What’s New in ECMO ARDS Management

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What is ECMO or ECLS?

- Mechanical device to provide prolonged pulmonary and/or cardiac support

Extracorporeal Membrane Oxygenation (ECMO) or better called Life Support (ECLS)

History of Cardiopulmonary Support

- Development of cardiopulmonary bypass 1935-1954
- 1952: first successful ASD closure
- Goals:
  - Support circulation
  - Oxygenation/ventilation
  - Bloodless surgical field
History of Cardiopulmonary Support

- Film oxygenator
- Bubble oxygenator
- Membrane oxygenator
- Hollow fiber oxygenator (now with second generation)

ECMO

- Silicone rubber membrane oxygenator
- First successful ECMO 1972
- First successful neonatal ECMO 1976

ECLS Components

- Vascular access catheters
- Connecting tubing
- Servo regulating blood pump
- Artificial lung
- Heat exchanger
- Various measuring & monitoring devices
ECMO Goals

- Support cardiac and respiratory systems until disease process resolves
- Disease process must be reversible
- Avoid end organ injury:
  - chronic lung injury
  - CNS injury
  - renal injury

ECMO Indications 2013?

- Reversible lung and cardiac disease
- Bridge to transplant both heart or lung
- ECPR
- Acute toxicity (calcium channel blocker ingestion)
- Septic Shock
- Hemorrhage (coated circuits, coated hollow fiber oxygenator)
- Trauma, pulmonary hemorrhage
- ARDS (both pediatric and adult)

ECMO for ARDS

- Does this mean ECMO for adults?
  - Why do we care?
  - Is it a good option?
WHAT IS ARDS?
- First described in 1967
- Acute onset of respiratory failure
- Severe acute lung injury involving diffuse alveolar damage, increased micro-vascular permeability and non-cardiogenic edema
- Acute refractory hypoxia
- Impaired oxygenation regardless of PEEP, with a PaO2/FiO2 ratio < 200
- Pulmonary artery occlusion pressure < 18 mmHg or the absence of left atrial hypertension
- Bilateral infiltrates on CXR

Stages of ARDS
- Exudative phase 0-4 days
- Proliferative phase 4-8 days
- Fibrotic phase > 8 days
- Recovery phase

NO ADULT ECMO (or big kid either)
- All the studies have shown it does not work.
- Too many complications
- “Who are you kidding?”
**Adult ECMO**

- First use of ECMO in an adult
- Clinical Trials
  - 1975 NIH adult ECMO trial
  - 1986 Milan ECCO₂R trial
  - 1994 LDS Hospital ECCO₂R trial
- Single Center Use
- CESAR Trial
- H1N1
- Management issues with ARDS

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**First Successful ECMO Case 1972**

- 24 year old involved in motorcycle crash
- Aortic rupture
- Orthopedic injuries
- ARDS on post op day #5
- Femoral venoarterial cannulation
- 3 – 3.5 L/min flow
- 75 hours on ECMO
- Pt survived

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**Initial ECMO Experience 1960 – 1970s**

- Each center devised their own circuits utilizing a variety of parts
- Many laboratories developed their own oxygenators
- Development of dimethylpolysiloxane membranes (silicone rubber) allowed exchange of O₂ and CO₂ at 10 X rate of previous materials
- Oxygenators then became available commercially
Early ECMO Experience with Acute Respiratory Insufficiency

- 1966 – 1976 voluntary survey
- 233 patients treated by 90 different teams in 7 countries (2.5 patients/center)
- Three types of cannulation: venovenous, arteriovenous, venoarterial
- 8 different types of oxygenators


Early ALI ECMO Experience

- No consensus on:
  - entry criteria
  - perfusion techniques
  - cannulation sites
  - oxygenators
- Favorable outcome = extubated, 21% O2 at 1 month after bypass
- FAVORABLE OUTCOME 15%


ECMO in Severe Acute Respiratory Failure

A Randomized Prospective Study

- 1974 NIH proposed multi-centered prospective randomized study of ECMO in adult respiratory failure
- Conventional mechanical ventilation versus VA ECMO
- Study began in 1975, completed in 1979
- 9 centers involved
- 300 patients to be enrolled

Zapol et al., JAMA 242:2193-2196, 1979
NIH Study Results

- Fast entry criteria
  - $\text{PO}_2 < 50$ for 2 hrs with $\text{FIO}_2$ 1.0 + Peep > 5 cm
- Slow entry criteria
  - $\text{PO}_2 < 50$ for > 12 hrs
  - $\text{FIO}_2$ 0.6 + Peep > 5 cm
  - 48 hrs maximal therapy

NIH

- Study planned for 300 patients but terminated after 92 as survival in both control and ECMO groups was less than 10%
- Death due to progressive pulmonary failure
- "We conclude that ECMO can support respiratory gas exchange but did not increase the probability of long-term survival in patients with severe ARF".

NIH

- Problems: centers with minimal or no ECMO experience, no lung rest (autopsy findings demonstrated fibrosis), severe bleeding complications (average blood loss > 2 L/day), no standardization of technique, 1976 – Influenza pneumonia outbreak
THIS STUDY IN CONCERT WITH INDIVIDUAL CENTER RESULTS EFFECTIVELY SLOWED ALL FURTHER ADULT ARDS ECMO RESEARCH IN THE UNITED STATES
But not in Europe & a few US centers!

Pivotal Studies

• **ARMA Trial**: 6 cc/kg (P_{plateau} max 30) vs 12 cc/kg (P_{plateau} max 50) tidal volume: 6 cc/kg group survival 40% vs 31%

• **Peep?** Diseased lungs opened by peep to avoid cyclic opening/closing but normal lung over-distended by peep

Pivotal Studies

• **ALVEOLI Trial**: 6 cc/kg TV with high peep compared to low peep/high FIO₂: no improvement in outcome with high peep
• **LOV Trial**: 6 cc/kg TV, P_{plateau} <30, vs 6 cc/kg TV, recruitment maneuvers (40 sec at 40 cm H₂O pressure with FIO₂ 1.0 up to 4 times a day), high peep, P_{plateau} <40 : no statistical difference in mortality
Pivotal Studies

• EXPRESS Trial: 6 cc/kg TV, high peep vs moderate peep (5-9). High peep adjusted by airway pressure (<30): no change in mortality although recruitment group had better oxygenation, more ventilator free days, more organ failure free days and decreased need for rescue therapy
• EPVENT 2 Trial: open lung strategy with 6 cc/kg TV + transpulmonary pressure (via esophageal pressure gauge) at end-expiration vs control 6 cc/kg TV with high peep strategy
  – Goal is to eliminate effects of poor chest wall compliance like obesity, pleural effusions

WHAT DO WE NOW KNOW ABOUT ARDS?

• Ventilator–induced lung injury plays a significant role in morbidity and mortality
  – Barotrauma
    • Excessive pressure leading to shear injury
  – Volutrauma
    • Overexpansion of alveoli
  – Atelectrauma
    • Repeated opening and closing of alveoli resulting in shearing
  – Biotrauma
    • Mechanical injury leading to inflammatory injury

Management of ARDS

The goal of mechanical ventilation in patients with ARDS is not to maintain "normal blood gas values", but rather to optimize oxygen delivery and the protection of the lung from ventilator-induced lung injury
Initial Adult ARDS ECMO Studies

There was excessive ventilator associated injury

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CESAR
Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

Giles J Peek MD FRCS CTh
CESAR Lead Clinical Investigator

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CESAR Trial

- Randomized clinical trial of ECMO vs. conventional mechanical ventilation
  - management in an ECMO center (17 years of ECMO experience, only ELSO recognized adult ECMO center in UK), with ECMO an expected, but optional, part of management VERSUS
  - management in non-ECMO centers using current mechanical ventilation techniques
- Primary outcome:
  - ECMO will increase survival without disability at 6 months
  - will be cost effective
CESAR Eligibility Criteria

- **Inclusion**
  - severe, potentially reversible respiratory failure
  - murry score ≥ 3
  - or uncompensated hypercapnea with pH < 7.20
  - age 18-65 years

- **Exclusion**
  - duration of high-pressure (>30 cm H₂O) high FiO₂ (>0.8) > 7 days
  - contraindicated to heparin
  - contraindication to continued active treatment

CESAR patient referral

ECMO Management

- Veno-venous ECMO preferred (drained RA via IJ or femoral, returned femoral)
- Circuits designed to deliver 120ml/kg/min flow
- Lung rest = PIP max 20 cm H₂O, Peep 10 cm H₂O, rate 10/min, FiO₂ 0.3
- Pts diuresed to dry weight
- Hemoglobin 14 g/dl
CESAR TRIAL

- 90 patients enrolled in each arm
- Survival at 6 months without disability
  - conventional arm survival 47%
  - ECMO arm survival 63%
- ECMO increases survival for adult patients with severe but potentially reversible acute respiratory failure
  - 1 extra survivor for each 6 patients treated
- Trial stopped at 180 pts for efficacy

CESAR CONTROVERSY

- 22 of 90 pts at ECMO center never received ECMO
  - Did that mean respiratory failure management was better in the ECMO center or pts were not as sick?
CESAR CONTROVERSY

- Pts in conventional sites did not receive a specific algorithm of respiratory care (although low tidal volume pressure-limited ventilation recommended)
  - Was this just a reflection of actual community care? Was the ECMO center ventilator care better so the superior “ECMO” results were just better overall ventilator care?

Adult ARDS ECMO Believers and Non-believers

- ECMO believers agreed with the results that ECMO improved outcome
- Non-believers found fault with the study design

Why Care about Adult ECMO?

- Data regarding adult ECMO has been extrapolated to pediatric ECMO
- Older children may not be offered ECMO as practitioners consider them young “adults”
- Some ECMO centers that traditionally only offer neonatal or pediatric ECMO are being asked to manage adults
**H1N1 2009-2010**

- On the heels of the CESAR Study, came H1N1
- Epidemic hit Australia/New Zealand before US/Canada
  - reports indicated most pts not very sick but of the hospitalized pts, 25% were in ICUs with severe respiratory failure
  - anecdotal reports from ECMO centers indicated they were putting H1N1 patients on ECMO

- When H1N1 reached the US, ECMO centers inundated with ECMO requests
- Don’t actually know totals
- ELSO developed a voluntary database
  - 263 pts with H1N1
  - 2/3 of patients over 18 years old
  - Substantial number of pregnant women
  - 63% survival

**Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome**

Paradigm Shift

• Before CESAR and H1N1
  – ECMO in adults was avoided
• After CESAR and H1N1
  – ECMO in adults is encouraged

• Between January 2009 and May 2011 over 1000 papers have been published on ECMO

EOLIA Trial

(ECMO To Rescue Lung Injury in severe ARDS)

• Multicenter, randomized, open trial
• ECMO initiated ASAP for every pt randomized, ethical crossover for patients with refractory hypoxemia
• Evaluate the impact of ECMO initiated after 3 hrs of optimal ventilator management (6 cc/kg TV, $P_{\text{plateau}}$ max 30) for ARDS
• Study start 2011, completion 2014

2013

Where are we now?
Goals for ARDS/ECMO Patient

• Keep patient alive with good end organ function without destroying the lungs
• Watch for complications
• Expect a long run (weeks and weeks and weeks)
• BE PATIENT – DON’T RUSH OR YOU WILL HURT THE PATIENT
• BE PATIENT
• BE PATIENT

VV ECMO

• Plan on VV ECMO
• Be comfortable with saturations ≥ 70%
• How do congenital cardiac patients survive with a low saturation?
  – HEMOGLOBIN
• Keep hemoglobin at 15
• Watch end organ function (brain, kidney, heart)

Level of Consciousness

• Keep as awake as possible
• Consider nasal intubation (more comfortable)
• Consider tracheostomy
• Consider extubation
• Decrease sedatives daily
  – Helps decrease tolerance
**Why Avoid Paralytics?**

- Expect patient to be on ECMO for weeks so prolonged paralytic use will result in injury to neuromuscular junction
- Deconditioning of muscles
- Difficult to assess neurologic status

**Protective Lung Strategy**

- Avoid oxygen toxicity
- Minimize alveolar overinflation
- Prevent atelectasis

**Ventilation Strategy Lung Rest**

- What is lung rest?
  - small tidal volume
  - avoid high inspiratory pressures
  - relatively high peep but not excessively high peep (7-10)
  - Slow rates
- Be gentle
- Be patient
- Try to avoid atelectasis but if it occurs – don’t beat up the lung trying to re-inflate
What are Lung Rest Settings?

I don't know!

WHAT HAVE WE LEARNED?

- We need to be flexible as caregivers
- Good flow is imperative to survival and lung rest
- Cannulation may not be "standard" may need to add extra cannula for adequate flow
- We need to get out of the box. Standard wait and see philosophy may lead to more multi-organ failure
“BE PATIENT” DOES NOT MEAN “BE PASSIVE”

Active Management Team Approach

- BAL
- Chest CT
- Light sedation
- Extubation versus tracheostomy
- Early mobilization
- Cannula configuration

BRONCHOALVEOLAR LAVAGE

- Get a BAL soon after going on ECMO
- Patient may have mucus plugs, airway edema, inflammation that is unrecognized
- Look even in pts too small to lavage as you can adjust your pulmonary therapy
  - Dornase, more aggressive pulmonary toilet and so forth
**Chest CT**

- Helps evaluate extent of lung injury
- May change management
- Weekly chest CT will help follow progress of lung disease

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**Extubation**

- Decrease and assess level of sedation (sedation versus delirium)
- Avoids injurious positive pressure ventilation
- Pt moves around better
- Interacts with family

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**So Who Cares if the Patient Moves Around More!**

**Functional Disability 5 Years after Acute Respiratory Distress Syndrome**

- 100 patients 5 year follow-up
- No recognizable weakness but all had perceived weakness + inability to perform physical work to previous intensity
- Oral/airway damage
  - Tracheal stenosis
  - Vocal cord injury
  - Reactive airway disease
  - Dental implants from intubation damage
- Pulmonary
  - Most had near normal pulmonary function testing
  - 25/100 had chest CT 7-9 years post ARDS: most common finding minor fibrotic areas consistent with ventilator induced lung injury, also bullae, bronchiectasis, pleural thickening

NEJM 364, 14 April 7, 2011
**Functional Disability 5 Years after Acute Respiratory Distress Syndrome**

- Foot amputation from vasoconstrictive medications
- Hearing loss or tinnitus from ototoxic medications
- Depression/anxiety/post-traumatic stress disorder
- By 5 years, 77% patients had returned to work
- These findings are often found in survivors of critical illness not just ARDS

**Can we prevent these long-term sequelae?**

**YES!**

**Extubation**

- Anecdotally pts improving faster, shorter runs with less morbidity
- Hopefully less chronic lung disease
- So far 20 pts extubated on ECMO

Off ECMO: 10 days later, home 2 weeks later
**Extubation Lessons**

- Patient may look uncomfortable on low vent settings (tachypnea, nasal flaring, retractions, anxious) but once extubated, they are very comfortable.
- They still may have tachypnea etc. but are comfortable.
- Better if patient awake enough to breath.
- But lungs easier to re-inflate even if patient is so comfortable, they are not breathing.

**15 Days after Extubation!**

**ECMO Day 1**
Day 6 VV ECMO
4 Days Post Extubation
6 Weeks VV ECMO
Just Decannulated

3 months post VV ECMO

Early Mobilization
- Lung transplant centers
- Adults and teenagers cannulated in neck are awake, extubated or with tracheostomy tubes
- Out of bed
- Walking around ICU
- Faster recovery once off ECMO without needing rehabilitation
**Pitfalls**

- Cannot wean ventilator or extubate without adequate flow, often need extra cannula
- Femoral cannula limit movement like walking
- Consider double lumen VV cannula
- Consider extra cannula
  - femoral, cephalad

**Conclusions**

- ECMO management in ARDS patients, while controversial, continues to improve
- Large children/teenagers can benefit from ECMO
- ARDS patients benefit from gentle low pressure low volume ventilation or no mechanical ventilation
- Our care needs to progress to prevent long term injury
- Over the last 5 years, there has been significant change in ECMO support