Early ECMO is better than conventional MV in patients with ARDS: CON

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The timing to initiate extracorporeal membrane oxygenation in pH1N1 acute respiratory distress syndrome.

Table 1. Patients treated in the ECMO center

Age (Years)	Sex	Duration of Ventilation Before ECMO	Time on ECMO	Outcome
39	Female	30 Days	17 Days	Weaned from ECMO; died 4 days later of sepsis
30	Male	14 Days	14 Days	Died of sepsis
38	Male	2 Days	12 Days	Survived
30[a]	Female	>7 Days	14 Days	Died
39	Female Post partum	21 Days	21 Days	Died of sepsis waiting for lung transplant

ECMO, extracorporeal membrane oxygenation.
[a]No exact data on pre-ECMO period.

Critical Care Medicine. 38(12):2427-2428, December 2010.

The timing to initiate extracorporeal membrane oxygenation in pH1N1 acute respiratory distress syndrome.

- We would suggest to change the time limit for initiation of ECMO in pH1N1 to <5 days.

- Use of ECMO should be a "rescue therapy" rather than a "desperate therapy."

Critical Care Medicine. 38(12):2427-2428, December 2010.

H1N1 Specific Supplements to the ELSO General Guidelines

- Indications:
- An estimate of 50% mortality risk is requirement for FiO2 0.8 and/or requirement for 2 vasoactive drugs.
- An estimate of 80% mortality risk (indication for cannulation) is P/F under 80 on FiO2 1.0 and PPlat or HHOV P over 30 cmH2O, and/or ongoing requirement for vasoactive drugs.
- All this despite optimal treatment, but **in H1N1 disease progression can be very fast (12-24hours to arrest), so have a low threshold for" failure of optimal Rx.**

- **Survival is approximately**
  - **72% for patients on ECMO within 6 days of intubation,**
  - **30% for patients on ECMO 7 or more days after intubation.**

November 2009

Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome (EOLIA)

Inclusion criteria :

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.

Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome (EOLIA)

Exclusion criteria :

1. **<u>Intubation and mechanical ventilation for ≥ 7 days</u>**
2. Age < 18 years
3. Pregnancy
4. Weight > 1 kg/cm or BMI > 45 kg/m²
5. Chronic respiratory insufficiency treated with oxygen therapy of long duration and/or long-term respiratory assistance
6. Cardiac failure requiring veno-arterial ECMO
7. Previous history of heparin-induced thrombopenia
8. Malignancy with fatal prognosis within 5 years
9. Patient moribund on the day of randomization or has a SAPS II > 90
10. Non drug-induced coma following cardiac arrest
11. Irreversible neurological pathology, for example, flat EEG tracing cerebral herniation…
12. Decision to limit therapeutic interventions
13. ECMO cannula access to femoral vein or jugular vein impossible.
14. CardioHelp device not immediately available

The impact of mechanical ventilation time before initiation of extracorporeal life support on survival in pediatric respiratory failure: A review of the extracorporeal life support registry*

Table 4. Multivariable regression analysis identifying factors independently associated with survival to hospital discharge

Pre-ECLS Variable Considered	Odds Ratio	95% Confidence Interval	*p*
Pre-ECLS mechanical ventilation time			
>7–10 days vs. 0–7 days	0.78	0.51–1.19	.25
>10–14 days vs. 0–7 days	0.70	0.44–1.10	.12
>14 days vs. 0–7 days	0.32	0.20–0.51	<.001
Pre-ECLS cardiac arrest	0.56	0.40–0.80	.001
Oxygenation index per 10 units	0.95	0.92–0.98	.002
pH per 0.1 units	1.15	1.09–1.23	<.001
Diagnosis			
"Other" vs. sepsis	2.24	1.44–3.42	<.001
Viral pneumonia vs. sepsis	3.14	1.92–5.14	<.001

The impact of mechanical ventilation time before initiation of extracorporeal life support on survival in pediatric respiratory failure: A review of the extracorporeal life support registry*

- There was a clear relationship between the number of mechanical ventilation days before the initiation of extracorporeal life support and survival.

- However; there was no statistically significant decrease in survival until >14 days of pre-extracorporeal life support ventilation was reached regardless of underlying diagnosis.

- **We found no evidence to suggest that prolonged mechanical ventilation should be considered as a contraindication to extracorporeal life support in children with respiratory failure before 14 days.**

Extracorporeal membrane oxygenation in adult patients with severe acute respiratory failure

Before September 2010 (100 pats)

Table 1

Inclusion criteria (before September 2010) (Multiply the value in kPa with 7.5 to convert in mmHg).

- Acute potentially reversible and potentially fatal respiratory failure.

Fast entry:

- $PaO_2 < 6.7$ kPa for more than 2 h with $FiO_2 = 1.0$ and PEEP > 10 cm H_2O.

Slow entry:

- $PaO_2 < 6.7$ kPa in > 24 h with $FiO_2 > 0.6$ and PEEP > 10 cm H_2O.

FiO_2, fraction of inspired oxygen; PaO_2, partial arterial oxygen concentration; PEEP, positive end expiratory

Table 2

Exclusion criteria (before September 2010).

- Mechanical ventilator therapy:

CNS, central nervous system; FiO_2, fraction of inspired oxygen.

After September 2010 (24 pts)

Table 3

Indications and contraindications after September 2010 (Multiply the value in kPa with 7.5 to convert in mmHg).

Indications

1. $PaO_2/FiO_2 < 10.7$ kPa on $FiO_2 > 90\%$ and Murray score 3–4
2. $PaCO_2 > 10.7$ kPa because of asthma or permissive hypercapnia (plateau ≤ 30 cm H_2O).
3. Severe air leak syndromes

Contraindications

Contraindications

There are no absolute contraindications to ECLS. Each patient is considered individually with respect to risks and benefits.

- Mechanical ventilator therapy:
  - Paediatric > 7 days and FiO2 1.0 > 3 days
  - Adults > 5 days and FiO2 1.0 > 3 days

Acta Anaesthesiol Scand 2013; ***57: 303–311***

Extracorporeal membrane oxygenation in adult patients with severe acute respiratory failure

Table 6

Fatal complications on and after extracorporeal membrane oxygenation (ECMO).

	Before or during ECMO	After ECMO
New cerebral infarction with haemorrhage	9	2
Sepsis	7	0
Liver failure/splanchnic ischaemia	3	1
Unable to restore pulmonary function	4	4
Failure to establish ECMO	2	0
Displaced cannulas	2	0
Cardiac death	0	1
Total pts 124	**37**	**8**

Acta Anaesthesiol Scand 2013; ***57: 303–311***

Extracorporeal membrane oxygenation in adult patients with severe acute respiratory failure

Table 4

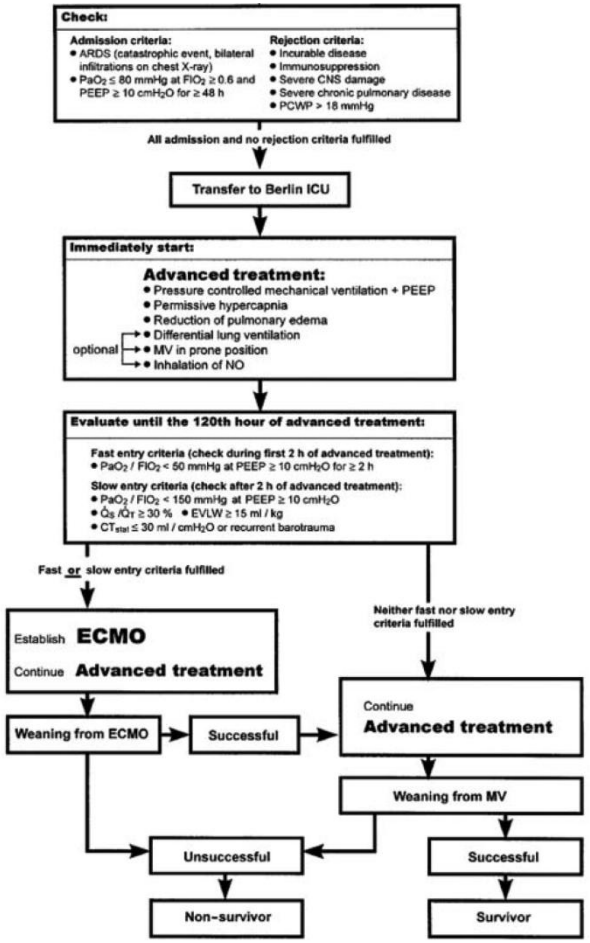
Age, gender, and primary and secondary cause of ARDS, acute lung injury score (Murray), simplified acute physiology score II (SAPS II) and sequential organ failure assessment (SOFA) scores. Numbers are in mean, or median and (range).

Diagnosis	Number (F/M) Percent of total	Mean age (range)	Number discharged from ICU (%)	Murray score Median (range)	SAPS II score Median (range)	SOFA score Median (range)
Primary lung injury	*n* = 91 (65%)		66/91 (73)			
Pneumonia bacterial	54 (28/26)	48 (17–66)	40/54 (74)	3.25 (2.5–4.0)	53 (19–81)	14 (7–20)
Pneumonia viral	25 (8/17)	46 (18–65)	17/25 (68)	3.75 (3.0–4.0)	42 (21–63)	12 (7–22)
Aspiration	83/5	40 (27–67)	6/8 (75)	3.75 (3.0–4.0)	47 (28–61)	11 (9–16)
Wegner's granuloma	41/3	40.5 (18–64)	3/4 (75)	3.5 (3.5–3.75)	55 (30–80)	9 (6–21)
Secondary lung injury	*n* = 33 (35%)		22/33 (67)			
Trauma	18 3/15	30.2 (20–59)	13/18 (72)	3.5 (2.5–4)	40 (24–67)	12 (6–15)
Sepsis	15 6/9	38.8 (16–67)	9/15 (60)	3.75 (3.5–4.0)	60 (19–74)	15 (10–23)
Total	124 49/75	41.8 (16–67)	88/124 (71)	3.7 (2.5–4.0)	50 (19–81)	13 (5–22)

SAPS-II, SOFA and Murray scores predicted the outcome.

Acta Anaesthesiol Scand 2013; ***57: 303–311***

High survival rate in 122 ARDS patients managed according to a clinical algorithm including extracorporeal membrane oxygenation



Intensive Care Med (1997) 23: 819–835

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Check:

Admission criteria:
- ARDS (catastrophic event, bilateral infiltrations on chest X-ray)
- $PaO_2 \leq 80$ mmHg at $FIO_2 \geq 0.6$ and PEEP ≥ 10 cmH_2O for ≥ 48 h

Rejection criteria:
- Incurable disease
- Immunosuppression
- Severe CNS damage
- Severe chronic pulmonary disease
- PCWP > 18 mmHg

- $PaO_2 \leq 80$ mmHg at $FIO_2 \geq 0.6$ and PEEP ≥ 10 cmH_2O for ≥ 48 h

All admission and no rejection criteria fulfilled

Transfer to Berlin ICU

Immediately start:

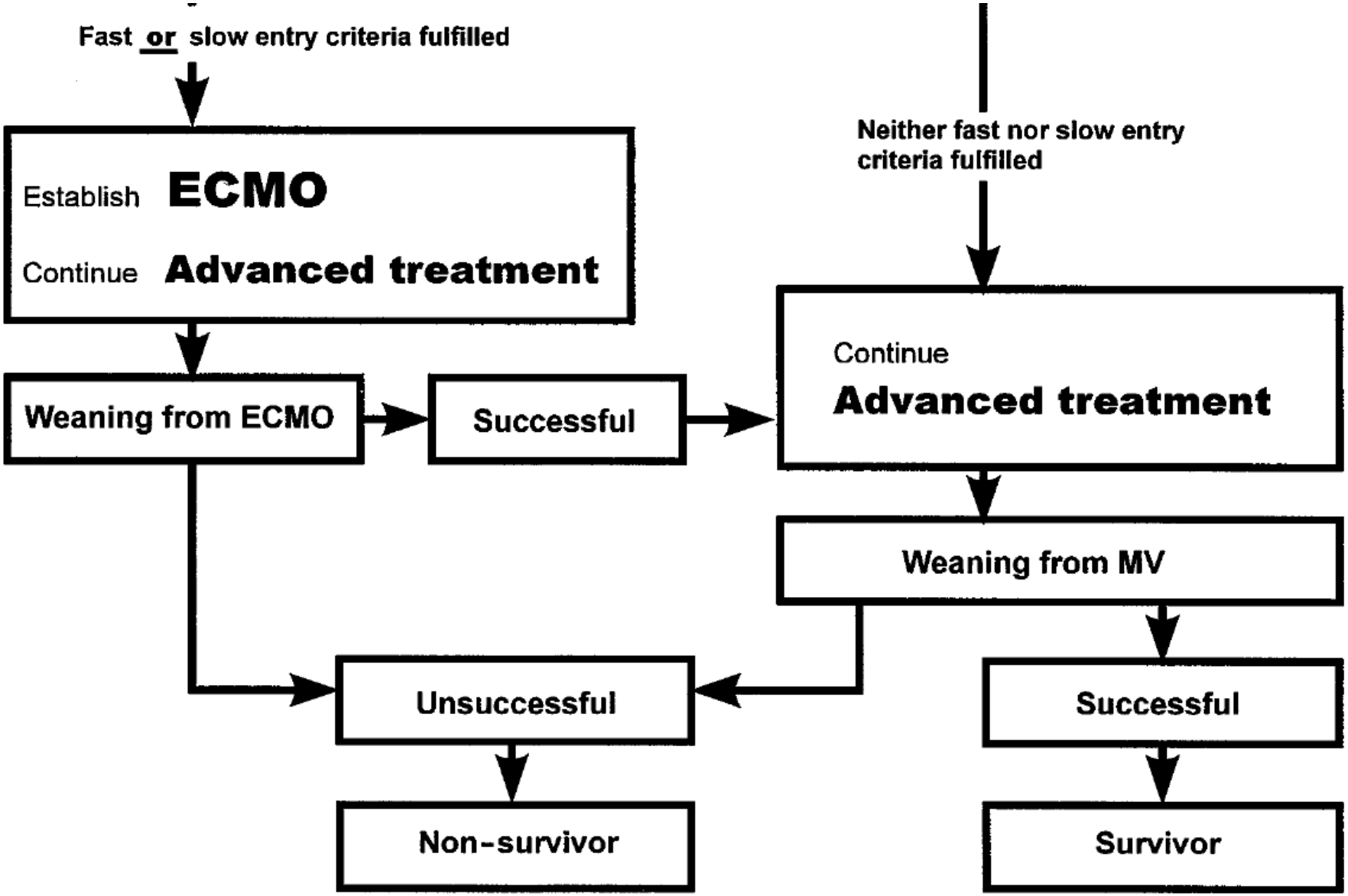
Advanced treatment:
- Pressure controlled mechanical ventilation + PEEP
- Permissive hypercapnia
- Reduction of pulmonary edema

optional
- Differential lung ventilation
- MV in prone position
- Inhalation of NO

Evaluate until the 120th hour of advanced treatment:

Fast entry criteria (check during first 2 h of advanced treatment):
- $PaO_2 / FIO_2 < 50$ mmHg at PEEP ≥ 10 cmH_2O for ≥ 2 h

Slow entry criteria (check after 2 h of advanced treatment):
- $PaO_2 / FIO_2 < 150$ mmHg at PEEP ≥ 10 cmH_2O



Intensive Care Med (1997) 23: 819–835

High survival rate in 122 ARDS patients managed according to a clinical algorithm including extracorporeal membrane oxygenation

Table 1 Characteristics and outcome of 122 patients with ARDS (*n* number of patients, *AT-sine-ECMO* advanced treatment without ECMO)

Patient group[a]	*n*	Age [years]	Sex [male/ female]	MV before admission [days]	APACHE II score [points]	Murray score [points]	Compliance on admission [ml/cmH_2O]	PEEP on admission [cmH_2O]	Baro-trauma [*n*]	ICU stay Berlin [days]	Survived/ died [*n*]	Survival [%]
AT-sine-ECMO	73	33.3 ± 13.3	46 M 27	**9.7 ± 8.6**	15.7 ± 5.0	3.20 ± 0.29	34.4 ± 12.4	10.7 ± 2.7	29 no 44 yes	31.2 ± 17.1	65 S 8 D	**89**
ECMO treatment	49	31.5 ± 14.4	28 M 21	**12.8 ± 8.7**	7.9 ± 4.7	3.40 ± 0.26	26.7 ± 11.5	12.0 ± 3.0	5 no 44 yes	50.1 ± 36.0	27 S 22 D	**55**
p values		0.5834[b]	0.6443[c]	0.0131[b]	0.0100[b]	0.0001[b]	0.0002[b]	0.0101[b]	0.0008[c]	0.0016[b]	0.0000[c]	
ECMO slow entry	28	33.4 ± 13.0	14 M 14	**11.8 ± 6.6**	7.4 ± 4.3	3.38 ± 0.28	29.8 ± 13.0	12.3 ± 3.1	2 no 26 yes	52.9 ± 39.9	16 S 12 D	**57**
ECMO fast entry	21	29.0 ± 16.2	14 M 7	**14.1 ± 10.9**	4 ± 5.3	3.43 ± 0.23	22.6 ± 7.6	11.6 ± 2.9	3 no 18 yes	46.3 ± 30.4	11 S 10 D	**52**
p values		0.2981[b]	0.3816[c]		0.0134[b]	0.7656[b]	0.1034[b]	0.4857[b]	0.6392[d]	0.7695[b]	0.9669[c]	**75**
All patients	122	32.6 ± 13.7	74 M 48	**10.9 ± 8.7**	5.5 ± 5.0	3.29 ± 0.29	31.1 ± 12.6	11.3 ± 2.9	34 no 88 yes	38.8 ± 27.8	92 S 30 D	

Intensive Care Med (1997) 23: 819–835

Indications for ECMO include (ELSO 2012)

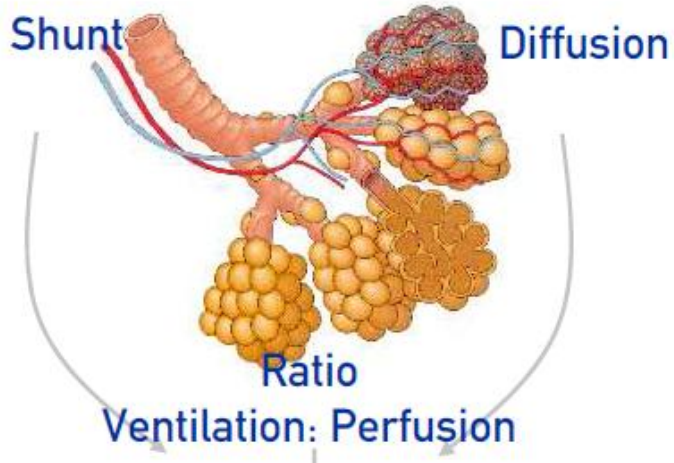
- **In hypoxic respiratory failure** due to any cause (primary or secondary) extracorporal life support (ECLS) **should be considered when the risk of mortality is 50%** (partial pressure of arterial oxygen for a given fraction of inspired oxygen (PaO_2/FiO_2) < 150 mm Hg on FiO_2 > 0.9, or Murray score 2 to 3 or greater) and is **indicated when the risk of mortality is 80% or greater** (80% mortality risk can be identified by a PaO_2/FiO_2 < 80 mm Hg on FiO_2 > 0.9, Murray score 3 to 4).
- **Carbon dioxide (CO_2) retention** due to asthma or permissive hypercapnia with a $PaCO_2$ > 80 mm Hg or inability to achieve safe inflation pressures (plateau pressure < 30 cm H_2O) is an indication for ECLS.
- **Severe air leak syndromes** are an indication for ECLS.

New Possibility

ALGORITHM INCLUDING ILA IN SEVERE ARDS

ACUTE RESPIRATORY FAILURE

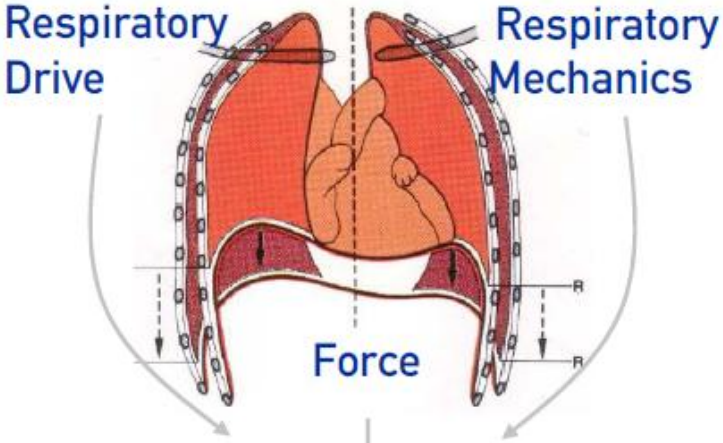
Lung failure:
Gas exchange disturbance



Hypoxemia

O_2-Supply

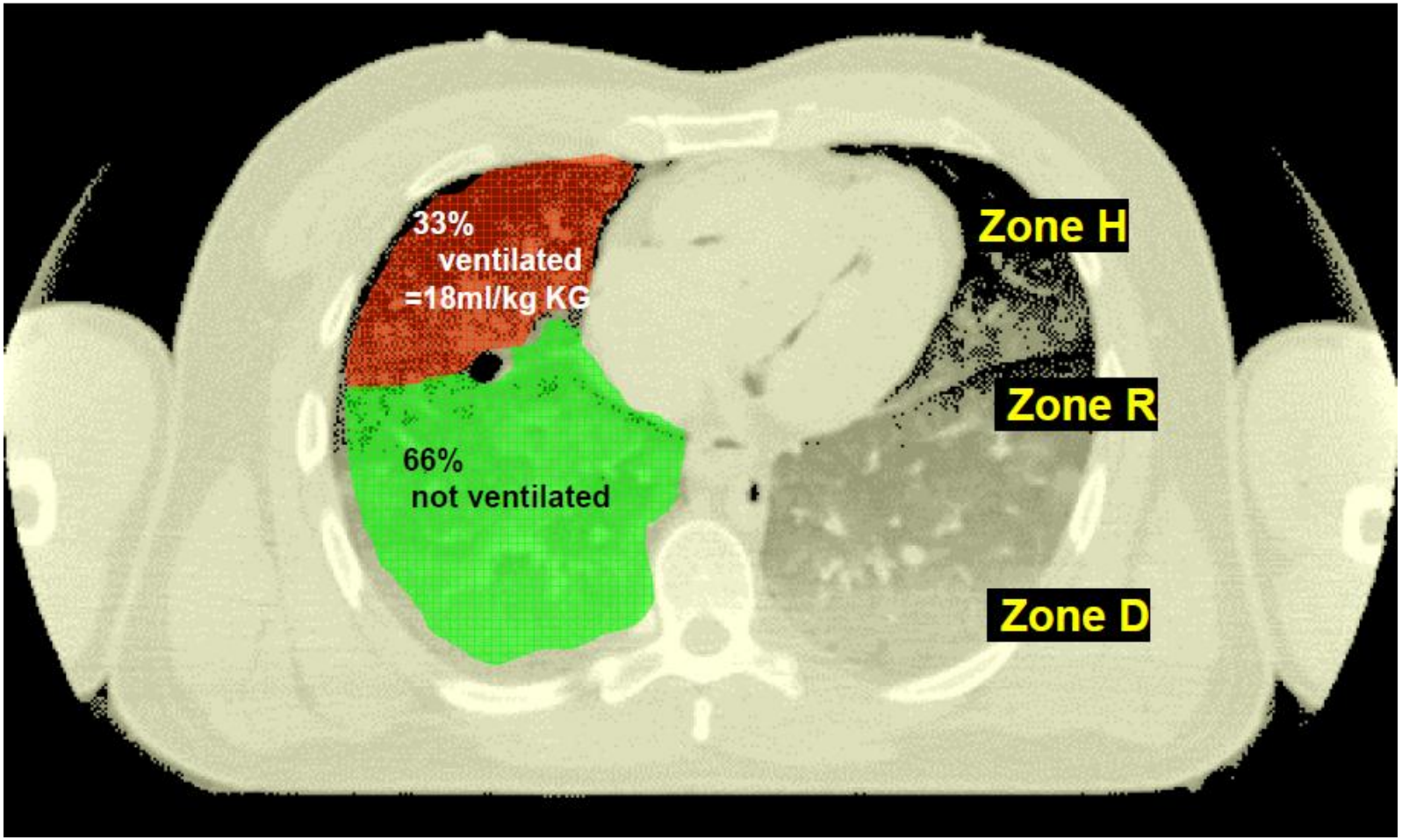
Breathing pump failure:
Ventilation disturbance



Hypercapnia

Mechanical ventilation

ALI/ARDS **„BABY LUNG“ – Vt 6ml/kgBW?**



Protective ventilation

Mechanical ventilation is always traumatic:

CT Scan Thorax: "one-third of patients experienced substantial tidal hyperinflation with tidal volumes of 6 ml/kg PBW" Terragni et al. Am J Resp Crit Care Med 2007;175:160-166

"[T]here is little evidence to support the safety of prolonged MV with P_{plat} as high as 30 to 35 cm H_2O."

Hager et al. Am J Resp Crit Care Med 2005;172:1241-1245

IN SUMMARY: Spontaneous breathing is the best protection!

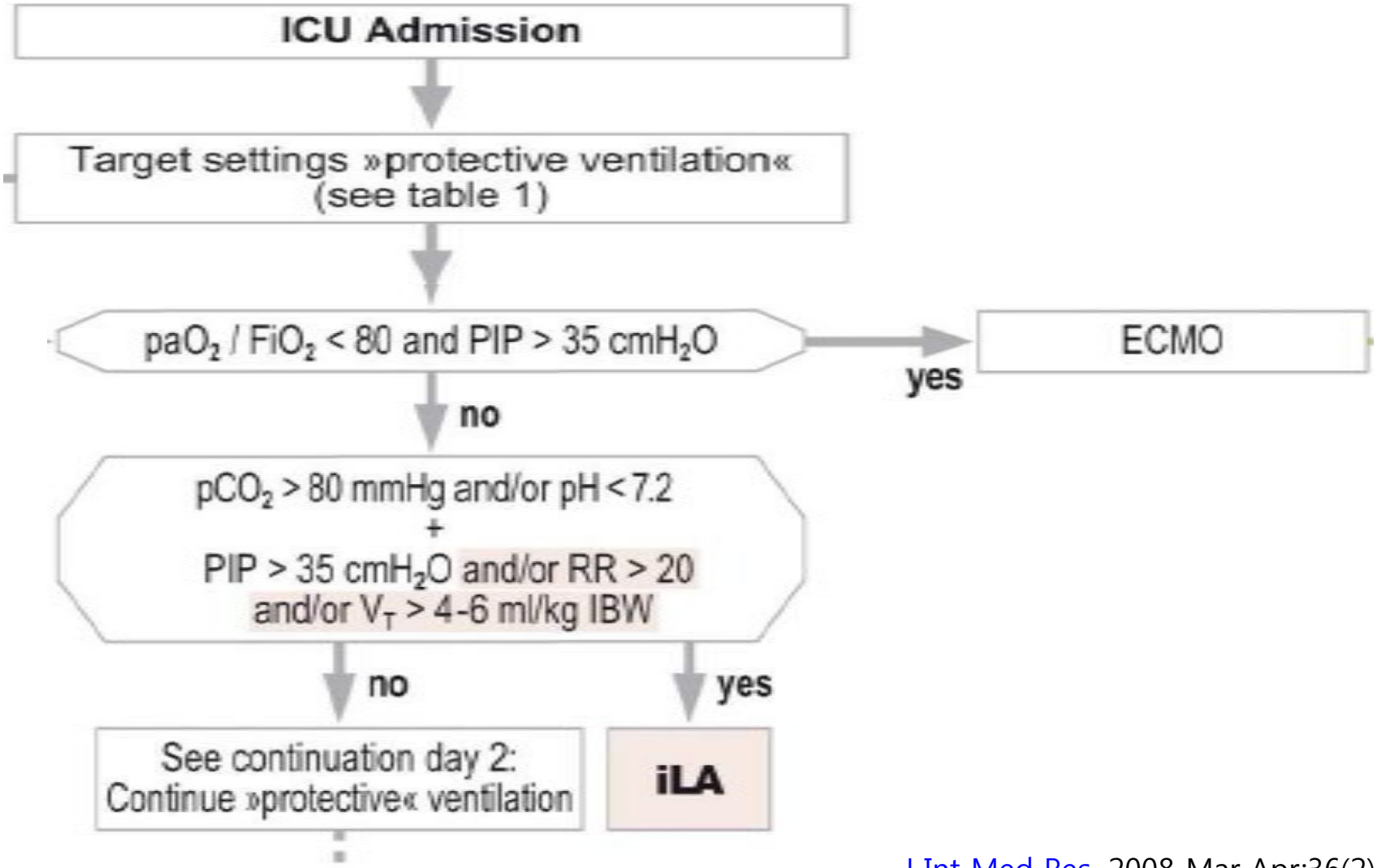
SUMMARY OF **„PROTECTIVE VENTILATION“**

- Spontaneous breathing when ever possible
- Small tidal volumes
- Low pressure amplitude
- Low inspiratory pressure
- High PEEP
- Permissive hypercapnia
- Low respiratory rate

- **Support !!**

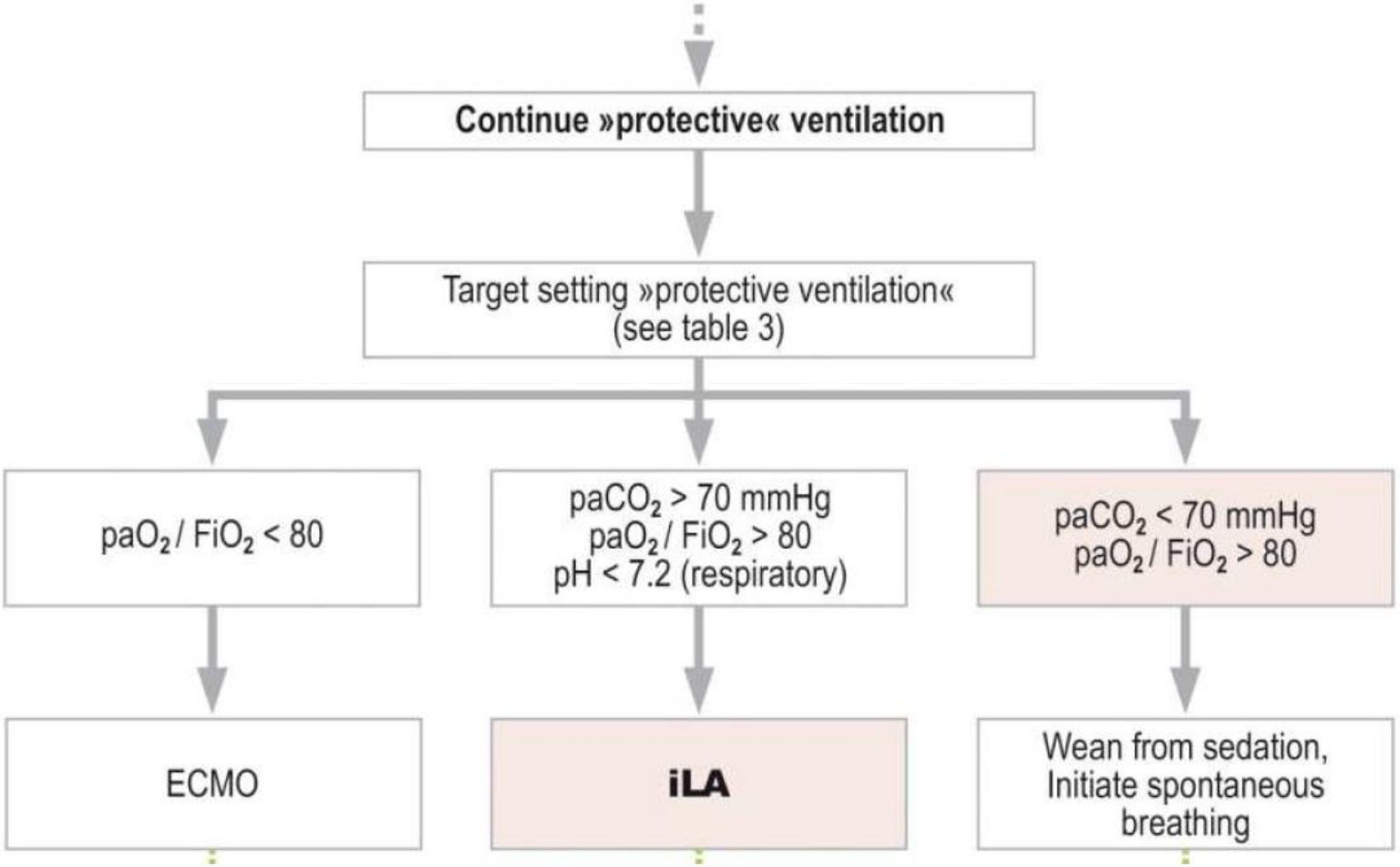
- Vt = 3 – 4 ml/kgIBW
- Δ P < 15 cmH2O
- PIP < 30 cmH2O
- Individual best level
- **No** (or pH $\geq$ 7,2)
- RR = 5 – 15 /min

ARDS ALGORITHM: FIRST 24 HOURS



J Int Med Res. 2008 Mar-Apr;36(2):211-21.

ARDS ALGORITHM: DAY 2



J Int Med Res. 2008 Mar-Apr;36(2):211-21.

ECMO 보험적용기준

기존의 치료법에 의해 교정되지 않는 중증 심부전 또는 **기존의 기계적 인공호흡기 치료로 생명유지가 불가능한 중증 급성 호흡부전 환자에서**, 심장 및 폐기능을 대치 또는 보조하여 전신 혈액 순환과 **조직의 적절한 산소화를 유지하기 위한 목적으로** 체외순환막형산화기(Extra Corporeal Membrane Oxygenator)를 이용한 체외순환을 시행할 수 있다.

다만, 이미 **진행된 다발성 장기부전으로 회복 가능성이 없는 경우**, **불가역적 중추신경 장애**, **지혈이 곤란한 출혈부위가 있어서 항응고요법의 절대적 금기증에 해당하는 경우, 말기 암환자 등 동 시술이 의의가 없다고 판단되는 경우에는 인정하지 않음.**

ILA 보험 적용기준(안)

기존의 인공호흡기 치료를 최적화하여 사용하여도 호전되지 않는 고이산화탄소혈증을 동반한 중증 급만성 호흡부전환자에서 pumpless arterio-venous membrance oxygenator를 사용한 체외막가스교환기를 시술할 수 있다.

조건

1) **인공호흡기유발 폐손상을 방지하기 위하여 , 고평부압(plateau pressure)을 30(~~35~~) cmH_2O이하로 유지시키면서, 일회호흡량(tidal volume)을 최대한 증가시켜도 70(~~80~~)mmHg 이상의 고이산화탄소혈증 또는(~~그리고~~) pH 7.2 미만의 호흡성 산증이 교정되지 않는 경우**

2) 시술 당시 환자는 혈역학적으로 안정되어 있어야 함(Cardiac Index가 3.0 L/min/m2이상 또는 **mean BP 65 mmHg 이상**)

다만, 이미 진행된 다발성 장기부전으로 회복 가능성이 없는 경우, 불가역적 중추신경 장애, 말기 암환자 등 동 시술이 의의가 없다고 판단되는 경우에는 인정하지 않음.

Conclusions

- Severe ARDS 치료에서 ECMO는 Rescue Tx로서 도움이 되며, indication 이 되는 경우에는 immediate start가 도움이 될수있다.

- 그러나 ECMO Tx는 well trained, well equipped state가 필수적이며, 합병증도 많은 highly invasive tx 임을 고려하여야 한다.

- ECMO 시작전의 MV 치료기간이 7일 이내여야 한다는 evidence는 확실치 않다(pandemic H1N1은 제외?).

- ECMO 치료를 고려하기 전에 protective ventilation strategy를 적용하는 것은 중요하다.

- Severe ARDS의 치료시 protective ventilation을 유지할 수 있는지 여부를 처음부터 계속 monitor 하면서, VILI를 피할 수 있는 ILA /ECMO 치료를 항상 적용할 수 있도록 준비하고 필요시에는 바로 적용하는 Algorithm에 따라 치료하는 것이 도움이 될 수 있다.