Extracorporeal membrane oxygenation:
the current role in acute respiratory distress syndrome

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전경만

Acute Respiratory Distress Syndrome (ARDS)

- Clinical syndrome of severe dyspnea of rapid onset, hypoxemia, and diffuse pulmonary infiltrates leading to respiratory failure
  - Syndrome of acute and persistent lung inflammation with increased vascular permeability
  - Caused by diffuse lung injury from many underlying medical and surgical disorders.

Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	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 assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation[b]	
Mild	200 mm Hg $<$ PaO_2/FIO_2 $\leq$ 300 mm Hg with PEEP or CPAP $\geq$5 cm H_2O[c]
Moderate	100 mm Hg $<$ PaO_2/FIO_2 $\leq$ 200 mm Hg with PEEP $\geq$5 cm H_2O
Severe	PaO_2/FIO_2 $\leq$ 100 mm Hg with PEEP $\geq$5 cm H_2O

Lancet 1967; 2: 319
N Engl J Med 2000;342:1334
JAMA 2012;307:2526

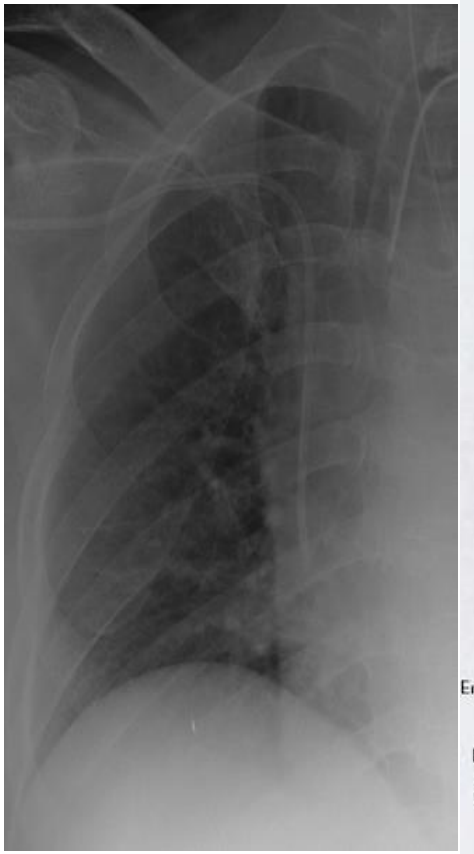
Risk Factors for ARDS

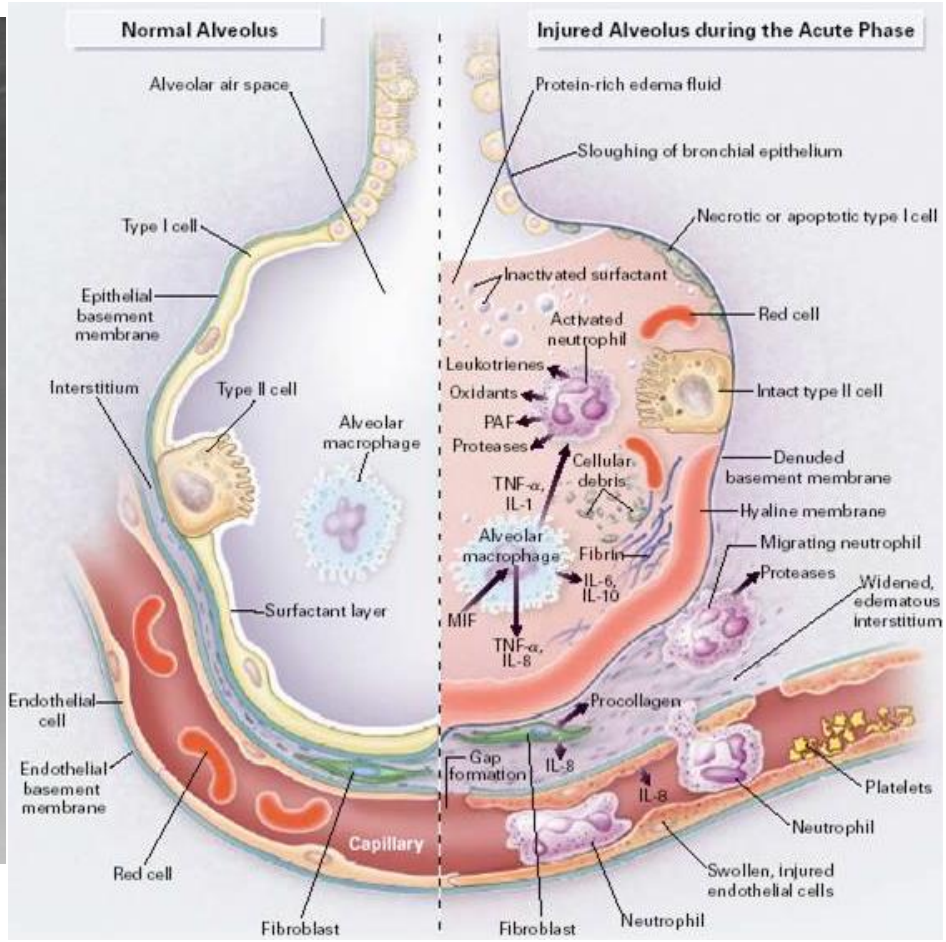
Direct lung injury	Indirect lung injury
Pneumonia	Sepsis
Aspiration of gastric contents	Nonthoracic trauma or hemorrhagic shock
Pulmonary contusion	Pancreatitis
Inhalation injury	Major burn injury
Near-drowning	Drug overdose
	Transfusion of blood products
	Cardiopulmonary bypass
	Reperfusion edema after lung transplantation or embolectomy

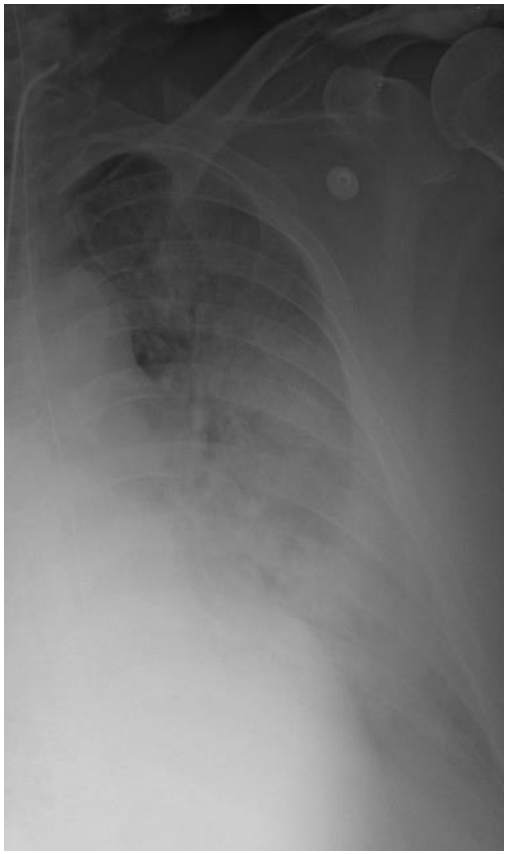
▶ Pneumonia, aspiration of gastric contents, and sepsis together account for more than 85% of cases of ARDS in recent clinical trials.

N Engl J Med 2017;377:562

Clinical Consequence of ARDS







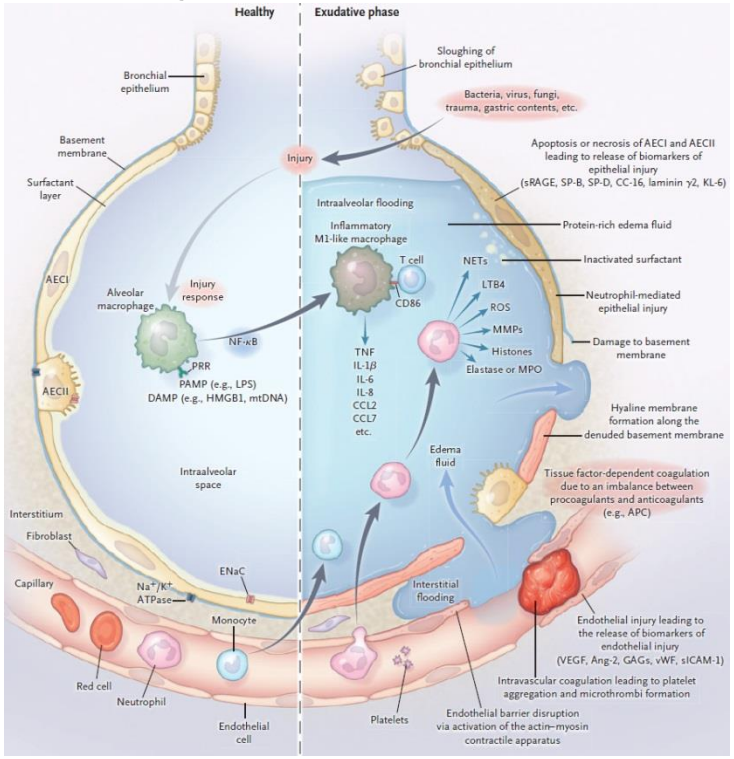
Permeability edema ▶Refractory hypoxemia

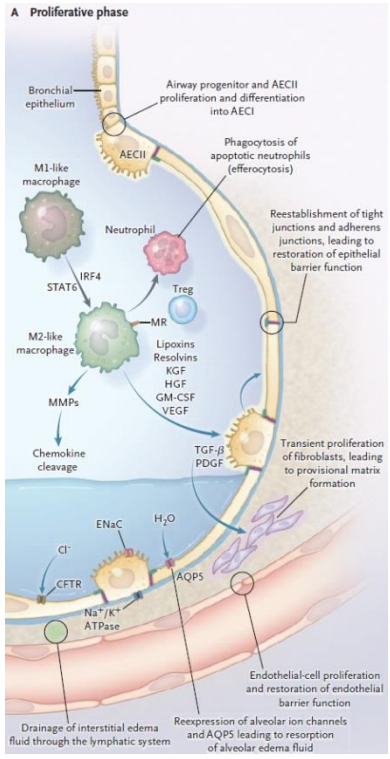
Clinical Course of ARDS

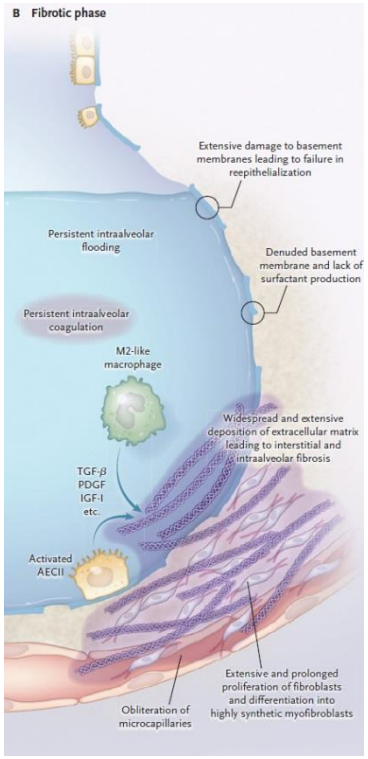
Exudative phase **Proliferative phase** **Fibrotic phase**

Edema Hyaline Membranes Interstitial Inflammation Fibrosis

Day: 0 2 7 14 21 . .







N Engl J Med 2017;377:562

Treatment of ARDS

No Specific Treatment

- General supportive care: mainstay of treatment
  - (1) recognition and treatment of the underlying medical and surgical disorders (e.g., sepsis, aspiration, trauma)
  - (2) minimizing procedures and their complications
  - (3) prophylaxis against venous thromboembolism, gastrointestinal bleeding, aspiration, excessive sedation, and central venous catheter infections
  - (4) prompt recognition of nosocomial infections
  - (5) provision of adequate nutrition
- Fluid management: restrictive fluid balance
  - Increased ventilator free days, ICU free days

N Engl J Med 2006;354:2564-75

- Corticosteroid ?
  - Improved mortality and morbidity outcomes

Crit Care Med 2009;37:1594-603

Evidence-Based Recommendations for ARDS

Harrison's Principles of Internal Medicine, 19th ed.

Treatment	Recommendation[a]
Mechanical ventilation	
Low tidal volume	A
Minimized left atrial filling pressures	B
High-PEEP or "open lung"	C
Prone position	C
Recruitment maneuvers	C
High-frequency ventilation	D
ECMO	C
Early neuromuscular blockade	A
Glucocorticoid treatment	D
Surfactant replacement, inhaled NO, inhaled epoprostenol, and other anti-inflam matory therapy (e.g., ketoconazole, PGE1, NSAIDs)	D

[a]Key: A, recommended therapy based on strong clinical evidence from randomized clinical trials; B, recommended therapy based on supportive but limited clinical data; C, recommended only as alternative therapy on the basis of indeterminate evidence; D, not recommended on the basis of clinical evidence against efficacy of therapy

Harrison's Principles of Internal Medicine, 19ed.

36 YO Male with Severe ARDS

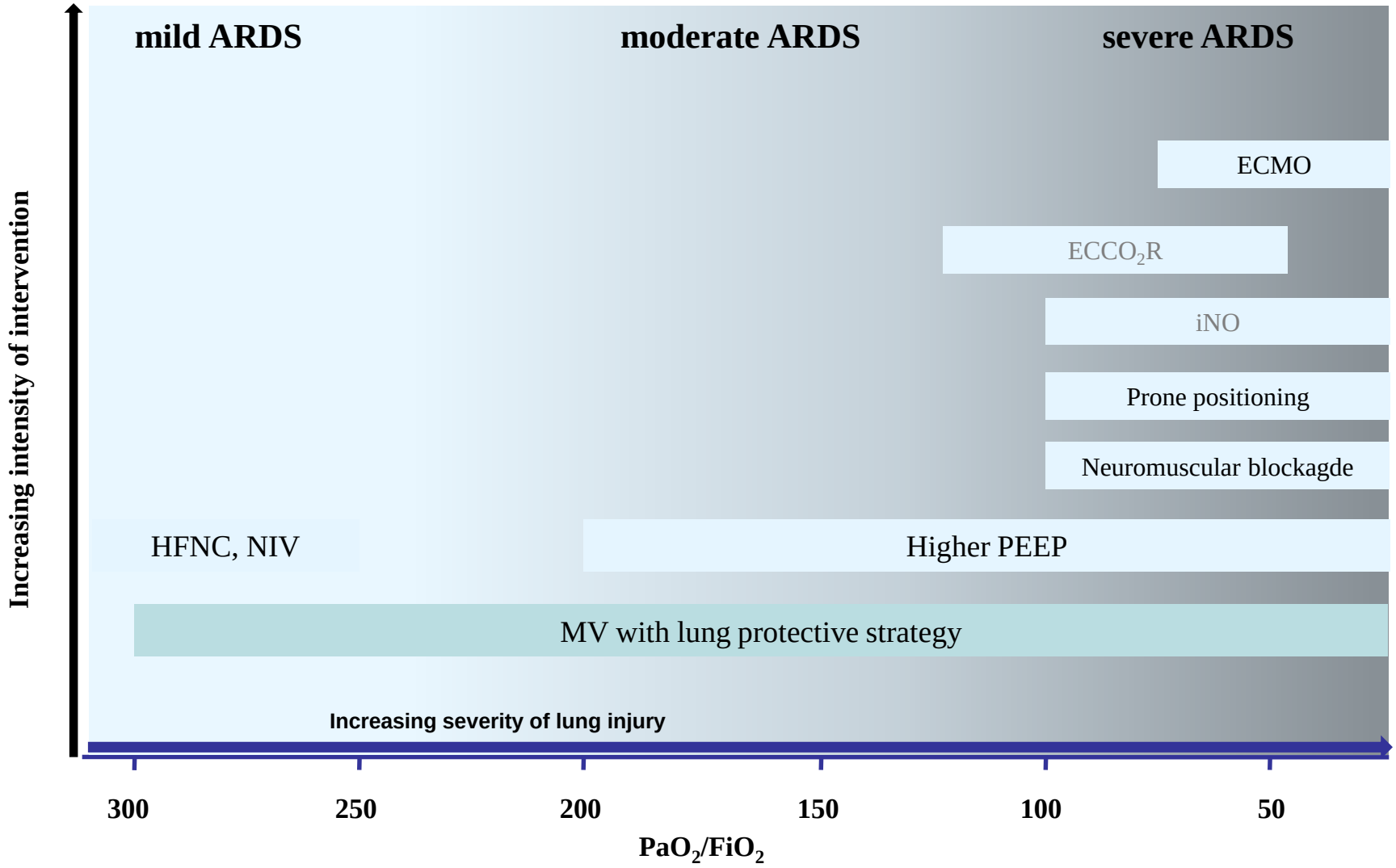
Interactive Medical Case at NEJM

- His heart rate is 124 beats per minute, and his blood pressure is 92/58 mm Hg. His height is 178 cm, and he weighs 75 kg. He is currently receiving ventilation with volume-assist control at a tidal volume of 400 ml (5.5 ml per kilogram of predicted body weight), a respiratory rate of 32 breaths per minute, positive end-expiratory pressure (PEEP) of 15 cm of water, and a fraction of inspired oxygen (FIO_2) of 1.0. The measured plateau pressure is approximately 30 cm of water. For the past 4 hours, he has had persistent hypoxemia, with arterial oxygen saturation between 80 and 82%. The most recent arterial blood gas measurement shows a pH of 7.22, partial pressure of oxygen (PaO_2) of 50 mm Hg, and partial pressure of carbon dioxide ($PaCO_2$) of 62 mm Hg.

- Which one of the following approaches would you recommend for this patient? Base your choice on the published literature, your own experience, guidelines, and other sources of information, as appropriate.
  1. Recommend initiation of venovenous ECMO.
  2. Continue current treatment with other therapies.

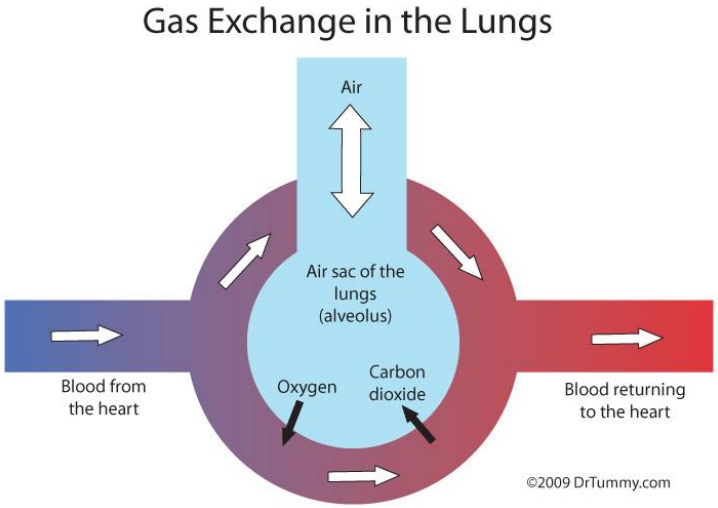
Key Components in Management of ARDS

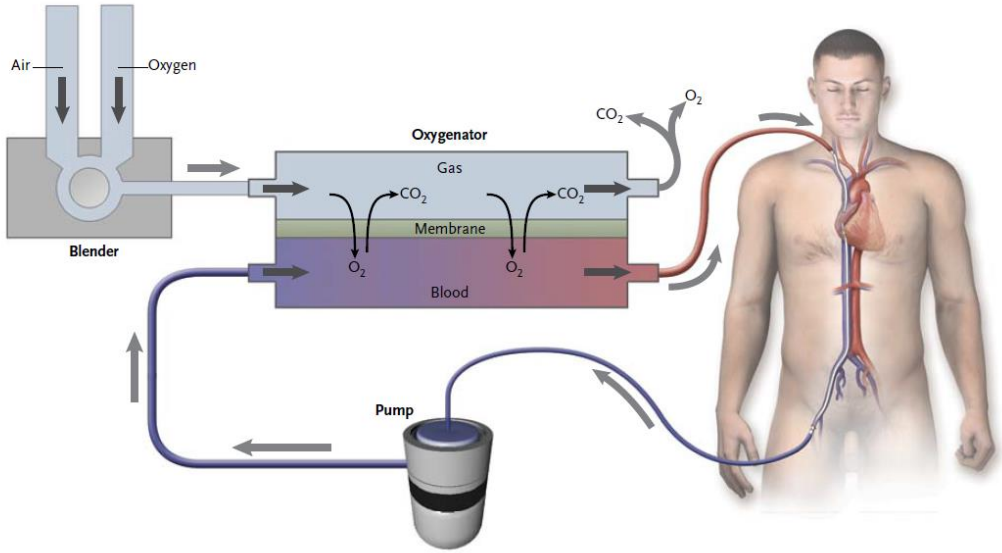
By Severity of Disease



Clinical Indication of VV ECMO

- VV ECMO
  - Provide adequate gas exchange and rest the lungs, decreasing the insult caused by mechanical ventilation





- Two distinct settings:
  - For rescue from refractory hypoxaemia, hypercapnia, or both
  - For prevention of mechanical ventilation induced lung injury

Rescue from Refractory Respiratory Failure
Case Selection for VV ECMO 1

- ECMO can be used in patients at high risk of death due to **non-response to conventional treatment**
  - Rescue from harmful effect of refractory hypoxemia, hypercapnia, or both

? Who is likely to benefit from EMCO

- ECMO can not treat the precipitating disease: reversibility
- Risk of ECMO complications

: There are as yet no standardized selection criteria for patients who will benefit from ECMO therapy.

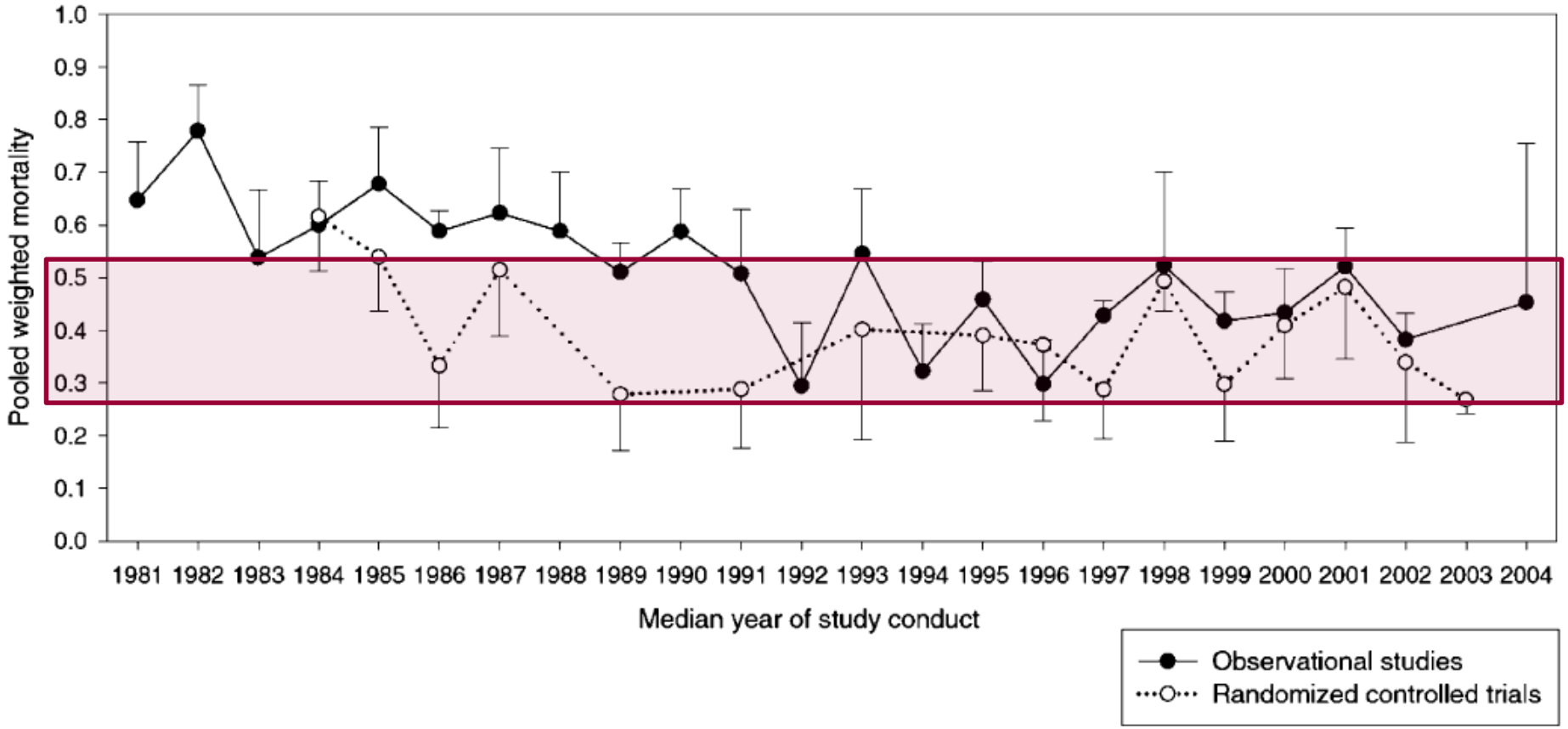
▶ Key to successful case selection

- Severity of illness and failure of conventional treatment
- Potentially reversible disease
- Contraindications

ECMO Extracorporeal Cardiopulmonary Support in Critical Care, 5th Ed.

Prognosis of ARDS

No Change of High Mortality Over Time



Am J Respir Crit Care Med 2009;179:220

High Risk of Death in Severe ARDS

Over 55% in Clinical Trials

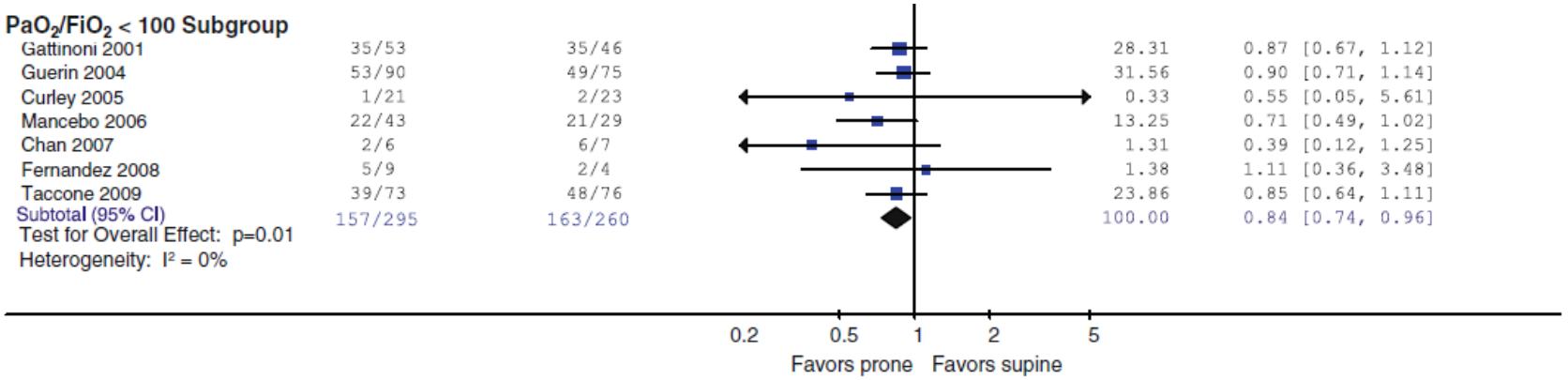
Table 7. Hospital Mortality Based on Severity of Lung Injury at Baseline

PaO_2/FIO_2	No. (%) Lung Open Ventilation	No. (%) Control	Relative Risk (95% Confidence Interval)	*P* Value[a]
Quartile 1: 41-106	57 (50)	77 (58)	0.86 (0.68-1.09)	.94
Quartile 2: >106-142	46 (39)	55 (43)	0.92 (0.68-1.24)	
Quartile 3: >142-180	43 (33)	40 (33)	0.99 (0.69-1.41)	
Quartile 4: >180-250	27 (25)	33 (26)	0.90 (0.58-1.40)	

54%

LOV study, JAMA 2008;299:637

58%



Systematic review on prone positioning Intensive Care Med 2010; 36:585

Indications for VV ECMO as Rescue Treatment

	ELSO	REVA	ANZ ECMO	ECMO Net	CESAR
Indications	Mortality >80%; PaO_2/FiO_2 <80 with FiO_2 >90%; Murray score 3.0–4.0	PaO_2/FiO_2 <50 despite PEEP 10–20 cm H_2O and FiO_2 >80%; Pplat >35 cm H_2O, despite the attempt to reduce Vt to less than 4 mL/kg PBW	PaO_2/FiO_2 <60; $PaCO_2$ >100 mm Hg with PaO_2/FiO_2 <100	Oxygenation index >30; PaO_2/FiO_2 <70 with PEEP ≥15 cm H_2O for patients already admitted to an ECMO center; pH <7.25 for ≥2 h; hemodynamic instability	Murray score ≥3.0; pH <7.20 despite optimum conventional treatment
Considerations	Mortality >50%; PaO_2/FiO_2 <150 with FiO_2 >90%; Murray score 2.0–3.0	None	None	PaO_2/FiO_2 <100 with PEEP ≥10 cm H_2O for patients awaiting transfer to ECMO center	Murray score ≥2.5

Illness Severity and Treatment Failure

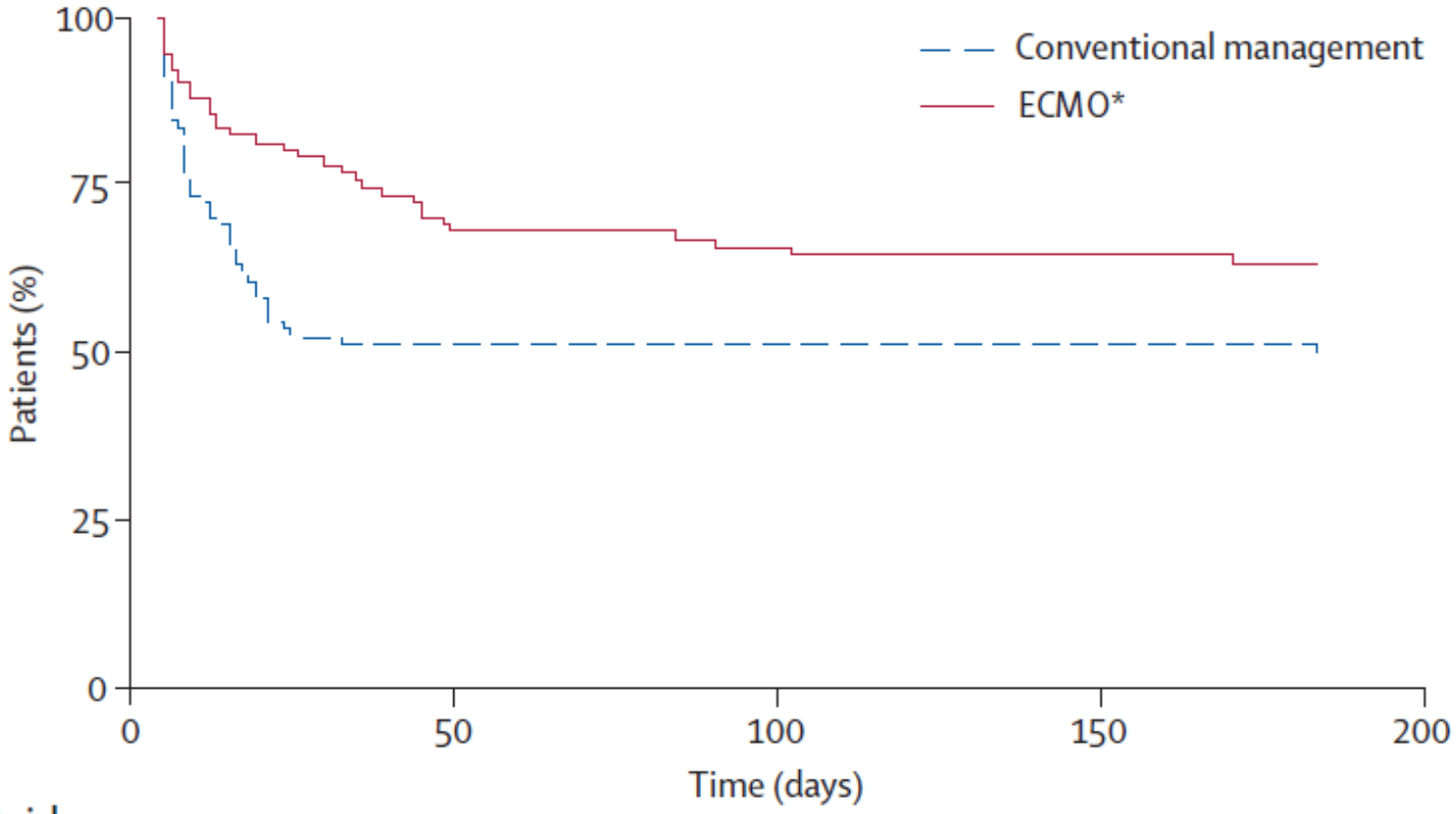
Table 1. Indications and Contraindications for ECMO in Severe Cases of ARDS.*

Indications
Severe hypoxemia (e.g., ratio of Pa_{O_2} to F_{IO_2} <80, despite the application of high levels of PEEP [typically 15–20 cm of water]) for at least 6 hr in patients with potentially reversible respiratory failure†
Uncompensated hypercapnia with acidemia (pH <7.15) despite the best accepted standard of care for management with a ventilator
Excessively high end-inspiratory plateau pressure (>35–45 cm of water, according to the patient's body size) despite the best accepted standard of care for management with a ventilator
Relative contraindications
High-pressure ventilation (end-inspiratory plateau pressure >30 cm of water) for >7 days
High F_{IO_2} requirements (>0.8) for >7 days
Limited vascular access
Any condition or organ dysfunction that would limit the likelihood of overall benefit from ECMO, such as severe, irreversible brain injury or untreatable metastatic cancer
Absolute contraindication
Any condition that precludes the use of anticoagulation therapy‡

N Engl J Med 2011;365:1905

CESAR Trial

Conventional Ventilation vs. ECMO for Severe Adult Respiratory Failure



Patients at risk					
Conventional management	90	45	44	44	0
ECMO*	90	61	59	58	0

Lancet 2009; 374: 1351

Murray Lung Injury Score (LIS)

Variables	Value
Chest radiograph score	
No alveolar consolidation	0
Alveolar consolidation confined to 1 quadrant	1
Alveolar consolidation confined to 2 quadrants	2
Alveolar consolidation confined to 3 quadrants	3
Alveolar consolidation in all 4 quadrants	4
Hypoxemia score	
PaO_2/FIO_2 ≥ 300	0
PaO_2/FIO_2 225 to 299	1
PaO_2/FIO_2 175 to 224	2
PaO_2/FIO_2 100 to 174	3
PaO_2/FIO_2 < 100	4
PEEP score (when ventilated)	
PEEP ≤ 5 cm H_2O	0
PEEP 6 to 8 cm H_2O	1
PEEP 9 to 11 cm H_2O	2
PEEP 12 to 14 cm H_2O	3
PEEP ≥ 15 cm H_2O	4
Respiratory system compliance score (when available)	
Compliance ≥ 80 ml/cm H_2O	0
Compliance 60 to 79 ml/cm H_2O	1
Compliance 40 to 59 ml/cm H_2O	2
Compliance 20 to 39 ml/cm H_2O	3
Compliance ≤ 19 ml/cm H_2O	4

Am Rev Respir Dis. 1988;4:720

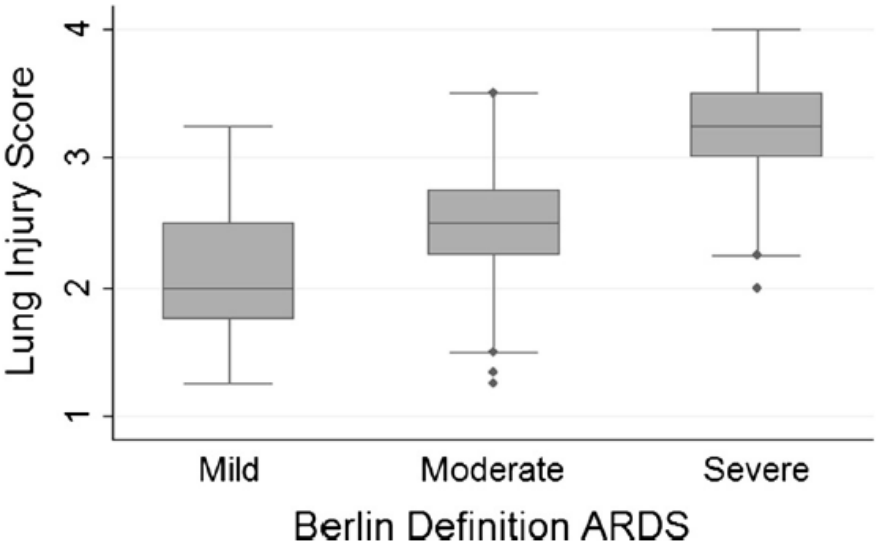
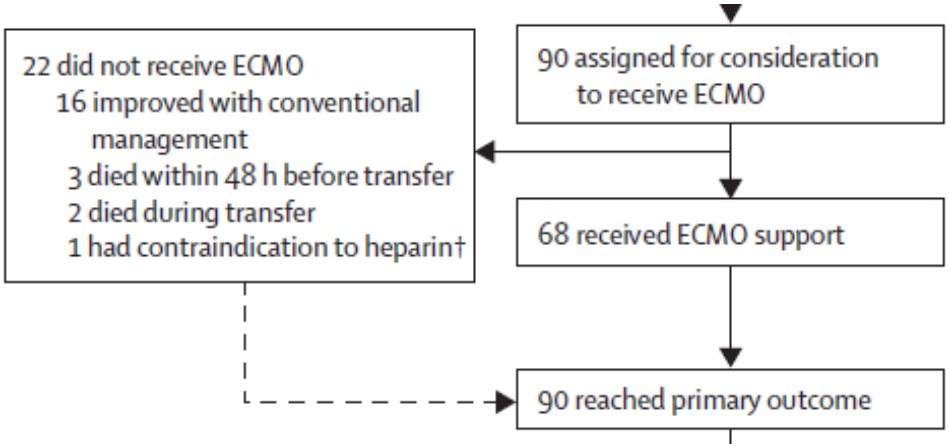


Table 3 Lung Injury Score (LIS) and component scores according to in-hospital mortality in 550 patients on day of acute respiratory distress syndrome (ARDS) diagnosis[a]

Overall	Died N = 135	Lived N = 415	*P*-value
LIS score, mean ± SD	2.9 ± 0.6	2.7 ± 0.6	0.006[b]
Chest radiograph score	4 (3 to 4)	4 (3 to 4)	0.77
PaO_2/FiO_2 category	4 (3 to 4)	3 (2 to 4)	< 0.001
PEEP category	2 (1 to 3)	2 (0 to 3)	0.02
Compliance category	3 (3 to 3)	3 (3 to 3)	0.48

Ann Intensive Care 2014;4:4

CESAR Doesn't Answer the ECMO Debate



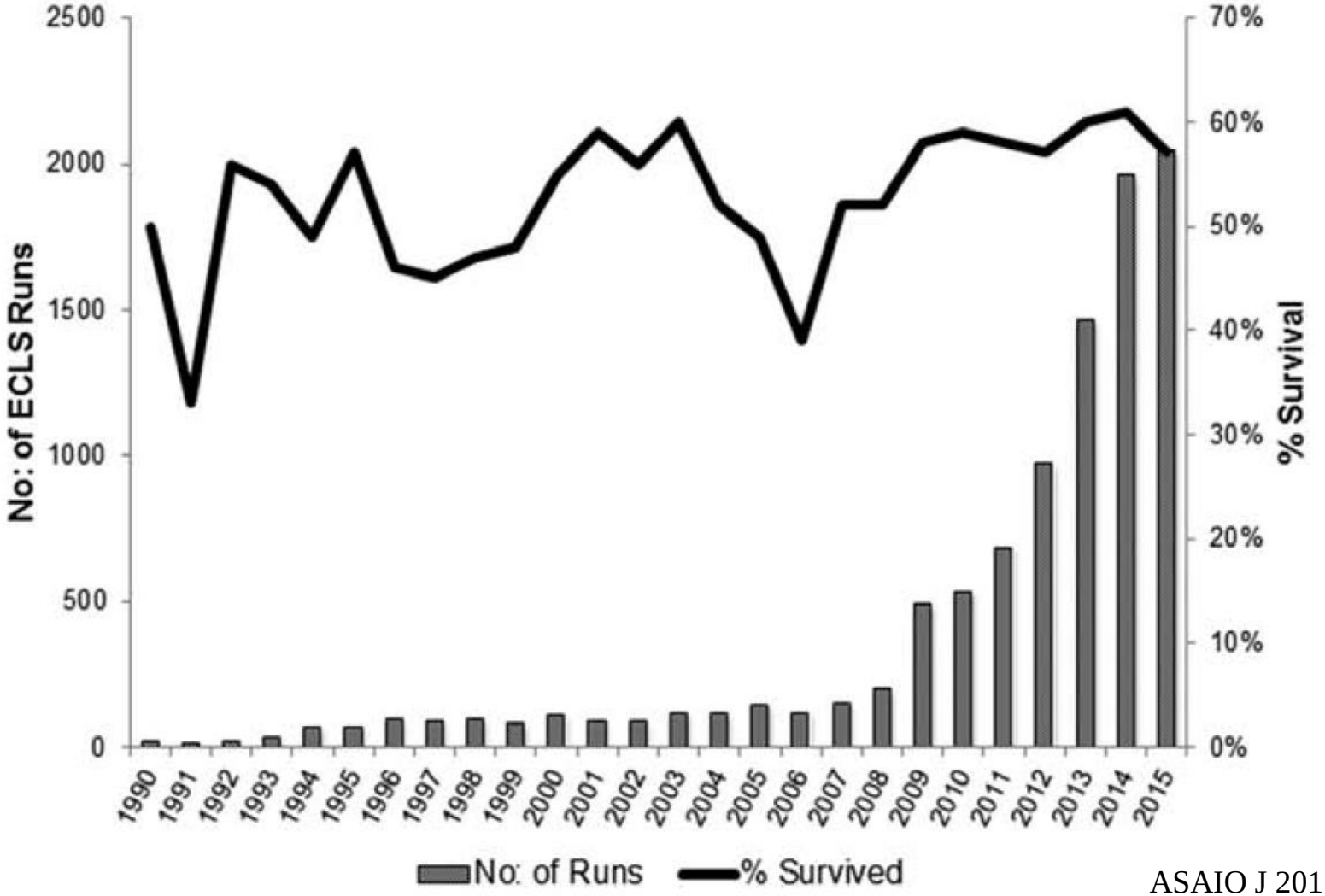
	ECMO group (n=90)*†	Conventional management group (n=90)	p value
Treatment by other management			
Missing all data	2 (2%)	0	NA
High-frequency oscillation or jet ventilation	6 (7%)	13 (14%)	0·21
Nitric oxide	9 (10%)	6 (7%)	0·60
Prone position	32 (4%)	38 (42%)	0·58
Steroids	76 (84%)	58 (64%)	0·001
MARS	15 (17%)	0	<0·0001
Continuous venovenous haemofiltration	72 (80%)	76 (84%)	0·61
Treatment by low-volume low-pressure ventilation strategy at any time	84 (93%)	63 (70%)	<0·0001
Time under strategy (days)	23·9 (20·4)	15·0 (21·1)	<0·0001

	ECMO group (n=90)*	Conventional management group (n=90)	Relative risk (95% CI, p value)
Death or severe disability at 6 months	NA	NA	0·69 (0·05–0·97, 0·03)†
No	57 (63%)	41 (47%)‡	NA
Yes	33 (37%)	46 (53%)‡	NA
No information about severe disability	0	3 (3%)§	NA
Died at ≤6 months or before discharge	NA	NA	0·73 (0·52–1·03, 0·07)
No	57 (63%)	45 (50%)	NA
Yes	33 (37%)	45 (45%)	NA

Lancet 2009; 374: 1351

ECMO Use and Survival in Respiratory Failure

ELSO Registry Data



ASAIO J 2017;63:60

ANZIC ECMO for H1N1 ARDS

Table 2. Severity of ARDS Before Commencement of ECMO

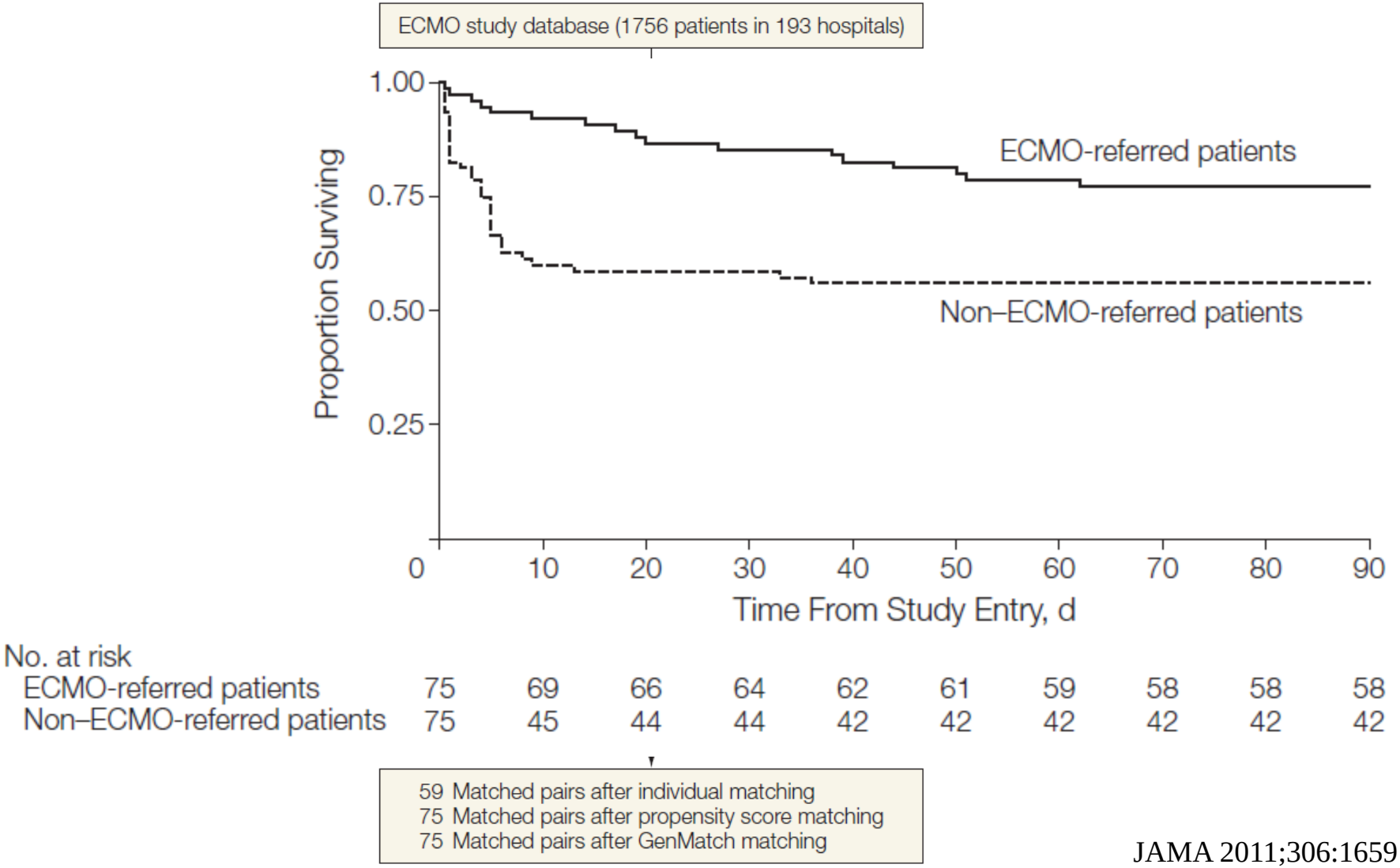
Characteristics	All Infections (N = 68)
Ventilation parameters, median (IQR)	
Lowest PaO_2/FIO_2 ratio	56 (48-63)
Highest FIO_2	1.0 (1.0-1.0)
Highest PEEP, cm H_2O	18 (15-20)
Highest peak airway pressure, cm H_2O	36 (33-38)
Lowest pH	7.2 (7.1-7.3)
Highest $PaCO_2$, mm Hg	69 (54-83)
Highest tidal volume, mL/kg	5.6 (4.6-6.7)
Quadrants of radiograph infiltrate, No.	4 (4-4)
Acute lung injury score[a]	3.8 (3.5-4.0)
Pneumothorax pre-ECMO, No. (%)	10 (15)
Rescue ARDS therapies used, No. (%)	
Recruitment maneuver	38 (67)
Prone positioning	12 (20)
High-frequency oscillation	3 (5)
Nitric oxide	20 (32)
Prostacyclin	14 (22)

Table 3. Patient Outcomes[a]

Outcome Measure	All Infections (N = 68)
Length of stay, median (IQR), d	
ICU	27 (16-37)
Hospital	39 (23-47)
Duration, median (IQR), d	
Mechanical ventilation	25 (13-34)
ECMO support	10 (7-15)
Survival at ICU discharge	48 (71)
Still in ICU	6 (9)
Survival at hospital discharge	32 (47)
Still in hospital[b]	16 (24)
Ambulant at hospital discharge[c]	31 (97)
SaO_2 on room air at hospital discharge, median (IQR), %[c]	97 (95-98)
Discharge destination	
Died	14 (21)
Home	22 (32)
Other hospital	1 (1)
Rehabilitation facility	9 (13)
Cause of death[d]	
Hemorrhage	4 (29)
Intracranial hemorrhage	6 (43)
Infection	1 (7)
Intractable respiratory failure	4 (29)

JAMA 2009;302:1888

UK Referral to ECMO Center for H1N1 ARDS



JAMA 2011;306:1659

French REVA Report

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 pa

um pericarditis

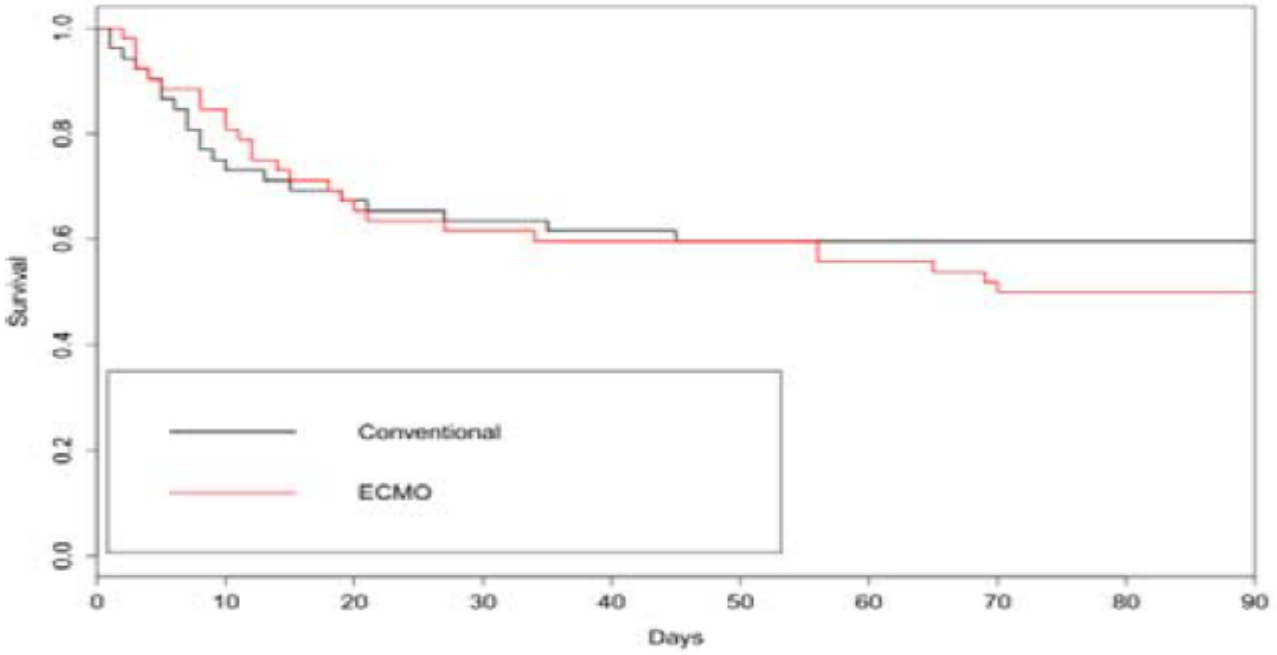
rrest

Excluded :

103 Not « severe »

arted after the
f MV

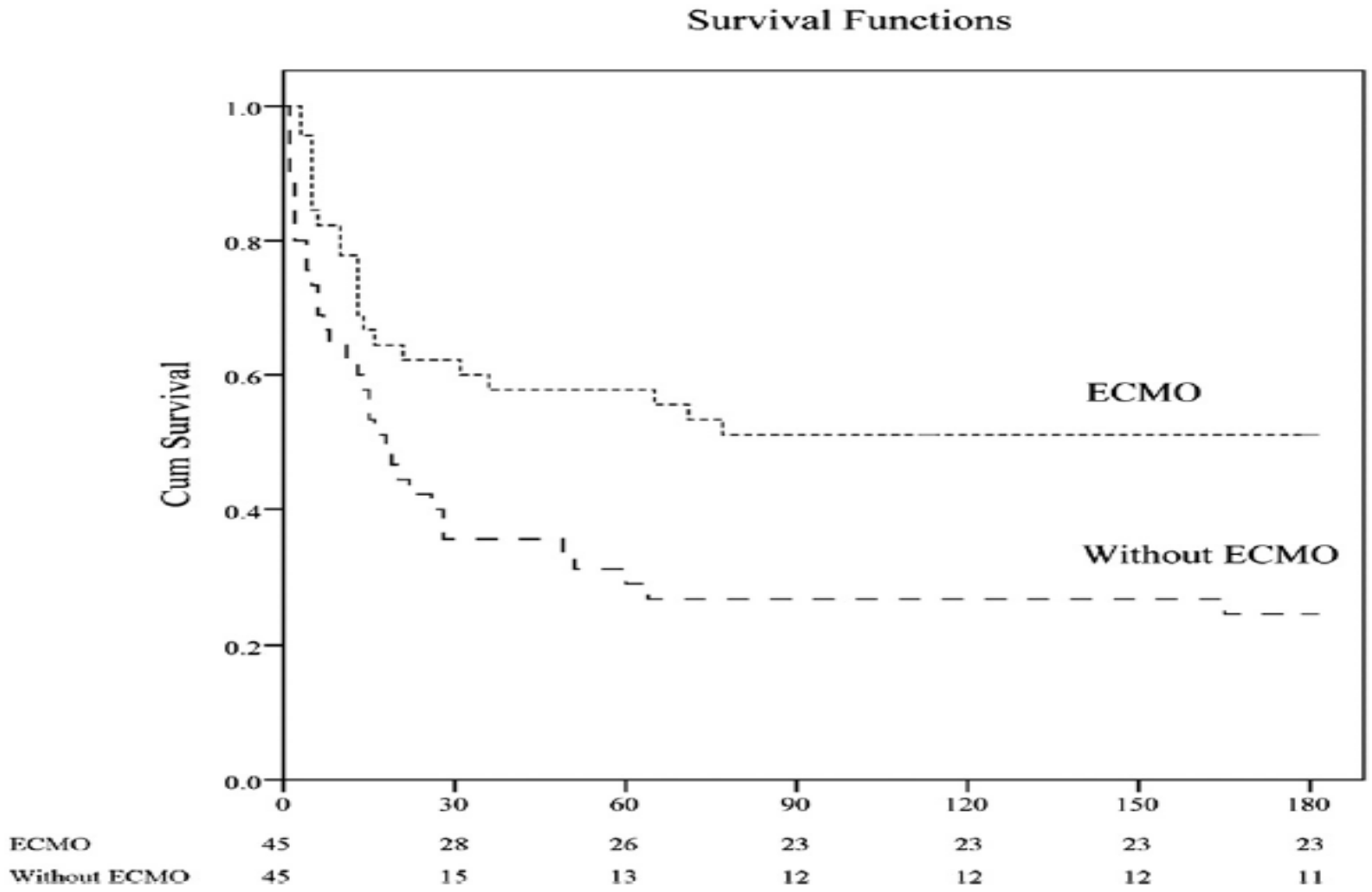
REVA main analysis
(matched sample without replacement)



52 Matched pairs

Am J Respir Crit Care Med 2013;187:276

Taiwan Score Matched Study



Ann Thorac Surg 2015;100:458

ELSO Suggestion
Adult Respiratory Failure, 2013 & 2017

VV ECMO as Rescue Therapy for Severe Hypoxemia/Hypercapnia Not Responding to Maximized Conventional Ventilatory Treatment

1. In hypoxic respiratory failure due to any cause (primary or secondary) ECLS should be considered when the risk of mortality is 50% or greater, and is indicated when the risk of mortality is 80% or greater.

a. 50% mortality risk is associated with a PaO2/FiO2 < 150 on FiO2 > 90% and/or Murray score 2-3, AOI, or APSS score .

b. 80% mortality risk is associated with a PaO2/FiO2 < 100 on FiO2> 90% and/or Murray score 3-4, AOI >80, or APSS score >7 despite optimal care **for 6 hours or less**.

The best outcome in ECMO for adult respiratory failure occurs when ECMO is instituted early after onset (1-2 days)

2. CO2 retention on mechanical ventilation despite high Pplat (>30 cm H2O)

3. Severe air leak syndromes

4. Need for intubation in a patient on lung transplant list

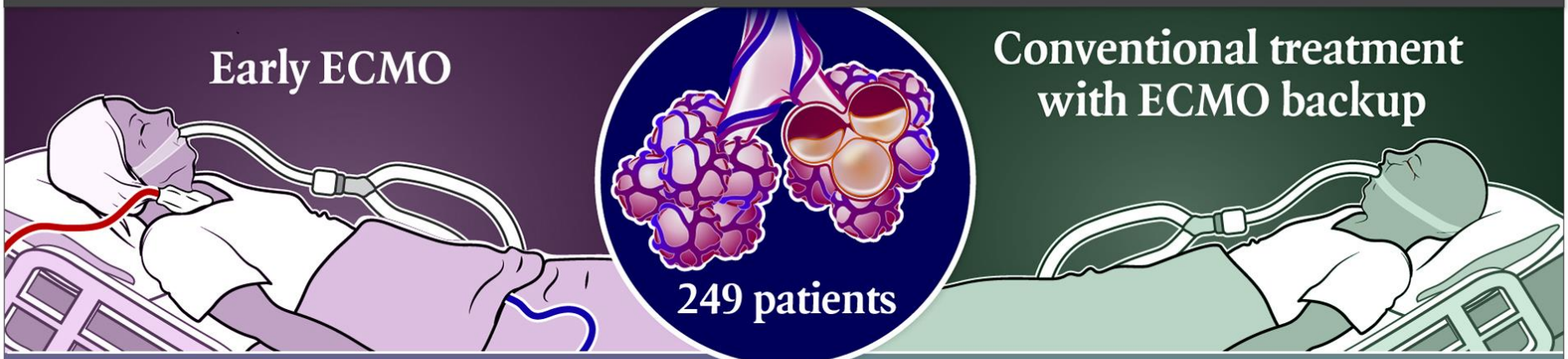
5. Immediate cardiac or respiratory collapse (PE, blocked airway, unresponsive to optimal care)

EOLIA Trial

ECMO to Rescue Lung Injury in Severe ARDS

Extracorporeal Membrane Oxygenation (ECMO) for Severe ARDS

INTERNATIONAL, RANDOMIZED CLINICAL TRIAL



35% (44/124)

60-day Mortality
(P = 0.09)
Stopped early for futility

46% (57/125)

Crossover for refractory hypoxemia (35 patients)

More bleeding, more severe thrombocytopenia, and fewer ischemic strokes in the early ECMO group

The NEW ENGLAND JOURNAL of MEDICINE

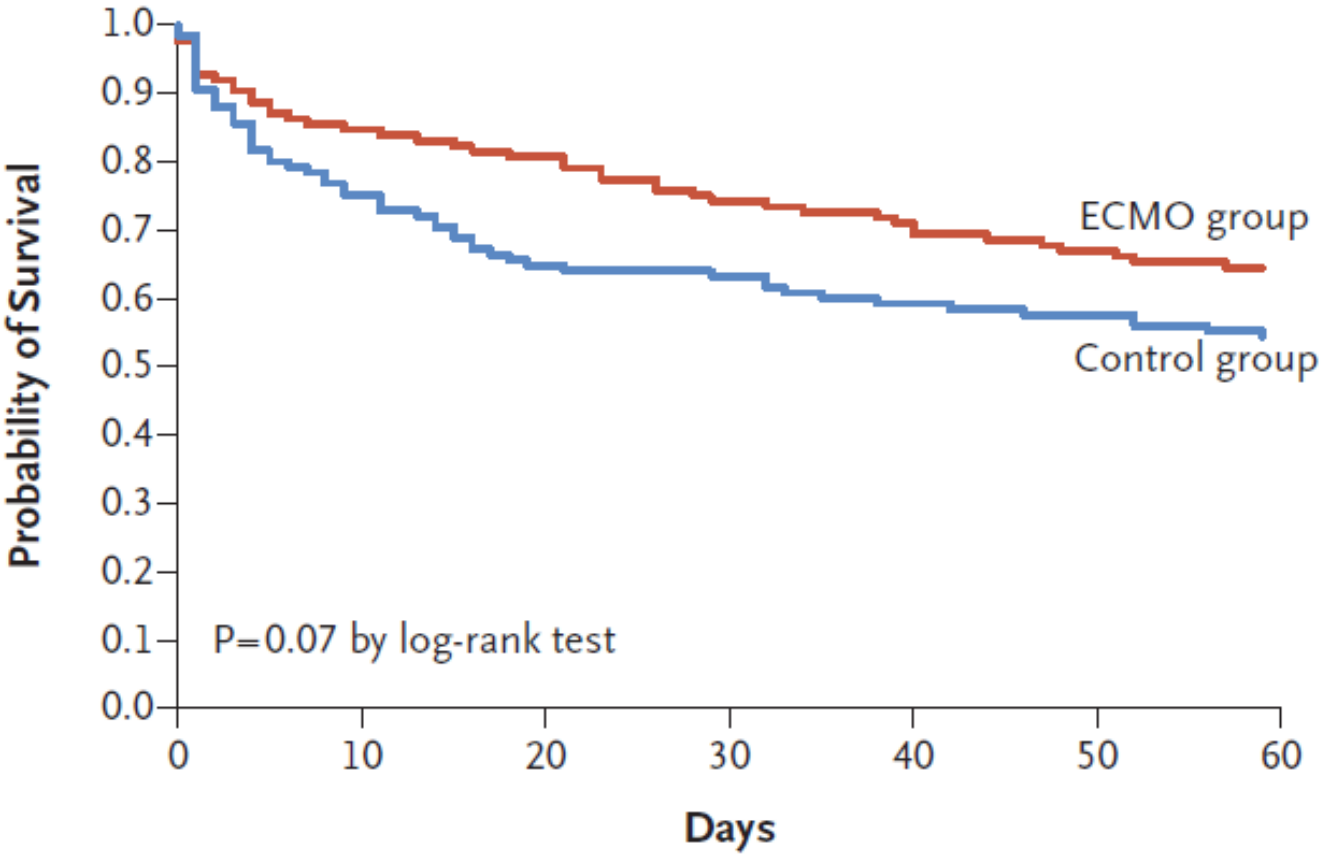
Combes et al. 2018

Inclusion Criteria for EOLIA Trial

- One of the 3 following criteria of disease severity:
  - i. PaO2/FiO2 < 50 mm Hg with FiO2 ≥ 80% for > 3 hours, despite optimization of mechanical ventilation (Vt set at 6 ml/kg and trial of PEEP ≥ 10 cm H2O) and despite possible recourse to usual adjunctive therapies (NO, recruitment maneuvers, prone position, HFO ventilation, almitrine infusion) OR
  - ii. PaO2/FiO2 < 80 mm Hg with FiO2 ≥ 80% for > 6 hours, despite optimization of mechanical ventilation (Vt set at 6 ml/kg and trial of PEEP ≥ 10 cm H2O) and despite possible recourse to usual adjunctive therapies (NO, recruitment maneuvers, prone position, HFO ventilation, almitrine infusion) OR
  - iii. pH < 7.25 for > 6 hours (with respiratory rate increased to 35/min) resulting from MV settings adjusted to keep plat ≤ 32 cm H2O (first, tidal volume reduction by steps of 1 mL/kg to 4 mL/kg then PEEP reduction to a minimum of 8 cm H2O

ECMO for Severe ARDS

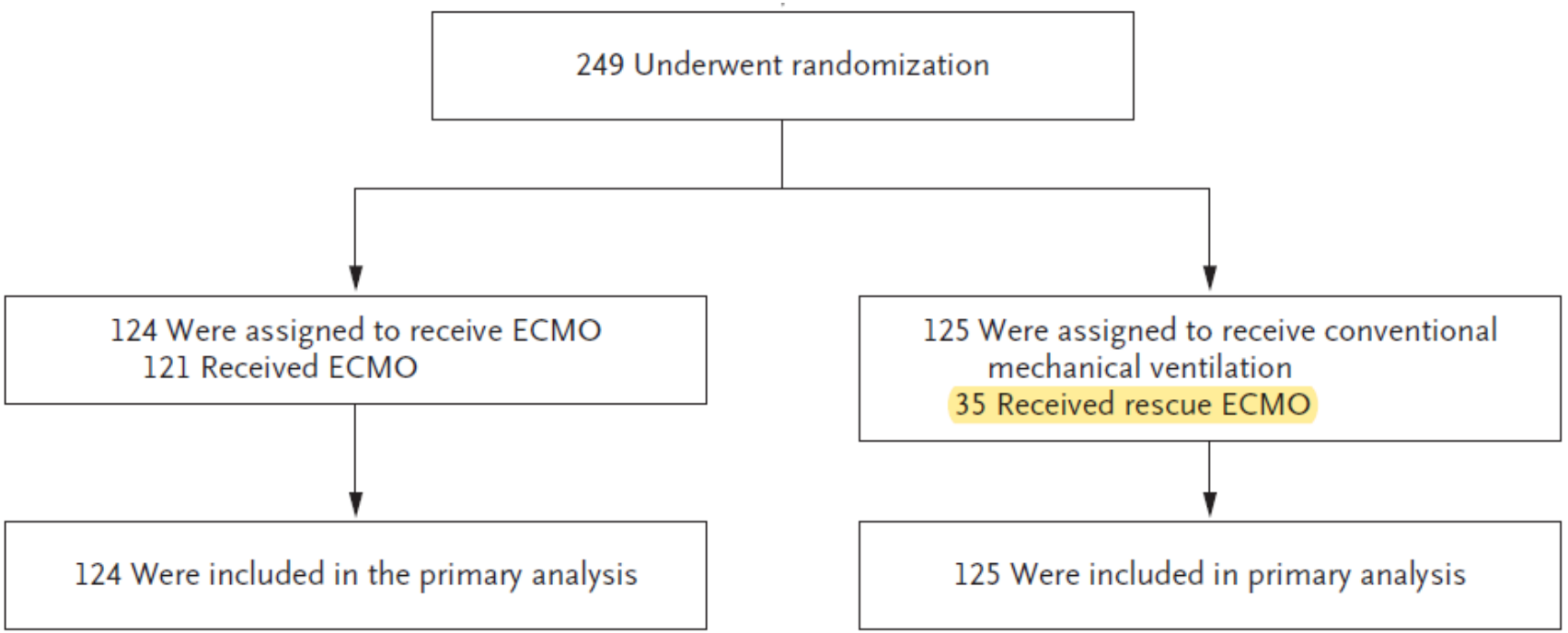
EOLIA Trial



No. at Risk							
ECMO	124	105	100	92	88	83	80
Control	125	94	81	79	74	72	69

N Engl J Med 2018;378:1965

Crossover to ECMO in the Control Group



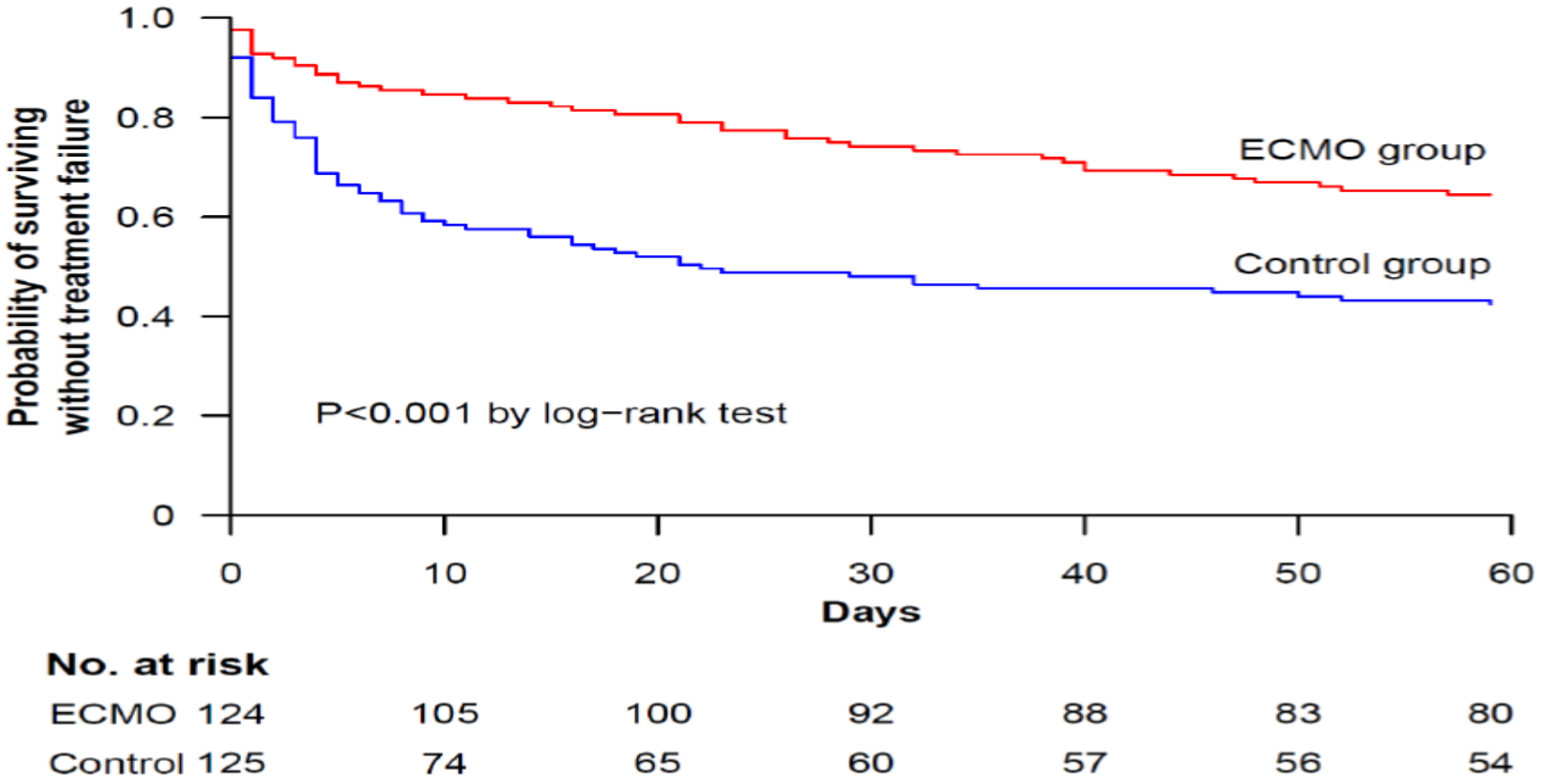
- A major limitation of the trial was that 28% of control group patients ultimately crossed over to ECMO, which diluted the effect of ECMO observed in the intention-to-treat analysis.
- Mortality of these crossed over patients was 57 vs. 41% among the other patients in the control group (RR 1.39, 95% CI 0.95–2.03).

Rank-Preserving Structural Failure Time Analysis

- Rank-Preserving Structural Failure Time (RPSFT) analysis
  - Method used to adjust for treatment switching in trials with survival outcomes

- The RPSFT analysis of overall survival may be more appropriate to estimate the "actual and unbiased" ECMO effect (i.e. if no crossover had occurred in the control group). As expected, this analysis showed that the effect of the experimental treatment increased after adjusting for crossover, from HR = 0.70 (95% CI 0.47 to 1.04, ITT analysis, P = 0.074) to HR = 0.51 (95% CI 0.24 to 1.02, RPSFT analysis), but without reaching statistical significance (P = 0.055).
  - Although it did not reach statistical significance, this more conservative estimation of the treatment effect may be viewed as the closest to the actual treatment effect, even though it may be sensitive to unverifiable modeling assumptions.

Survival without Treatment Failure



Kaplan–Meier estimates of survival without treatment failure, defined as crossover to ECMO or death for the control group and death for the ECMO group in the intention-to-treat population during the first 60 study days.

N Engl J Med 2018;378:1965

Key Secondary Outcomes
EOLIA Trial

End Point	ECMO Group (N=124)	Control Group (N=125)	Relative Risk or Difference (95% CI)†	P Value
Primary end point: mortality at 60 days — no. (%)	44 (35)	57 (46)	0.76 (0.55 to 1.04)	0.09
Key secondary end point: treatment failure at 60 days — no. (%)‡	44 (35)	72 (58)	0.62 (0.47 to 0.82)	<0.001
Other end points				
Mortality at 90 days — no. (%)	46 (37)	59 (47)	−10 (−22 to 2)	
Median length of stay (interquartile range) — days				
In the ICU	23 (13–34)	18 (8–33)	5 (−1 to 10)	
In the hospital	36 (19–48)	18 (5–43)	18 (6 to 25)	
Median days free from mechanical ventilation (interquartile range)§	23 (0–40)	3 (0–36)	20 (−5 to 32)	
Median days free from vasopressor use (interquartile range)§	49 (0–56)	40 (0–53)	9 (0 to 51)	
Median days free from renal-replacement therapy (interquartile range)§	50 (0–60)	32 (0–57)	18 (0 to 51)	
Prone position — no. (%)¶	82 (66)	113 (90)	−24 (−34 to −14)	
Recruitment maneuvers — no. (%)¶	27 (22)	54 (43)	−21 (−32 to −10)	
Inhaled nitric oxide or prostacyclin — no. (%)¶	75 (60)	104 (83)	−23 (−33 to −12)	
Glucocorticoids — no. (%)¶	80 (65)	82 (66)	−1 (−13 to 11)	

N Engl J Med 2018;378:1965

Does the EOLIA Trial Really Help?
Comments by Luciano Gattinoni

Two hypotheses of ECMO trial

a) Emergency ECMO improves outcome by "buying time" in extremely hypoxemic patients.

- Of the 35 patients switched from conventional therapy to rescue ECMO (median SaO2 77%; nine cardiac arrest events), 15 survived. It is unlikely that they would have survived without ECMO, regardless of the statistical relevance of these observations.

b) ECMO improves outcome by reducing the invasiveness of mechanical ventilation.

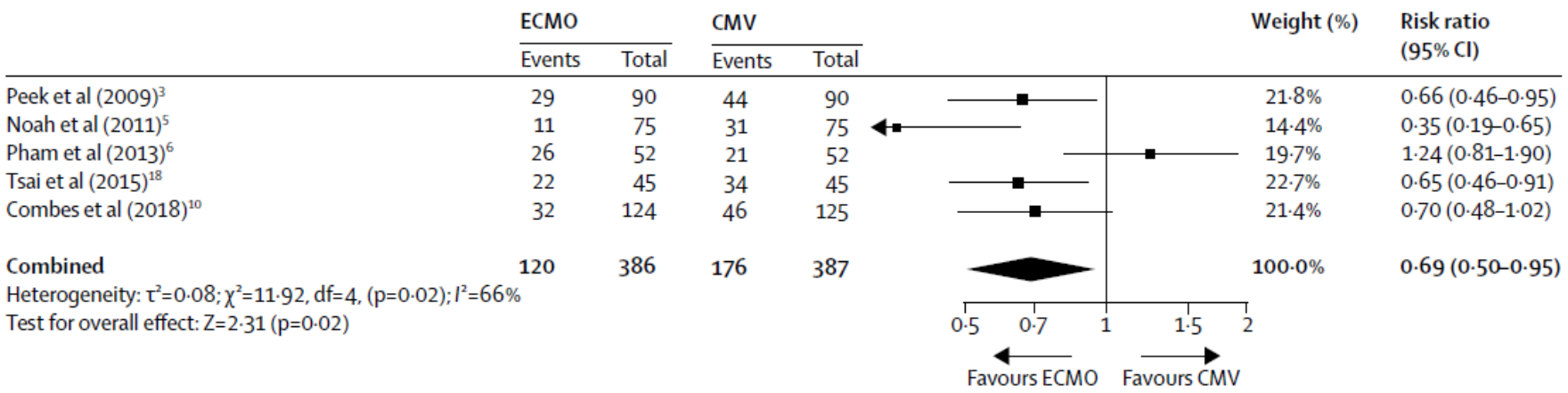
- During ECMO, tidal volume was reduced by 43% and respiratory rate by 23%, while PEEP remained essentially unchanged. This represents an estimated 66% reduction in the mechanical power applied to the lungs (from 28 J/min to 10 J/min). This reduction was associated with a higher survival rate (81/124 patients) in the ECMO group (vs 68/125 controls).

Critical Care 2018; 22:171

Venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis

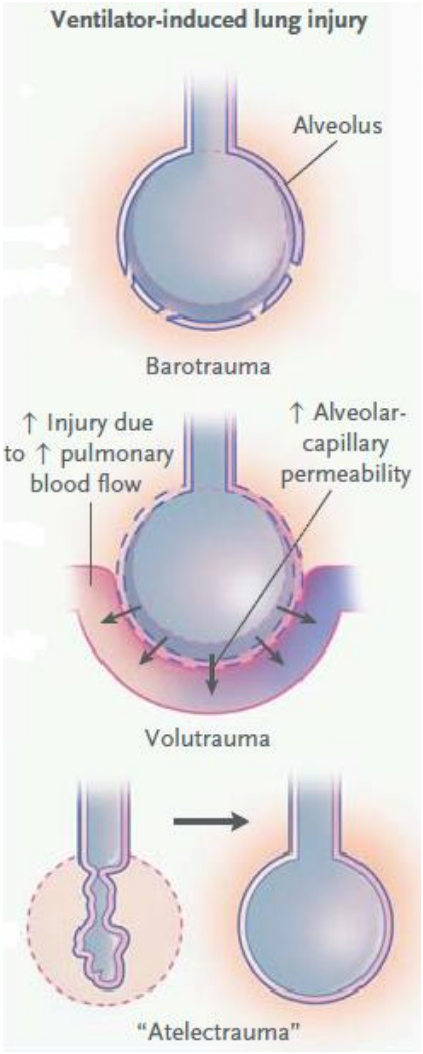
Laveena Munshi, Allan Walkey, Ewan Goligher, Tai Pham, Elizabeth M Uleryk, Eddy Fan

	Peek et al (CESAR),[3] 2009	Noah et al,[5] 2011	Pham et al,[6] 2013	Tsai et al,[18] 2015	Combes et al (EOLIA),[10] 2018
Study type	Randomised controlled trial	Observational	Observational	Observational	Randomised controlled trial
n					
Overall	180	150	260 (104)*	216	249
ECMO group	90	75	103 (52)*	81 (45)†	124
Indication for ECMO	Severe but potentially reversible ARDS‡; Murray score ≥3·0 or uncompensated hypercapnia with pH <7·2 despite optimal conventional treatment	Age 18–65 years; severe but potentially reversible ARDS; Murray score ≥3·0 or uncompensated hypercapnia with pH <7·2 despite optimal conventional treatment; infection with H1N1 influenza	Severe ARDS, which was defined as ARDS due to H1N1 influenza, and any one of a modified lung injury score ≥3·0, an arterial pH <7·21, PaO_2:FiO_2 <100 mm Hg, or arterial oxygen saturation <90%	Moderate-to-severe ARDS (more specific criteria for ECMO indications not described)	PaO_2:FiO_2 <50 for 3 h, PaO_2:FiO_2 <80 for 6 h, or $PaCO_2$ >60 mm Hg and pH <7·25 for 6 h
Mean PaO_2:FiO_2 (SD)					
ECMO	76 (30)	55 (14)	70 (26)	93 (13)	73 (30)
CMV	75 (36)	55 (12)	68 (20)	124 (12)	72 (24)



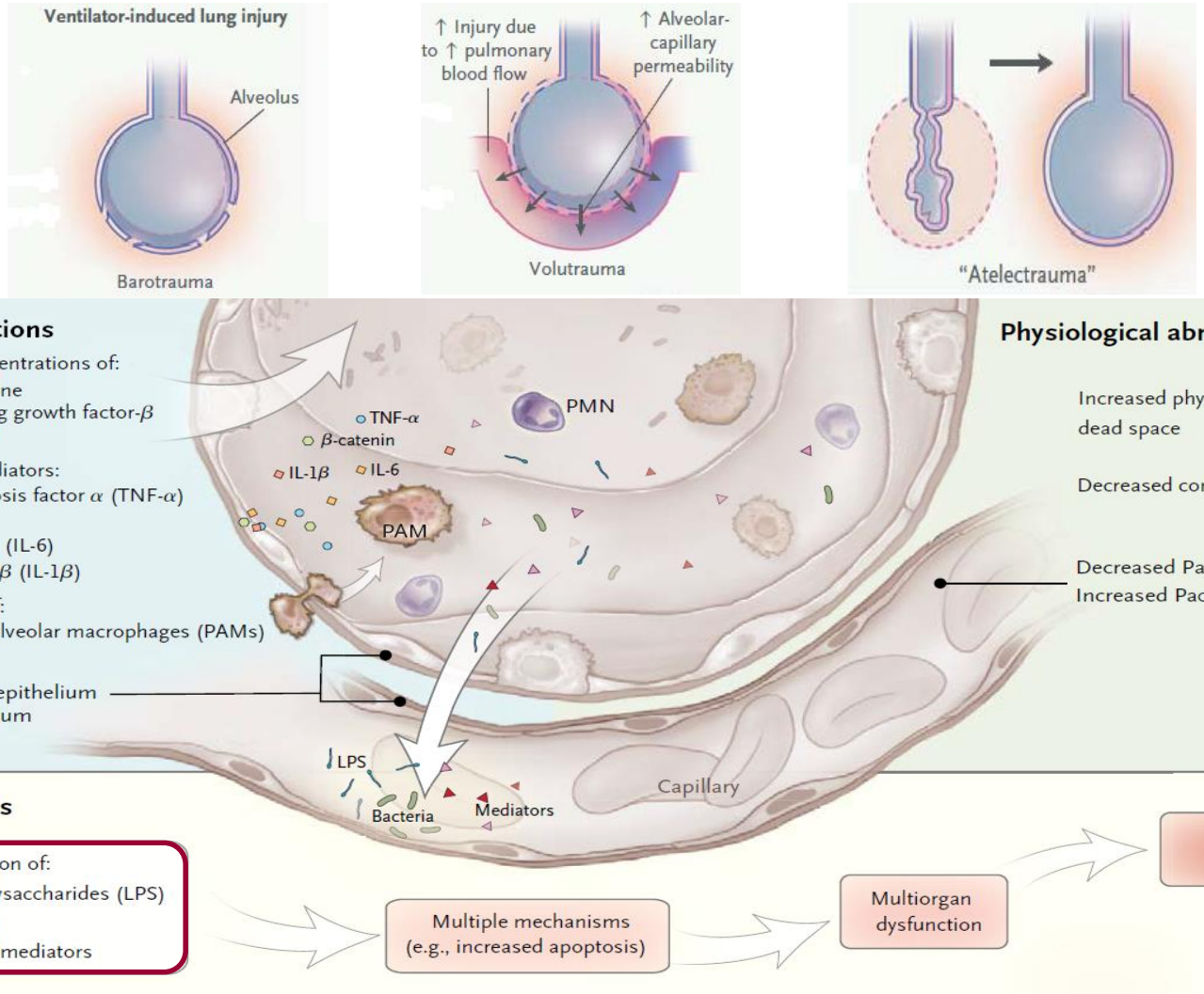
Lancet Respir Med 2019;7:163

Ventilator Induced Lung Injury (VILI)



- Barotrauma
  - High airway pressure
- Volutrauma
  - High tidal volume (high transpulmonary pressure)
  - Alveolar overdistension
- Atelectrauma
  - Repeated opening & closing of collapsed lung units
  - Cyclic atelectasis
    - shear stress
    - surfactant alteration

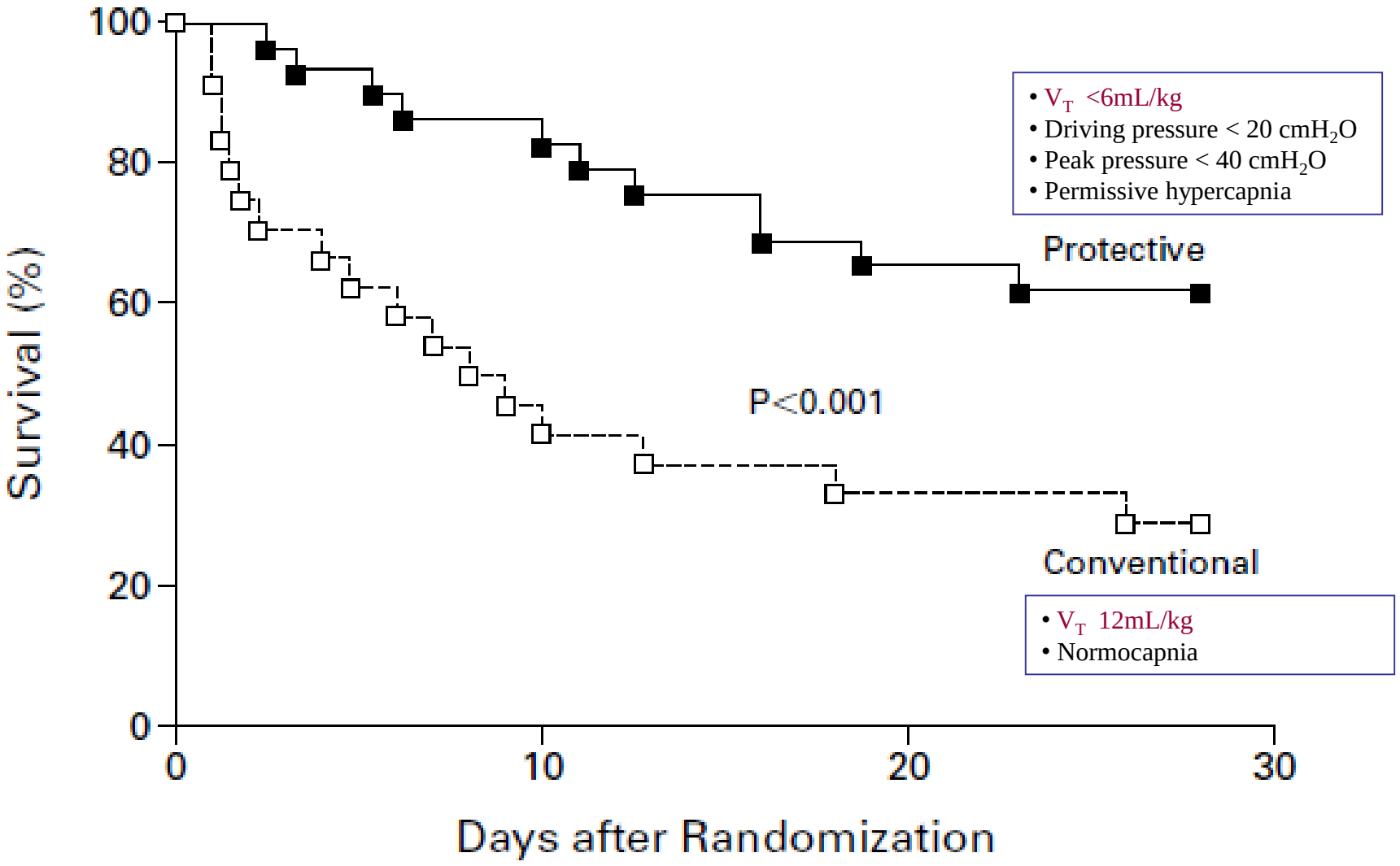
VILI and Organ Dysfunction



N Engl J Med 2013; 369:2126

Low V_T in ARDS

Amato et al. 1998



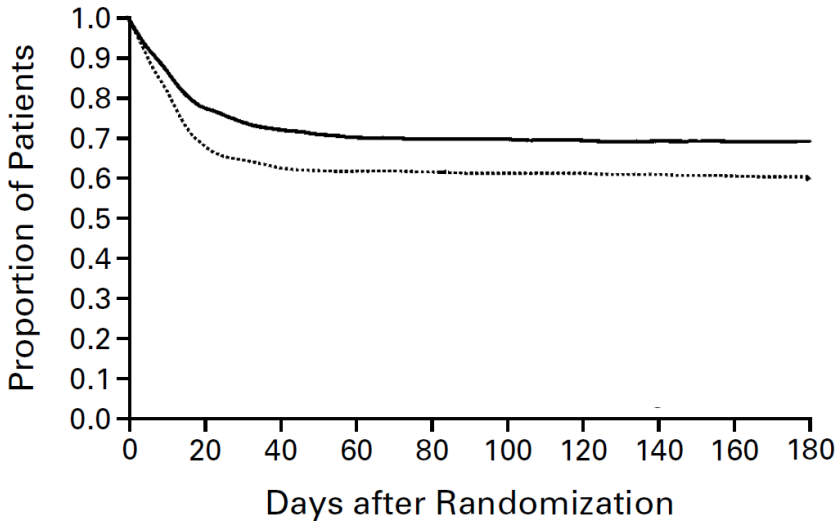
N Engl J Med 1998;338:347

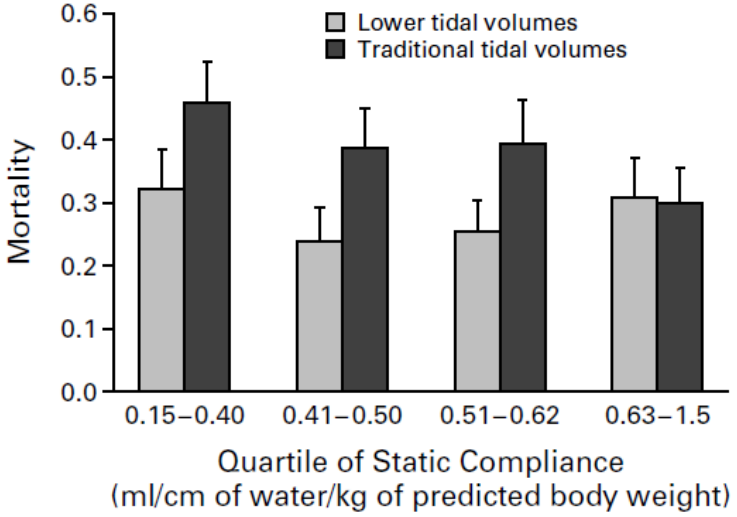
Low Tidal Volume Ventilation
ARDS Network

VOLUME 342 MAY 4, 2000 NUMBER 18

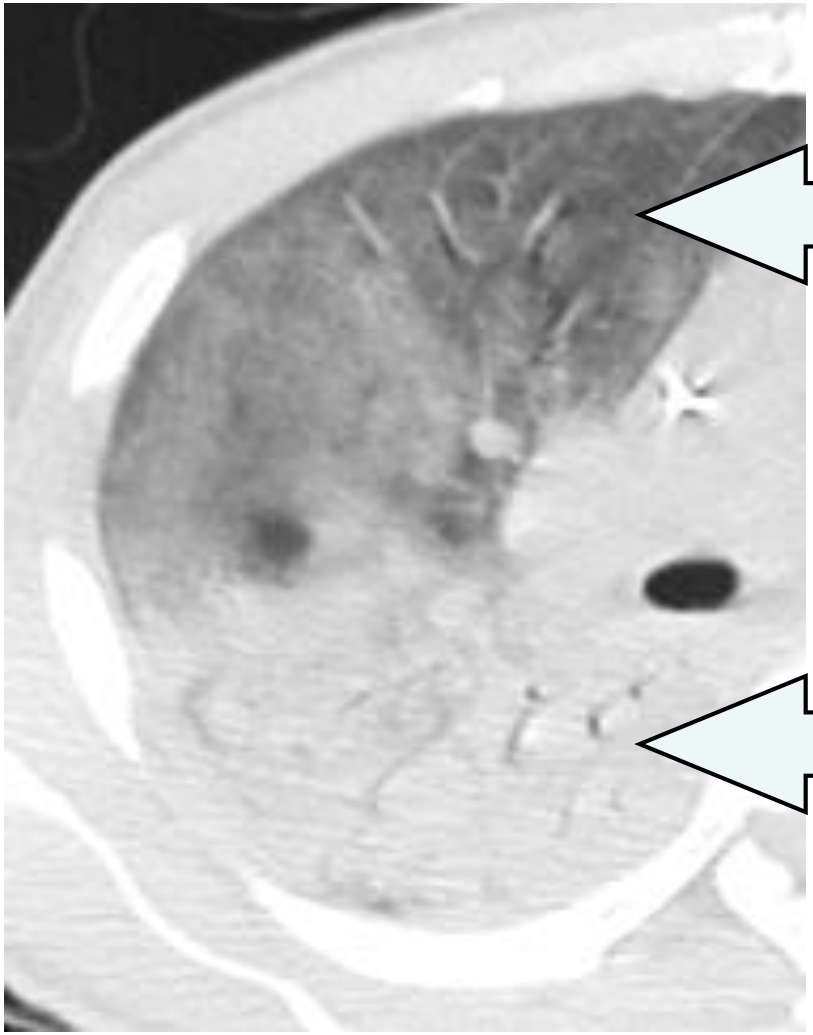
VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*





Lung Protective Ventilation



Avoid overdistension

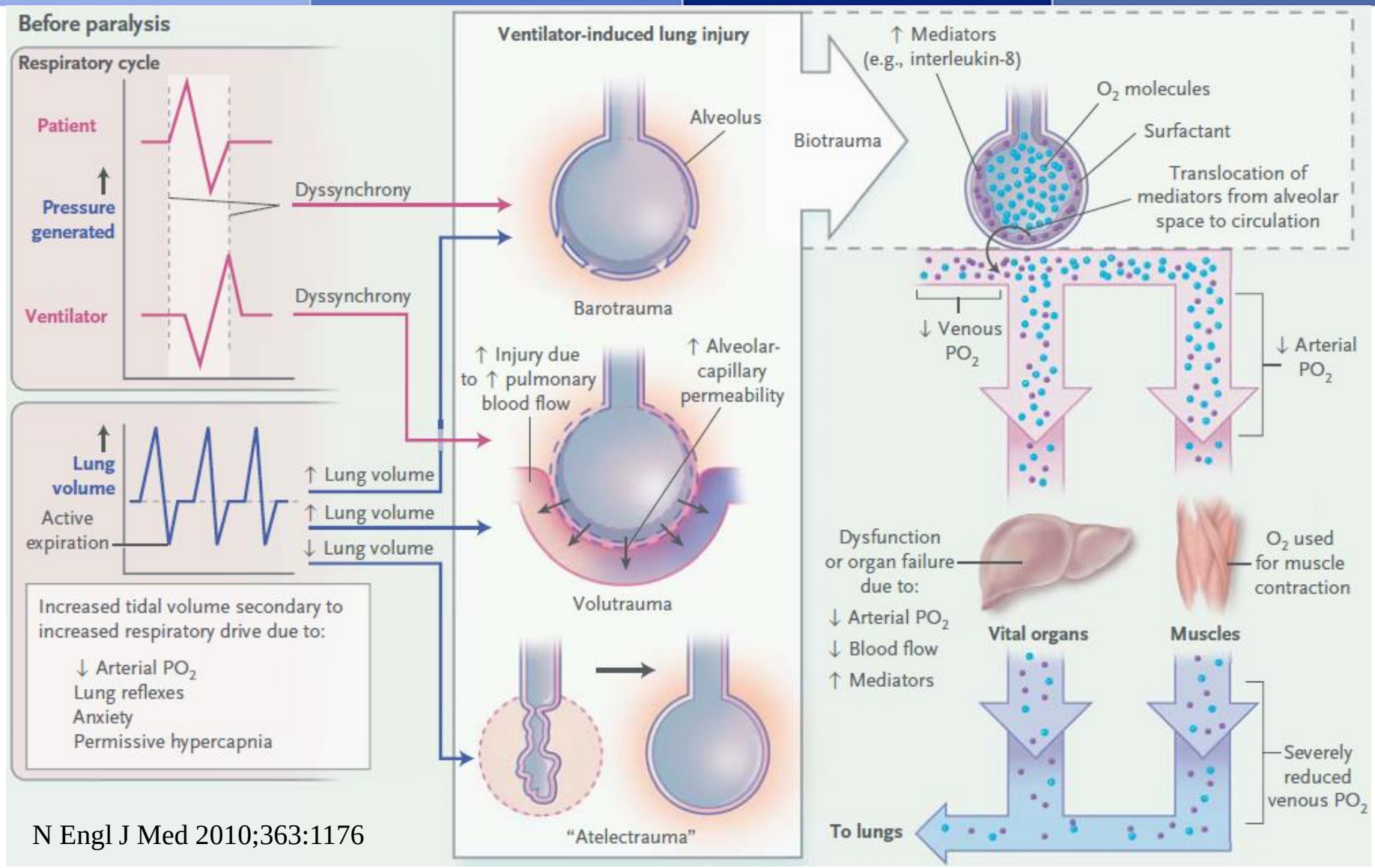
: Low tidal volumes (low driving pressure)

Keep the lung open at end expiration

: PEEP (high PEEP in severe form)

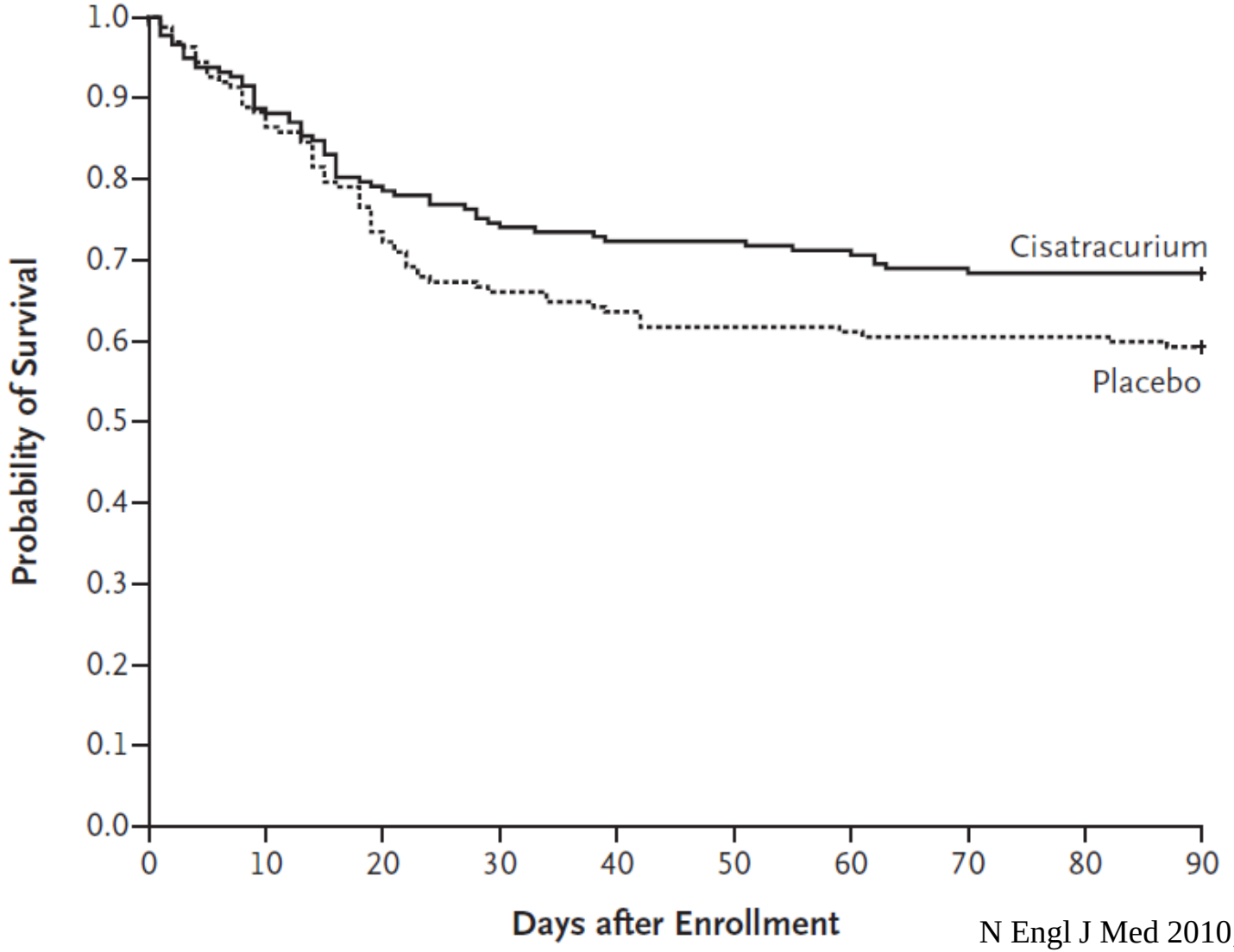
N Engl J Med 2017;377:562

Ventilator Dyssynchrony



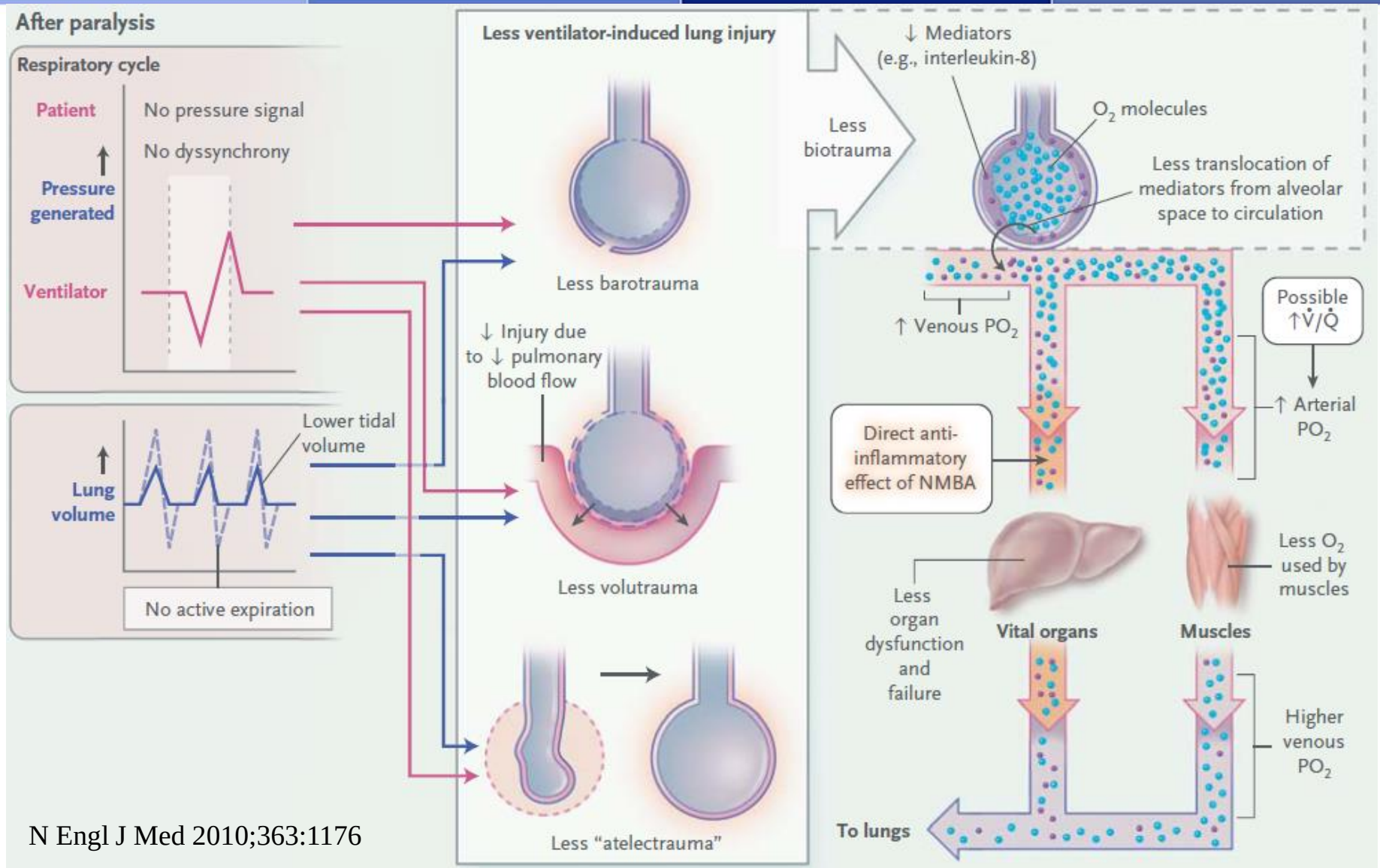
N Engl J Med 2010;363:1176

NM Blocking for 48 Hrs in ARDS
ACURASYS Study



N Engl J Med 2010;363:1107

Prevent VILI with NM Blocking



N Engl J Med 2010;363:1176

Prevention of VILI
Case Selection for VV ECMO 2

- ECMO might be suitable for use in patients with early acute respiratory distress syndrome who would otherwise require injurious levels of mechanical ventilation to maintain adequate gas exchange.
  - Lowering of plateau pressure, tidal volume, or both, has been associated with decreased mortality

Am J Respir Crit Care Med 2005;172:1241

BMJ 2012;344:e2124

Am J Respir Crit Care Med 2017;195:1161

▶ Rest the lung with ECMO even in case of that gas exchange is adequate but require injurious levels of mechanical ventilation to maintain adequate gas exchange

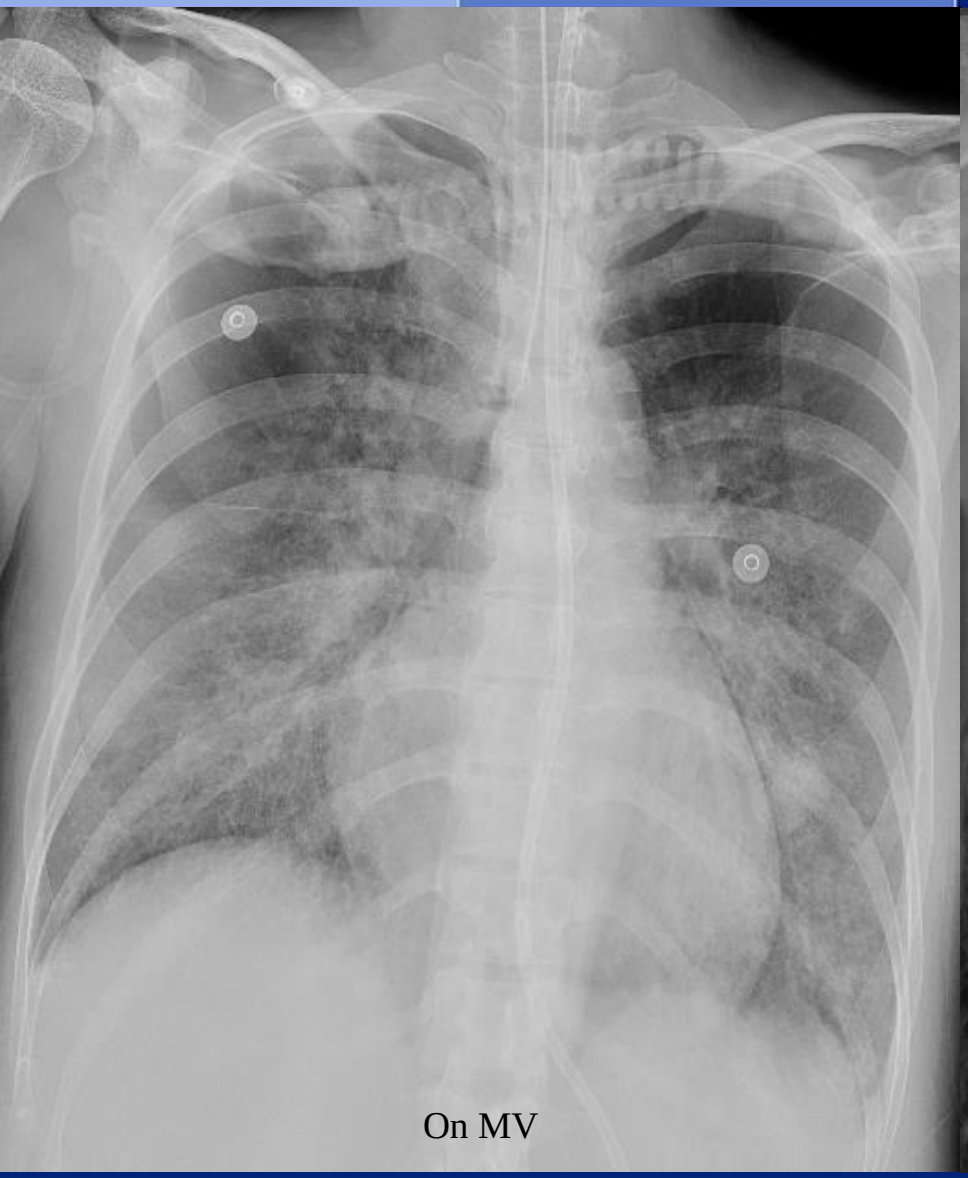
▶ Ultraprotective mechanical ventilation with ECMO or ECCO2R could further improve outcomes in patients with acute respiratory distress syndrome

Crit Care 2012; 16: 232

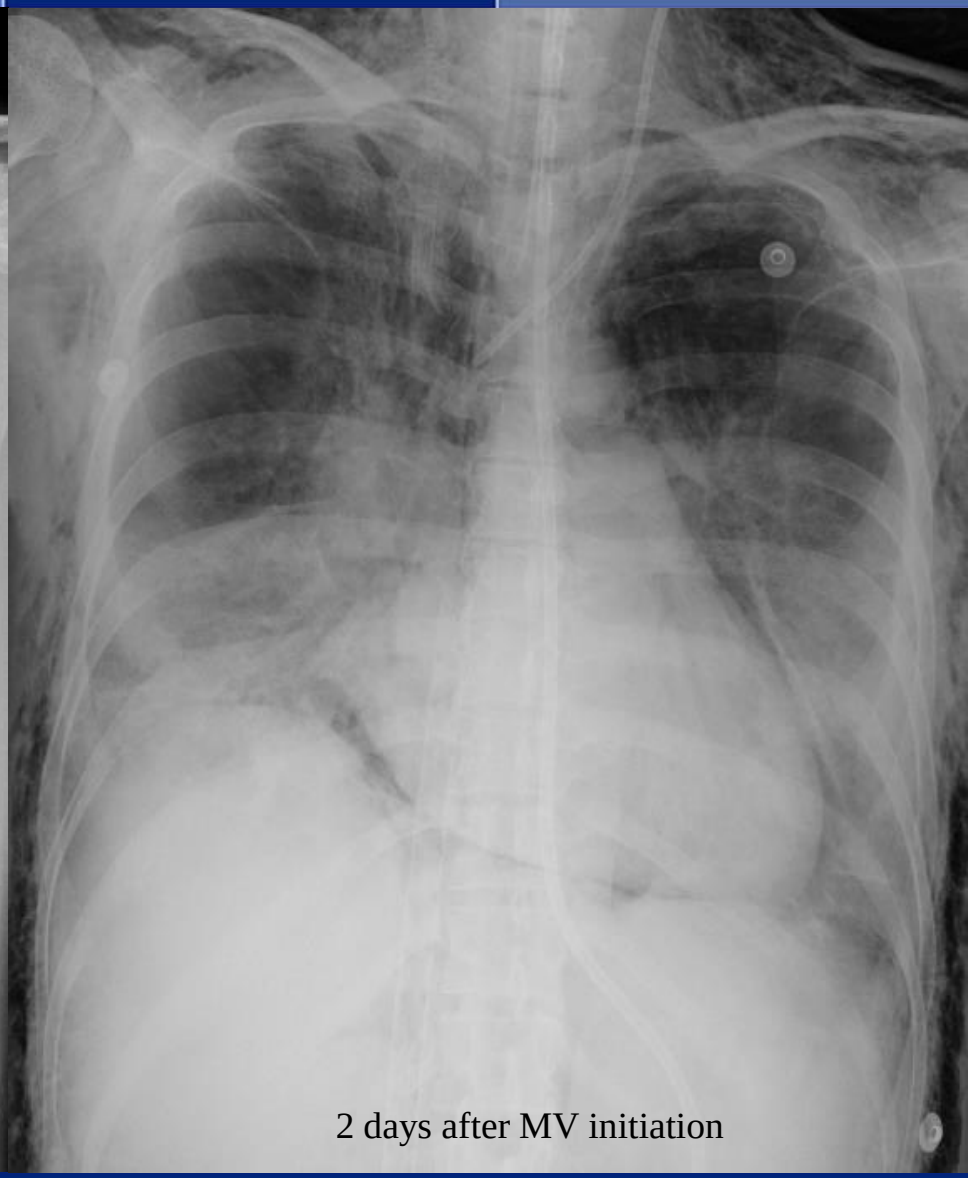
Intensive Care Med 2019 (in press)

35 YO Female with Influenza Pneumonia

Progression of Pneumomediastinum

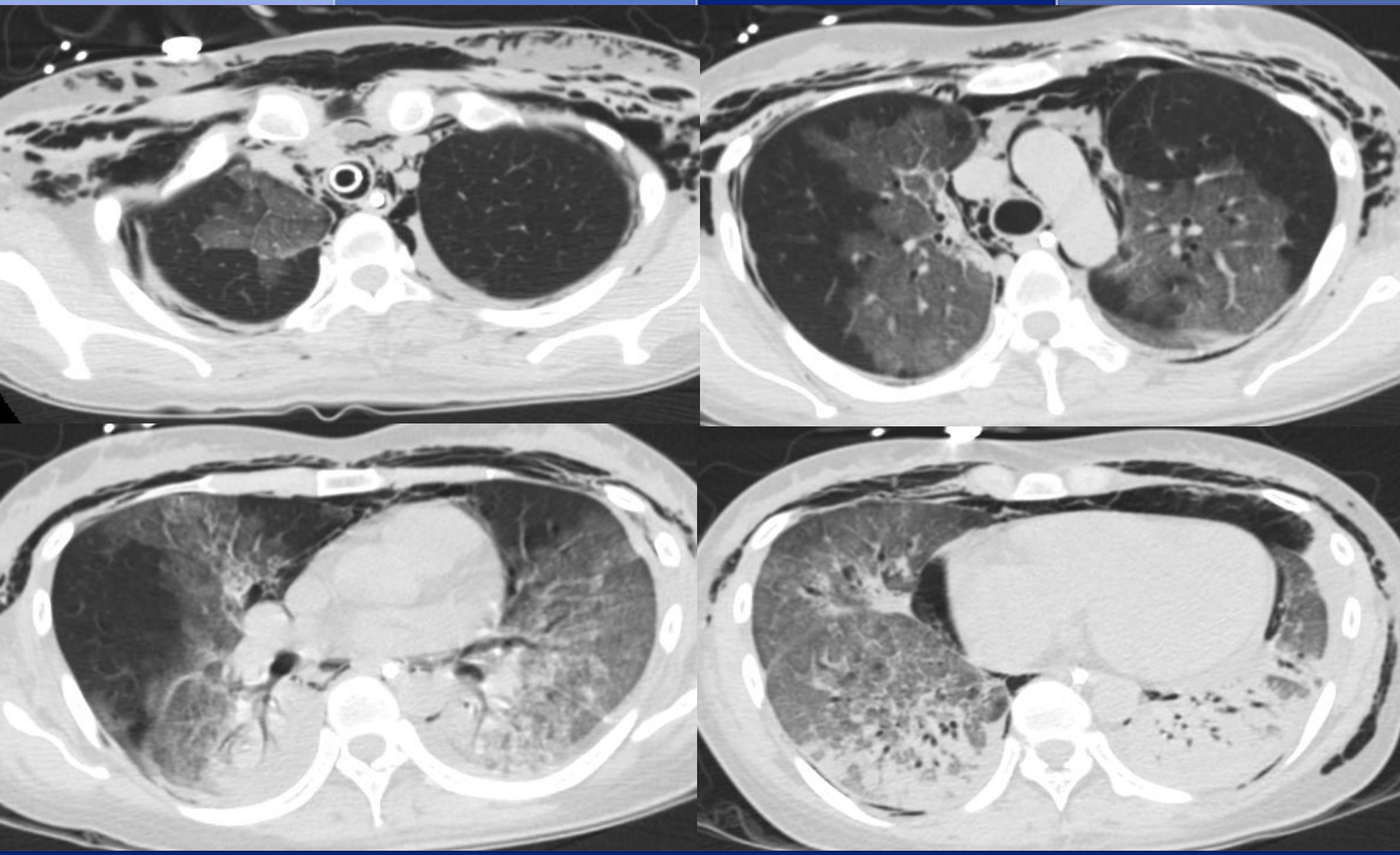


On MV

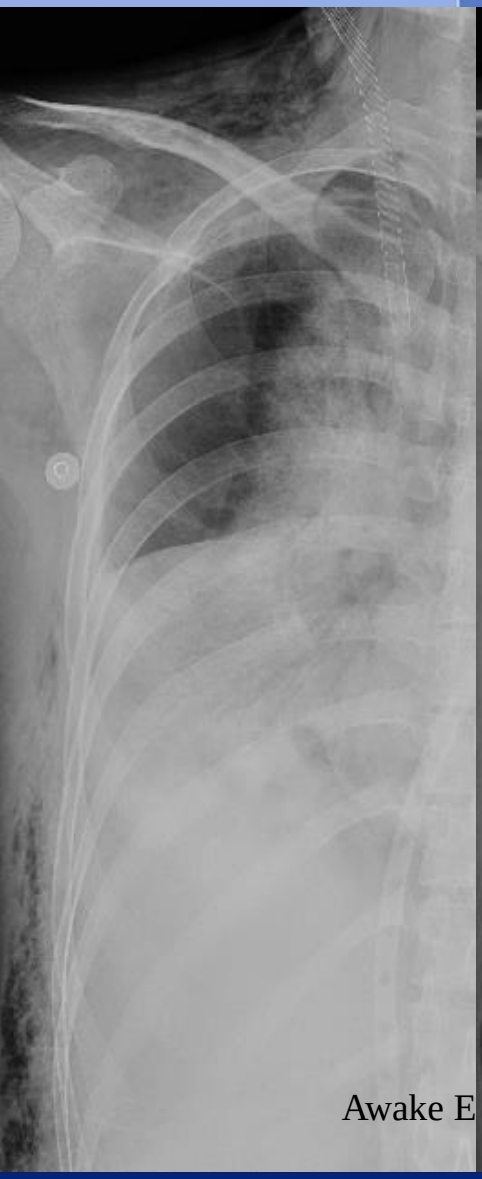


2 days after MV initiation

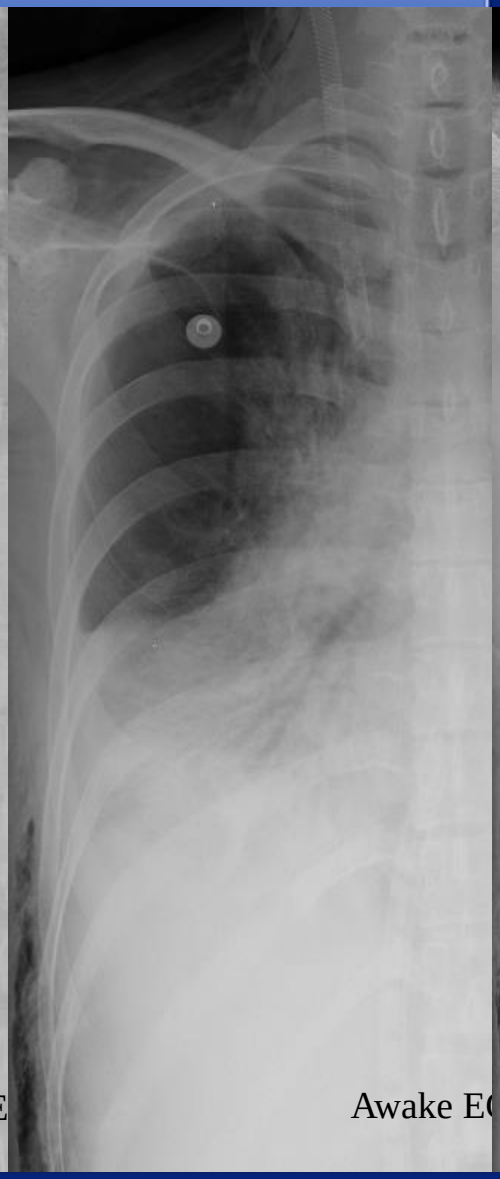
Chest CT Scans



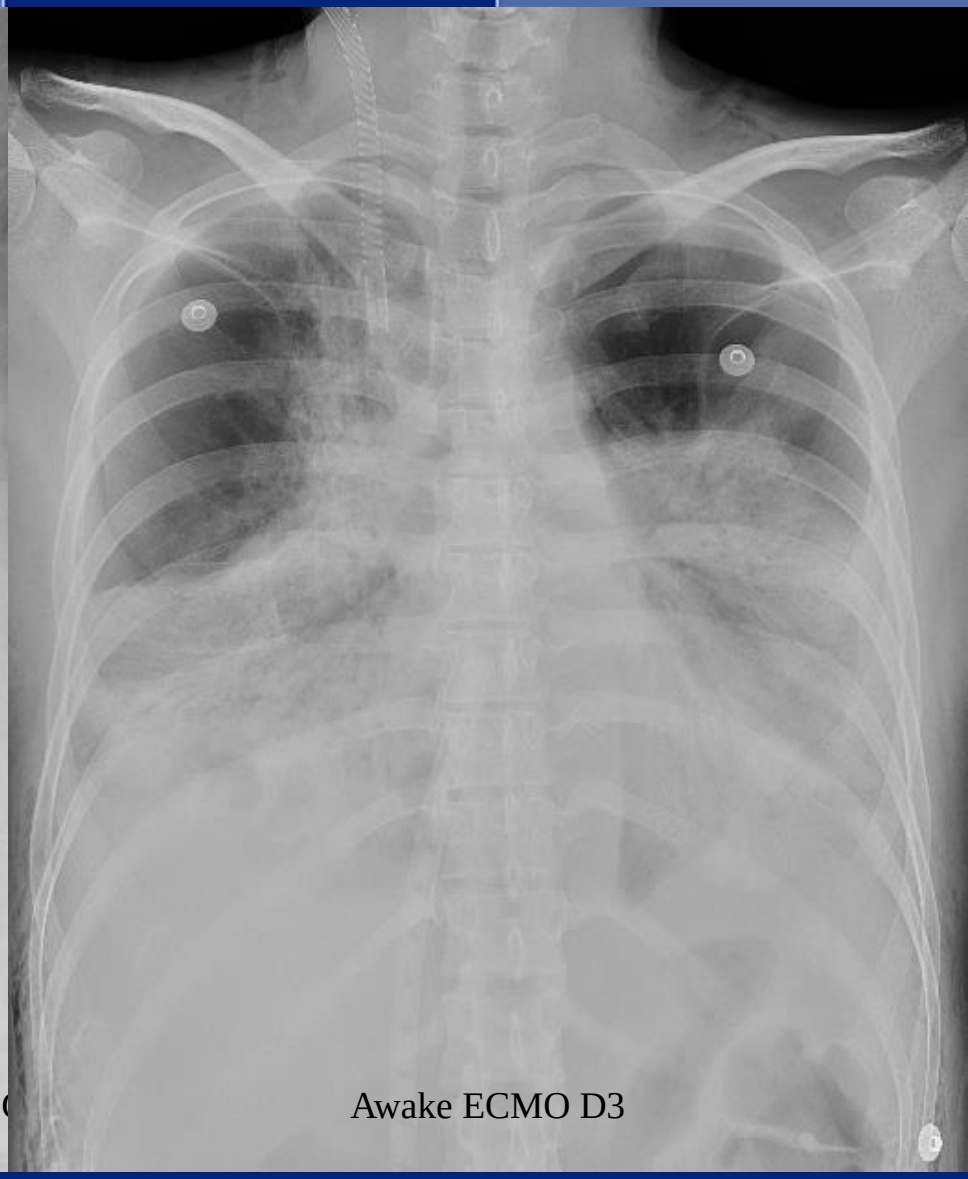
Resolution of Pneumomediastinum



Awake E

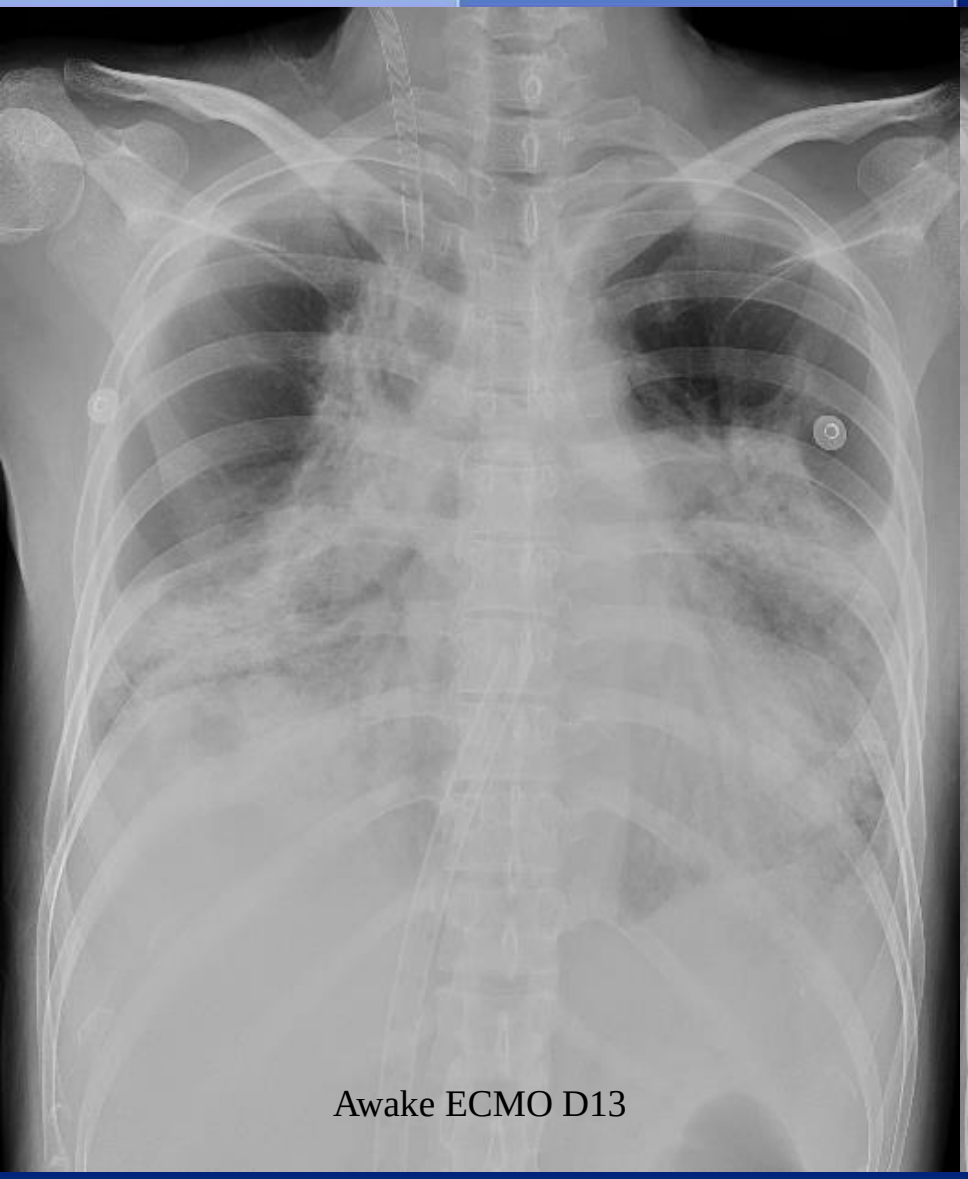


Awake E

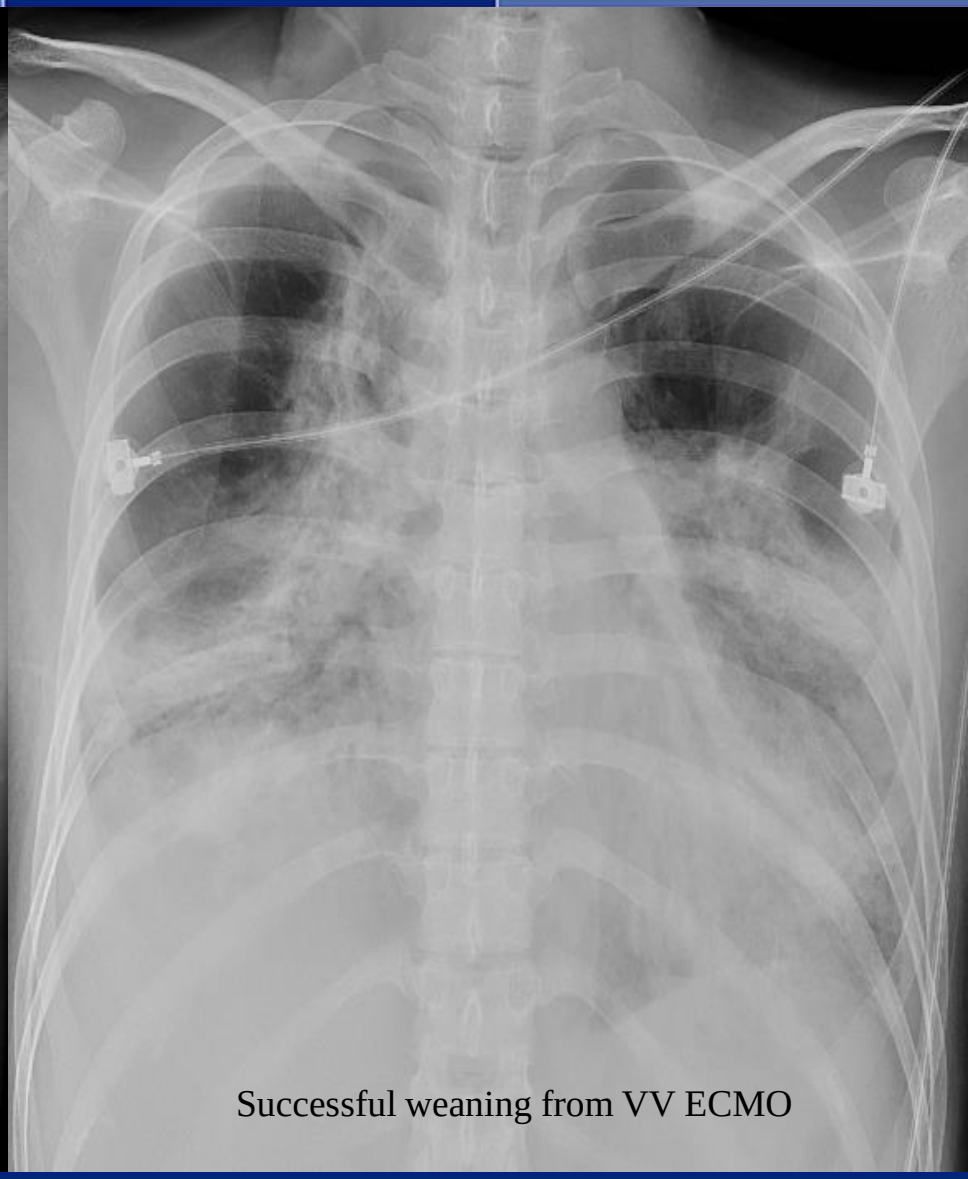


Awake ECMO D3

Weaning from VV ECMO

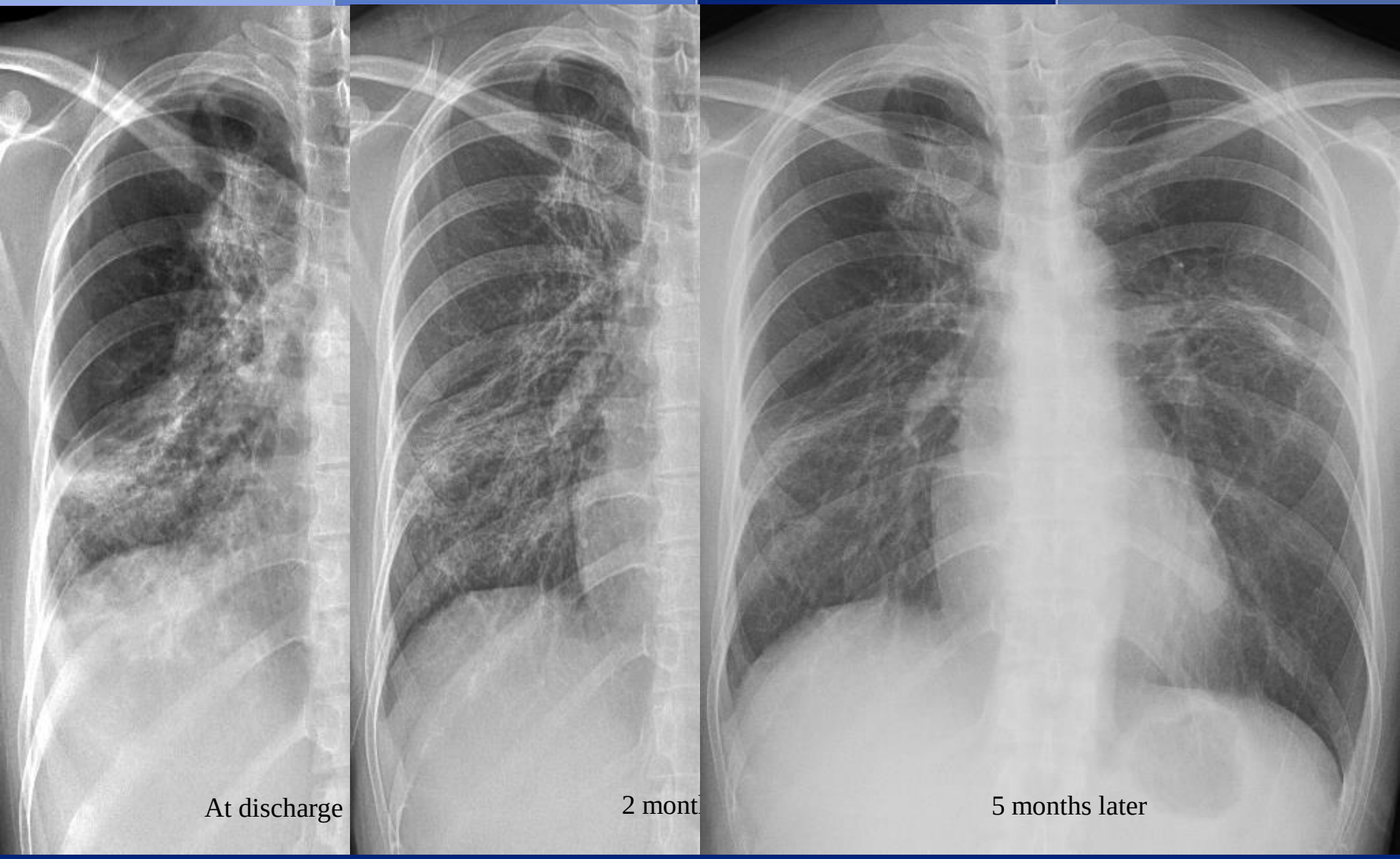


Awake ECMO D13



Successful weaning from VV ECMO

Regeneration of Injured Lung



ECMO instead of Invasive MV

- Single-center, uncontrolled pilot trial designed to assess the feasibility of VV ECMO in awake, non-intubated, spontaneously breathing patients with ARDS

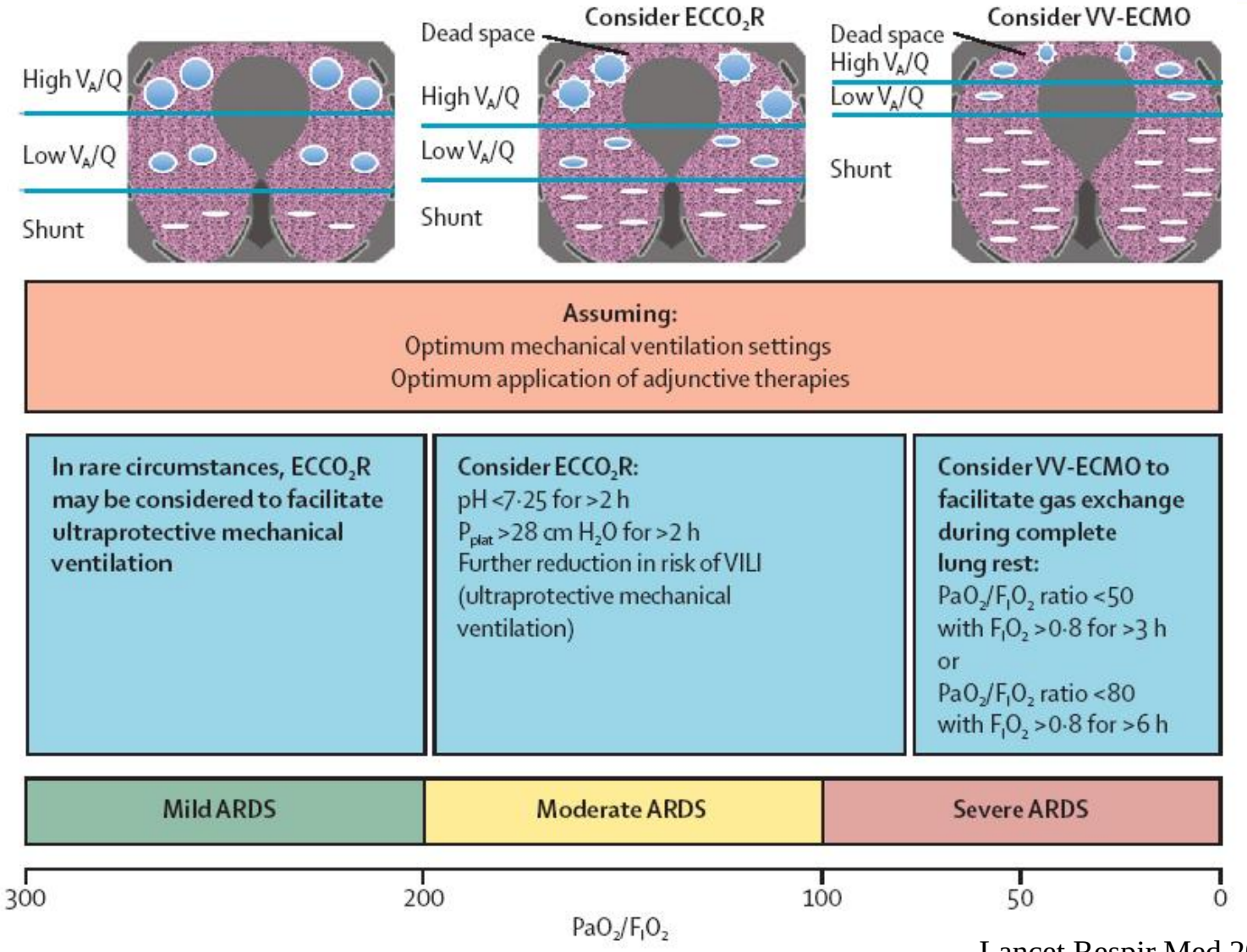
Table 1 Patient characteristics and outcomes

Patient	Sex	Age (years)	Cause of ARDS	Underlying disease	Last measurements before ECMO			ECMO duration (days)	Invasive ventilation	Duration ICU stay (days)	Last status
					FiO_2	PaO_2/FiO_2 (mmHg)	MV (l/min)				
1	M	60	Pneumonia (unidentified organism)	AML	0.8	82	19.7	10	No	13	Alive, discharged from hospital
2	M	56	Pneumonia (unidentified organism)	BLTx	0.9	100	28.0	8	Yes	50	Alive, discharged from hospital
3	M	72	Pneumonia (unidentified organism)	None	1.0	80	18.2	4	Yes	14	Died
4	F	59	Pneumonia (unidentified organism)	ALL	1.0	61	16.5	5	No	7	Alive, discharged from hospital
5	M	53	Pneumonia (*Pneumocystis jirovecii*)	AIDS	1.0	87	24.6	7	No	10	Alive, discharged from hospital
6	M	62	Pneumonia influenza A (H1N1)	None	1.0	51	22.1	27	Yes	28	Died

ARDS denotes acute respiratory distress syndrome, *AML* acute myelogenous leukemia, *ALL* acute lymphatic leukemia, *BLTx* bilateral lung transplantation, *AIDS* acquired immunodeficiency syndrome, *ICU* intensive care unit, *ECMO* extracorporeal membrane oxygenation, *MV* minute ventilation, *NIV* noninvasive ventilation

Intensive Care Med 2013;39:2056

Possible Clinical Criteria for ECMO



Lancet Respir Med 2014;2:154

Feasibility of ECCO2R to Enhance LPV

SUPERNOVA Trial (N = 95)

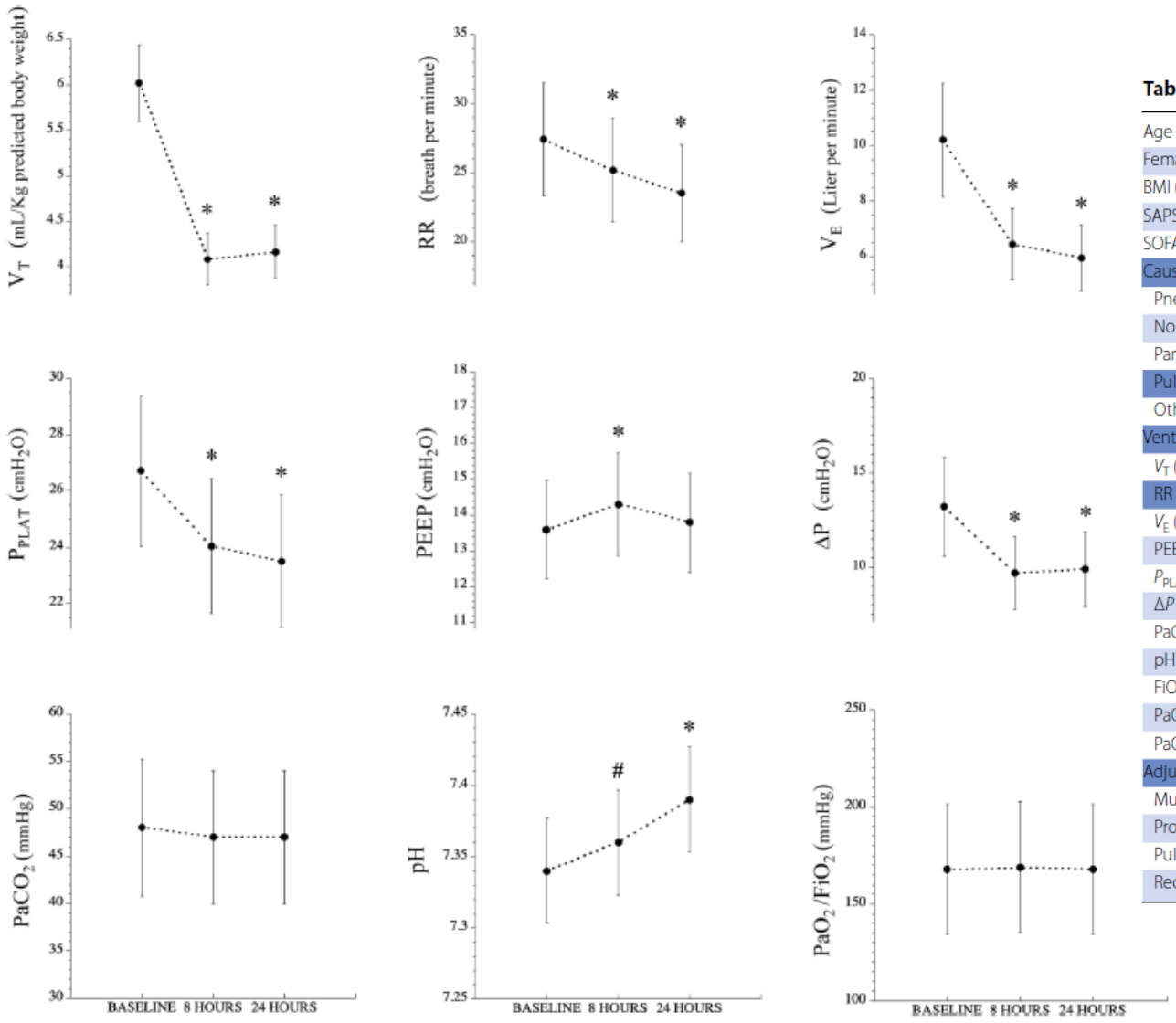


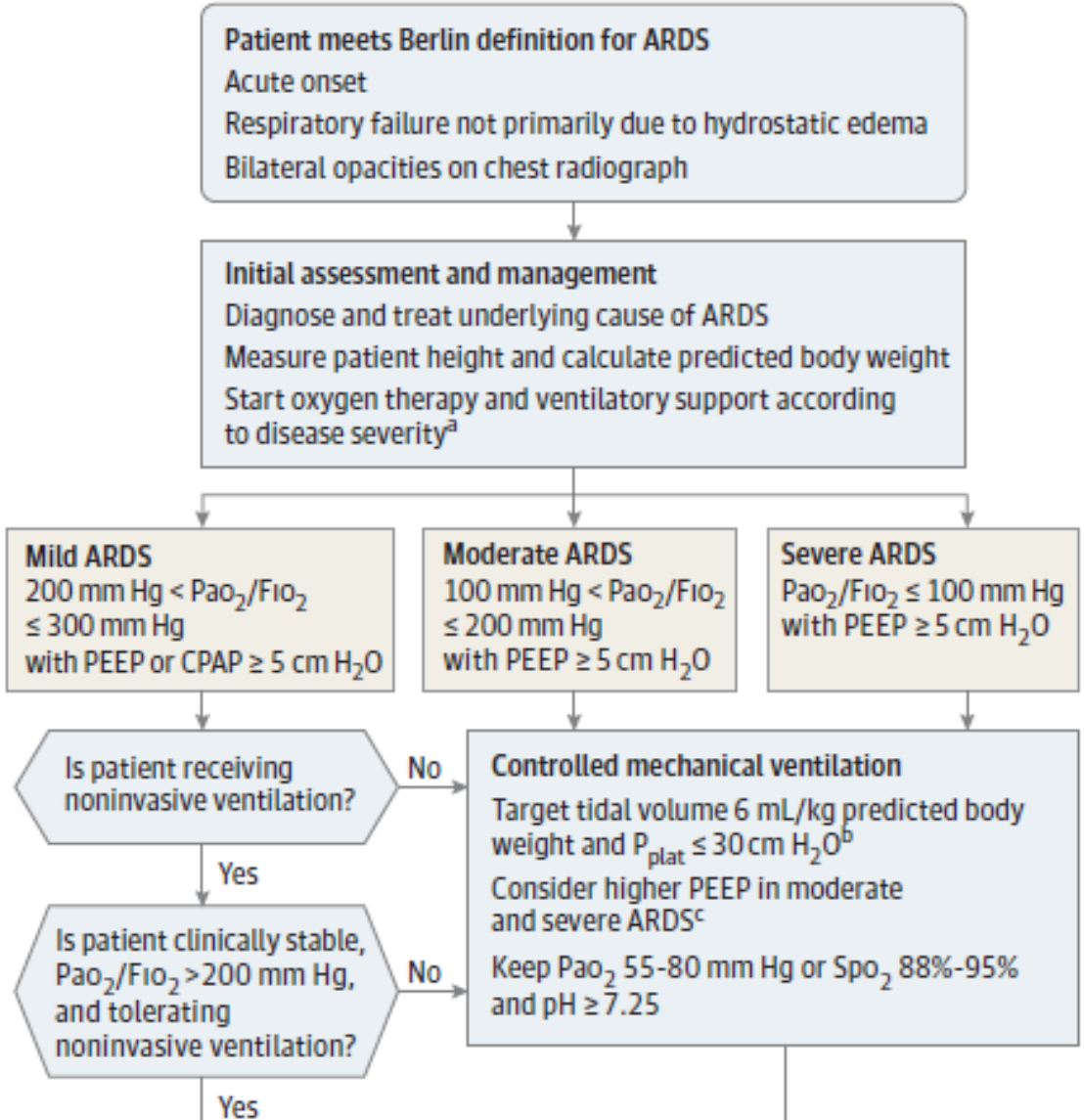
Table 1 Characteristics of patients at study inclusion

Age (years)	60.2 ± 14.0
Female (*n*, %)	31 (32.6%)
BMI (kg/m^2)	29.2 ± 8.79
SAPS II	45.9 ± 15.5
SOFA score	7.42 ± 3.22
Cause of ARDS (*n*, %)	
Pneumonia	78 (82.1%)
Non-pulmonary sepsis	3 (3.2%)
Pancreatitis	2 (2.1%)
Pulmonary contusion	2 (2.1%)
Other	10 (10.5%)
Ventilatory settings	
V_T (mL/kg)	6.0 ± 0.2
RR (breaths/min)	27.3 ± 4.8
V_E (L/min)	10.2 ± 2.3
PEEP (cmH_2O)	15.5 [10.0;16.0]
P_{PLAT} (breaths/min)	26.6 ± 3.0
ΔP (cmH_2O)	13.2 ± 4.3
$PaCO_2$ (mmHg)	47.8 ± 9.4
pH	7.34 ± 0.08
FiO_2	0.57 [0.50;0.70]
PaO_2 (mmHg)	101.2 ± 34.5
PaO_2/FiO_2	173 ± 61
Adjunctive treatments before inclusion (*n*, %)	
Muscle paralysis	80 (84.2%)
Prone position	23 (24.2%)
Pulmonary vasodilator	8 (8.42%)
Recruitment maneuvers	26 (27.4%)

Intensive Care Med 2019 (in press)

Treatment Algorithm for ARDS

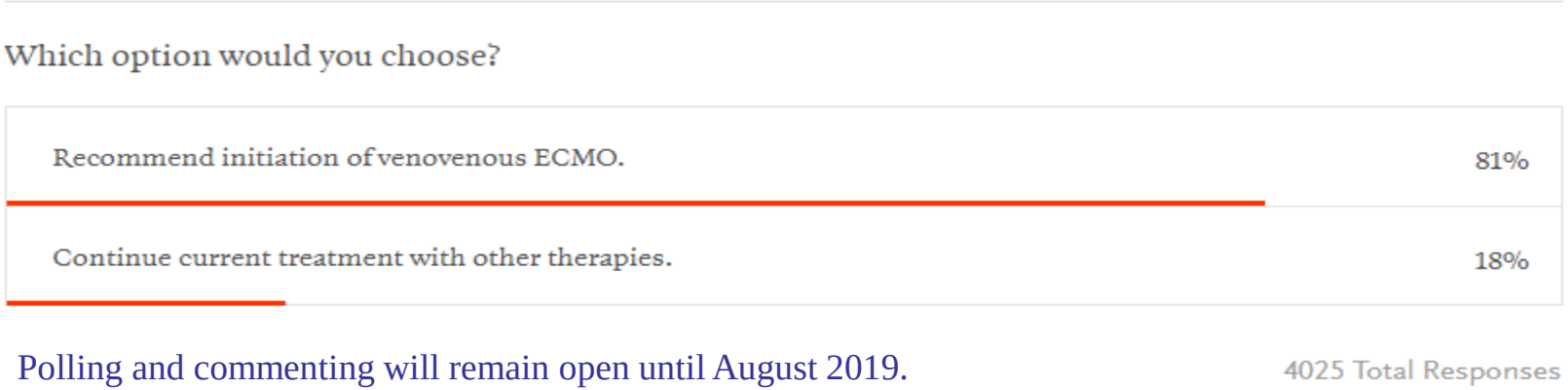
Recent Recommendation



MA 2018;319:698

Interim Analysis of Polling Results
Interactive Medical Case at NEJM

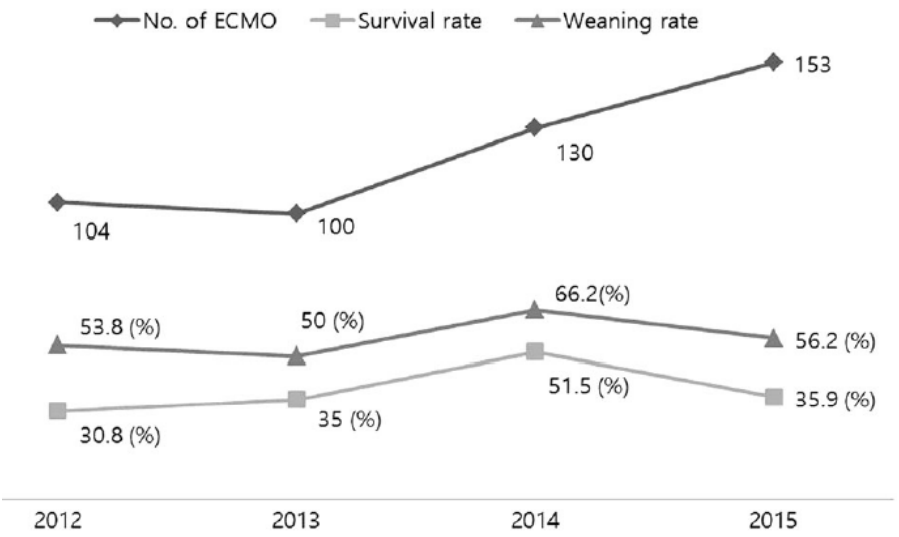
- During the **first 3 weeks of polling**, 3492 readers from 107 countries voted. The largest percentage of votes was received from the United States (43.2% [1507 votes]), followed by the United Kingdom (4.4% [153]), Australia (4.1% [142]), and Germany (4.0% [137]).
- The majority of voters (82.2% [2870]) favored initiating venovenous ECMO. Support for ECMO was shared across all regions of the globe, with 81.2% of voters from the United States and 82.9% of voters from the rest of the world voting in favor of initiating ECMO.

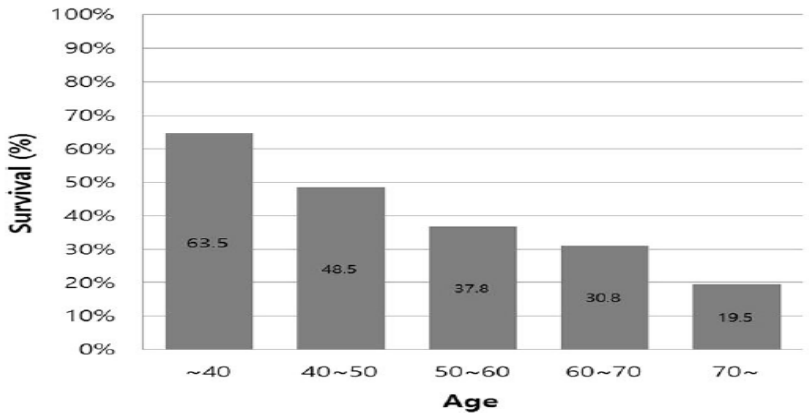


Polling and commenting will remain open until August 2019.

Korean Perspective
Retrospective Data Registry from 16 Hospitals

Variable	Total ($n = 487$)
Ventilation parameters	
PaO_2/FiO_2	65 (53, 90)
FiO_2	100 (90, 100)
PEEP (cmH_2O)	10 (6, 12)
PIP (cmH_2O)	28 (24, 32)
Tidal volume (ml/kg)	7 (6, 9)
Driving pressure (cmH_2O)	18 (15, 24)
Minute ventilation (L/min)	9.6 (7.4, 12.4)
Interval MV–ECMO (days)	1 (0, 5)
ECMO duration (days)	8 (4, 18)
Hospital stay (days)	35 (18, 61)
Tracheostomy	199 (41.8)
Weaning rate	278 (57.1)
Survival rate	189 (38.8)





Crit Care 2019;23:1

Adverse Events during ECLS

Event	Rate
	%
Directly related to the ECMO circuit	
Oxygenator failure	17.5
Blood clots	
Oxygenator	12.2
Other circuit	17.8
Cannula-related problems	8.4
Other mechanical complications	7.9
Not directly related to the ECMO circuit†	
Bleeding	
Surgical-site bleeding	19.0
Cannulation-site bleeding	17.1
Pulmonary hemorrhage	8.1
Gastrointestinal hemorrhage	5.1
Intracranial hemorrhage	3.8
Hemolysis	6.9
Disseminated intravascular coagulation	3.7
Culture-confirmed infection at any site (related or unrelated to ECMO)‡	21.3

$ECCO_2R$-related adverse events	Patients experiencing $ECCO_2R$-related adverse events, *n* (%)
Mechanical	
Membrane lung clotting	13 (14)
Leading to circuit change	6 (6)
Leading to $ECCO_2R$ discontinuation	7 (7)
Pump malfunction	3 (3)
Catheter displacement	2 (2)
Clinical	
Hemolysis	11 (12)
Bleeding	13 (14)
Related to cannula insertion	3 (3)
At cannula site	7 (7)
Significant	6 (6)
Infectious complications	2 (2)
Thrombocytopenia	12 (13)
Hypofibrinogenemia	2 (2)

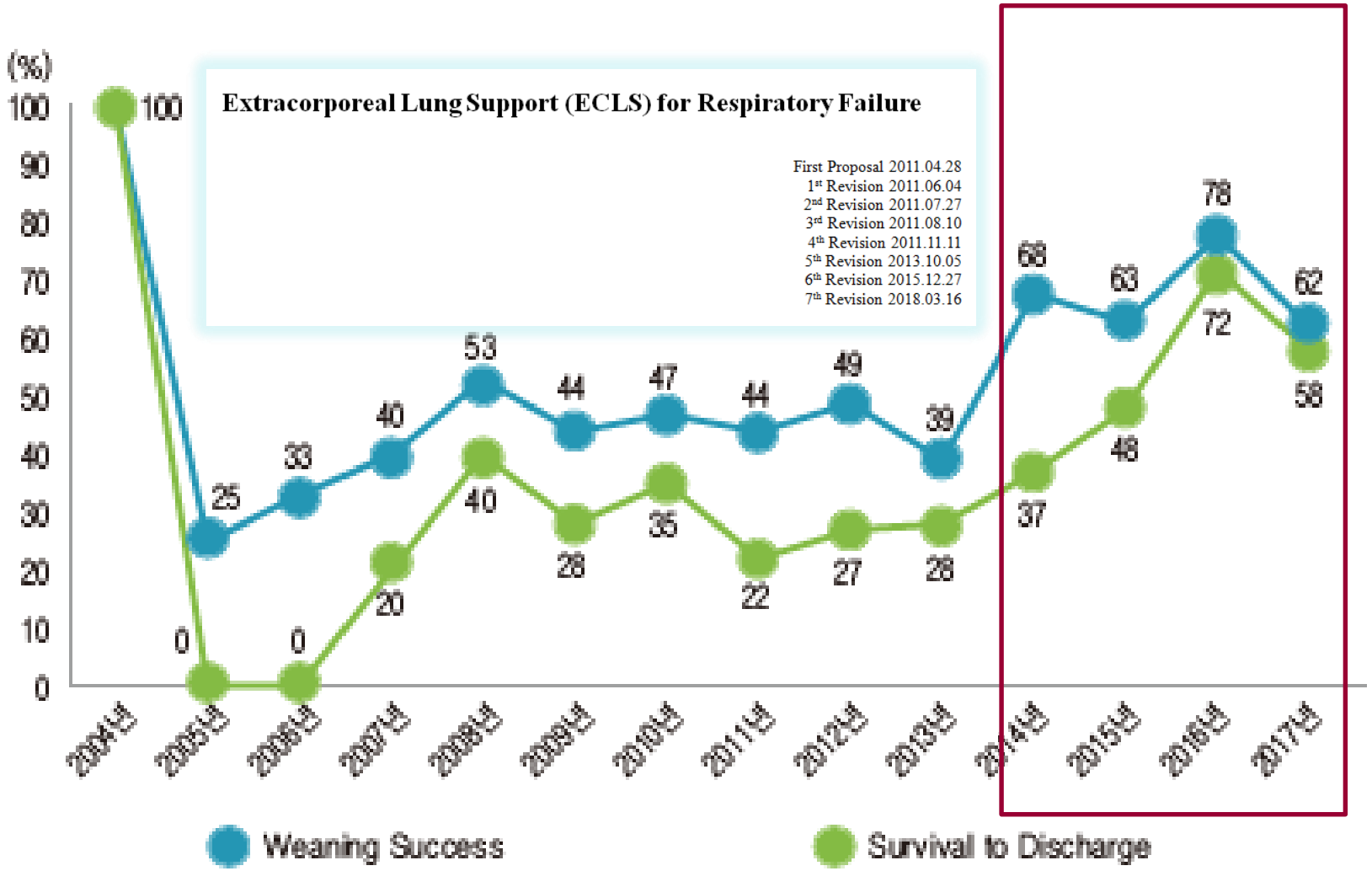
$ECCO_2R$ extracorporeal carbon dioxide removal. *Hemolysis*: serum free hemoglobin ≥ 100 mg/L or hematocrit reduction not related to hemorrhage or other causes of blood loss, jaundice, hemoglobinuria, impaired renal function; *significant bleeding*: any bleeding event requiring administration of 1 unit of packed red cells; *thrombocytopenia*: platelet count below 50,000 per microliter; *hypofibrinogenemia*: fibrinogen < 1.5 g/L

N Engl J Med 2011;365:1905

Intensive Care Med 2019 (in press)

Outcome of VV ECMO in SMC

SMC ECMO Team since 2014



Effect of Multidisciplinary ECMO Team

SMC Experience

	Pre-ECMO team period ($n = 70$)	Post-ECMO team period ($n = 46$)	*P* value
Adverse events during ECMO			
ECMO-related complications			
Cannula	23 (32.9)	7 (15.2)	0.034
Malposition requiring repositioning	21	5	
Vessel perforation	1	0	
Arterial cannulation	1	0	
Accidental decannulation	0	2	
Other	11 (15.7)	11 (23.9)	0.271
Patient complications			
Hematological	20 (28.6)	10 (21.7)	0.411
Neurological	9 (12.9)	1 (2.2)	0.086
Cardiovascular[a]	62 (88.6)	30 (65.2)	0.002
Inotrope or vasopressor use	51	30	
Myocardial stunning	3	0	
Arrhythmia	19	5	
Cardiac tamponade	1	0	
Cardiac arrest	10	1	
Pulmonary	23 (32.9)	15 (32.6)	0.978
Renal	36 (51.4)	23 (50.0)	0.880
Infection	36 (51.4)	19 (41.3)	0.285

Ann Intensive Care 2018;8:31

Proposal of Early ECMO for ARDS