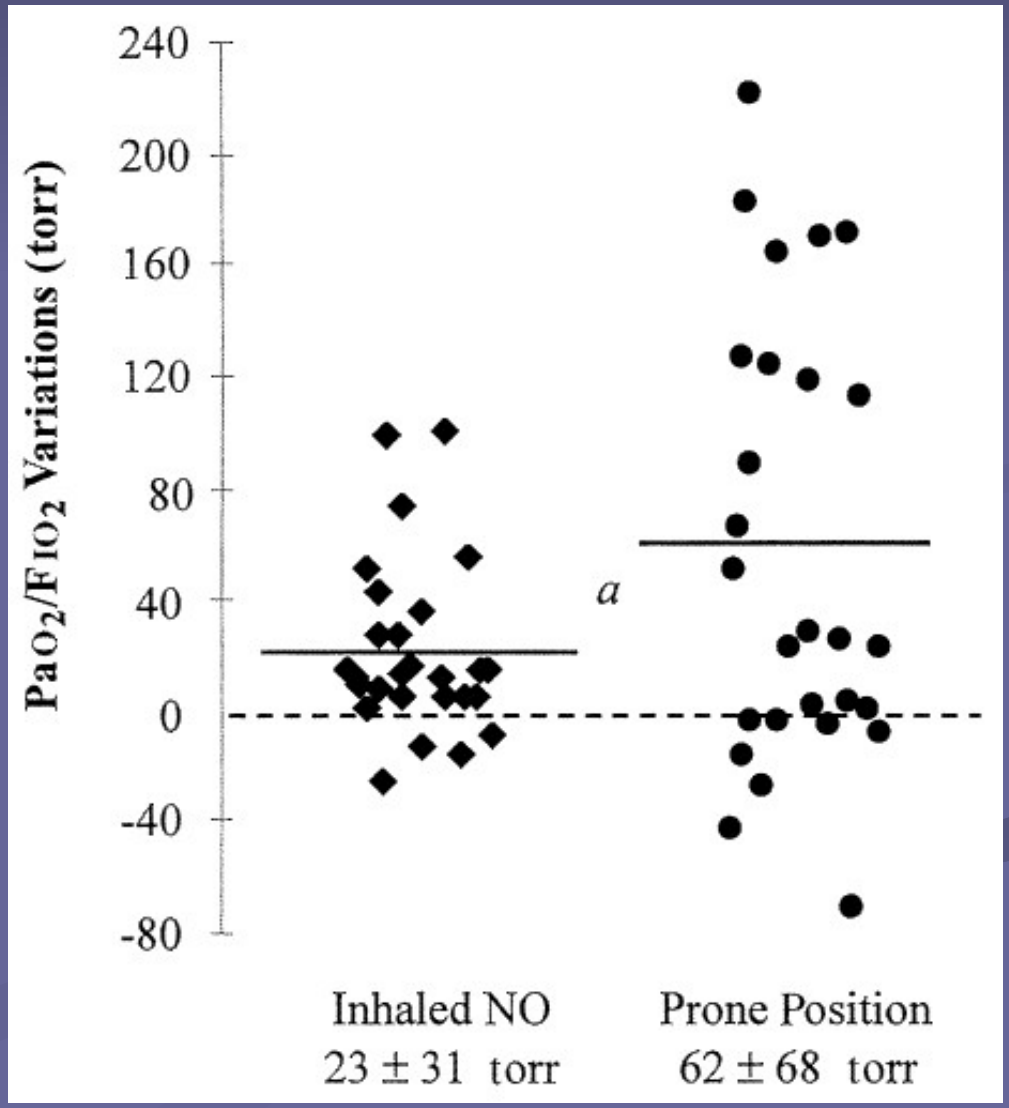
- Bez vlivu na mortalitu či délku UPV

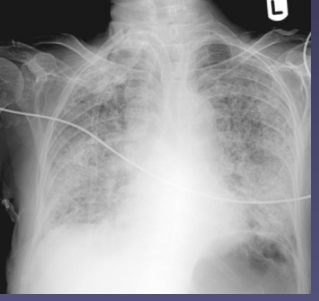
Doporučení: jako rescue terapie u ARDS s refrakterní hypoxemií



Critical Care Medicine: Volume 28(2) February 2000 pp 304-308
Short-term effect of inhaled nitric oxide and prone positioning on gas exchange in patients with severe acute respiratory distress syndrome
Dupont, Hervé MD; Mentec, Hervé MD; Cheval, Christine MD; Moine, Pierre MD; Fierobe, Lisiane MD; Timsit, Jean-François MD

- 27 pacientů
- Pronační poloha X NO
- NO: 5 až 20 ppm
- pronace: 4 hodiny

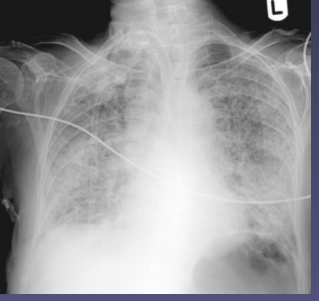




Prostaglandin E1

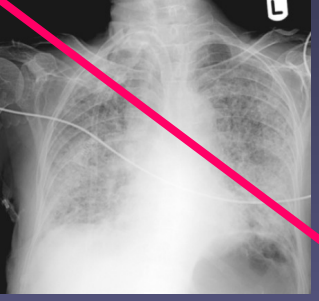
- Fce:
  - Plicní vasodilatátor
  - Snižuje aktivaci neutrofilů
  - Snižuje agregaci trombocytů
- Prostaglandin E1 (ALPROSTADIL)
  - 7 studií (693 pacientů)
  - Podání: bolusové X kontinuální
  - Forma: standartní X liposomální
  - Dávka: 7,2 až 43,2 μg/kg/den
- Výsledky:
  - bez efektu na časnou mortalitu
  - 1 studie snížení nutnosti ventilace den 8.
  - ALE: časté nežádoucí účinky (CNS, kardiovaskulární)

Aktuálně není možné doporučit PGE1 v léčbě ALI/ARDS



Ostatní

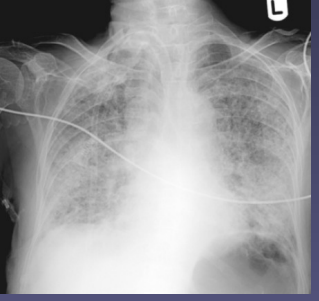
- Partial liguid ventilation
- Tracheal gas insufflation (TGI)
- HFOV
- Kinetická terapie
- Neinvazivní ventilace (?)



Neprokázaná

1. Acetylcysteine
2. Dazoxiben
3. GM-CSF
4. Indomethacin
5. Ketokonazol (Nizoral)
6. Lisofyllin
7. Pentoxifylin (Agapurin)
8. Acyclovir (Herpesin)
9. NEI – neutrofil elastase inhibitor
10. IL-10

UNPROVED



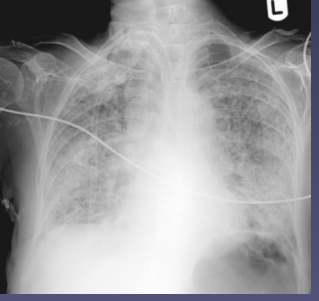
TERAPIE

I. NEFARMAKOLOGICKÁ

II. FAMAKOLOGICKÁ

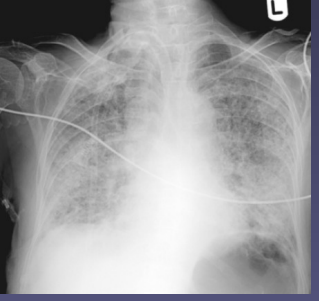
III. Podpůrná

1. Léčba vyvolávající příčiny
2. Nutrice
3. Léčba infekce
4. Management hemodynamiky
5. Prevence VAP



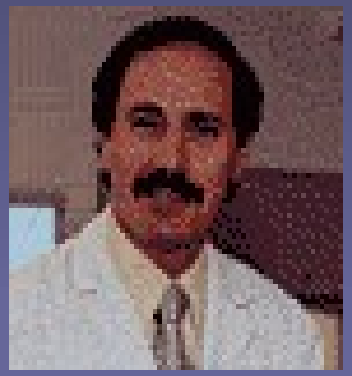
EBM x patient-oriented physiological thinking

- do RCT je zařazováno jen **zlomek** pacientů (interní x externí validita studií)
- intervence na ICU jsou **komplexní** prováděné u diagnóz, které jsou extrémně patofyziologicky složité a **heterogenní** (septický šok, PAC)
- máme intervence, které **nejsou** EBM-prooved a **provádíme** je (PPI, furosemid, sPO_2)
- máme intervence, které **jsou** EBM-prooved a **neprovádíme** je (SDD)
- **Je mnoho studií, které vzbuzují žhavé pro-con debaty v rámci kongresů, ale selhaly ve zlepšení péče o pacienta!**



RCT vs. critical care

Randomized, Controlled Trials in Critical Care: An Expert Interview With John J. Marini, MD from Medscape General Medicine™ posted 06/03/2003



Some compare evidence-based medicine (EBM) to a modern religion. Do you believe that EBM limits independent thinking and personal initiative? Is this necessarily detrimental in everyday clinical practice?

Dr.Marini: k řešení většiny problémů v intenzivní péči mají RCT k dispozici jen zlomky relevantních dat a nemohou tedy nabízet návody k postupu….

…..jejich závěry lze brát pouze jako rámcové pro pacienty podobné těm ve studii a starat se o ně podobně