

ECMO: The best therapy for severe ARDS



Ashok Babu

Alan Hopeman Lectureship

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“DeMong Lung”

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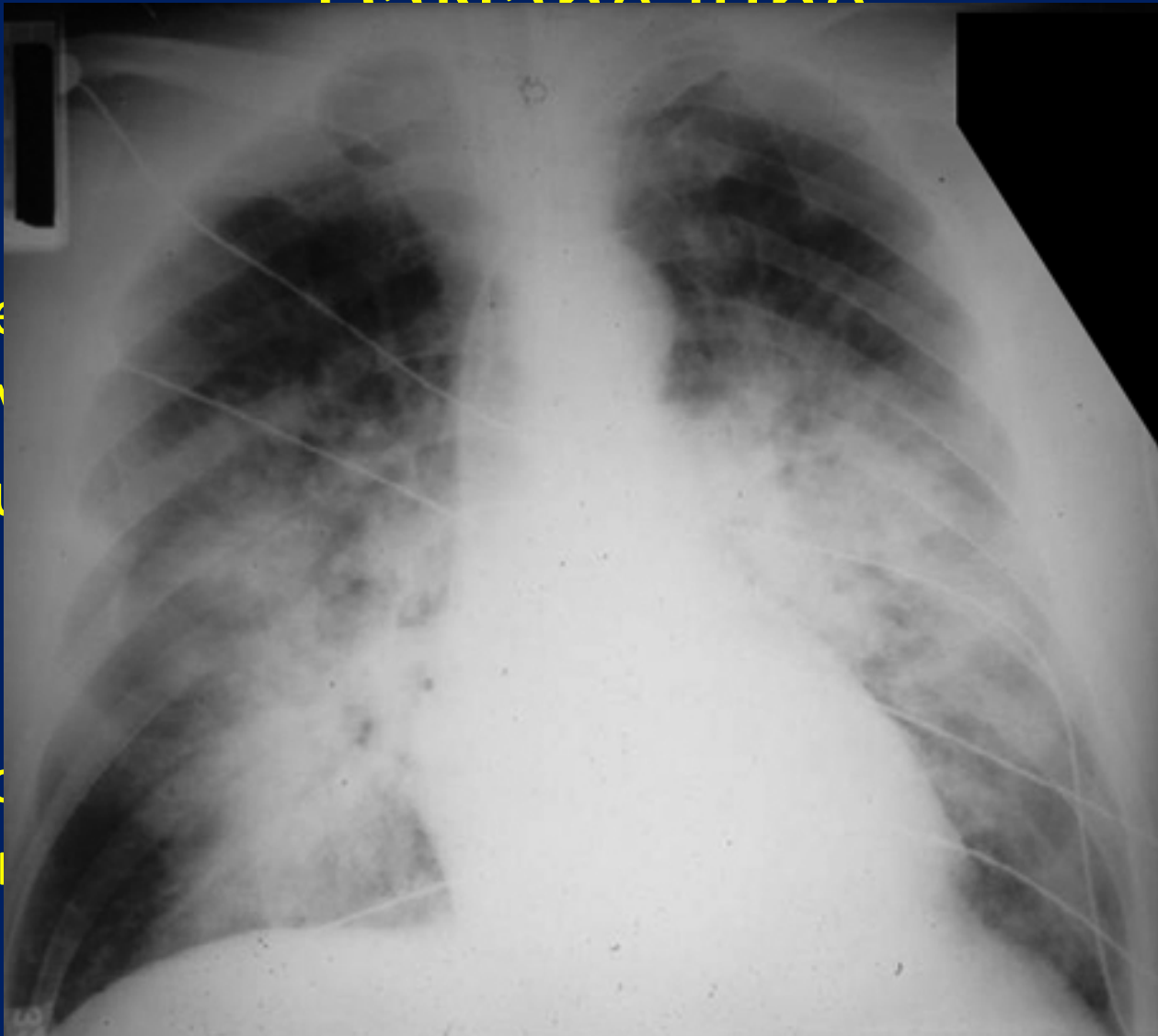
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“DaNang Lung”

- Progressive respiratory failure req. mechanical ventilation
 - Stiff lungs
 - Hypoxemia
- autopsy
 - HETEROGENEOUS
 - Vascular congestion / Interstitial / alveolar edema
 - Focal atelectasis
 - Hyaline membranes
 - (late) fibrosis

The Lancet · Saturday 12 August 1967

ACUTE RESPIRATORY DISTRESS IN ADULTS

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of lung compliance, and diffuse alveolar infiltration seen on chest X-ray.

No patient had a previous history of respiratory failure. 1 patient gave a history of mild asthma since childhood but had no disability or recent attacks. Another patient had a chronic cough that was attributed to cigarette smoking. The remaining 10 patients did not have any previous pulmonary disease.

Severe trauma preceded respiratory distress in 7 patients (table 1). Viral infection in 4 patients and acute pancreatitis in 1 patient were precipitating factors in the remainder. Respiratory distress occurred as early as one hour and as late as ninety-six hours after the precipitating illness or injury. Shock of varying degree and duration was present in 5 patients and excessive fluid administration occurred in 7 patients. 4 patients developed acidosis with pH less than 7.3 before the onset of respiratory distress.

Methods

All patients were admitted to intensive-care units of the surgical or medical services. Blood-gas studies were performed on arterial blood drawn by percutaneous puncture of either brachial or femoral artery. In most instances, blood was drawn

Surg Gynecol Obstet. 1977 Mar;144(3):323-6.

Multiple organ failure.

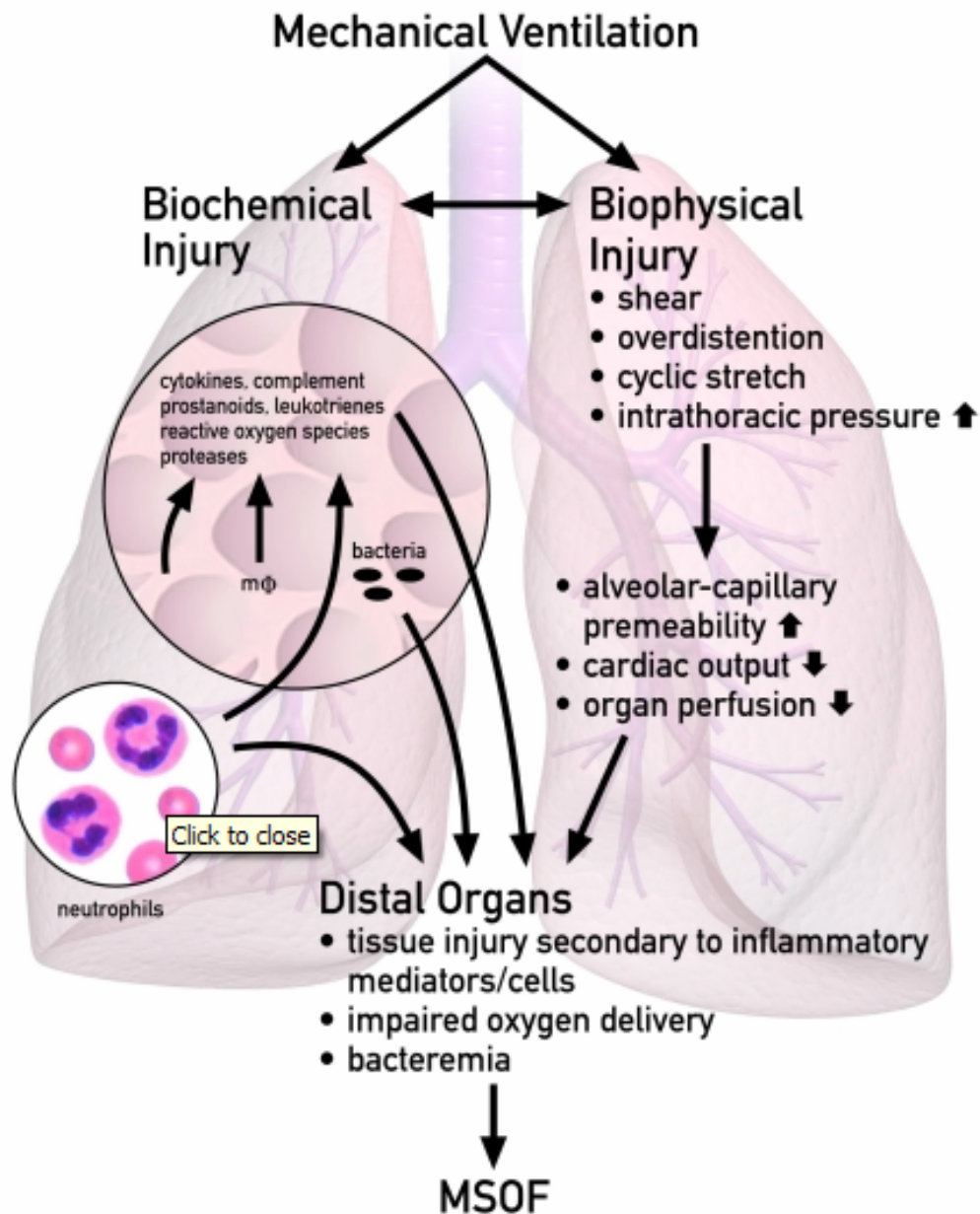
Eiseman B, Beart R, Norton L.

Abstract

Forty-two postoperative patients, each with demonstrable failure of two or more vital organ systems, have been studied as they define a syndrome of multiple organ failure. They typify the emerging clinical entity of patients kept alive solely by reason of specific mechanical and pharmacologic support. Trauma initiated hospitalization in 40 per cent and major bleeding, in 11 per cent. Sepsis was judged to be of etiologic significance in 69 per cent. Complications in clinical management were, in retrospect, thought to be of contributory etiologic significance in 57 per cent. Twenty-nine of 42 patients died; a mortality of 69 per cent. Mean duration of multiple organ failure was 30.5 days. Hospital cost, omitting the physician's fees, was conservatively estimated at \$700 per day. Scientific, social, moral, ethical and legal factors emphasize the need to establish a statistically valid large data base concerning this new man-made syndrome which has both important scientific and social implications. This study is a first step in this direction.

ARDS

- Acute onset
 - Bilateral infiltrates
 - PCWP < 18mmHg
 - PaO₂ / FiO₂ < 200
-
- Usually develops 48-72 hrs after an inciting event



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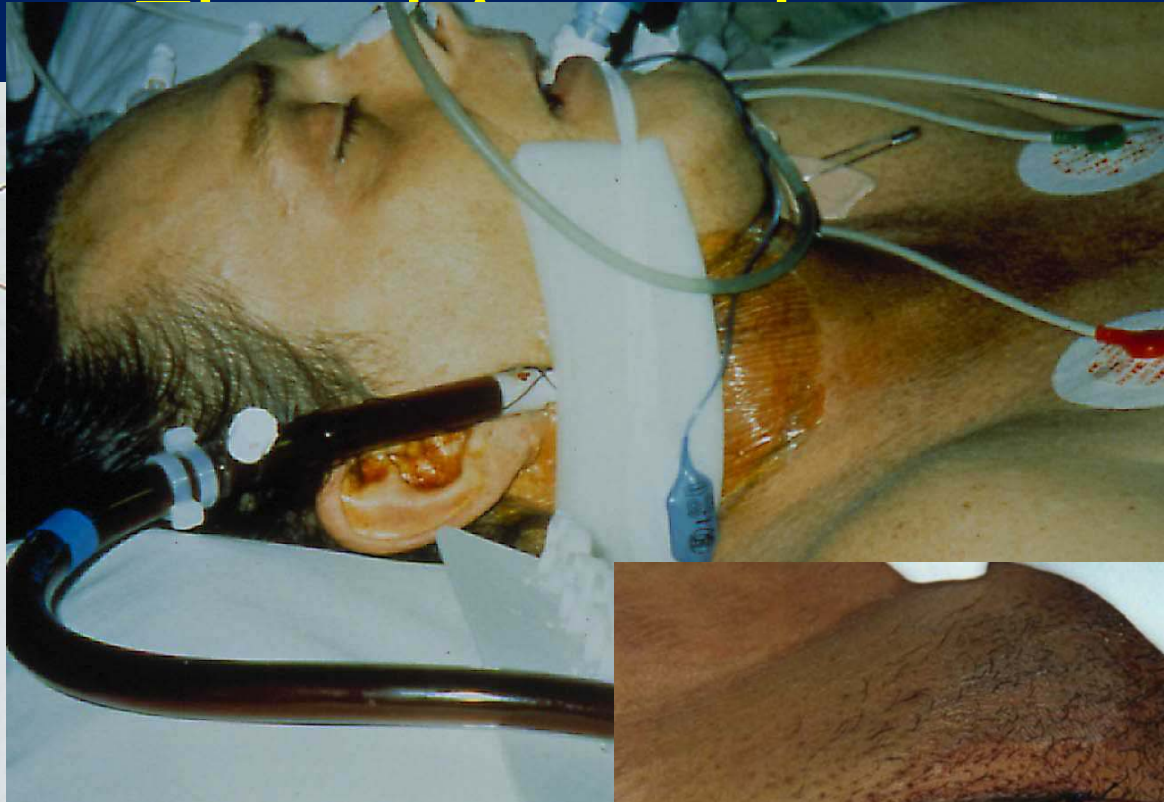


VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH
TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY
AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

- “What do you mean you can’t ventilate him? Turn the pressure control up to 80. Let’s show them lungs who’s boss!!”
- “anuric renal failure?!?! Just give a gram of lasix! That’ll teach them kidneys!”

ECMO



ECMO in neonates

- Experience began in 1960's.
 - Bartlett reported 1st neonatal success in 1975
- Bartlett reported 1st 100 patients (V-A ECMO) in 1986 with 72% survival
- Bartlett, Zwisch reported PRCT in neonates with 100% vs. 0% survival (11:1 randomization!)
- UK collaborative PRCT (185 pts):
 - 68% survival vs. 41% in ECMO vs. conventional
 - Low rate of severe disability
- In 2001, 20,638 pts worldwide with 77% survival

ELSO registry report 2001.

Bartlett, Zwisch et.al. Pediatrics. 1985.

Bartlett et.al. Ann Surg. 1986.

UK Collaborative ECMO group. 1996.

Moving target

- Since 1970's, survival of ARDS with conventional management has increased from 10% to as high as 50-70%
 - Low Vt, PEEP, iNO, prone position
- ECMO technology continues to evolve
 - VA and VV ECMO
 - Extracorporeal CO₂ removal (ECCO₂R)
 - arteriovenous CO₂ removal (AVCO₂R)
 - expertise

NIH randomized trial

- 9 centers, 90 patients with all cause ARDS
- Fast entry
 - $\text{PaO}_2 < 50$ on 100% with PEEP > 5
- Slow entry
 - $\text{PaO}_2 < 50$ on 60% with PEEP > 5
 - Shunt fraction $> 30\%$
 - Included only after 48hrs max medical therapy
- exclusion:
 - Insult > 21 days
 - PCWP > 25
 - Chronic systemic disease

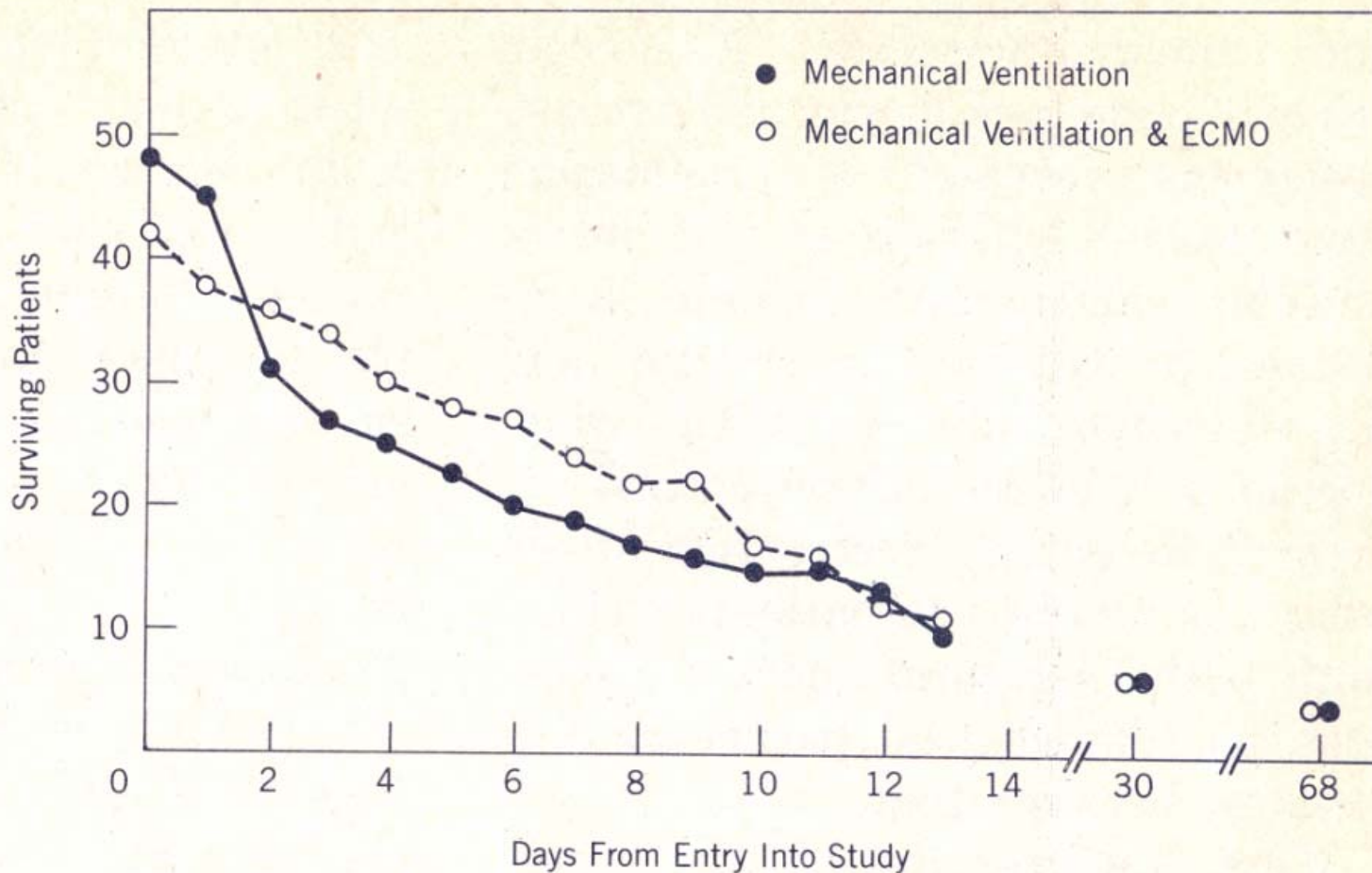
patients

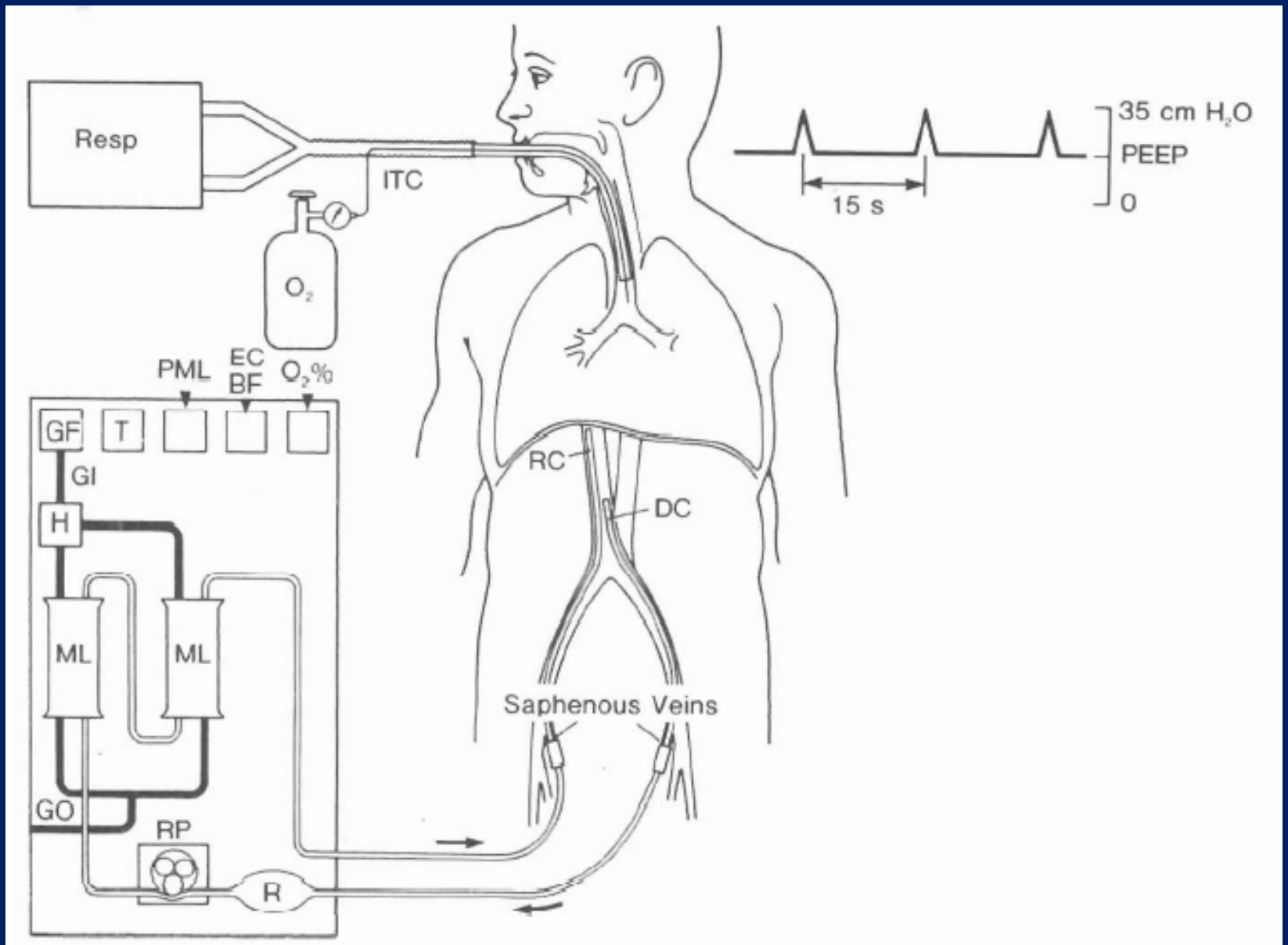
- 65% pneumonia
- 10% PE
- 10% post-traumatic

NIH randomized trial

- ECMO regimen
 - Veno-arterial ECMO (VA)
 - Roller pump with membrane oxygenator
- Termination endpoint
 - $\text{PaO}_2 > 70$ on 60% and 5 PEEP
 - Or
 - No improvement after 5 days

NIH randomized trial





Gattinoni et.al. JAMA. 1986.

management

- LFPPV: PEEP range 15-25
 - 3 to 5 breaths with PIP 35-45 every minute
 - Mean airway pressure slightly above PEEP
 - V_t dependent on compliance
 - Once down to 40% FiO_2 , PEEP progressively decreased
- ECCO2R: 20-30% of cardiac output
 - heparinized

Weaning protocol

- Taken off bypass when able to exchange gas on 40%, PEEP 10-15, and compliance > 30

Patients

- 43 patients
- Compliance < 30 AND
- Fast: pO₂ <50 on 100% / 5
- Slow (88% of pts): after 48 hrs therapy, pO₂ <50 on 60% / 5 with shunt fraction > 30%
- 50% PNA, 20% post-traumatic, 10% PE

Results

- 73% had improvement in lung function
 - Always occurred within 48hrs
- 49% (21 pts) survived to discharge
- 2/4 pts survived with >21 days pre-op ventilation
 - Survivors mean ventilation 7.9 days vs 11.9
- 67% survival in 12 patients with 4 organ failure
- 1.8 liters of whole blood per day

Utah trial of ECCO2R

- 40 pts randomized to PCIRV vs. ECCO2R
- Patients with ARDS
 - P:F <100, compliance < 50
 - bilat infiltrates, PCWP < 15
- Rapid entry:
 - pAO₂ < 50 on 100%/5
- Slow entry
 - pAO₂ < 50 on 60%/5 with shunt > 30%
- Exclusion:
 - Mech vent > 21 days

Utah trial of ECCO2R

- Survival 33% in ECCO2R vs. 42% conventional
- 1.8L pRBC/day
- 1.6L FFP/day
- 21 major bleeding complications
- 7 ECCO2R discontinued due to bleeding
- Mean PIP 55!
- 70% incidence of barotrauma in ECCO2R group

Landmark trial from the UK

- Conventional ventilation vs. ECMO in Severe Acute Respiratory failure (CESAR)
- Funded by national health service
- Purpose was to determine efficacy of VV ECMO in adults ARDS vs. modern ARDS management

CESAR

- Inclusion:
 - Adults aged 18-65 with severe but reversible respiratory failure
 - Murray Score ≥ 3.0 or pH < 7.20 due to hypercapnea
- Exclusion:
 - High pressure ($>30\text{cmH}_2\text{O}$) ventilation > 7 days
 - High FiO₂ (0.8 or greater) for > 7 days
 - Contraindication to heparin
 - Thought to be moribund by ECMO consultant

Murray Score

- $\text{PaO}_2/\text{FiO}_2$: $\geq 300 = 0$, $225-299 = 1$, $175-224 = 2$, $100-174 = 3$, $<100 = 4$
 - CXR: normal = 0, 1 point per quadrant infiltrated.
 - PEEP: $\leq 5 = 0$, $6-8 = 1$, $9-11 = 2$, $12-14 = 3$, $\geq 15 = 4$.
 - Compliance ($\text{ml}/\text{cmH}_2\text{O}$): $\geq 80 = 0$, $60-79 = 1$, $40-59 = 2$, $20-39 = 3$, and $\leq 19 = 4$
-
- pO_2 60, FiO_2 100%, PEEP 12.5, PIP 35, V_t 400, diffuse infiltrate
– 3.75
 - pO_2 100, FiO_2 100%, PEEP 10, PIP 25, V_t 550, diffuse infiltrate

Centers

- ECMO: Glenfield Hospital in Leicester, UK
- conventional treatment centers (CTC) (92):
 - Critical care certified hospitals or those that treat >350 ARDS cases per year
 - HD capability
- Referral hospitals (11):
 - hospitals with patients meeting entry criteria
 - Transfer to CTC if randomized to non-ECMO

Interventions: conventional

- Treatment at a CTC—may involve transfer from smaller hospital
- Optimal therapy at discretion of intensivist
 - Recommended to follow low tidal volume
 - Keep plateau <30 and 4-8 ml/kg tidal volumes
 - Can include iNO, oscillator, prone position, steroids

Interventions: ECMO

- Once randomized, transferred to Leicester
 - If too unstable, will remain there until stable or dead on conventional mgmt.
 - Intention-to-treat analysis
 - On arrival, patients are re-evaluated
 - ECMO instituted only if patient cannot be managed with:
 - Plateau pressure <30
 - FiO₂ <60
 - 17 pts did not get ECMO for this reason (14 survived)

VV ECMO

- Percutaneous cannulation
 - R atrial drainage via femoral vein or IJ
 - Blood return via contralateral femoral
- Flow: 120ml/kg/min
- Oxygenator: Medos HiLite 7000LT
- Pump: Sorin Stockert roller pump
- VA ECMO used if HD unstable



Management during ECMO

- ACT 160-220
- PIP <20, PEEP 10, FiO₂ 30%
- Diuresed to dry weight
- Hb=14 mg/dL
- Plts>100K
- When CXR and compliance improve, “trial off” ECMO attempted
 - Must oxygenate and ventilate using no more than PIP 30 and 60% FiO₂

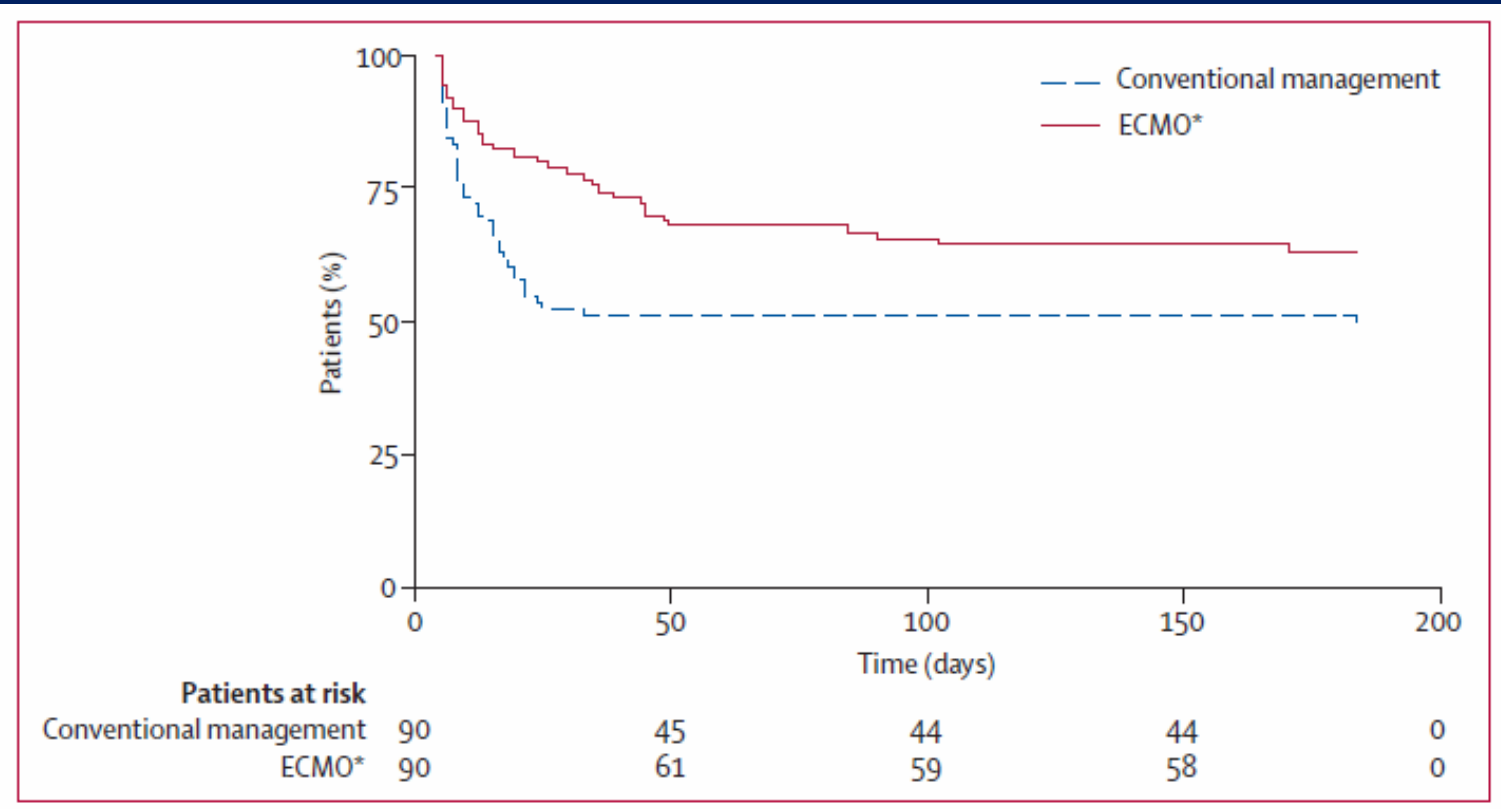
outcomes

- Primary endpoint: Death or disability at 6 months
- Secondary: time on vent, LOS, ICU LOS, use of oscillator, use of iNO, prone position

demographics

- About 55% PNA, 5% post-trauma
- Mean age 40
- 70% had 1-2 organ failure
- 30% had 3 or more organ failure
- 95% entered on Murray score—not hypercapnia
- 65% were on high pressure or FiO₂ for <2 days

Results



results

- CVVH about 80% in both groups
- 93% ARDSNet compliance in ECMO vs. 70% in controls
- deaths due to resp failure 24% in ECMO vs. 60% controls
- 42% deaths related to MOF in ECMO group
- One major cannulation complication
 - No other sig bleeding complications reported

cost

- \$70K USD additional cost per ECMO patient (about double the cost of conventional treatment)
- \$33,000 per QALY
- Need to treat 6 people to save one

	ECMO group (n=90)*	Conventional management group (n=90)
All patients		
Critical care (days)	24.0 (13.0–40.5)†	13.0 (11.0–16.0)
Hospital (days)	35.0 (15.6–74.0)	17.0 (4.8–45.3)
Patients who died‡		
Critical care (days)	11.0 (2.0–28.0)†	5.0 (2.0–13.5)
Hospital (days)	15.0 (3.0–40.5)	5.0 (2.0–13.5)

Data are median (IQR). ECMO=extracorporeal membrane oxygenation. *Patients were randomly allocated to consideration for treatment by ECMO, but did not necessarily receive this treatment. †Excludes one patient whose notes are still with the coroner. ‡Data for 33 patients receiving extracorporeal membrane oxygenation, and 45 patients receiving conventional management.

Table 4: Length of stay

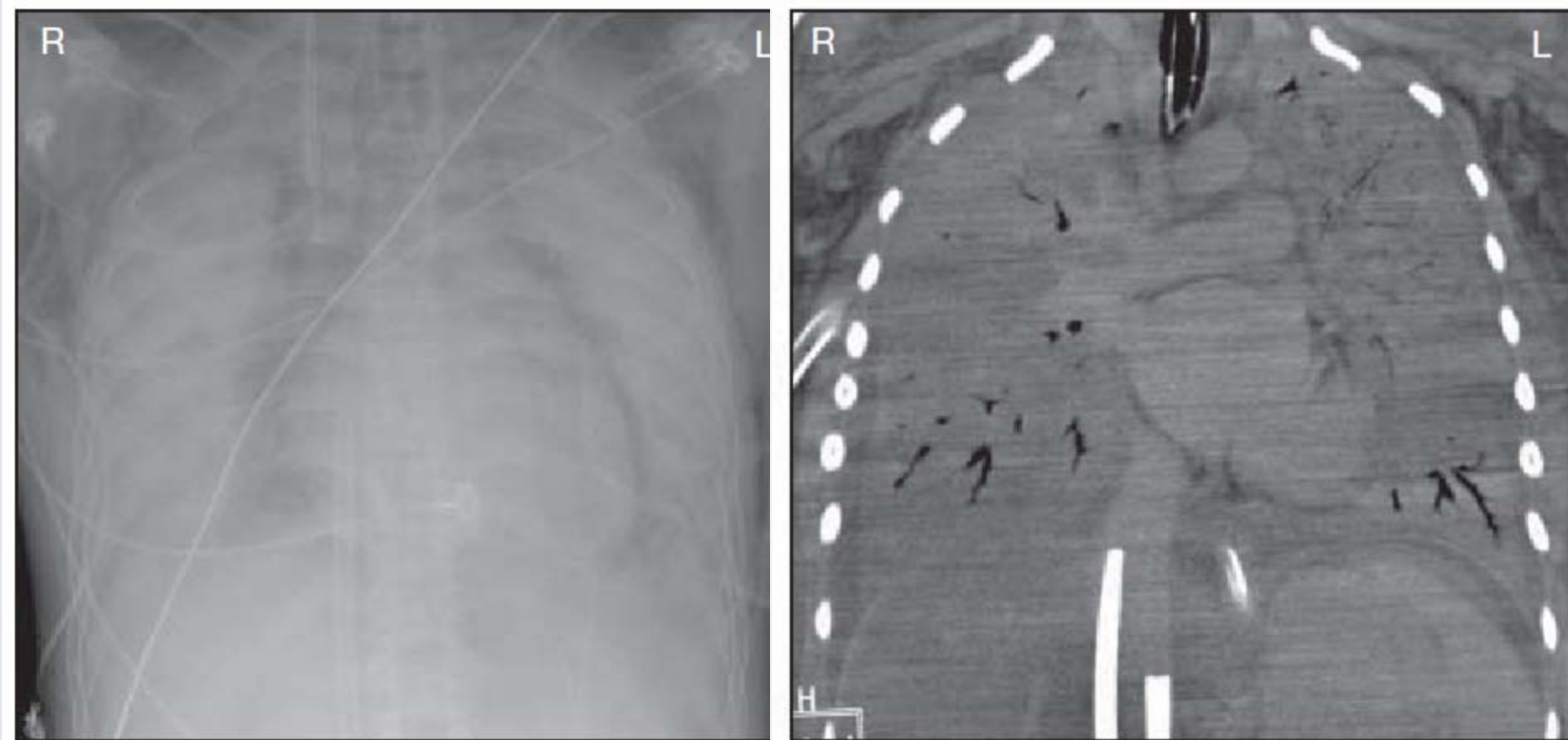
H1N1 2009 in Australia

- NONRANDOMIZED retrospective cohort
- June, July, August 2009
 - 201 pts req. mech vent. for H1N1 ARDS
 - Those with most severe disease received ECMO
 - Decision made by clinician to place on ECMO
 - VV ECMO with centrifugal pump
 - Heparin bonded cannulas
 - 68 ECMO, 133 deemed to not need it

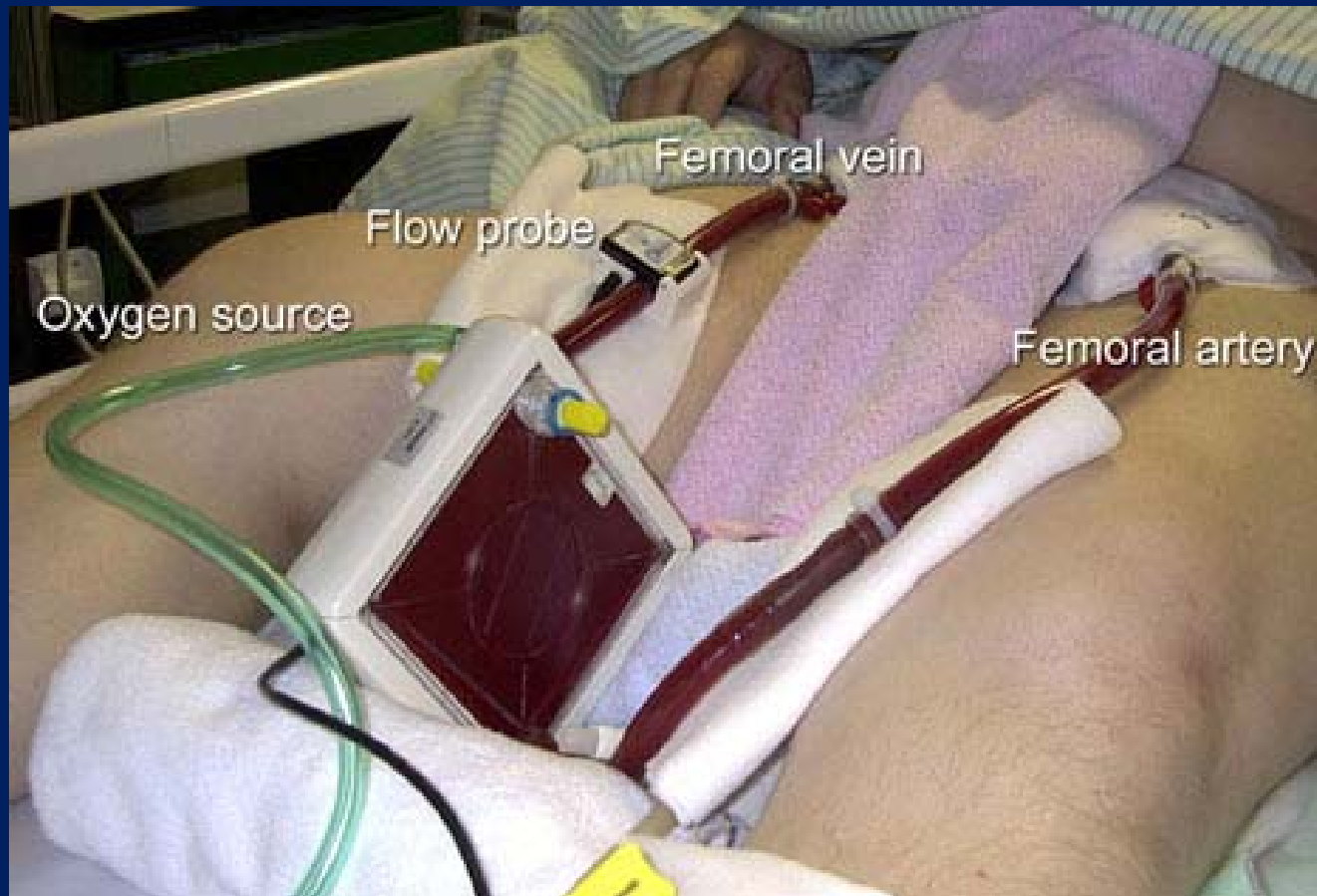
Characteristics of ECMO pts.

- pH 7.2, pCO₂ 69, P:F 55, PEEP 18, FiO₂ 100%
- Murray score 3.8
- 81% had attempted one or more of following:
 - Prone, prostacyclin, iNO, HFOV

Results



Arteriovenous CO₂ removal



Arteriovenous CO2 removal

- Effective at scavenging CO2
- May improve hemodynamics by correcting pH, decreasing airway pressures
- Robs 25% systemic blood flow
- No pump, small circuit volume
- Less anticoag requirements (800u/hr)
- Not appropriate for those with very severe hypoxia

Summary

- In the last 30 years, both ECMO and ARDS management have evolved tremendously
- Both will continue to evolve
- ECMO clearly has the ability to save lives in ARDS with today's technology
- Major referral centers in the US need to establish ECMO protocols to standardize application to ARDS patients