

ECMO for ARDS

Unproven,
Expensive,
Dangerous!

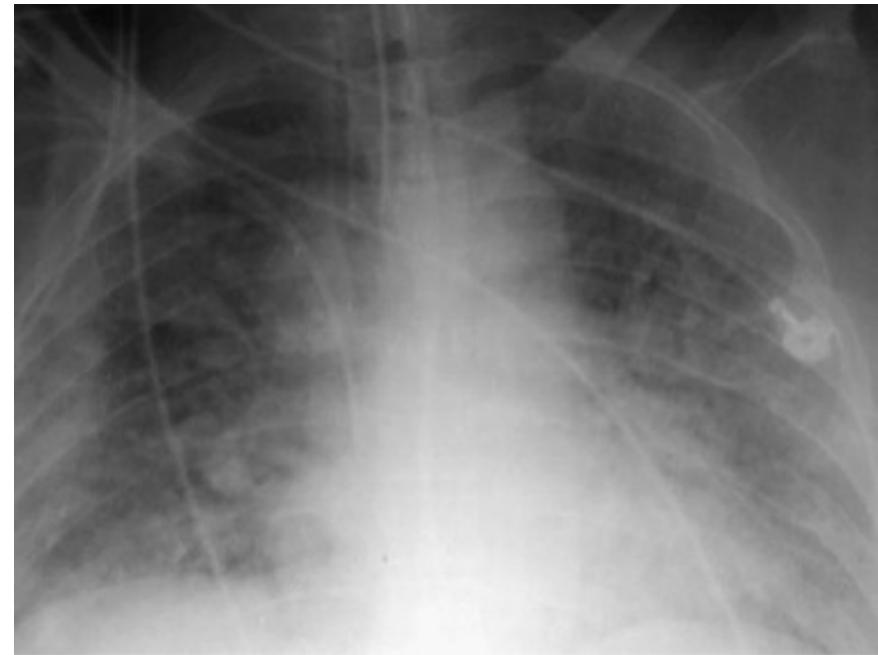
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Grand Rounds

September 27, 2010

ALI/ARDS

- Definition (A/E Consensus conference)
 - Acute Onset
 - Bilateral infiltrate
 - R/O cardiogenic (PCWP <18)
 - Hypoxemia
 - $\text{PaO}_2/\text{FIO}_2 < 300$ = ALI
 - $\text{PaO}_2/\text{FIO}_2 < 200$ = ARDS
- Criticisms of definition
 - What constitutes B infiltrates?
 - No head-nod to etiology
 - FIO₂ +/- PEEP
- Conclusion: Very heterogenous population of patients



Epidemiology

- 2-75/100,000. Best study ~ 22/100,000
 - Risks
 - #1 Sepsis
 - 40% of patients with sepsis develop ARDS
 - Gastric aspiration, blood transfusions, trauma, alcoholism, pulm contusions, pneumonia, smoke inhalation
- => Direct (pulm) vs. indirect (non-pulm causes)

Pulm vs Non-Pulm Causes

Sepsis	Pneumonia
Major trauma	Aspiration
Multiple blood transfusions	Pulmonary contusion
Pancreatitis	Toxic inhalation
Cardiopulmonary bypass	Near-drowning
Drug overdose	Reperfusion injury (e.g., post lung transplant)
Adverse effect of medication	

? Different mechanisms and pathologies

Pathology In ARDS

- Macro Level
 - Exudative Phase (5-7 days)
 - Proliferative Phase
 - Fibrotic Phase (2 weeks)
- Micro Level
 - Endothelial & Epithelial Damage
 - Surfactant loss (cause vs. effect)
 - Neutrophil activation
 - Coag cascade

What is ECMO?

- Extracorporeal = outside of body
- Membrane = membrane
- Oxygenation = put oxygen in blood
- Main purpose: Replace gas exchange function of lungs (CO₂, O₂)
- Second purpose:
 - In ARDS, to throw away money...



ECMO for ARDS: Data

- “ARDS” => 9712
- “ECMO” => 2774
- ARDS and ECMO => 207
- ARDS and ECMO and RCT => 3

Extracorporeal Membrane Oxygenation in Severe Acute Respiratory Failure

A Randomized Prospective Study

Warren M. Zapol, MD; Michael T. Snider, MD, PhD; J. Donald Hill, MD;

Robert J. Fallat, MD; Robert H. Bartlett, MD; L. Henry Edmunds, MD; Alan H. Morris, MD;

E. Converse Peirce II, MD; Arthur N. Thomas, MD; Herbert J. Proctor, MD; Philip A. Drinker, PhD;

Philip C. Pratt, MD; Anna Bagniewski, MA; Rupert G. Miller, Jr, PhD

Zapol WM. **JAMA**
1979; 242: 2193-
2196.

- JAMA !!!
- Randomized, prospective, multicenter trial
- 9 centers
- 2 years, 90 patients randomized
- Entry criteria
 - “Fast-entry”: $\text{PaO}_2 < 50$ for > 2 hrs on $\text{FIO}_2 1.0$ and $\text{PEEP} \geq 5$.
 - “Slow-entry”: 48 hrs of medical therapy then $\text{PaO}_2 < 50$ for > 12 hrs @ $\text{FIO}_2 0.6$ and $\text{PEEP} \geq 5$, and shunt $> 30\%$ of CO .
- Exclusion criteria
 - < 12 or > 65 yo
 - > 21 days of pulm therapy
 - $\text{PCWP} > 25$
 - Other diseases

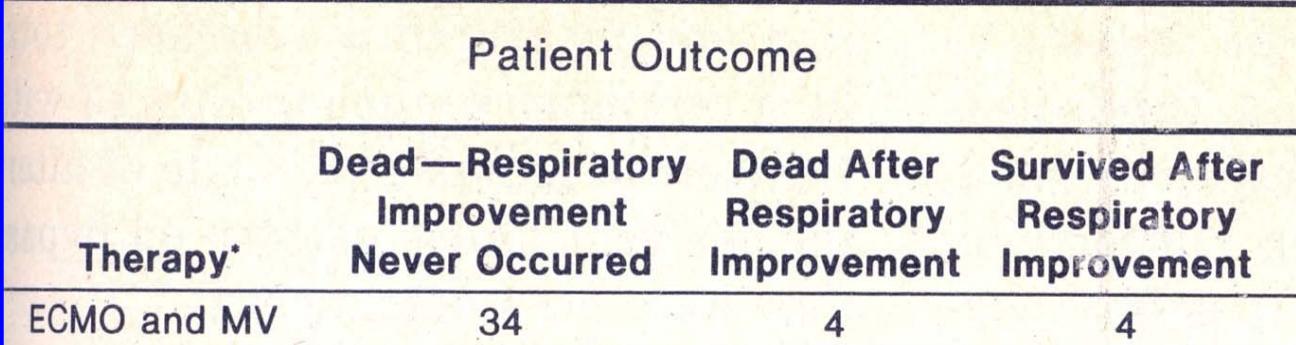
Extracorporeal Membrane Oxygenation in Severe Acute Respiratory Failure

A Randomized Prospective Study

- Methods
- Mechanical vent
 - Not clearly specified.
 - “Although specific mech vent patterns may have differed between centers, each patient was treated in an established ICU employing broadly accepted regimens of medical therapy.”
- ECMO
 - Venoarterial partial bypass
 - Total amount not specified
 - Q 12 hours flows dropped to 0.5 L to test ABG
 - Reduced pulm flow from 3.5 to 2.4
 - Reasons to stop ECMO:
 - Improved: $\text{PaO}_2 \geq 70$ with $\text{FIO}_2 0.6$ and PEEP 5 on flow of 0.5 L/min
 - Technical complications or bleeding
 - No improvement in 5 days

Extracorporeal Membrane Oxygenation in Severe Acute Respiratory Failure

A Randomized Prospective Study

-  s on

Therapy*	Patient Outcome		
	Dead—Respiratory Improvement Never Occurred	Dead After Respiratory Improvement	Survived After Respiratory Improvement
ECMO and MV	34	4	4

- Results
 - Demographics and diseases similar in both groups
 - Mortality: No different
 - ECMO added more deaths to control arm
 - Respiratory improvement DID NOT improve mortality.

Conclusions from JAMA 1979

- “Patients with severe ARF treated with bypass on a membrane oxygenator experienced NEITHER a significantly increased respiratory recovery NOR a greater long-term survival than those treated with standard therapy for severe ARF.”
- Whatever benefit there may be with ECMO is negated by the negative effects of bypass.

Criticisms

- High death rate: 90-92%
 - Will not see a benefit
- Not standard therapy of MV anymore
 - That would improve mortality in BOTH groups
 - 45 % PTX rate in this study

My Conclusions

- Although two groups well matched, no benefit from this “novel therapy.”
- It’s a miracle ECMO did not kill more patients.
- Proof that ECMO can be done safely...in healthier patients.

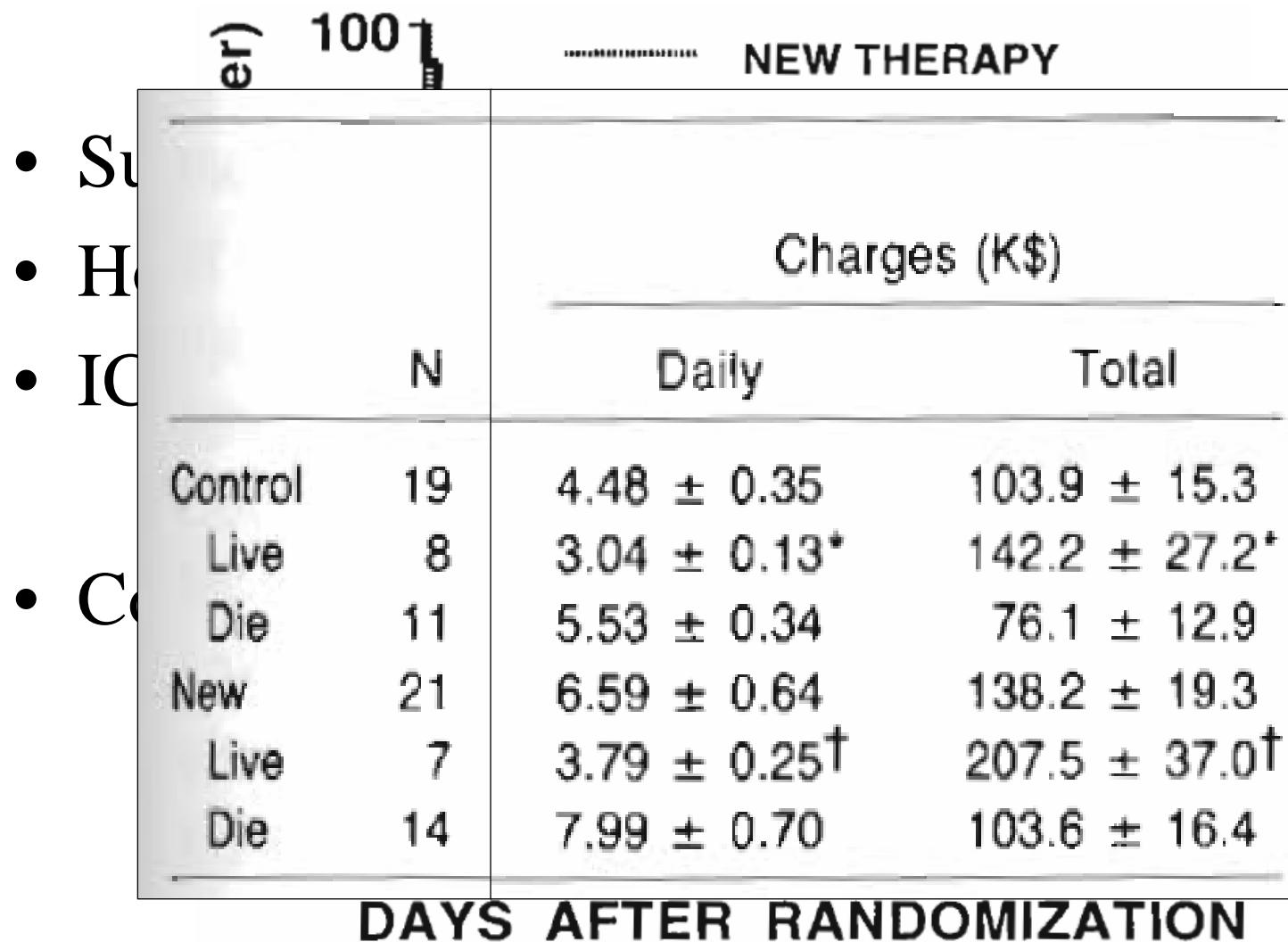
Randomized Clinical Trial of Pressure-controlled Inverse Ratio Ventilation and Extracorporeal CO₂ Removal for Adult Respiratory Distress Syndrome

Design

- Randomized, controlled
- 40 patients
 - 19 Control
 - 21 in “PCIRV”
 - Attempted PCIRV first and if failed, then LFPPV-ECCO2R
 - Only 1 patient “succeeded @ PCIRV”
- Outcomes
 - Survival, LOS, ICU days etc
 - Cost: Not including disposable items for ECCO2R

Randomized Clinical Trial of Pressure-controlled Inverse Ratio Ventilation and Extracorporeal CO₂ Removal for Adult Respiratory Distress Syndrome

Results



Conclusions

“In summary, we failed to find a statistically significant difference in survival between control and extracorporeal treatment patient groups.”

CESAR- The last hope

- On the surface:
 - Sick patients with severe ARDS, anticipated mortality of ~ 60%
 - 180 patients randomized to Best Conventional Therapy vs. BCT/ECMO
 - Dedicated centers
 - 92 for BCT and 1 for ECMO
 - Outcomes: Death or Disability @ 6M. Cost

CESAR- Surface Results

- Death/ Disability @ 6M
 - 37% vs. 53%
- Cost
 - \$65,500 difference in ECMO vs. BCT
 - But, \$31,000 per QALY**
 - Somehow, this is “well within the range regarded as cost effective.”

CESAR- The fine print...A bunch of lies

- “Best standard practice”
 - 92 conventional tx centers without protocols
 - Could be placed in other ARDS studies
 - ARDS Network suggested, not required

Are you determining how we treat these patients conventionally?

We are not dictating how intensivists treat their patients. We accept that there are many ways of treating ARDS e.g. prone, steroids, nitric oxide and oscillation. We will be recording how each patient is treated during the course of the trial. We do however, strongly advise that you follow the ARDS network recommendations i.e. low volume and pressure ventilation. (If you require a copy of this, we can send it out to you). This strategy is the only ventilator protocol **proven** to increase survival in ARDS. The CESAR trial is pragmatic in its aim to compare ECMO with conventional treatments currently available.

CES

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	ECMO group (n=90)*†	Conventional management group (n=90)	p value
Treatment by ECMO	68 (76%)	NA	NA
Transport to treatment centre	62 (69%)	NA	NA
Air (with or without ground transport)	24 (27%)	NA	NA
Ground	38 (42%)	NA	NA
Not transferred‡	6 (7%)	NA	NA
Time between randomisation and treatment (h)	6·1 (4·0-7·1)§	NA	NA
Duration of treatment (days)	9·0 (6·0-16·0)	NA	NA
Treatment by conventional management	22 (24%)	90 (100%)	NA
Transport to treatment centre	19 (21%)	11 (12%)	NA
Air (with or without ground transport)	5 (6%)	2 (2%)	NA
Ground	14 (1%)	9 (10%)	NA
Not transferred	3 (3%)	79 (88%)	NA
Duration of treatment (days)	10 (4·8-22·8)	11 (4·0-20·3)	NA
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

of

CESAR- The fine print...A bunch of lies

- “ECMO is more cost effective.”
 - ECMO costs more than just the cost to each patient
 - Cost to set up more “ECMO” centers
 - Cost to maintain ECMO skills and equipment
 - Cost for transport
 - Not equivalent in US or other developed countries

CESAR “Real” Conclusions

- Death or Disability @ 6M
 - 3 patients without followup in BCT arm
 - Including these patients makes the difference NON-significant
- ECMO keeps patients alive longer to die 2/2 other causes.
- Embarrassing that with the boat loaded towards the ECMO group they could not show a better difference?
- The BEST therapy is STILL ARDS network recs.!

ECMO For Select Few

- Can't have ECMO if...
 - C/I to heparin
 - Some series, as high as 10% of patients.

Proven Therapies for ARDS

- Lung-Protective Strategies
 - In-hospital mortality
 - 30-day mortality
 - Days on Vent (+/-)
 - Long-term O₂ use (+/-)
- PEEP
 - Esp for ARDS. Less for ALI



Conclusions

- ECMO for ARDS should be put in the same box as some other bright ideas:



Conclusions, Seriously

- Why is ECMO NOT the choice for everyone?
 - No Prospective Data
 - Too much bias
 - Few patients will actually benefit
 - Cost
 - Too many unknowns about ECMO
 - Other proven therapies

- Everyone keeps saying that ECMO is the answer, but we just don't know how to use it.
- Type of ECMO VV vs VA
- Flows
- Anticoag
- Timing
- Etc

LPS Cochrane Graphs

Analysis I.1. Comparison I protective versus conventional, Outcome I Mortality at the end of the follow up period for each trial.

