ADULT EXTRACORPOREAL SUPPORT

울산의대 서울아산병원
홍상범

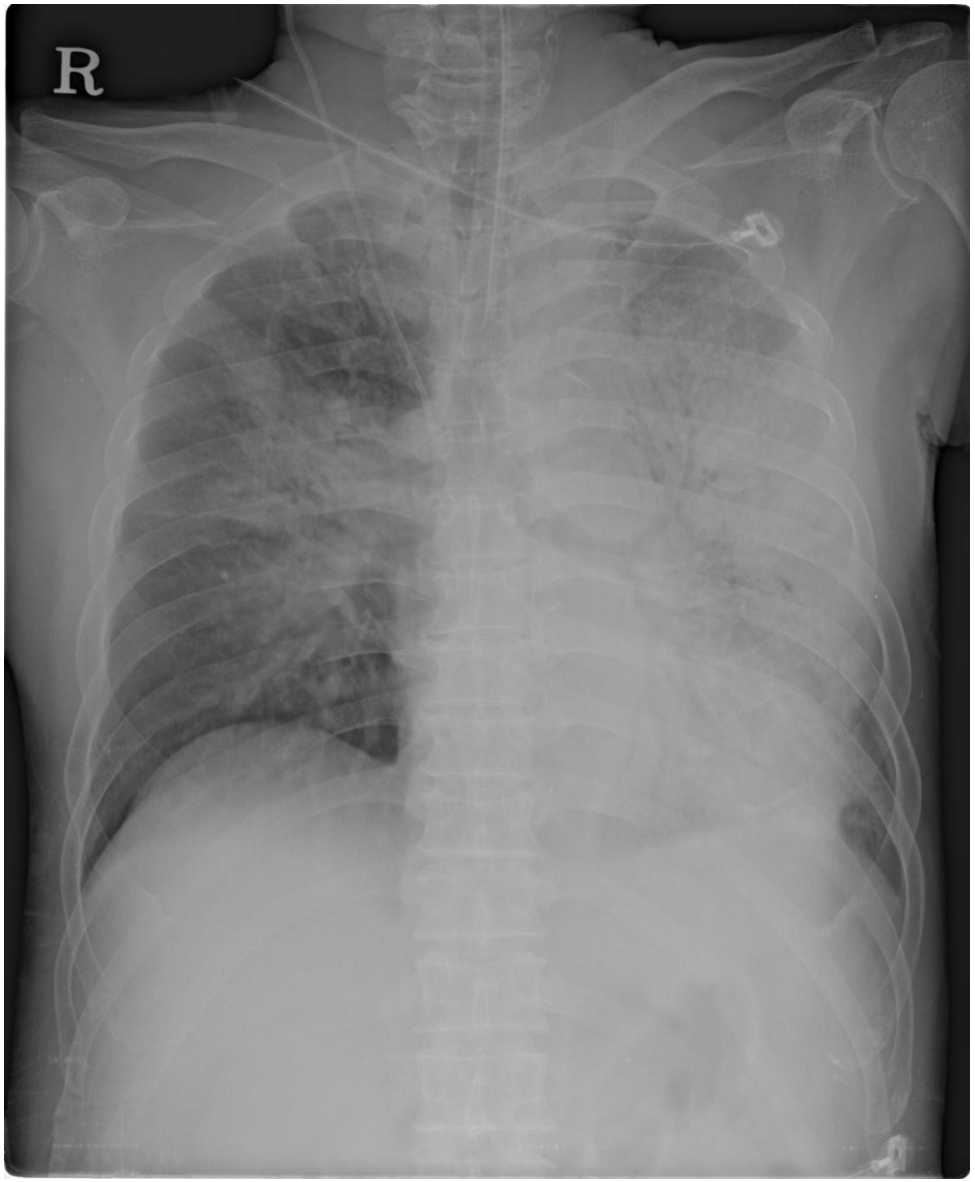
CASE 1

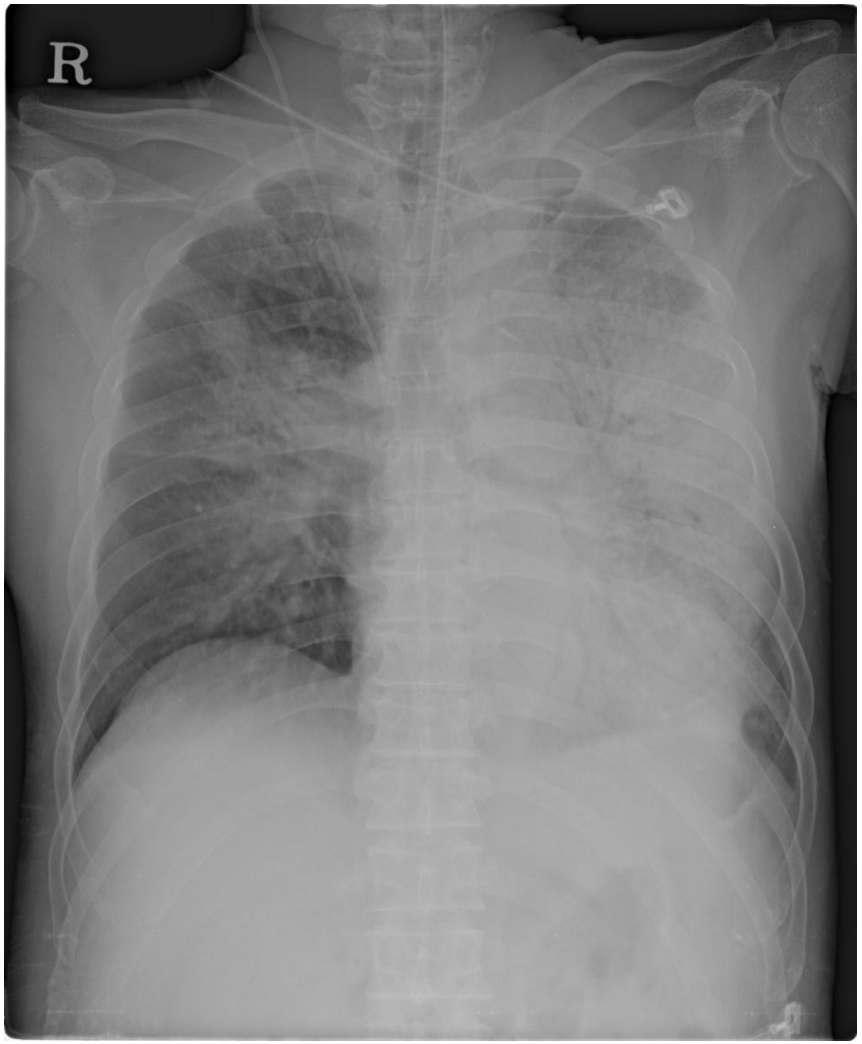
64/M
Chief complaints : Dyspnea
(onset : 1 day ago)

내원 4-5일 전부터 fever 및 myalgia 증세로
primary clinic 에서 medication 처방 받아 복용하였으나
증상 호전 없었고, 내원 1일전부터 cough 및 dyspnea
발생하여 본원으로 전원됨.

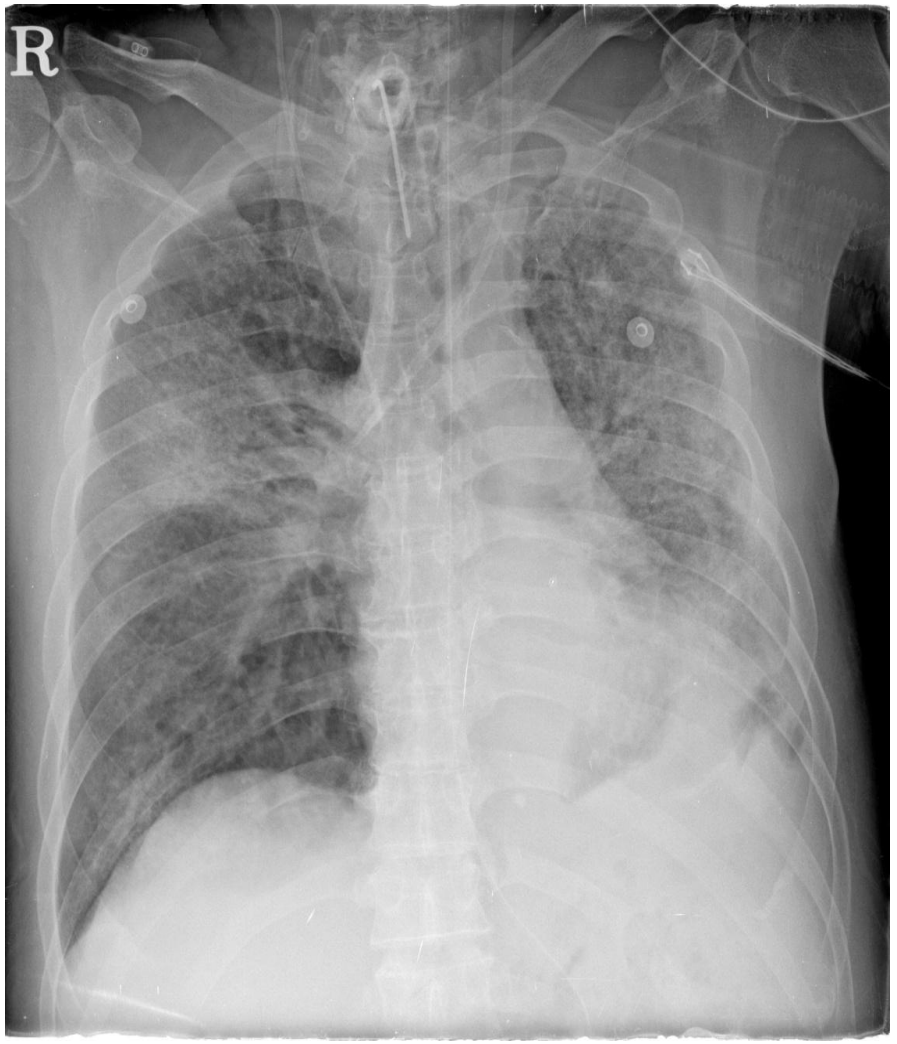
PMHX : DM (+) HTN (+)
SHX : heavy smoker & alcholics

Initial chest x-ray

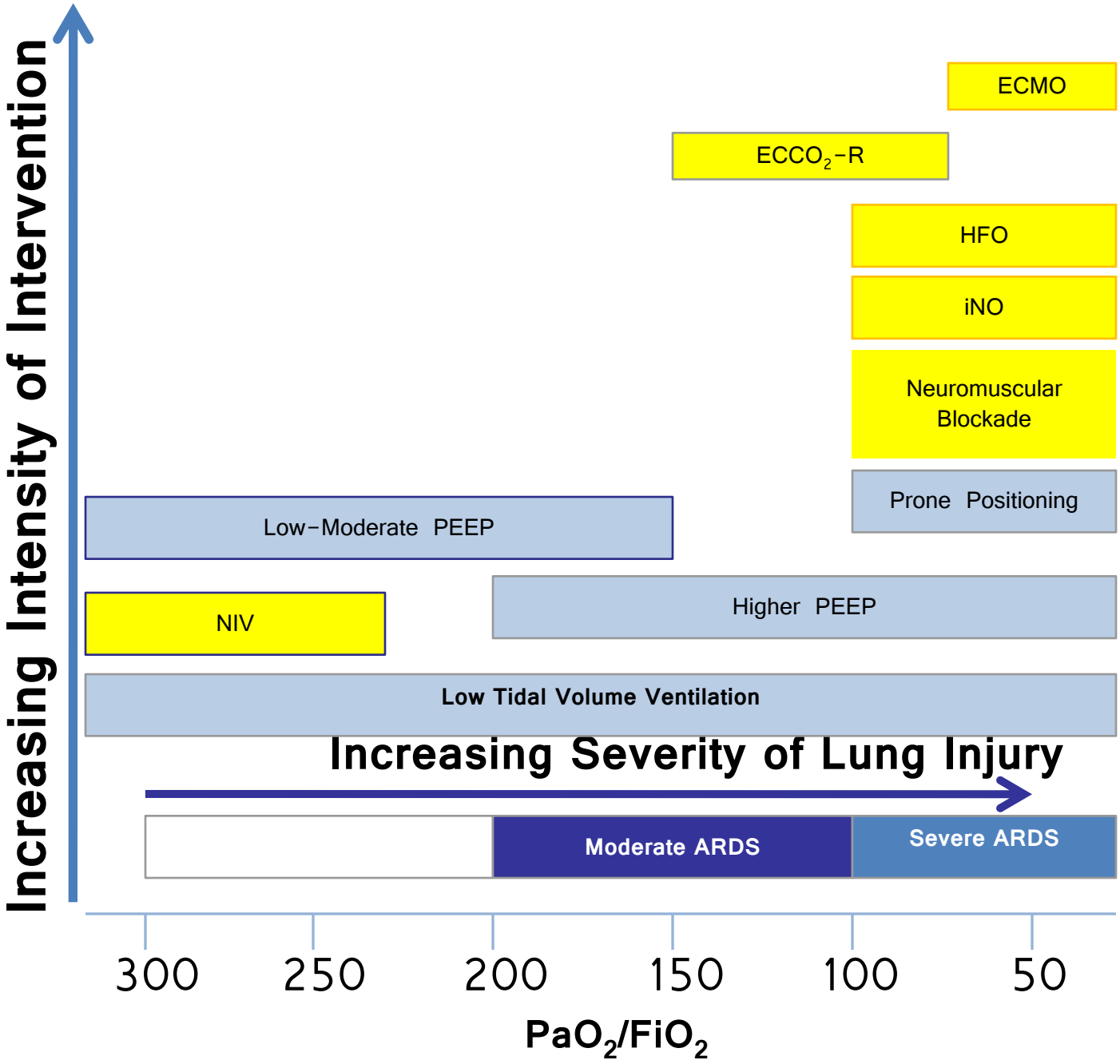




2010.7.19

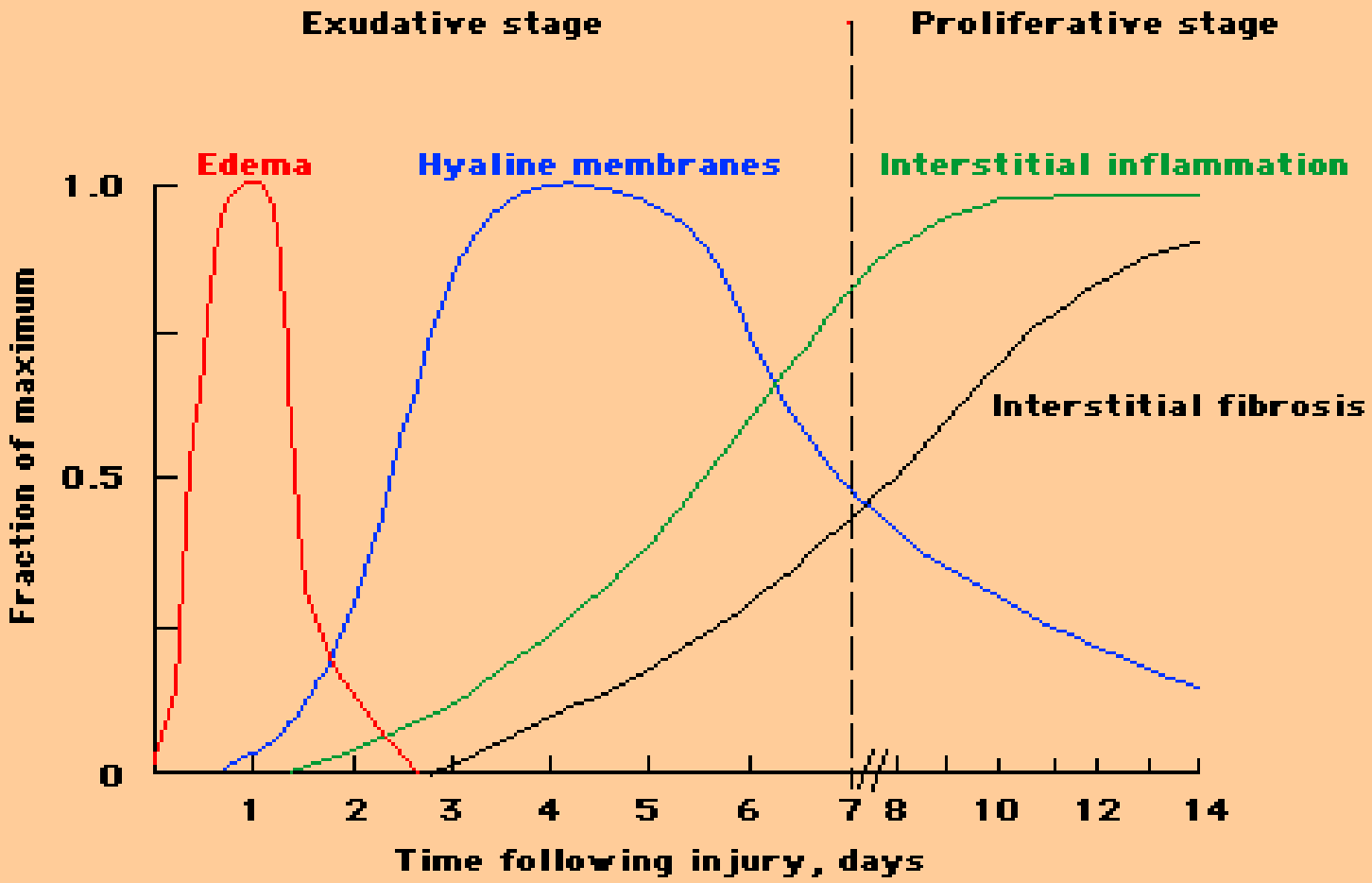


2010.7.27

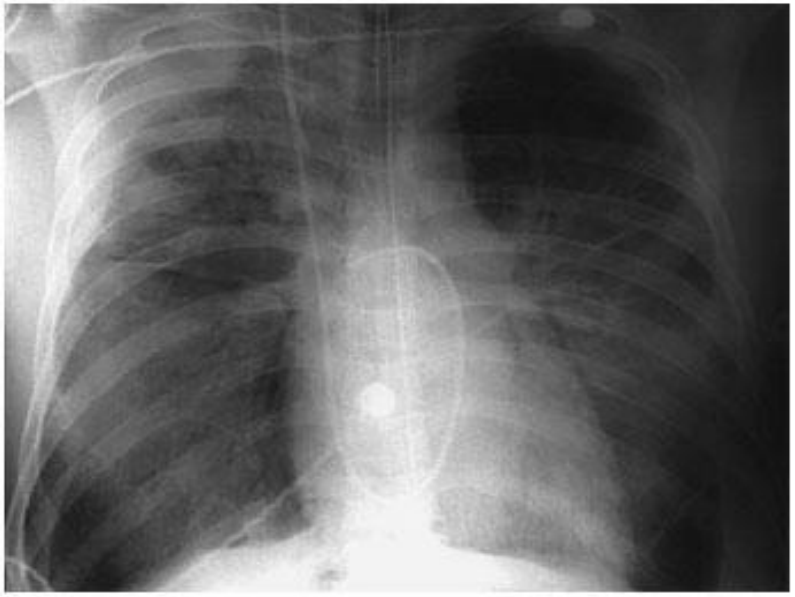

Increasing Intensity of Intervention
ECMO
ECCO2-R
HFO
iNO
Neuromuscular Blockade
Prone Positioning
Low-Moderate PEEP
Higher PEEP
NIV
Low Tidal Volume Ventilation
Increasing Severity of Lung Injury
Moderate ARDS
Severe ARDS
300
250
200
150
100
50
PaO2/FiO2

Before ECMO

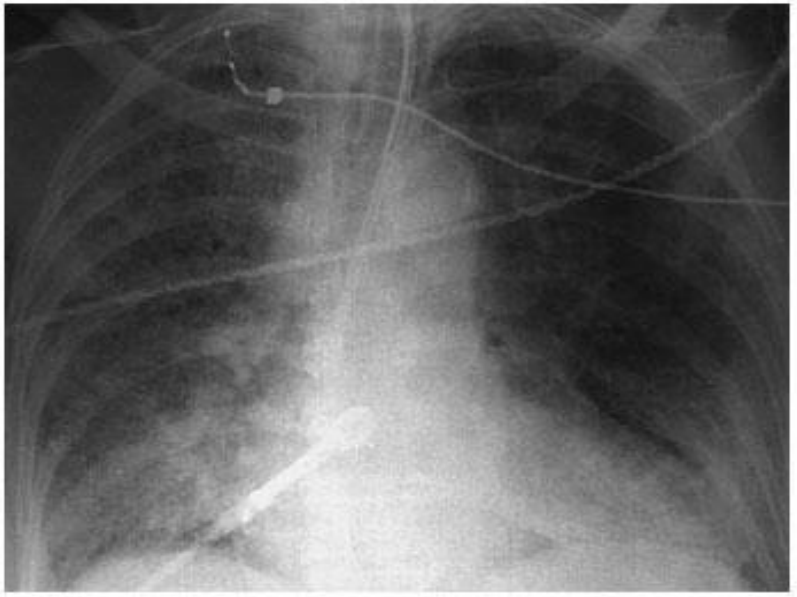
- Drain effusions, pneumothorax
- Consider pulmonary embolism
- Suction
- Increase DO_2: Transfuse
- Consider intracardiac shunt
- Recruitment maneuver
- Neuromuscular blockade
- Prone
- Diurese; consider albumin
- iNO or iProstacyclin



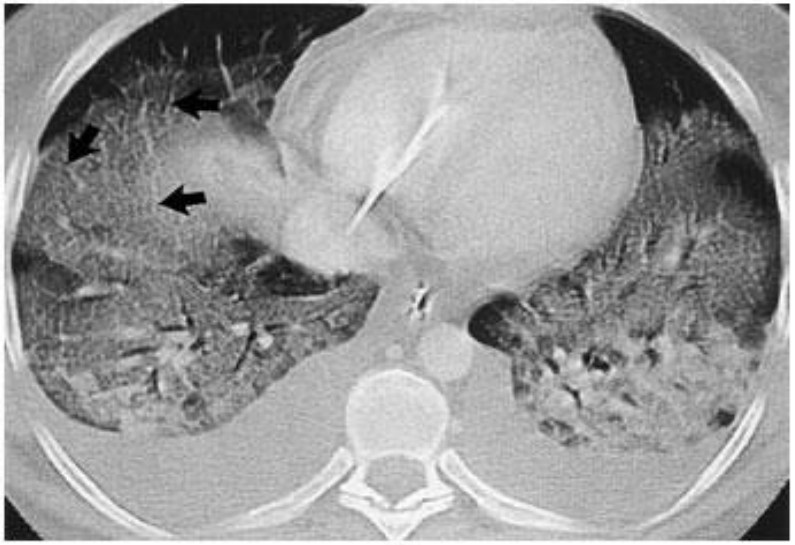
Time course of ARDS Schematic representation of the time course of the acute respiratory distress syndrome (ARDS). During the early or exudative phase, the lesion is characterized by high permeability pulmonary edema followed by the formation of hyaline membranes. After 7 to 10 days, a proliferative phase may develop, with marked interstitial inflammation, fibrosis, and disordered healing. (Redrawn from Katzenstein AA, Askin FB. Surgical Pathology of Non-neoplastic Lung Disease. Saunders, Philadelphia, 1982.)



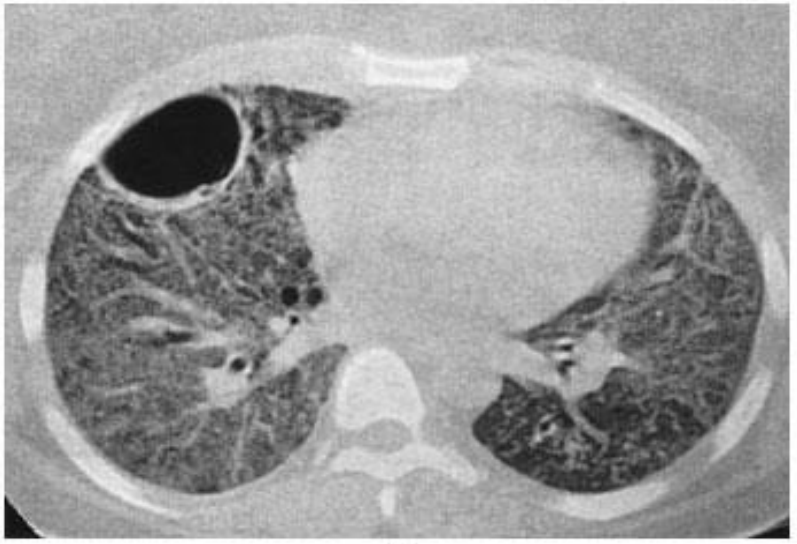
A



B



C



D

Journal of Critical Care (2013) xx, xxx–xxx

ELSEVIER

Journal of Critical Care

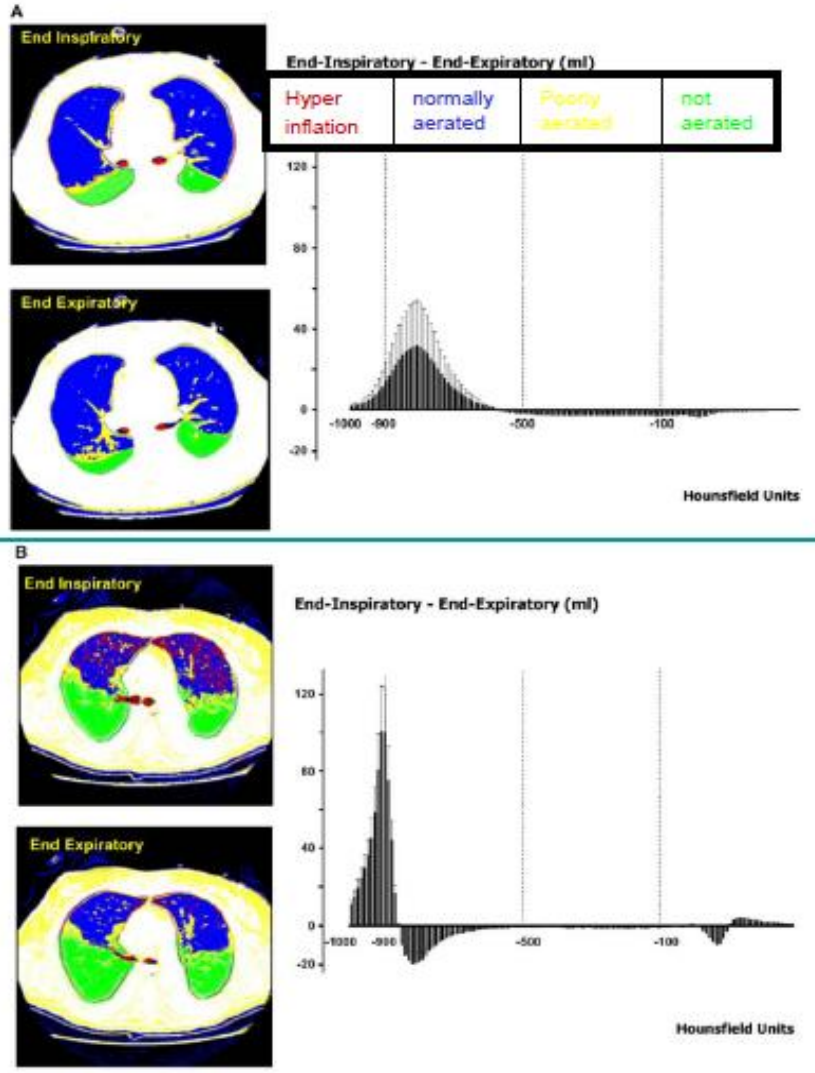
Low-tidal volume mechanical ventilation in patients with acute respiratory distress syndrome caused by pandemic influenza A/H1N1 infection☆

Dong Kyu Oh MD[a], Myung Goo Lee MD[b], Eun Young Choi MD[c], Jaemin Lim MD[a], Hyun-Kyung Lee MD[d], Seok Chan Kim MD[e], Chae-Man Lim MD, PhD[a], Younsuck Koh MD, PhD[a], Sang-Bum Hong MD, PhD[a,□]
for the Korean Society of Critical Care Medicine H1N1 collaborative

Tidal Hyperinflation during Low Tidal Volume Ventilation in Acute Respiratory Distress Syndrome

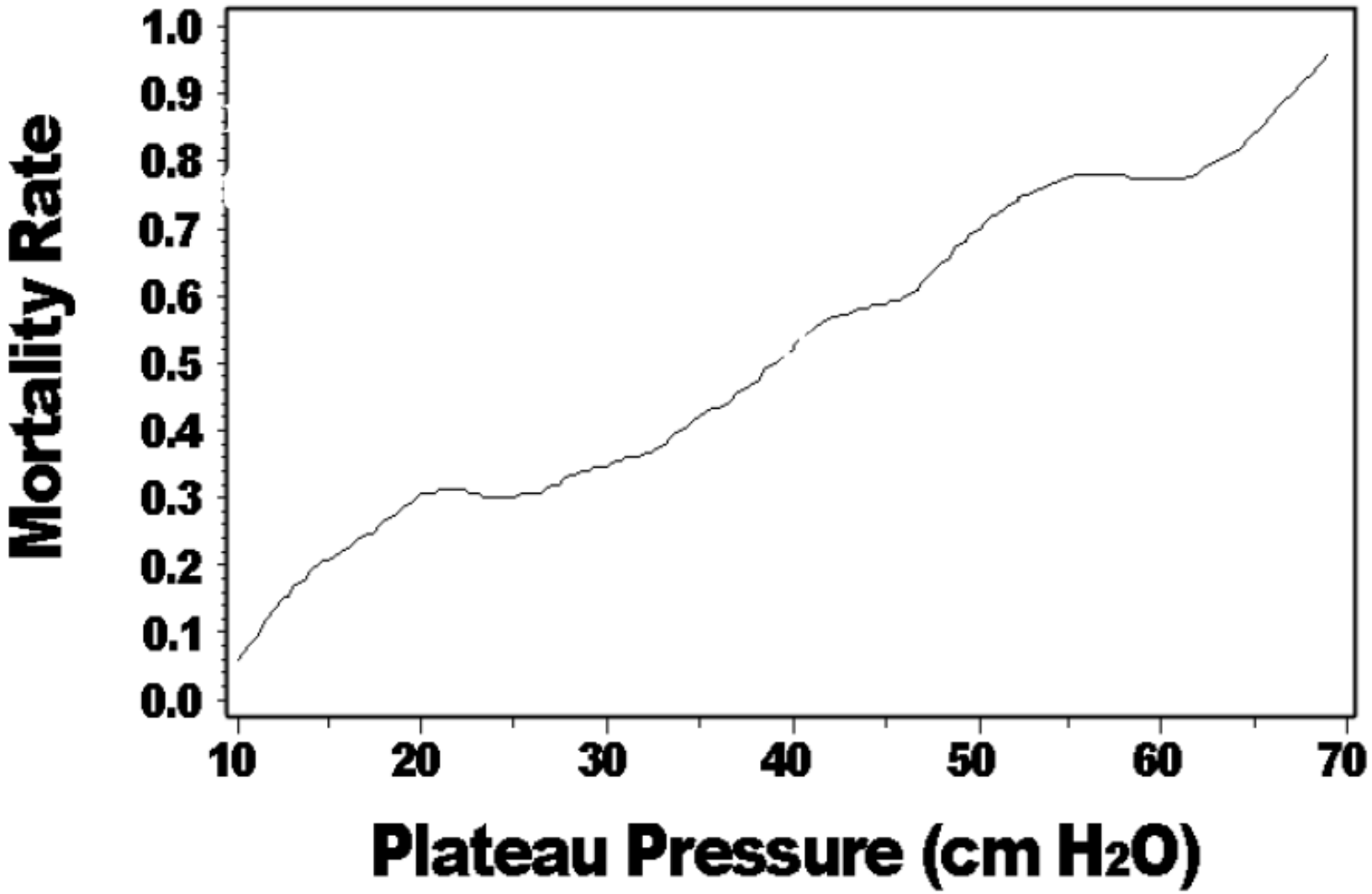
Pier Paolo Terragni, Giulio Rosboch, Andrea Tealdi, Eleonora Corno, Eleonora Menaldo, Ottavio Davini, Giovanni Gandini, Peter Herrmann, Luciana Mascia, Michel Quintel, Arthur S. Slutsky, Luciano Gattinoni, and V. Marco Ranieri

- n = 30, T_V 6 mL/kg pred. BW
- CT scan →
- <u>in 10 patients:</u>
  - inspiratory hyperinflation
  - plateau pressure 28 – 30 cm H_2O
  - time on ventilation ↑
  - cytokines in BAL ↑
- <u>conclusion:</u>
  - 6 mL/kg pred. BW may be too much in severe ARDS:
  - tidal volumes should be adjusted individually to aerated lung volumes



AJRCCM 2007;175:160-66

Mortality and Plateau Pressure



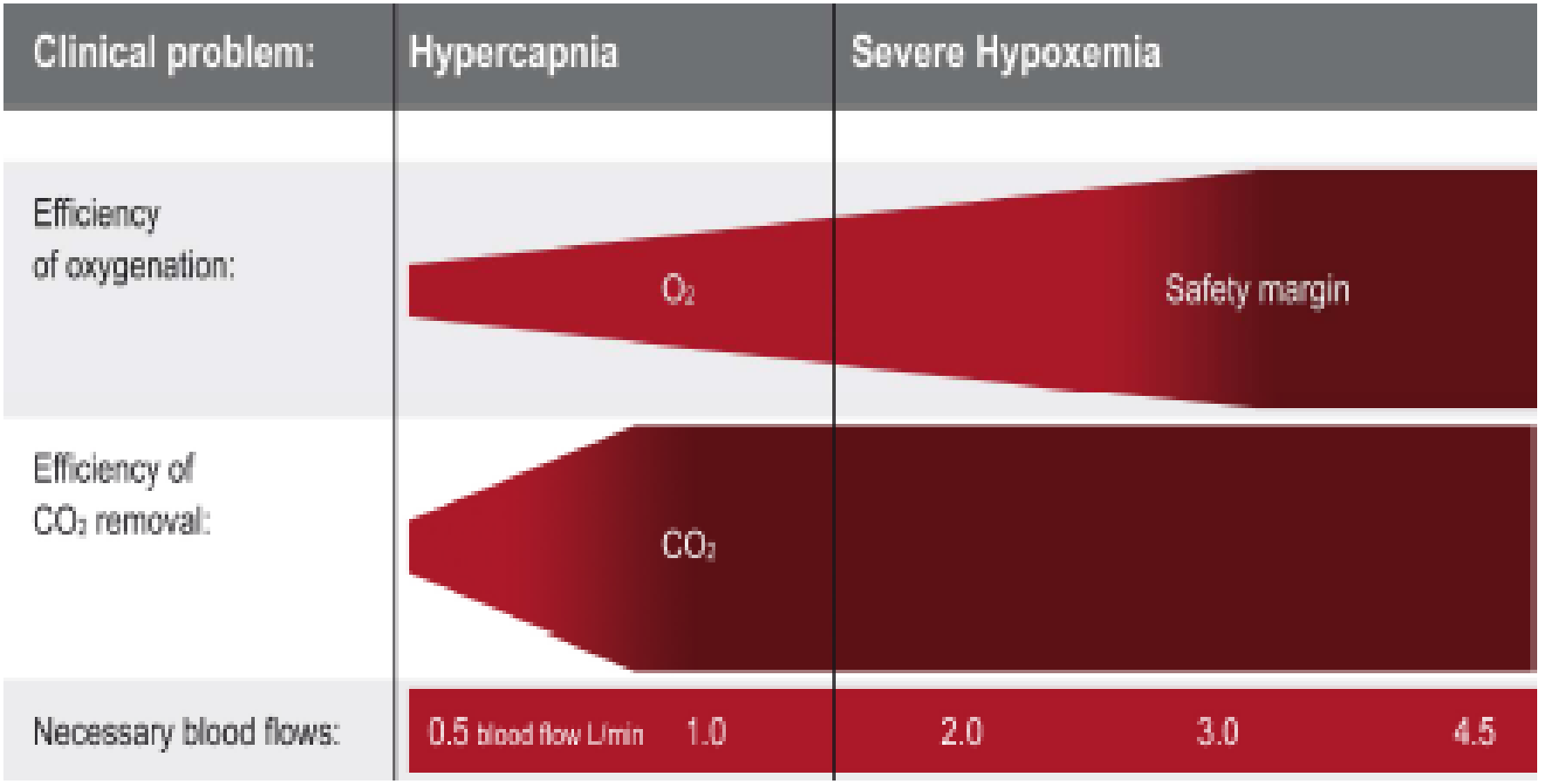
Brower et al Amer J Resp Crit Care Med 2002

Overall concept

- Artificial ventilation
- Less invasive than full ECMO
- Lower flows = lower gas exchange rates
- Partial-to-total lung support
- Envisioned as adjunct to mechanical ventilation
- Allow reduction in mechanical ventilation settings (...beyond ARDSNet recommendations)

	pumpless A-V ECMO (Novalung)	V-V ECMO	V-A ECMO
Indication	Hypercapnic respiratory failure	Hypoxic respiratory failure	Cardiac failure Respiratory failure with unstable vital sign
Blood pumping	Optional	Required	Required
Hemodynamic change	Negligible	Negligible	Major (preload↓, afterload↑, pulmonary a. pr ↓)
Oxygenation	moderate	80-95%	100%
Vascular access	Artery & Vein	Vein & Vein	Vein & Artery
Surgical complexity **Complexity of equipment**	Simple	Complex	Advanced
Requirement for heparin	Small	Moderate	Large

Blood flow & breathing gases

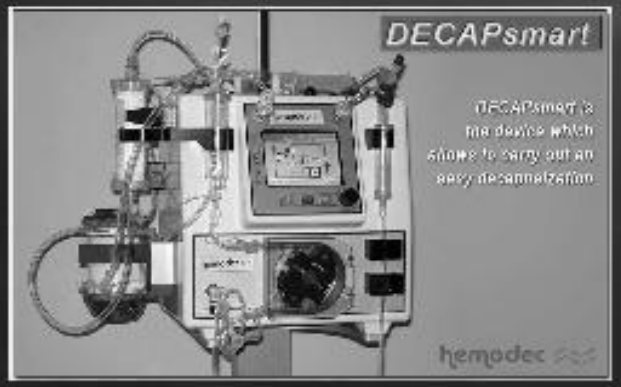


Basic rule for venovenous therapy: oxygen:blood flow ratio = 2.5 : 1 to maximize gas exchange performance and while using the lowest possible blood flow.

Novel devices available today

novalung®

ALUNG.

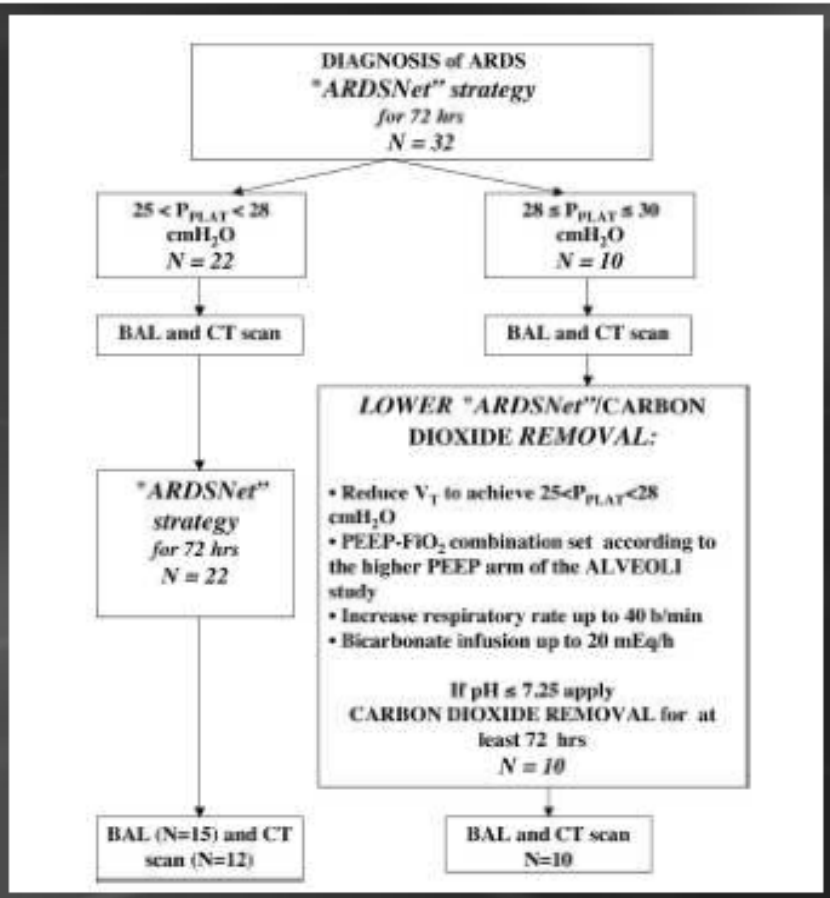


Anesthesiology 2009; 111:826–35

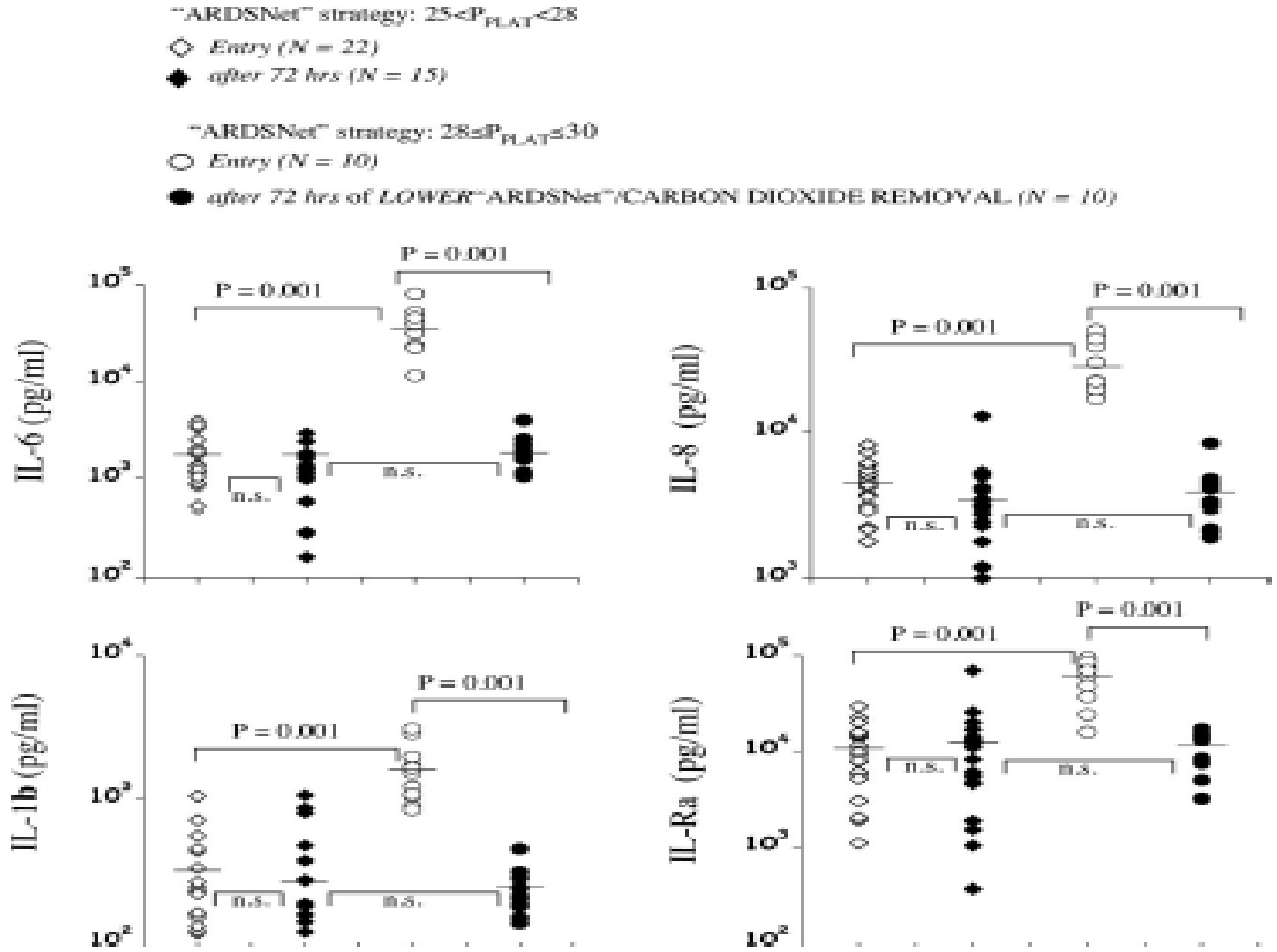
Tidal Volume Lower than 6 ml/kg Enhances Lung Prolection

Role of Extracorporeal Carbon Dioxide Removal

Pier Paolo Terragni, M.D., Lorenzo Del Sorbo, M.D.,* Luciana Mascia, M.D., Ph.D.,* Rosario Urbino, M.D.,* Erica L. Martin, Ph.D.,* Alberto Birocco, M.D.,† Chiara Faggiano, M.D.,† Michael Quintel, M.D.,‡ Luciano Gattinoni, M.D.,§ V. Marco Ranieri, M.D.‖*



Terragni et al. Anesthesiology, 2009


"ARDSNet" strategy: 25<P$_{PLAT}$<28
Entry (N = 22)
after 72 hrs (N = 15)
"ARDSNet" strategy: 28≤P$_{PLAT}$≤30
Entry (N = 10)
after 72 hrs of LOWER "ARDSNet"/CARBON DIOXIDE REMOVAL (N = 10)
IL-6 (pg/ml)
IL-8 (pg/ml)
IL-1b (pg/ml)
IL-Ra (pg/ml)
P = 0.001
n.s.

Intensive Care Med
DOI 10.1007/s00134-012-2787-6

ORIGINAL

Thomas Bein
Steffen Weber-Carstens
Anton Goldmann
Thomas Müller
Thomas Staudinger
Jörg Brederlau
Ralf Muellenbach
Rolf Dembinski
Bernhard M. Graf
Marlene Wewalka
Alois Philipp
Klaus-Dieter Wernecke
Matthias Lubnow
Arthur S. Slutsky

Lower tidal volume strategy ($\approx$3 ml/kg) combined with extracorporeal CO_2 removal versus 'conventional' protective ventilation (6 ml/kg) in severe ARDS

The prospective randomized Xtravent-study

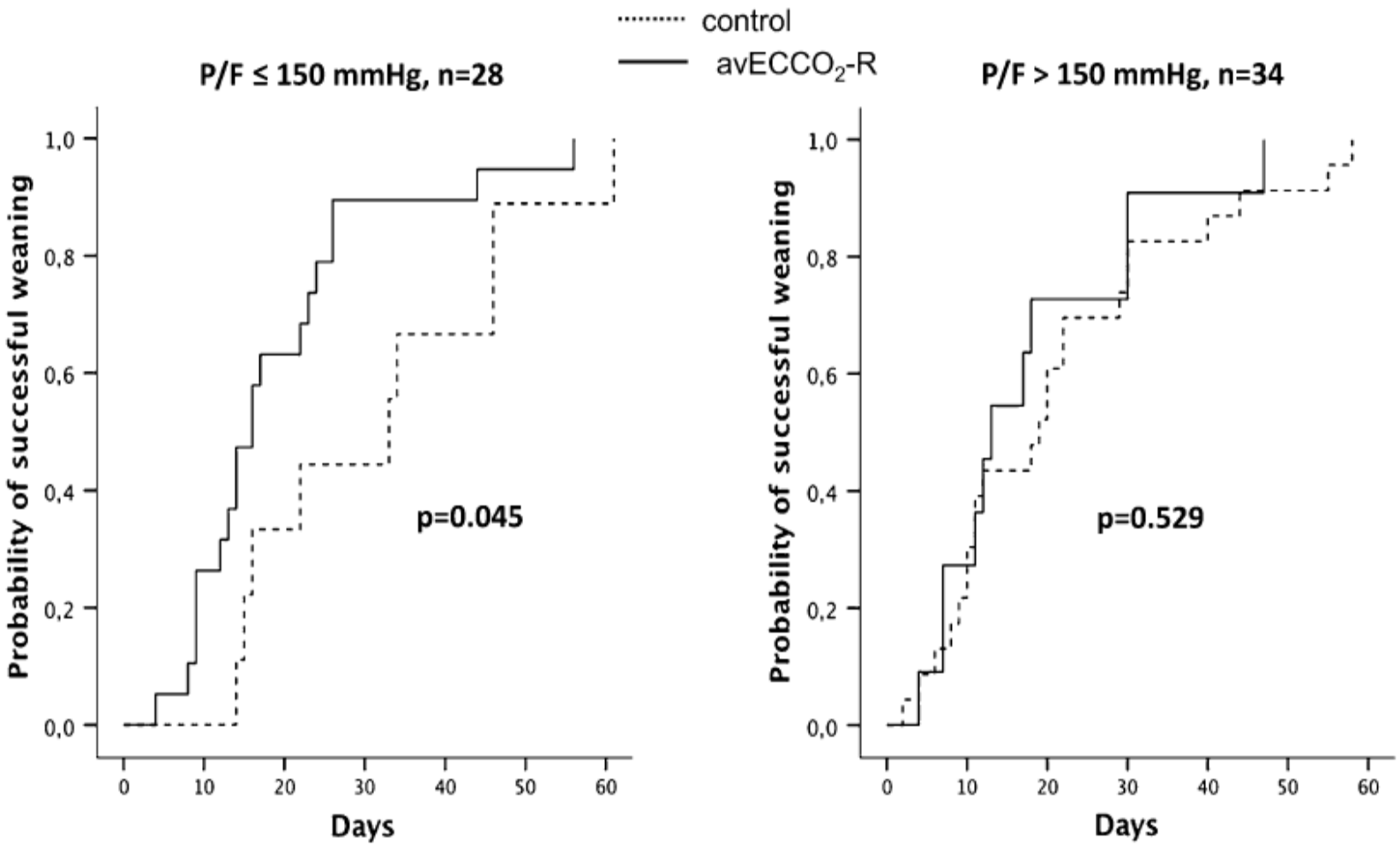


Fig. 2 Post-hoc analysis: probability of successful weaning in patients presenting with PaO_2/FIO_2 ≤150 versus >150 (only surviving patients)

Physiologic Effect and Safety of the Pumpless Extracorporeal Interventional Lung Assist System in Patients With Acute Respiratory Failure—A Pilot Study

*Woo Hyun Cho, †Kwangha Lee, ‡Jin Won Huh, ‡Chae-Man Lim, ‡Younsuck Koh, and ‡Sang-Bum Hong

*Department of Internal Medicine, *Pusan National University Yangsan Hospital and †Pusan National University Hospital, Pusan National University School of Medicine, Busan; and ‡Department of Internal Medicine, Division of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea*

Artif Organs, Vol. 36, No. 4, 2012

CESAR study in 2009

Conventional ventilatory support	ECMO

Severe Adult Respiratory Failure

Significantly greater survival at 6-month without disability in ECMO group (47% vs 63%)

In severe refractory hypoxemia from ARDS,
Transfer patients to a center providing ECMO
: Potentially life-saving

ANZ ECMO study in 2009

- ECMO for severe influenza-associated ARDS
- 61 patients during H1N1 pandemic
- Survival rate 79%

Complicated interpretation due to confounding factors (age, severity, pre-existing co-morbidities) in patients selection and outcome

ARDSnet H1N1 registry

The NEW ENGLAND JOURNAL of MEDICINE

Critical Care Services and 2009 H1N1 Influenza in Australia and New Zealand

The ANZIC Influenza Investigators*

682 patients in 12 mths		748
ECMO	4%	11%
HFOV	8%	6%
28 day mortality	21.8%	N/A
Hospital mortality	24%	16.2% (2.3% unknown)
Death due to ARF	43%	N/A

ARDSnet (Rice T). ATS 2011

ANZIC Influenza Investigators. NEJM 2009

The aim of study

Non-ECMO-referred Pts **(85 hospitals)**

VS

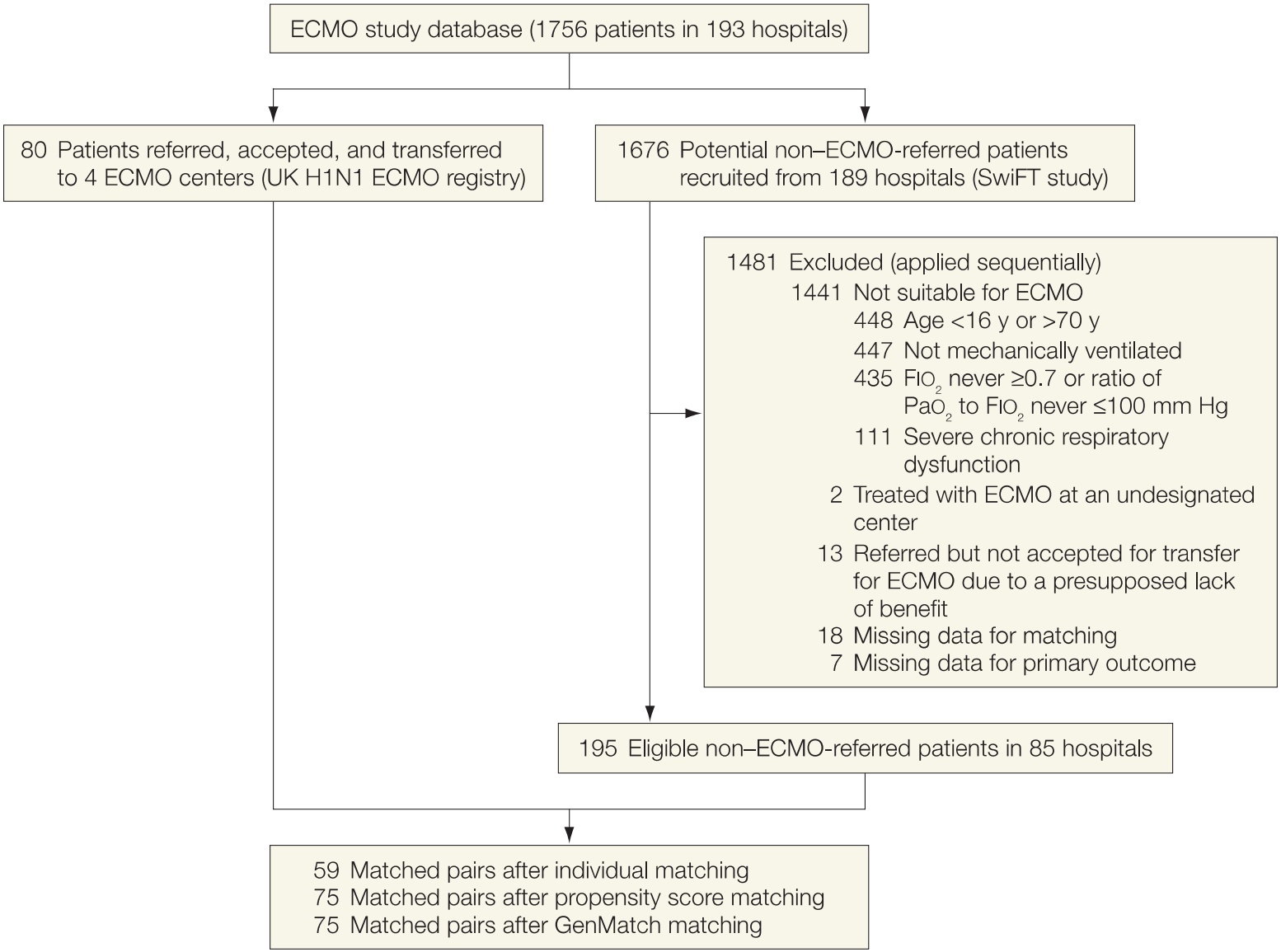
ECMO-referred Pts **(UK ECMO centers)**

H1N1-related ARDS

by matching patients

- Noah et. JAMA 2011 36(15):1659-1668

Figure 1. Enrollment and Matching of Patients



Outcome

- 22 pts (27.5%) died in 80 pts transferred

Table 2. Deaths Analyzed by Matching Methods

	No. of Deaths/ Total No. of Patients (%)			
	ECMO-Referred	Non–ECMO-Referred	RR (95% CI)	*P* Value
Matching method				
Propensity score	18/75 (24.0)	35/75 (46.7)	0.51 (0.31-0.84)	.008
GenMatch	18/75 (24.0)	38/75 (50.7)	0.47 (0.31-0.72)	.001
Individual	14/59 (23.7)	31/59 (52.5)	0.45 (0.26-0.79)	.006

Abbreviations: ECMO, extracorporeal membrane oxygenation; RR, relative risk.

Extracorporeal Membrane Oxygenation for Pandemic Influenza A(H1N1)–induced Acute Respiratory Distress Syndrome

A Cohort Study and Propensity-matched Analysis

Tài Pham[1,2], Alain Combes[3,4], Hadrien Rozé[5], Sylvie Chevret[2,6], Alain Mercat[7,8], Antoine Roch[9,10], Bruno Mourvillier[11,12], Claire Ara-Somohano[13,14], Olivier Bastien[15,16], Elie Zogheib[17], Marc Clavel[18,19], Adrien Constan[1], Jean-Christophe Marie Richard[20,21,22], Christian Brun-Buisson[1,23,24], and Laurent Brochard[20,21,24]; for the REVA Research Network*

Am J Respir Crit Care Med Vol 187, Iss. 3, pp 276–285, Feb 1, 2013

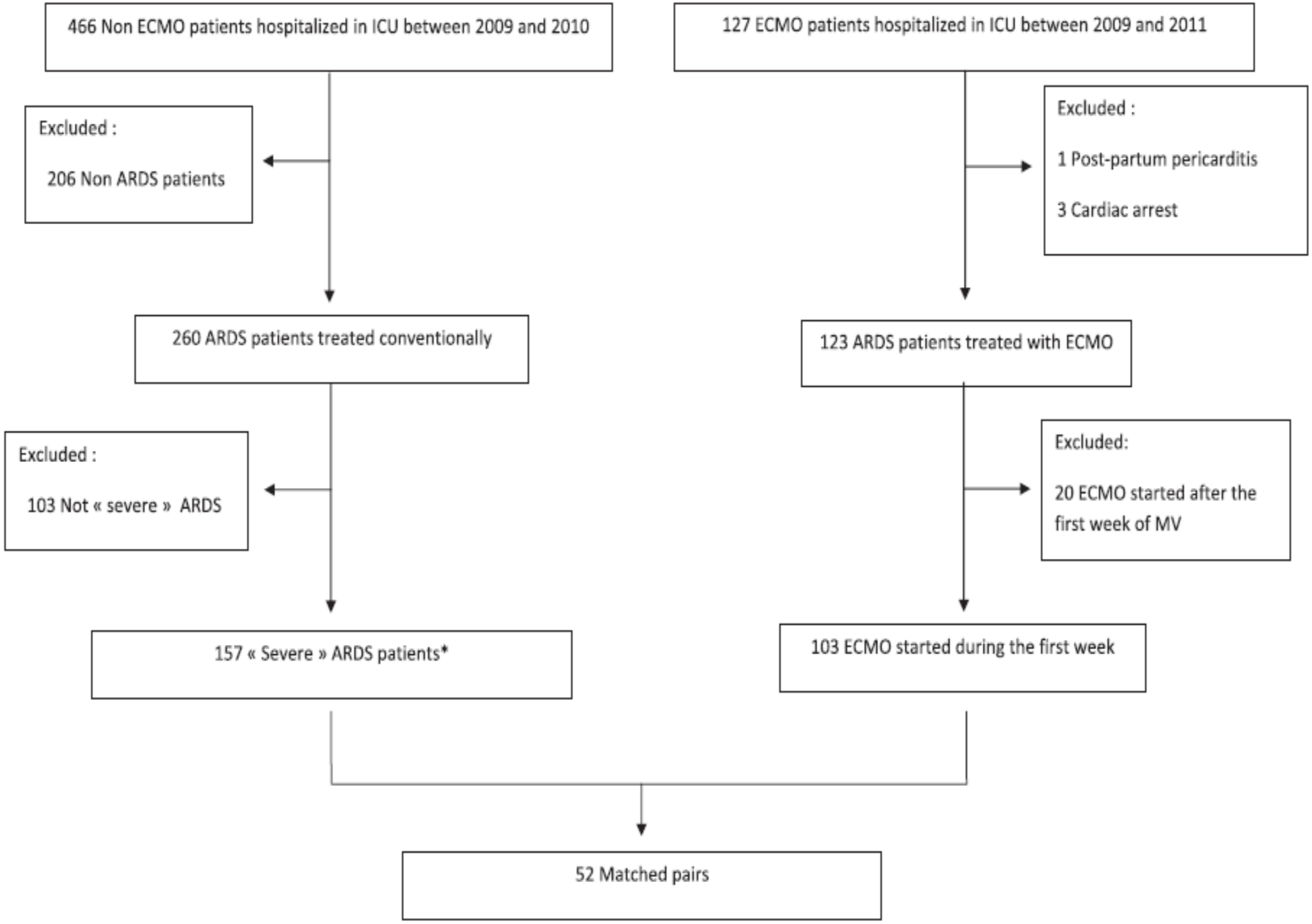

466 Non ECMO patients hospitalized in ICU between 2009 and 2010
127 ECMO patients hospitalized in ICU between 2009 and 2011
Excluded :
206 Non ARDS patients
Excluded :
1 Post-partum pericarditis
3 Cardiac arrest
260 ARDS patients treated conventionally
123 ARDS patients treated with ECMO
Excluded :
103 Not « severe » ARDS
Excluded:
20 ECMO started after the first week of MV
157 « Severe » ARDS patients*
103 ECMO started during the first week
52 Matched pairs

TABLE 1. BASELINE CHARACTERISTICS, MANAGEMENT, AND OUTCOME OF 123 PATIENTS TREATED WITH ECMO FOR INFLUENZA A/H1N1PDM–RELATED ACUTE RESPIRATORY DISTRESS SYNDROME

	Mean (SD), Median (IQR), or N (%)
Baseline characteristics	
Age, yr	42 (13)
Male sex	61 (50%)
MacCabe 1*	108 (88%)
Risk factor for influenza complication	93 (76%)
Pregnancy or postpartum	18 (15%)
BMI, kg/m^2	30.5 (8.5)
On admission	
SAPS3	58 (14)
SOFA	9.5 (4)
Bacterial coinfection	28 (23%)
Before ECMO	
Shock	60 (49%)
Corticosteroid therapy	42 (34%)
Rescue therapy	91 (74%)
Inhaled nitric oxide	83 (72%)
Prone positioning	51 (45%)
Almitrine	7 (7%)
HFOV	3 (2%)
Time from MV to ECMO, d	2 (1–5)
V-V ECMO	107 (87%)

	Pre-ECMO	First Day on ECMO
Tidal volume, ml/kg PBW	6.7 (1.6)	3.9 (1.4)
Respiratory rate, min^{-1}	27 (6)	19 (8)
PEEP, cm H_2O	13 (4)	13 (4)
Plateau pressure, cm H_2O	32 (5)	26 (4)
Pa_{O_2}/FI_{O_2} ratio, mm Hg	63 (21)	109 (74)
Sa_{O_2}, %	84 (11)	95 (5)
Arterial pH	7.26 (0.12)	7.39 (0.12)
Pa_{CO_2}, mm Hg	57 (18)	38 (9)
Arterial lactate, mM	2.9 (3)	4.2 (5.6)
Driving pressure, cm $H_2O^{\dagger}$	19 (6)	14 (5)
LIS	3.4 (0.6)	Not collected
Complications and outcome		
Nosocomial pneumonia		68 (62%)
Length of ECMO, d		11 (8–22)
Length of MV, d		28 (15–44)
Length of ICU stay, d		33 (17–59)
Mortality		44 (36%)

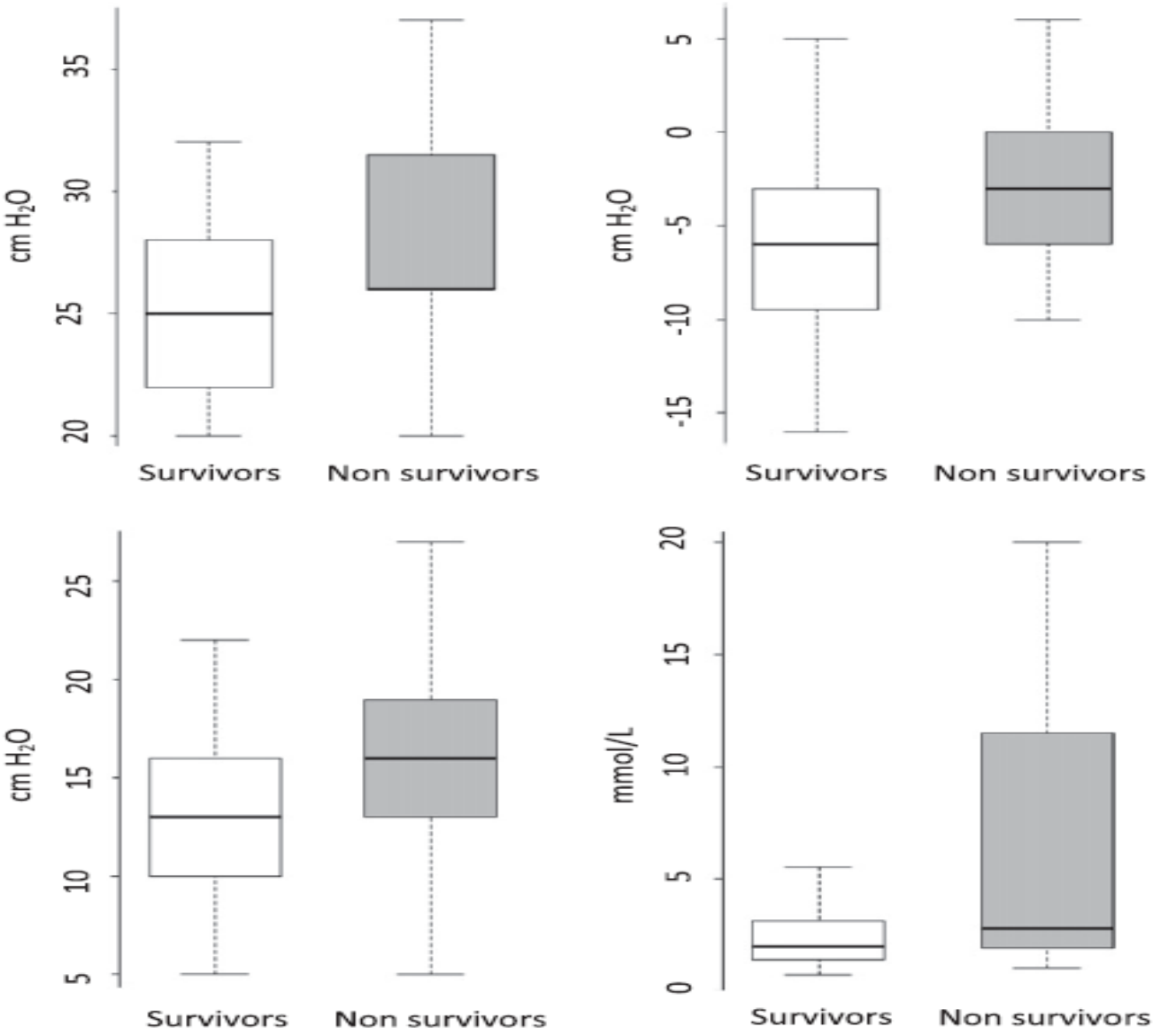


Figure 2. Boxplots of arterial lactate and respiratory parameters according to intensive care unit outcome for the 123 patients who received extracorporeal membrane oxygenation (ECMO) support. *Top left*: Plateau pressure (Pplat) on the first day under ECMO. *Top right*: Pplat under ECMO − Pplat before ECMO. *Bottom left*: Driving pressure on the first day under ECMO. *Bottom right*: Arterial lactate on the first day under ECMO.

TABLE 4. BASELINE CHARACTERISTICS, ICU MANAGEMENT, AND OUTCOME OF ECMO PATIENTS SELECTED AND EXCLUDED FROM THE MATCHED ANALYSES

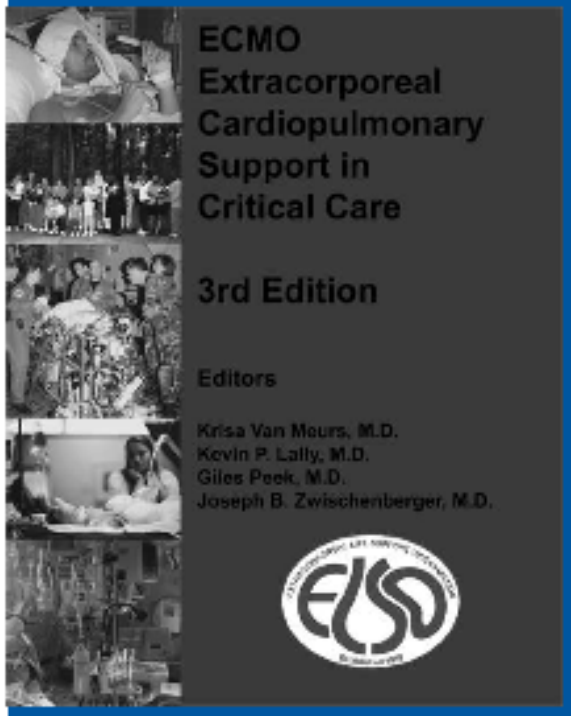
	Selected for Matching (*52*)	Not Selected for Matching (*51*)	*P* Value
Baseline characteristics			
Age, yr	45 (13)	38 (13)	<0.01
Male sex	30 (58%)	19 (37%)	0.06
MacCabe 1*	45 (87%)	47 (92%)	0.55
Risk factor for flu complication	37 (71%)	44 (86%)	0.10
Pregnancy or postpartum	3 (6%)	13 (25%)	0.01
BMI, kg/m^2	30 (8)	33 (10)	0.03
Obesity	17 (33%)	29 (57%)	0.04
Immunosuppression	12 (23%)	6 (12%)	0.21
On admission			
SAPS3 score	61 (14)	58 (14)	0.28
SOFA score	9.6 (4.8)	10 (3.7)	0.70
Bacterial coinfection	13 (25%)	9 (18%)	0.50
Shock	40 (77%)	37 (73%)	0.78
Before ECMO			
Steroids	24 (46%)	8 (16%)	<0.01
Rescue therapy	40 (77%)	44 (86%)	0.33
Time from MV to ECMO	2 (1–4)	1 (0–3.5)	0.47
V-V ECMO	44 (85%)	44 (86%)	0.97

Complications and outcome			
Nosocomial pneumonia, n	32 (61%)	22 (43%)	0.09
Length of ECMO, d	9 (7–18)	13 (9–23)	0.31
Length of MV, d	22 (12–35)	30 (15–42)	0.11
Length of ICU stay, d	27 (11–52)	34.5 (21–58)	0.72
In-ICU mortality, n	26 (50%)	11 (22%)	<0.01

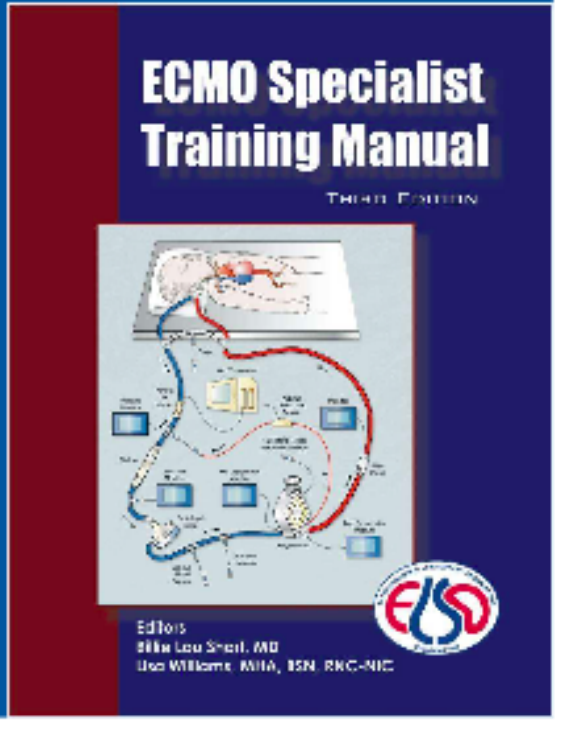
summary

- Pplat to around 25 cmH2O
- No benefit of ECMO on ICU survival in matched patients (50%)
- Young patients with severe respiratory failure receiving ECMO remained unmatched and had a more favorable outcome.

Extracorporeal Life Support Organization (ELSO)



- Now 22 years old
- Over 45,000 patients in database
- Meetings (2-4 major/yr)
- Quarterly reports
- Increased Asian/European involvement
  - ?joint meeting
- Small grants given for research
- <$1000/yr



Evaluation until the 120th hours of advanced treatment for ECMO entry criteria

Slow entry criteria :

- when despite maximum therapy of more than 120 hrs no improvement occurs and
- PaO_2 < 100 - 150 mmHg at FIo_2 1.0
- PEEP ≥10 cmH_2O

Fast entry criteria :

when despite maximum therapy > 2h :

PaO_2 < 50 mmHg resp. SaO_2 < 85 - 90 % at FIO_2 1.0

PEEP ≥ 10 cmH_2O

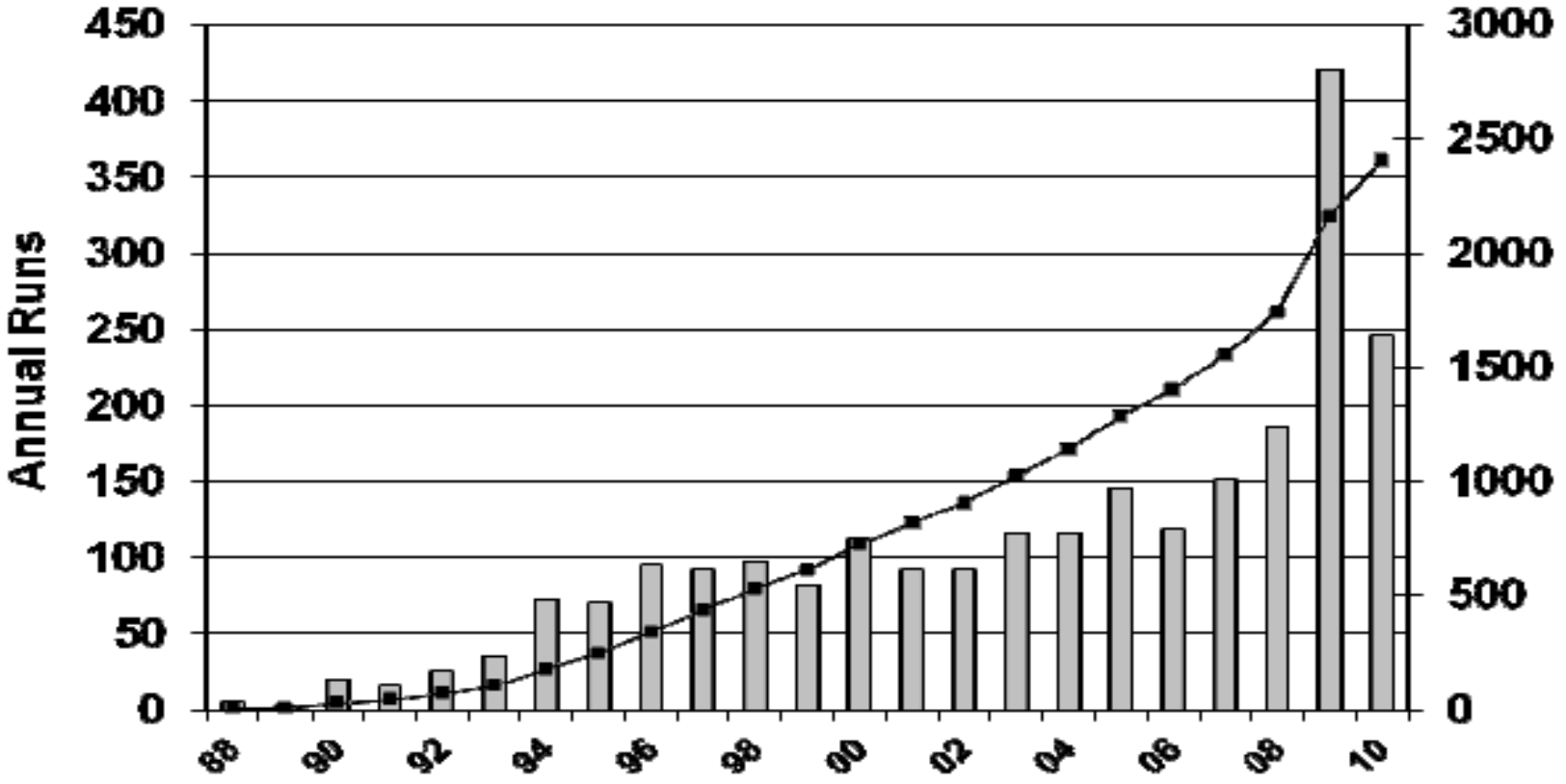
Lewandowski et al.:Intensive Care Med (1997) 23:819-835

II. Contraindication

1) High pressure (peak inspiratory pressure >30 cm H2O) or high FiO2(>0.8) ventilation for more than 168 h (7 days)
2) Signs of intracranial bleeding; any other contraindication to limited heparinisation
3) Any contraindication to continuation of active treatment
4) Major pharmacologic **immunosuppression** (ANC < 400)

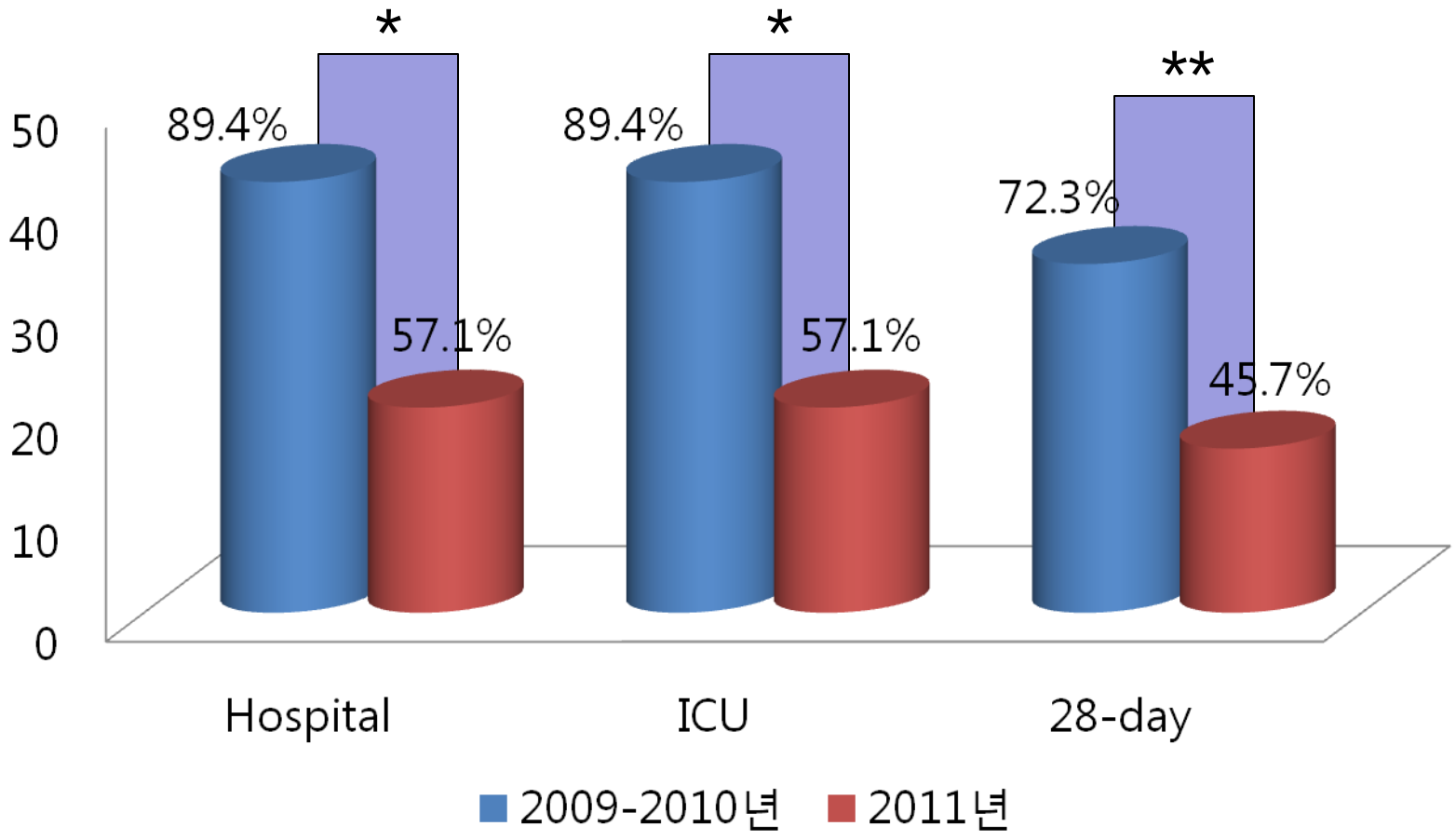
Ventilation	ECMO
• Baro-, Volu-, Atelektrauma ↑ • “stress and strain” ↑ ⇒ VILI ↑	• Blood flow ↑, larger cannulas, out-flow- and back-flow pressure ↑ • “blood trauma” and activation of coagulation ↑ • Platelet destruction, bleeding, thrombosis ↑ ⇒ ECMO-induced lung injury (EILI) ↑ (?)

Adult Respiratory Cases



ELSO Registry January 2011

ECMO Mortality in AMC



* : p<0.001, **: p<0.05

Initiation – keep bedside & V/S

MV	ECMO
•Airway •Intubation •ETT •tidal volume •often deep sedation	•Catheter •Insertion •Circuit •flow •often light sedation

Initial VV ECMO Management

- Vent to "lung rest" : PIP 22-26, PEEP10-14, fio2 40%
- Volume resuscitation and pressor wean
- Wean pressors to off
- D/C paralytics, hold sedation for N/E
- Tx of primary ds – AB, Antiviral, steroid
- no prophylactic AB

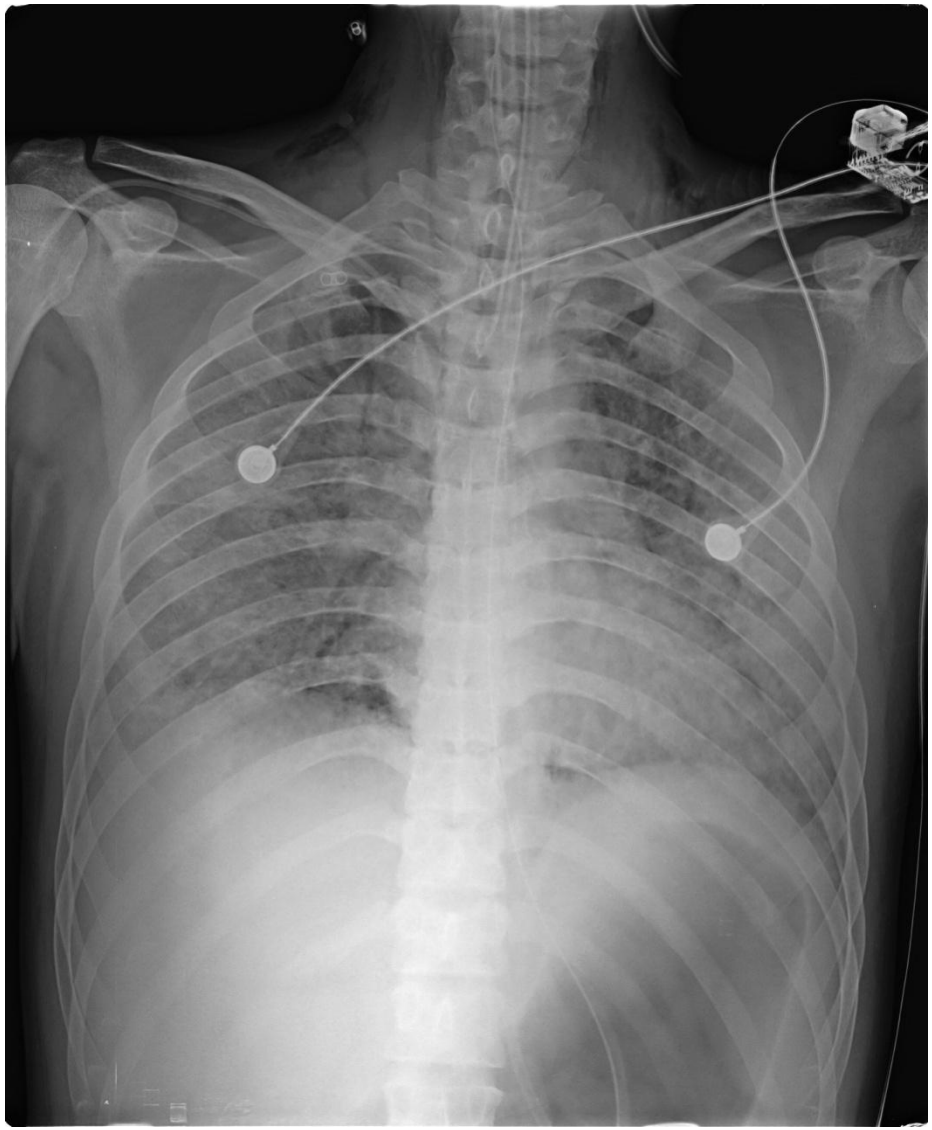
complications of ECMO

- Hemorrage
- CNS injury
- infection

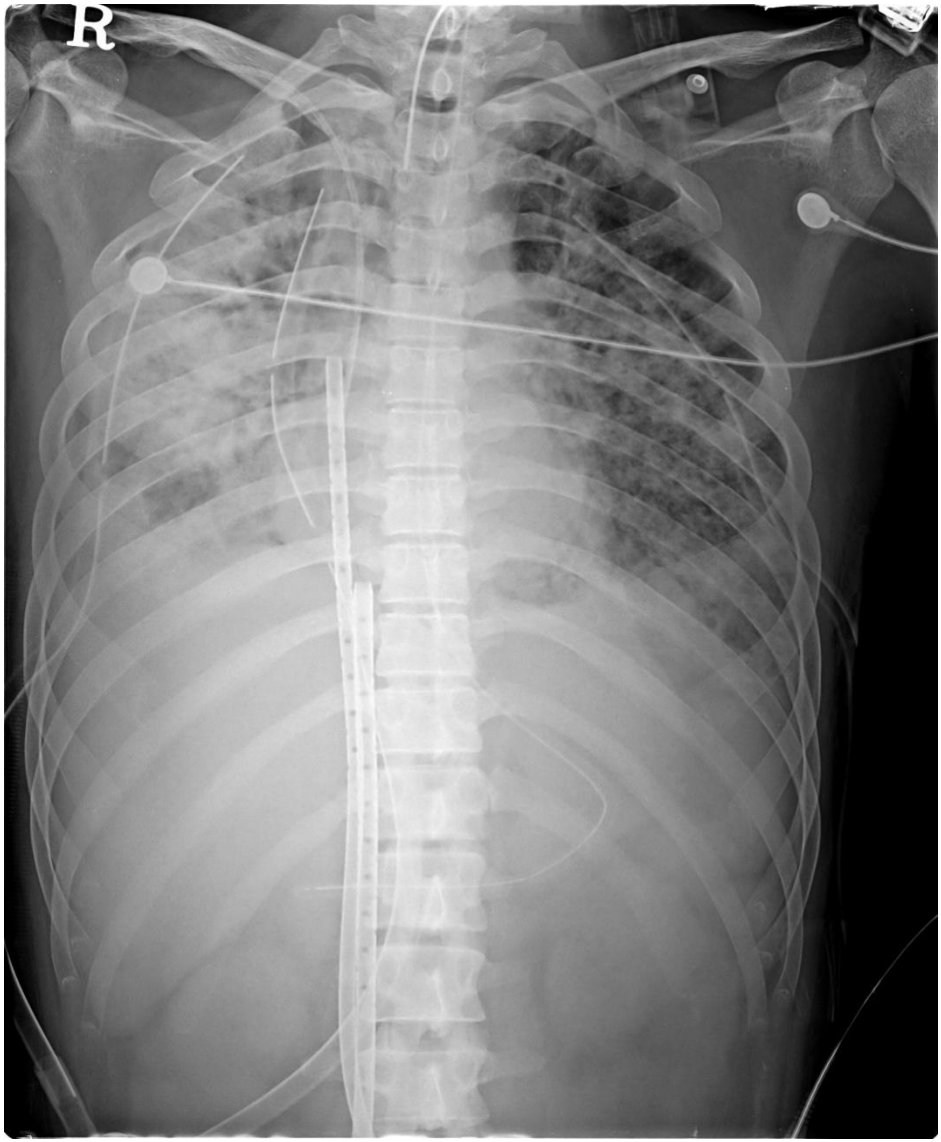
M/27

- Hospital course
  - old pul. Tbc. 외 특이병력 없던 자로 diarrhea를 주 증상으로 크론병 의심하에 타원 입원 치료 중 HAP 발생하였고, 이후 ARDS develop 되어 입원 10일째 기계환기 시작
  - 입원 28일째 Rt. spontaneous pneumothorax develop 되었고, hypercapnia 로 iLA insertion
  - 입원 42일째 hypoxia 진행되어 VV ECMO 시행

Ventilator strat day

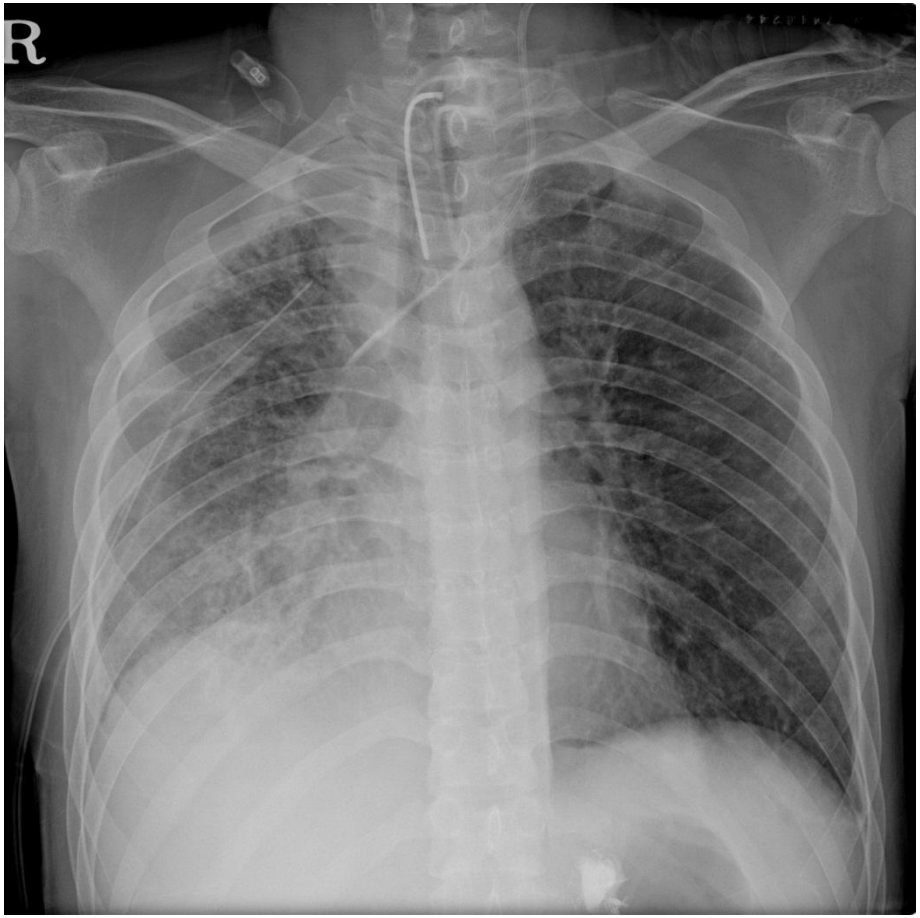


ECMO start day

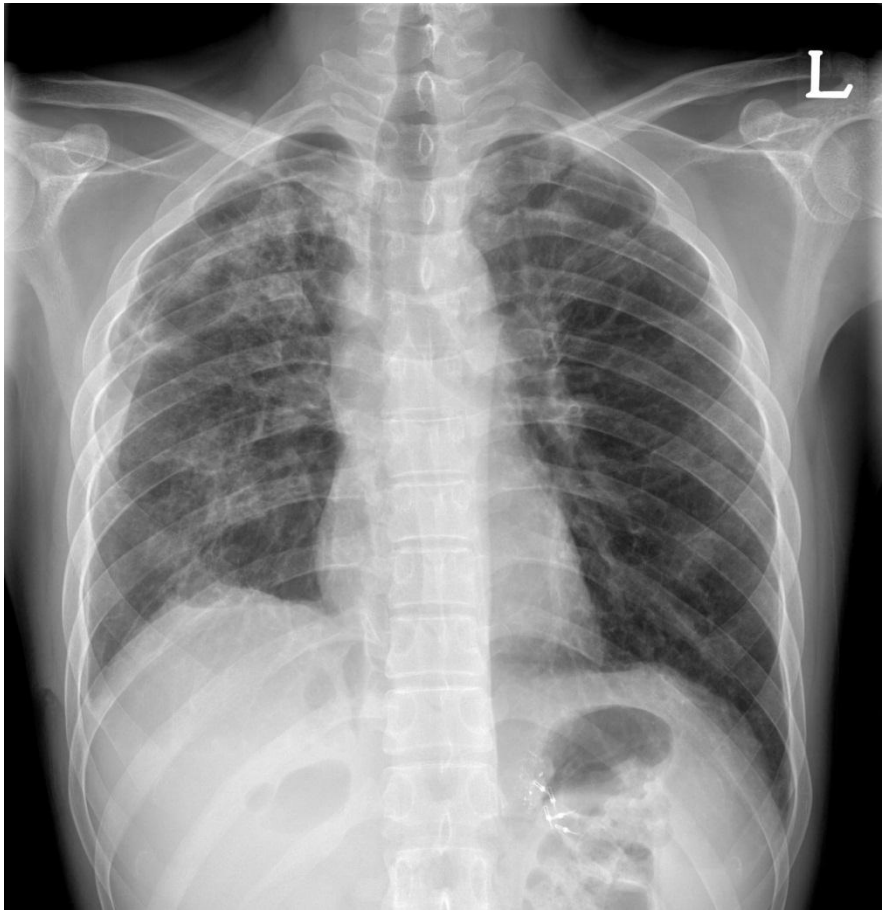


- 입원 77일째 폐이식을 고려하여 본원 의료진들이 방문하여 VV ECMO 유지한 채 본원 전원
- CRPA bacteremia, CRAB pneumoina, septic shock, DIC 진단하에 manage 하였고, recurrent hemorrhagic complication으로 본원 전원 후 anticoagulation free ECMO 시행
- 입원 108일째 CXR상 호전 시작 및 TV 점차 증가
- 입원 126일(ECMO 85일)째 ECMO weaning
- 입원 139일(ventilator day 129일) ventilator weaning, 이후 GW 전동
- 입원 172일째 discharge

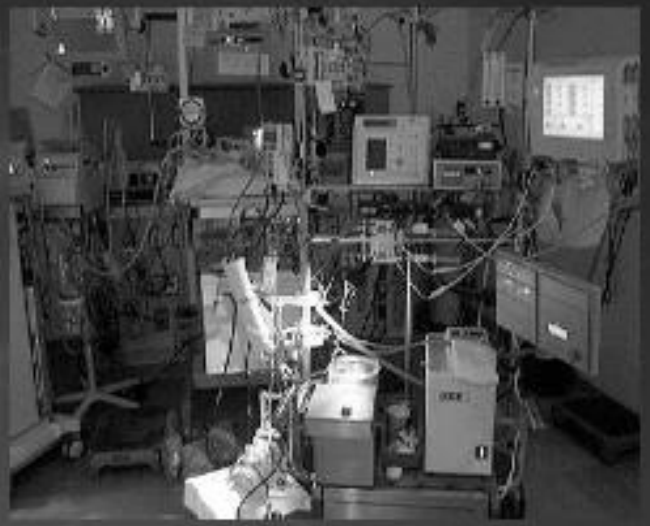
ECMO weaning day



Discharge day



Fact: ECMO became less complicated



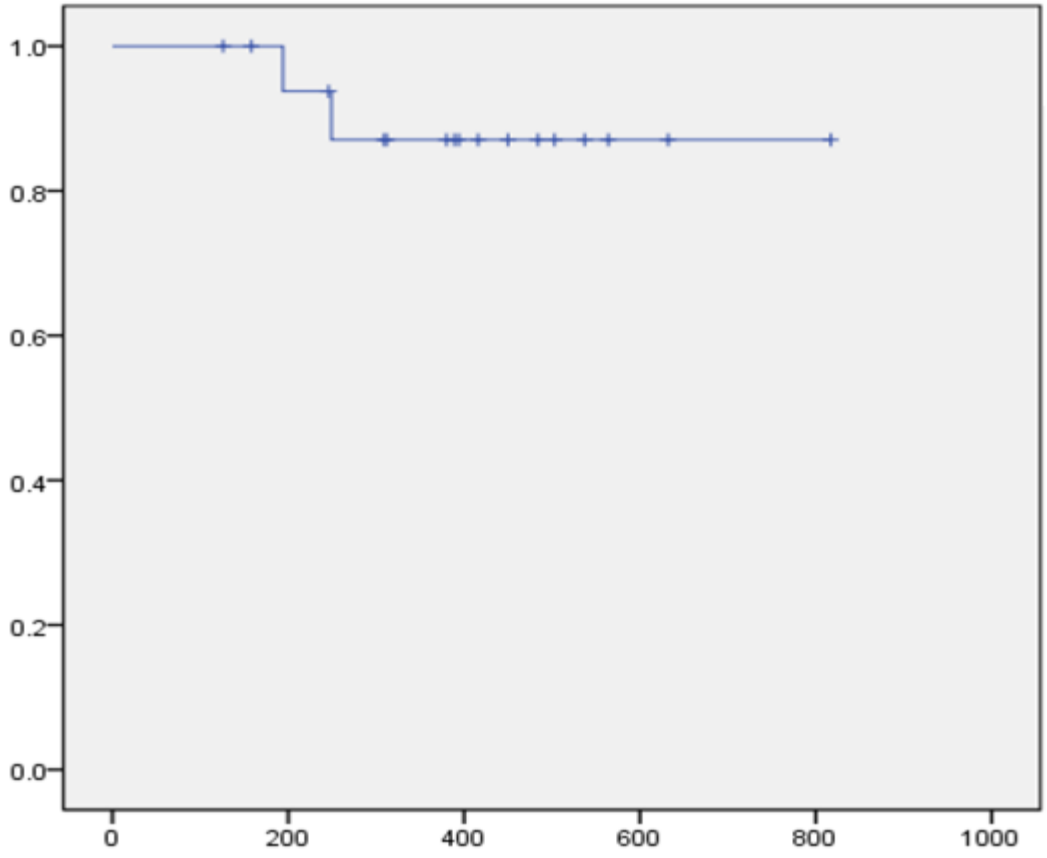
Solutions for respiratory failure

Up to 2008
Patient sedated

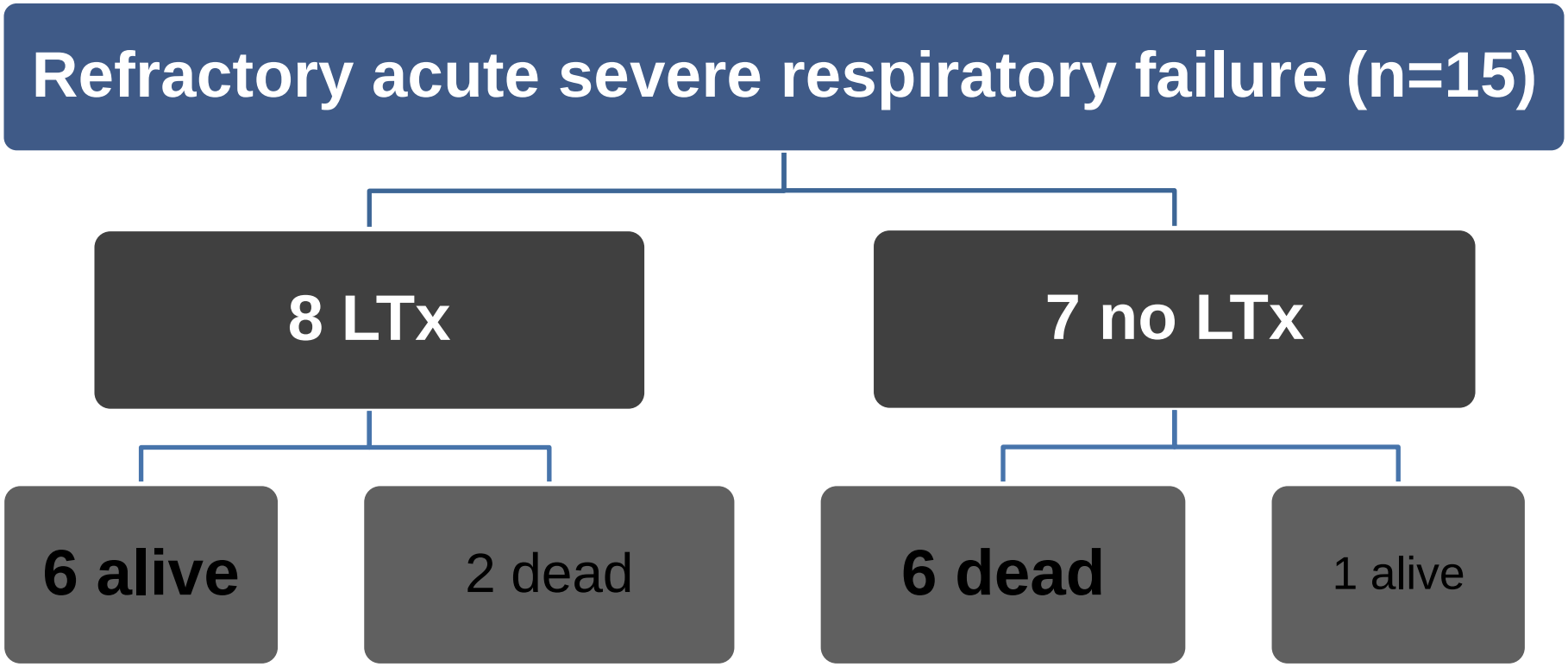
2009
Patient awake

2011
Patient mobile

Kaplan-Meier survival estimates (n=18)



LTx recipients in AMC



*MV=mechanical ventilation, LTx=lung transplantation, HLTx=heart-lung transplantation

Early ECMO has better aspects

- Apply ECMO < 7d (before fibrosis)
- Lower plateau pressure : VILI
- Before high lactate concentration
- Awake and communication
- No NMB
- Apply long days (healing time)
- Getting smarter and smarter ECMO
- Combined tx : novalung + CRRT