Principle, management & monitoring of patients on ECMO
Role of ECMO & ECCO2 R in ARDS

Kodati Rakesh
HISTORY
ECLS (Extracorporeal life support)

- Encompasses all extracorporeal technologies and life support components including oxygenation, carbon dioxide removal, and haemodynamic support; renal and liver support may also be incorporated

- ECMO (VA & VV ECMO)
- ECPR
- ECCO2R
History

• 1971 – first successfully treated case of ARDS
• 1975 – first neonatal case
• 1978 – first description of ECCO2R
• 1989 – foundation of ESLO (Extracorporeal life support organisation)
• 2009 – renewed interest in ARDS (CESAR trial)
• 2009 – H1N1 pandemic, lead to widespread use
PROLONGED EXTRACORPOREAL OXYGENATION FOR ACUTE POST-TRAUMATIC RESPIRATORY FAILURE (SHOCK-LUNG SYNDROME)

Use of the Bramson Membrane Lung

First successful ECMO patient in 1971

Figure 3.4. The first successful extracorporeal life support patient, treated by J. Donald Hill using the Bramson oxygenator (foreground), Santa Barbara, 1971.
## ECLS registry report 2016

<table>
<thead>
<tr>
<th></th>
<th>No. Cases</th>
<th>Survived ECLS, N (%)</th>
<th>Discharged, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neonatal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>29,153</td>
<td>24,488 (84)</td>
<td>21,545 (74)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>6,475</td>
<td>4,028 (62)</td>
<td>2,695 (42)</td>
</tr>
<tr>
<td>ECPR</td>
<td>1,336</td>
<td>859 (64)</td>
<td>547 (41)</td>
</tr>
<tr>
<td><strong>Pediatric</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>7,552</td>
<td>5,036 (67)</td>
<td>4,371 (58)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>8,374</td>
<td>5,594 (67)</td>
<td>4,265 (51)</td>
</tr>
<tr>
<td>ECPR</td>
<td>2,996</td>
<td>1,645 (55)</td>
<td>1,232 (41)</td>
</tr>
<tr>
<td><strong>Adult</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>10,601</td>
<td>6,997 (66)</td>
<td>6,121 (58)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>9,025</td>
<td>5,082 (56)</td>
<td>3,721 (41)</td>
</tr>
<tr>
<td>ECPR</td>
<td>2,885</td>
<td>1,137 (39)</td>
<td>848 (29)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>78,397</td>
<td>54,866 (70)</td>
<td>45,345 (58)</td>
</tr>
</tbody>
</table>
ECLS registry report 2016

RR Thiagarajan et al, ELSO registry, ASAIO Journal 2017
ECLS registry report 2016

RR Thiagarajan et al, ELSO registry, ASAIO Journal 2017
ECLS in respiratory failure

RR Thiagarajan et al, ELSO registry, ASAIO Journal 2017
BASIC PRINCIPLES
Principles

• To provide cardiopulmonary support in cases refractory to conventional management

• To correct gas exchange abnormalities not maintained by conventional support

• Used to prevent ventilator associated lung injury
  – Reducing the delivered volumes and airway pressures
  – Low FiO2 levels
Principles

• Bridging therapy, not a cure
  – Bridge to recovery – buying time for the patient to recover
  – Bridge to decision – temporary step till further decision
  – Bridge to transplant
Different from CPB..

<table>
<thead>
<tr>
<th>CPB (cardiopulmonary bypass)</th>
<th>ECMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperatively during cardiac sx</td>
<td>Intensive care units</td>
</tr>
<tr>
<td>Few hours</td>
<td>Longer duration of support</td>
</tr>
<tr>
<td>Low blood flow rates (2 l/min)</td>
<td>Higher flow rates ( &gt;4 l/min)</td>
</tr>
<tr>
<td>More anticoagulation</td>
<td>Less anticoagulation</td>
</tr>
</tbody>
</table>
Physiology - oxygenation

- Direct function of the blood flow
- Usual blood flow required is b/n 3 to 6 L/min
- Factors determining oxygenation
  - Thickness of the blood film
  - Fraction of inspired oxygen (FIO2)
  - Hemoglobin concentration
  - Oxygenation of the blood prior to membrane

Gattinoni et al. Critical Care 2011, 15:243
Physiology – CO2 removal

• Direct function of “Sweep gas” flow rate
• Sweep flow – measure of gas flow across the membrane oxygenator
• CO2 exchange is much more efficient than O2 exchange
• May necessitate adding CO2 to the sweep gas to prevent excessive CO2 removal and respiratory alkalosis in neonates

Gattinoni et al. Critical Care 2011, 15:243
Physiology - Artificial lung

Oxygenation
- High extracorporeal blood flow
- Low sweep flow

CO2 removal
- High sweep flow
- Low blood flow

Gattinoni et al. Critical Care 2011, 15:243
Physiology - Artificial lung

Murray Nadel Textbook of Respiratory Medicine, 6th Ed
Modes of access

• Veno - venous (V-V)
  – Isolated respiratory failure

• Veno - arterial (V-A)
  – Isolated cardiac failure
  – Cardiorespiratory failure
Venovenous ECMO

- Blood is extracted from the vena cava or right atrium and returned to the right atrium
- Provides respiratory support, but the patient is dependent upon his or her own hemodynamics
- Systemic blood flow and pressure are the result of the native cardiac function unrelated to the extracorporeal flow
Venovenous ECMO

• The PaO2 is determined by the mixing effect of oxygenated blood returning from the ECMO circuit to the right heart and deoxygenated blood returning from the bronchial admixture, coronary sinus, and vena cava.

• Connected in series with lungs and heart.
Venovenous ECMO

- Most frequently used
- Drainage though femoral venous cannula in IVC
- Infusion through IJV cannula proximal to RA

Femoral vein (drainage)
Jugular vein (infusion)
Venovenous ECMO

- Higher risk of recirculation

- Tip of the drainage cannula at the level of L1–L2, in order to receive the blood contribution of the renal veins

- Tip of the reimmission cannula should be placed close to the junction between the IVC & RA

Femoral vein (drainage)
Femoral vein (infusion)
Venovenous ECMO

- Cannula must cross the RA with the tip in the IVC
- Blood is drained from both the SVC & IVC
- Reinfusion occurs through a separate lumen into the RA just facing the tricuspid valve
- Early mobilisation & less need of sedatives

Single cannulation with double lumen
Venoarterial ECMO

- Blood is extracted from the right atrium or vena cava (for drainage), and returned to the arterial system either through peripheral cannulations via femoral, axillary or carotid arteries (for infusion)
- Connected in parallel with heart and lungs
Venoarterial ECMO

• Systemic flow, PO2 and CO2 levels are determined by combination of the blood added from the extracorporeal circuit plus the amount of blood passing through the native heart and lungs
Venoarterial ECMO

Femoral vein (drainage)
Femoral artery (infusion)

Femoral vein (drainage)
Axillary artery (infusion)

Femoral vein (drainage)
Carotid artery (infusion)
Central venoarterial ECMO

Right atrium (drainage)
Ascending aorta (infusion)

Post cardiotomy - Cannulas of CPB are transferred to the ECMO circuit

Larger cannulas with low resistance
# ECMO

<table>
<thead>
<tr>
<th>V-V ECMO</th>
<th>V-A ECMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does not provide cardiac support</td>
<td>Provides cardiac support to assist systemic circulation</td>
</tr>
<tr>
<td>Connected in series</td>
<td>Connected in parallel</td>
</tr>
<tr>
<td>Low PaO2 achieved -</td>
<td>Higher PaO2 achieved</td>
</tr>
<tr>
<td>• Blood with high oxygen saturation reaches the PA, ↑V/Q mismatch of the native lung due to the loss of hypoxic vasoconstriction</td>
<td>• artificially oxygenated blood mixes with arterial blood and directly perfuses distal organs</td>
</tr>
<tr>
<td>• Recirculation of oxygenated blood within the circuit</td>
<td>• no loss of hypoxic vasoconstriction, in lungs</td>
</tr>
<tr>
<td>Less complications</td>
<td>More complications</td>
</tr>
</tbody>
</table>

- V-V ECMO: Venous-to-venous ECMO
- V-A ECMO: Venous-to-arterial ECMO

- **PaO2**: Partial pressure of oxygen in arterial blood
- **V/Q**: Ventilation to perfusion ratio
INDICATIONS & CONTRAINDICATIONS
Indications of ECLS

• Hypoxic respiratory failure due to any cause
  - P/F ratio < 100 and/or Murray score ≥ 3
• Hypercapnic failure on MV despite high Pplat (pH <7.2)
• Need for intubation in a patient on lung transplant list
• Immediate cardiac or respiratory collapse (PE, blocked airway, unresponsive to optimal care)
• Refractory cardiogenic shock

ELSO General guidelines Ver 1.3 Dec 2013
Contraindications

- Mechanical ventilation at high settings (FiO2 > 0.9, Pplat > 30) for ≥ 7 days
- Major pharmacologic immunosuppression (absolute neutrophil count <400/mm³)
- CNS hemorrhage that is recent or expanding
- Non recoverable co morbidity such as major CNS damage or terminal malignancy
- Age: no specific age contraindication but consider increasing risk with increasing age
ECMO CIRCUITRY & COMPONENTS
ECMO circuitry
Components

• Cannulas
• Pumps
• Oxygenator / Membrane lung
• Heat exchanger
• Tubings
Components - Cannulas

• Best cannulation technique should be chosen on the basis of patients and clinical settings
• Intrathoracic or extrathoracic
• Percutaneous or surgical
• Percutaneous approach is standard of care in VV ECMO
  — Less risk of bleeding
  — Short operative time
  — Easier mobilization & nursing

Laurance Lequier et al; Pediatr Crit Care Med. 2013
Components - Cannulas

• Cannula size
  – Big enough to ensure adequate flow with relatively low suction pressure
  – Shouldn’t exceed 2/3 rd of vessel diameter

• Positioning
  – Important to minimise recirculation
  – Tip should be in a high flow vessel
# Components - Pumps

<table>
<thead>
<tr>
<th>Roller pump</th>
<th>Centrifugal pump</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compresses the circuit tubing and pushes the blood through the raceway of the pump</td>
<td>Driven by electromagnetic induction motors and uses the principles of centrifugal force to generate a flow</td>
</tr>
<tr>
<td>Constant flow provided independent of circuit preload</td>
<td>Inability to maintain a set flow Back flow at low flow rates</td>
</tr>
<tr>
<td>Risk of cavitation and hemolysis Circuit disruption due to excessive pressure</td>
<td>Less risk of cavitation and air embolism Reduced blood trauma</td>
</tr>
</tbody>
</table>

*Laurance Lequier et al; Pediatr Crit Care Med. 2013*
Components - Oxygenator

• Blood and gas flow in counter-current directions within the silicone lung and gas exchange occurs by diffusion across the membrane

• Hollow fiber devices with polymethylpentene surface (PMP) replaced silicone ones
  — efficient at gas exchange
  — minimal plasma leakage
  — low resistance to blood flow

*Laurance Lequier et al; Pediatr Crit Care Med. 2013*
Components – heat exchanger

• Principle is counter current flow
• A great deal of heat is lost while a patient is on ECMO as a result of the large extracorporeal surface area to which the patient’s blood is exposed
• The water is warmed to 37 °C to 40 °C to compensate for the heat loss in the circuit
• Kept less than 42 °C to prevent hemolysis and formation of bubbles

Laurance Lequier et al; Pediatr Crit Care Med. 2013
Components - Tubings

• Polyvinylchloride (PVC) – based plastic compound
• Minimal resistance to venous drainage
• Non-biologic surfaces of a circuit – activation of coagulation pathway and the inflammatory response
• Blood flow and pressure monitors
• Continuous oxyhemoglobin saturation monitors
• Circuit access sites

Laurance Lequier et al; Pediatr Crit Care Med. 2013
Components - Tubings

- Biocompatible lining to reduce the systemic inflammatory response and risk of thrombosis and bleeding
- Fewer the connectors and stopcocks – less is the flow turbulence and blood stasis

*Laurance Lequier et al; Pediatr Crit Care Med. 2013*
Components - Bridge

• Connection between the venous (drain) and arterial (return) components of the circuit

• Bypass to allow the isolation of the patient from the circuit

• If adequate gas exchange and hemodynamics can be maintained while flow continues through the bridge after its opening
INITIATION & MAINTENANCE
Technique of ECMO

- Should only be performed by clinicians with training and experience in its initiation, maintenance, and discontinuation
- The patient is anticoagulated with IV heparin
- Cannulae are inserted into the vessels
- Cannulae are connected to the limbs of circuit
- ECMO support is initiated after that
Circuit initiation

- Flow rate: 50-80 cc/dry kg/min

- BF required during VV bypass for acceptable arterial oxygenation is usually 3 to 6 L/min, partially depending on the cardiac output of the patient, on hemoglobin concentration and on saturation

- Maximum initially, then lowest flow to maintain SaO2 > 80-85% at rest vent settings in VV ECMO

Gattinoni et al. Critical Care 2011, 15:243
S Allen et al; Journal of Intensive Care Medicine 2011
Circuit initiation

• In contrast, the flow rate used during VA ECMO
  *high enough to provide adequate perfusion pressure and venous oxyhemoglobin saturation
  *low enough to provide sufficient preload to maintain left ventricular output

• Sweep gas flow is titrated to maintain PaCO$_2$ at 40 mmHg

Gattinoni et al. Critical Care 2011, 15:243
S Allen et al; Journal of Intensive Care Medicine 2011
Titration & targets

• An arterial oxyhemoglobin saturation
  – VA ECMO: > 90% ; VV ECMO: 80-85%
• SvO2 25-30% less than SaO2, measured on the venous line
• Higher SaO2 targets would require high flows predisposing to volume overload and hemolysis in VV bypass
• Adequate tissue perfusion, as determined by the ABP, venous oxygen saturation, and blood lactate level

Gattinoni et al. Critical Care 2011, 15:243
S Allen et al; Journal of Intensive Care Medicine 2011
Oxygenation monitoring

• If the FIO2 of the sweep gas is 1, the expected PO2 in the output blood (PO2out) should be high (generally > 300 to 400 mm Hg)

• Drop in pO2 in post oxygenator blood
  Oxygenator failure
  Recirculation

Gattinoni et al. Critical Care 2011, 15:243
S Allen et al; Journal of Intensive Care Medicine 2011
Oxygenation monitoring

- Suspect **recirculation**
  - $\text{SaO}_2$ below 80% with reasonable ECMO flows
  - minimal improvement in saturation with higher flows
- Confirmed by decreased difference b/n pre and post oxygenator blood saturations
- Decreased by distancing the inflow and outflow cannula
- Even after readjusting, it can occur secondary to increased pulmonary vascular resistance leading to preferential flow thru ECMO circuit

*Gattinoni et al. Critical Care 2011, 15:243*
*S Allen et al; Journal of Intensive Care Medicine 2011*
Pressure monitoring

Ensure excessive suction is avoided

Detect resistance in oxygenator (or) post oxygenator circuit
Flow monitoring

- Drop in flow at stable RPM
  - Decrease in preload
    - Hypovolemia / bleeding
    - Obstructive process – tamponade, tension PTX & Abd CS
  - Increase in after load
    - Kink in outflow cannula
    - Membrane oxygenator thrombus
    - High SVR in VA circuit

- Negative pressure – hemolysis - chattering

*M Chung et al, Scientific World Journal 2014*
MAP monitoring

• Essential in case of VA ECMO bypass - MAP > 65 mm Hg
• MAP should not exceed 90 mm Hg in order to limit the afterload
• MAP can be increased by administering the volume or by increasing the RPM
• Correction of volume status and vasopressor support as indicated to maintain MAP

M Chung et al, ScientificWorld Journal 2014
LV monitoring - VA ECMO

VA ECMO

Decrease in preload to the heart
Decrease in volume work

Increase in after load
Increase in pressure work

Overall effect is determined by level of ECMO support and myocardial function
LV monitoring - V A ECMO

• Left ventricular output can be closely monitored by pulsatility in the arterial line's waveform & frequent echocardiography

• Insufficient unloading of the distended LV due to ongoing blood flow to LV from the bronchial circulation and right ventricle – pulmonary edema

M Chung et al, Scientific World Journal 2014
LV monitoring - V A ECMO

• Failing left ventricular contractility despite ECMO
  – Inotropic support
  – Intra aortic balloon pulsation

• Refractory LV depression
  – LV decompression
  – transatrial balloon septostomy or insertion of a left atrial or ventricular drainage catheter
Systemic anticoagulation

- Intended to prevent thrombotic complications
- UFH most commonly used
- Classical dose is b/n 20 and 70 IU/kg/hr
- Sensitivity of UFH depends on endogenous AT3 levels and platelets
- If AT 3 deficiency, replace by FFP
Systemic anticoagulation

• ACT (activated clotting time) - standard of monitoring during heparin anticoagulation
• Target of ACT is 180 to 210 sec
• Target has to be individualised based on signs of hypo or hypercoagulability and ECMO flow rates
• Alternatives of ACT
  • PTT (1.5 times the baseline)
  • anti-Factor Xa activity (anti Xa) levels
  • thromboelastography (TEG)
Systemic anticoagulation

- Systemic anticoagulation in VV ECMO

Systematic review, 18 studies including a total of 646 patients
Rate of major bleeds was 16%
Rate of clotting episodes was 53%

<table>
<thead>
<tr>
<th>7 studies aPTT (n =199)</th>
<th>2 studies ACT (n =37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleeding episodes - 37 (19%)</td>
<td></td>
</tr>
<tr>
<td>Major thromboses - 53 (27%)</td>
<td></td>
</tr>
<tr>
<td>Major bleeding episodes - 23 (62%)</td>
<td></td>
</tr>
<tr>
<td>Major thromboses - 23 (62%)</td>
<td></td>
</tr>
</tbody>
</table>

aPTT targets ≥ 60 seconds (n =43, 5 studies) reported 24 (56%) bleeds & 3 (7%) clot
aPTT target < 60 seconds(n = 156, 3 studies) reported 13 (8%) bleeds & 50 (32%) clots

Michael C Sklar et al, Annals ATS. 2016
Systemic anticoagulation

• Optimal therapeutic targets for anticoagulation during ECMO are unclear
• Previously studies are retrospective, observational design, small cohorts, and patient heterogeneity
• Clinical significance of reported thrombotic complications is largely unknown
• Need for RCTs of anticoagulation strategies for patients undergoing ECMO

*Michael C Sklar et al, Annals ATS. 2016*
MV - ECMO

- Significant knowledge gap in understanding the benefits and risks of MV during ECMO
- Risk of VILI
  - Limitation of the alveolar strain by decrease in Vt
  - High PEEP with low Vt to prevent atelectrauma
  - Avoid oxygen toxicity to the lung from a high FiO2 & reabsorption atelectasis

*Schmidt et al. Critical Care 2014, 18:203*
MV - ECMO

- Cardiovascular effects
  - Increase in pulmonary vascular resistance, RV overload, causing adverse effects in pts of RV failure
  - Conversely, pts with predominately LV failure may develop pulmonary edema requiring high PEEP
  - ↓ lung perfusion may accelerate pulmonary vascular thrombosis in severe lung injury

Schmidt et al. Critical Care 2014, 18:203
MV - ECMO

- Most appropriate settings are unknown
- FiO2 <0.4
- Non damaging “rest settings (P plat<25 cm H2O)”
- Tidal volumes are maintained below 4 ml/kg PBW
- Increased alveolar recruitment with PEEP to maintain airway patency at low lung volumes

ELSO General guidelinesVer 1.3 Dec 2013
## MV - ECMO

<table>
<thead>
<tr>
<th>First 24 hrs</th>
<th>24 – 48 hrs</th>
<th>After 48 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate to heavy sedation</td>
<td>moderate to minimal sedation</td>
<td>Minimal to no sedation</td>
</tr>
<tr>
<td>PCV 25/15</td>
<td>PCV 20/10</td>
<td>PCV as before or take on PSV as the condition improves</td>
</tr>
<tr>
<td>I: E 2:1</td>
<td>I: E 2:1</td>
<td></td>
</tr>
<tr>
<td>Rate 5/min</td>
<td>Rate 5/min + spontaneous breaths</td>
<td></td>
</tr>
<tr>
<td>FiO2 0.5</td>
<td>FiO2 0.2 - 0.4</td>
<td></td>
</tr>
<tr>
<td>FiN2 50 %</td>
<td>FiN2 60-80 %</td>
<td></td>
</tr>
</tbody>
</table>

ELSO General guidelines Ver 1.3 Dec 2013
## MV - ECMO

<table>
<thead>
<tr>
<th></th>
<th>European network</th>
<th>CESAR</th>
<th>EOLIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of MV</td>
<td>Volume AC</td>
<td>Pressure AC</td>
<td>Volume AC / APRV</td>
</tr>
<tr>
<td>PEEP</td>
<td>≥ 10</td>
<td>10 - 15</td>
<td>&gt; 10</td>
</tr>
<tr>
<td>FIO2</td>
<td>0.3 – 0.5</td>
<td>0.3</td>
<td>0.3 – 0.6</td>
</tr>
<tr>
<td>Pressure limit</td>
<td>≤ 20 to 25 cm H$_2$O</td>
<td>20 to 25 cm H$_2$O</td>
<td>25 cm H$_2$O</td>
</tr>
<tr>
<td>RR (/min)</td>
<td>6 - 20</td>
<td>10</td>
<td>10 - 30</td>
</tr>
<tr>
<td>Tidal volume</td>
<td>Targeted to above pressure</td>
<td>-</td>
<td>Targeted to above pressure</td>
</tr>
</tbody>
</table>

*To what extent we should reduce both the tidal volume and the plateau pressure to allow lung rest remains unknown*
Transfusion support

• The benefit of enhanced oxygen delivery must be weighed against the potential harm of transfusion

• Many centers recommend transfusion who are receiving ECMO until their hematocrit levels are in the normal range

• Lesser blood flows in the circuit are required if hematocrit is maintained

Transfusion support

• Platelets are continuously consumed during ECMO because they are activated by exposure to the foreign surface area

• Platelet counts should be maintained greater than 50,000/microL, which may require platelet transfusion

Weaning from ECMO

• Progressive reduction of the ECMO contribution to oxygenation and CO2 removal as the gas exchange capability of the native lung improves and the patient’s clinical conditions stabilize

• Requires regular monitoring the pts respiratory function (gas exchange function, respiratory mechanics) and hemodynamics
Weaning from ECMO

• Respiratory failure
  – when 50% to 80% of total gas exchange is by the native lungs
  – when the patient’s lung compliance improves
  – improving chest x-ray

• Cardiac failure
  – Enhanced aortic pulsatility correlates with improved left ventricular output
  – Decrease in mixed-venous oxygenation saturation
  – MAP > 60 mmHg in the absence of “high-dose” inopressors
Weaning from ECMO

• VV ECMO trials
  – Sweep low rate is slowly decreased
  – Ventilator is placed on full support
  – Successful weaning is confirmed if the patient remains stable at a FGF of 0 L/min for a period of 4 to 24 hours
Weaning from ECMO

• VA ECMO trials
  – Require temporary clamping of both the drainage and infusion lines, while allowing the ECMO circuit to circulate through a bridge between the arterial and venous limbs
  – If the patient manifests signs of deterioration, the bridge is clamped and flow is re-directed to the patient as before

*Steve Allen et al, Journal of Intensive Care Medicine 26(1) 13-26*
COMPLICATIONS
Complications ECLS

Circuit related complications

• Blood clots and thromboembolism
  — Failure of the oxygenator
  — Platelet consumption
  — Pulmonary or systemic embolism

• Gas entrapment and embolism

• Circuit fractures
Complications ECLS

Circuit related complications

• Recirculation – minimizing the oxygenation efficiency

• Shaking or “chatter” of the tubing - hypovolemia, cannula malposition, pneumothorax, and pericardial tamponade

• Manifests as caused by excessive negative pressure (created by the pump in the venous system) as well as a drop in pump output
Complications ECLS

Patient related complications

• Vascular access complications
  – Perforation of posterior wall, hematoma
  – Dissection of the vessel
  – AV fistula or pseudo aneurysm

• Leg ischemia in femoral arterial cannulation
  – Requires insertion of peripheral perfusion cannula distally
Complications ECLS

Patient related complications

• Bleeding – surgical site, GI, airway bleed
• Coagulopathy (TCP, HIT & DIC)
• Neurologic complications – intracranial hemorrhage
• Cardiac complications – insufficient unloading of the distended LV due to ongoing blood flow to LV from the bronchial circulation and right ventricle
• Sepsis
# Complications ECLS

<table>
<thead>
<tr>
<th></th>
<th>Neonate (%)</th>
<th>Pediatric (%)</th>
<th>Adult (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical: pump malfunction</td>
<td>1.6</td>
<td>2.2</td>
<td>1.5</td>
</tr>
<tr>
<td>Mechanical: oxygenator failure</td>
<td>5.7</td>
<td>10.6</td>
<td>9.1</td>
</tr>
<tr>
<td>Cannula hemorrhage</td>
<td>7.9</td>
<td>18.3</td>
<td>13.2</td>
</tr>
<tr>
<td>Surgical hemorrhage</td>
<td>6.3</td>
<td>12.6</td>
<td>10.5</td>
</tr>
<tr>
<td>Pulmonary hemorrhage</td>
<td>4.5</td>
<td>8.1</td>
<td>6.1</td>
</tr>
<tr>
<td>CNS hemorrhage</td>
<td>7.6</td>
<td>6.4</td>
<td>3.9</td>
</tr>
<tr>
<td>CNS infarction</td>
<td>6.8</td>
<td>4.2</td>
<td>2.0</td>
</tr>
<tr>
<td>Renal failure</td>
<td>7.8*</td>
<td>12.9*</td>
<td>9.3†</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>7.3</td>
<td>5.2</td>
<td>8.7</td>
</tr>
<tr>
<td>Infection</td>
<td>5.8</td>
<td>16.8</td>
<td>17.5</td>
</tr>
</tbody>
</table>

RR Thiagarajan et al, ELSO registry, ASAIO Journal 2017
ECMO - ARDS
ECMO in ARDS

- Currently a *salvage therapy* for the most severe cases of ARDS
- Benefit of ECMO as compared to conventional, standard of care management for ARDS has yet to be demonstrated
- Increasing potential for ECMO to enhance the way ARDS is managed

*M Parekh et al; Ann Transl Med 2017*
Benefit in ARDS

- Complete lung rest – Lung protective ventilation
- Complete avoidance of VILI
- Adequate gas exchange extracorporeally
- Decreases Oxygen toxicity to lung

*M Parekh et al; Ann Transl Med 2017*
Indications in ARDS

* Threshold for the initiation of ECMO varies considerably across studies and guidelines

• Severe hypoxemia (P/F ratio <80, despite the application of high PEEP) for at least 6 hr in patients with potentially reversible respiratory failure

• Considered after a shorter interval if P/F ratio < 50

• Uncompensated hypercapnia with acidemia (pH <7.15)

• Murray score > 3.0

Contraindications in ARDS

- High-pressure ventilation (Pplat > 30 cm of water) or high Fio2 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
- Any condition that precludes the use of anticoagulation therapy
ECMO

• First prospective randomised study in severe ARF
• 9 medical centres, 90 subjects
• Majority - acute bacterial or viral pneumonia (57%)
• Conventional MV (n=48) Vs MV + VA ECMO (42)
• MV before entry  7 days in control group vs 9.6 in test group
• 4 survived in each group

Zapol WM et al, JAMA 1979;242(20):2193–2196
Pts had significantly high PaO2, low PaCO2 in study group
Reduction of FiO2 from 0.74 to 0.48 seen in ECMO group
High mean daily transfusion support (1 to 2.5 L)
ECMO can support respiratory gas exchange but did not increase the probability of long-term survival in patients with severe ARF
ECMO

• 122 ARDS pts (PaO2 ≤ 80 mm Hg on FiO2 ≥ 0.6)
• Followed a predefined clinical algorithm
• Initially treated with advanced non invasive Rx options (PCV with PEEP, PHC, Reduction of pulmonary edema, optional proning and iNO)
• Those who are not responding to advanced Rx were taken onto VV ECMO by certain entry criteria

ECMO

- 122 consecutive patients according to a predefined treatment algorithm [(n=73), mean P/F 86] or to care involving ECMO [(n=49), mean P/F 67]
- The overall survival rate was 75%
- 89% in the AT-sine ECMO group & 55% in the ECMO treatment group (p < 0.001)
- Patients in the ECMO group were found to have higher severity of illness scores and worse oxygenation at baseline

ECMO

• Evidence from these studies suggested no definite benefit of ECMO over conventional mechanical ventilation
• Its usage was restricted to clinical trials and not got widely implemented
• However these studies have little relevance now due to changed ventilatory strategies, ECMO circuits, disease management and increased experience with it
H1 N1 Australia NZ report

• Retrospective study of ECMO receivers for H1 N1 ARDS in 15 ICUs from June to August 2009

• 68 patients were included
  – 53 patients (78%) were PCR / viral culture positive
  – 8 patients (12%) had serological evidence of recent influenza A
  – 7 patients (10%) had preceding symptoms of influenza like illness

Andrew R Davies et al, JAMA, Nov 2009; Vol 302, No. 17
# H1 N1 Australia NZ report

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Confirmed Infection (n = 53)</th>
<th>Suspected Infection (n = 15)</th>
<th>All Infections (N = 68)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation parameters, median (IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest PaO₂/FiO₂ ratio</td>
<td>55 (48-65)</td>
<td>57 (45-62)</td>
<td>56 (48-63)</td>
</tr>
<tr>
<td>Highest FiO₂</td>
<td>1.0 (1.0-1.0)</td>
<td>1.0 (1.0-1.0)</td>
<td>1.0 (1.0-1.0)</td>
</tr>
<tr>
<td>Highest PEEP, cm H₂O</td>
<td>18 (15-20)</td>
<td>15 (14-18)</td>
<td>18 (15-20)</td>
</tr>
<tr>
<td>Highest peak airway pressure, cm H₂O</td>
<td>36 (34-40)</td>
<td>34 (29-36)</td>
<td>36 (33-38)</td>
</tr>
<tr>
<td>Lowest pH</td>
<td>7.2 (7.1-7.3)</td>
<td>7.2 (7.1-7.3)</td>
<td>7.2 (7.1-7.3)</td>
</tr>
<tr>
<td>Highest Paco₂, mm Hg</td>
<td>69 (54-86)</td>
<td>67 (61-73)</td>
<td>69 (54-83)</td>
</tr>
<tr>
<td>Highest tidal volume, mL/kg</td>
<td>5.6 (4.8-6.6)</td>
<td>5.7 (4.4-6.7)</td>
<td>5.6 (4.6-6.7)</td>
</tr>
<tr>
<td>Quadrants of radiograph infiltrate, No.</td>
<td>4 (4-4)</td>
<td>4 (4-4)</td>
<td>4 (4-4)</td>
</tr>
<tr>
<td>Acute lung injury scorea</td>
<td>3.8 (3.3-4.0)</td>
<td>3.5 (3.3-3.8)</td>
<td>3.8 (3.5-4.0)</td>
</tr>
<tr>
<td>Pneumothorax pre-ECMO, No. (%)</td>
<td>9 (17)</td>
<td>1 (7)</td>
<td>10 (15)</td>
</tr>
<tr>
<td>Rescue ARDS therapies used, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recruitment maneuver</td>
<td>30 (66)</td>
<td>8 (66)</td>
<td>38 (67)</td>
</tr>
<tr>
<td>Prone positioning</td>
<td>11 (22)</td>
<td>1 (8)</td>
<td>12 (20)</td>
</tr>
<tr>
<td>High-frequency oscillation</td>
<td>3 (6)</td>
<td>0</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Nitric oxide</td>
<td>19 (38)</td>
<td>1 (8)</td>
<td>20 (32)</td>
</tr>
<tr>
<td>Prostacyclin</td>
<td>12 (23)</td>
<td>2 (15)</td>
<td>14 (22)</td>
</tr>
</tbody>
</table>

*Andrew R Davies et al, JAMA, Nov 2009; Vol 302, No. 17*
## H1 N1 Australia NZ report

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Confirmed Infection (n = 53)</th>
<th>Suspected Infection (n = 15)</th>
<th>All Infections (N = 68)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Length of stay, median (IQR), d</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>26 (16-35)</td>
<td>31 (15-38)</td>
<td>27 (16-37)</td>
</tr>
<tr>
<td>Hospital</td>
<td>35 (24-45)</td>
<td>40 (27-54)</td>
<td>39 (23-47)</td>
</tr>
<tr>
<td><strong>Duration, median (IQR), d</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>24 (13-31)</td>
<td>28 (13-34)</td>
<td>25 (13-34)</td>
</tr>
<tr>
<td>ECMO support</td>
<td>10 (7-14)</td>
<td>11 (10-16)</td>
<td>10 (7-15)</td>
</tr>
<tr>
<td><strong>Survival at ICU discharge</strong></td>
<td>38 (72)</td>
<td>10 (67)</td>
<td>48 (71)</td>
</tr>
<tr>
<td>Still in ICU</td>
<td>4 (8)</td>
<td>2 (13)</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Survival at hospital discharge</td>
<td>22 (42)</td>
<td>10 (67)</td>
<td>32 (47)</td>
</tr>
<tr>
<td>Still in hospital&lt;sup&gt;b&lt;/sup&gt;</td>
<td>14 (26)</td>
<td>2 (13)</td>
<td>16 (24)</td>
</tr>
<tr>
<td>Ambulant at hospital discharge&lt;sup&gt;c&lt;/sup&gt;</td>
<td>21 (95)</td>
<td>10 (100)</td>
<td>31 (97)</td>
</tr>
<tr>
<td>Sao₂ on room air at hospital discharge, median (IQR), %&lt;sup&gt;c&lt;/sup&gt;</td>
<td>97 (95-98)</td>
<td>97 (95-98)</td>
<td>97 (95-98)</td>
</tr>
<tr>
<td><strong>Discharge destination</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td>11 (21)</td>
<td>3 (20)</td>
<td>14 (21)</td>
</tr>
<tr>
<td>Home</td>
<td>18 (34)</td>
<td>4 (27)</td>
<td>22 (32)</td>
</tr>
<tr>
<td>Other hospital</td>
<td>0</td>
<td>1 (7)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Rehabilitation facility</td>
<td>4 (8)</td>
<td>5 (33)</td>
<td>9 (13)</td>
</tr>
<tr>
<td><strong>Cause of death</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>3 (27)</td>
<td>1 (33)</td>
<td>4 (29)</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>4 (36)</td>
<td>2 (66)</td>
<td>6 (43)</td>
</tr>
<tr>
<td>Infection</td>
<td>1 (9)</td>
<td>0</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Intractable respiratory failure</td>
<td>3 (27)</td>
<td>1 (33)</td>
<td>4 (29)</td>
</tr>
</tbody>
</table>

Andrew R Davies et al, JAMA, Nov 2009; Vol 302, No. 17
## CESAR trial

### Efficacy of conventional ventilatory support versus ECMO for severe adult respiratory failure

| Participants | 180 adults of severe but potentially reversible respiratory failure (Murray score ≥ 3.0 / pH < 7.2) despite optimal conventional Rx |
| Methods      | Randomised in 1 : 1 fashion  
Conventional MV Vs Referral to consideration for ECMO  
68/90 (75 %) received ECMO |
| Outcome measure | Death or severe disability at 6 m of randomisation |
| Results      | Survival upto 6 months  
63% (57/90) of ECMO Vs 47% (41/87) of conventional MV  
RR of 0·69; 95% CI 0·05–0·97, p=0·03 |
| Conclusion   | Transfer of adult patients with severe but potentially reversible respiratory failure to a centre with an ECMO-based management protocol will significantly improve survival without severe disability |

*Giles J Peek et al;, Lancet 2009; 374: 1351–63*
## CESAR trial

<table>
<thead>
<tr>
<th>Outcome/Measure</th>
<th>ECMO group (n=90)*</th>
<th>Conventional management group (n=90)</th>
<th>Relative risk (95% CI, p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Death or severe disability at 6 months</strong></td>
<td></td>
<td></td>
<td><strong>0.69 (0.05-0.97, 0.03)</strong>†</td>
</tr>
<tr>
<td>No</td>
<td>57 (63%)</td>
<td>41 (47%)†</td>
<td>NA</td>
</tr>
<tr>
<td>Yes</td>
<td>33 (37%)</td>
<td>46 (53%)‡</td>
<td>NA</td>
</tr>
<tr>
<td>No information about severe disability</td>
<td>0</td>
<td>3 (3%)§</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Died at ≤6 months or before discharge</strong></td>
<td></td>
<td></td>
<td><strong>0.73 (0.52-1.03, 0.07)</strong></td>
</tr>
<tr>
<td>No</td>
<td>57 (63%)</td>
<td>45 (50%)</td>
<td>NA</td>
</tr>
<tr>
<td>Yes</td>
<td>33 (37%)</td>
<td>45 (45%)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Severe disability</strong></td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>No</td>
<td>57 (63%)</td>
<td>41 (46%)</td>
<td>NA</td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>1 (1%)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Cause of death</strong></td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>8 (9%)</td>
<td>24 (27%)</td>
<td>NA</td>
</tr>
<tr>
<td>Multiorgan failure</td>
<td>14 (16%)</td>
<td>15 (17%)</td>
<td>NA</td>
</tr>
<tr>
<td>Neurological disorder</td>
<td>4 (4%)</td>
<td>2 (2%)</td>
<td>NA</td>
</tr>
<tr>
<td>Cardiovascular disorder</td>
<td>1 (1%)</td>
<td>3 (3%)</td>
<td>NA</td>
</tr>
<tr>
<td>Related to ECMO</td>
<td>1 (1%)</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1%)</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (4%)</td>
<td>1 (1%)</td>
<td>NA</td>
</tr>
<tr>
<td>Time between randomisation and death (days)</td>
<td>15 (3–41)</td>
<td>5 (2–14)</td>
<td>NA</td>
</tr>
</tbody>
</table>
Limitations - CESAR trial

- No standardisation of Rx protocol
  - 30% of the patients in control arm did not get LPV
  - Steroid recipients more in study group

| 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 |
| Steroids | 76 (84%) | 58 (64%) | 0.001 |

Giles J Peek et al; Lancet 2009; 374: 1351–63
Limitations - CESAR trial

• Intervention in CESAR was *referral* to an ECMO center not *treatment* with ECMO
  ▪ 25% of patients in ECMO referral group did not receive ECMO

• Two serious adverse events noted
  – Mechanical failure of O2 supply during transport
  – Vessel perforation during cannulation

*Giles J Peek et al; Lancet 2009; 374: 1351–63*
Limitations - CESAR trial

• Three patients died before they could be transferred and two died in transit
• Risk of death during transfer of such patients
• Exclusion of pts ventilated with high pressure or high FiO₂ for more than 7 days
• Did improved care at the single ECMO hospital lead to the relative risk observed??

Giles J Peek et al; CESAR trial, Lancet 2009; 374: 1351–63
ECMO

• UK H1N1 2009-10
• H1N1-related ARDS transferred for ECMO Vs matched patients who were not referred for ECMO
• Of 80 ECMO-referred patients, 69 received ECMO (86.3%) and 22 died (27.5%) prior to discharge from the hospital
• Survival to acute hospital discharge

Noah et al, JAMA 2011;306(15):1659-1668
*For patients with H1N1-related ARDS, referral and transfer to an ECMO center was associated with lower hospital mortality compared to matched ones*

Noah et al, JAMA 2011;306(15):1659-1668
ECLS – In hospital mortality

- 4 RCTs, 6 observational studies (496/1248)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>ECLS Events</th>
<th>Total</th>
<th>MV Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio IV, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zapol 1979</td>
<td>38</td>
<td>42</td>
<td>44</td>
<td>48</td>
<td>14.8%</td>
<td>0.99 [0.87, 1.12] 1979</td>
</tr>
<tr>
<td>Morris 1994</td>
<td>14</td>
<td>21</td>
<td>11</td>
<td>19</td>
<td>10.0%</td>
<td>1.15 [0.71, 1.88] 1994</td>
</tr>
<tr>
<td>Lewandowski 1997</td>
<td>22</td>
<td>49</td>
<td>8</td>
<td>73</td>
<td>7.1%</td>
<td>4.10 [1.99, 8.45] 1997</td>
</tr>
<tr>
<td>Mols 2000</td>
<td>28</td>
<td>62</td>
<td>71</td>
<td>183</td>
<td>12.3%</td>
<td>1.16 [0.84, 1.62] 2000</td>
</tr>
<tr>
<td>Beiderlinde 2006</td>
<td>15</td>
<td>32</td>
<td>34</td>
<td>118</td>
<td>10.4%</td>
<td>1.63 [1.02, 2.59] 2006</td>
</tr>
<tr>
<td>Peek 2009</td>
<td>25</td>
<td>68</td>
<td>44</td>
<td>90</td>
<td>11.7%</td>
<td>0.75 [0.52, 1.10] 2009</td>
</tr>
<tr>
<td>Roch 2010</td>
<td>5</td>
<td>9</td>
<td>5</td>
<td>9</td>
<td>6.1%</td>
<td>1.00 [0.44, 2.29] 2010</td>
</tr>
<tr>
<td>Noah 2011</td>
<td>18</td>
<td>75</td>
<td>38</td>
<td>75</td>
<td>10.4%</td>
<td>0.47 [0.30, 0.75] 2011</td>
</tr>
<tr>
<td>Pham 2013</td>
<td>35</td>
<td>98</td>
<td>54</td>
<td>98</td>
<td>12.5%</td>
<td>0.65 [0.47, 0.89] 2013</td>
</tr>
<tr>
<td>Bein 2013</td>
<td>7</td>
<td>40</td>
<td>6</td>
<td>39</td>
<td>4.8%</td>
<td>1.14 [0.42, 3.08] 2013</td>
</tr>
</tbody>
</table>

| Total (95% CI)    | 496          | 752   | 100.0%    | 1.02  | [0.79, 1.33] |
| Total events      | 207          | 315   |           |       |             |

Heterogeneity: \( \tau^2 = 0.12; \chi^2 = 38.94, \text{df} = 9 (P < 0.0001); \, \, I^2 = 77\%

Test for overall effect: \( Z = 0.17 (P = 0.87) \)

Laveena Munshi et al, Annals ATS 2014
ECLS – In hospital mortality

<table>
<thead>
<tr>
<th>VV ECMO only</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
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<tbody>
<tr>
<td></td>
<td>25</td>
<td>68</td>
<td>44</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Peek 2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>32.8%</td>
</tr>
<tr>
<td>Noah 2011</td>
<td>18</td>
<td>75</td>
<td>38</td>
<td>75</td>
<td>21.9%</td>
</tr>
<tr>
<td>Pham 2013</td>
<td>35</td>
<td>98</td>
<td>54</td>
<td>98</td>
<td>45.3%</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>241</td>
<td>263</td>
<td>100.0%</td>
<td>0.64 [0.51, 0.79]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>78</td>
<td>136</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 2.35, df = 2 (P = 0.31); I² = 15%
Test for overall effect: Z = 4.12 (P < 0.0001)

Laveena Munshi et al, Annals ATS 2014
ECLS – complications

Laveena Munshi et al, Annals ATS 2014
ECLS mortality

- Systematic review of 56 studies
- Mortality rates range from 36 to 56% in the studies performed in the last 15 years and reporting outcomes of >30 ECMO patients
- Mortality rates for H1N1 ARDS ranged from 14 to 64% in the 16 studies from 11 countries

ECLS mortality

- Factors associated with poor outcomes after ECMO for acute respiratory failure
  - Older age
  - More days of mechanical ventilation before ECMO
  - More number of organ failures
  - Low pre ECMO respiratory system compliance
  - Immunosuppression

Respiratory ECMO survival prediction (RESP)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td></td>
</tr>
<tr>
<td>18 to 49</td>
<td>0</td>
</tr>
<tr>
<td>50 to 59</td>
<td>-2</td>
</tr>
<tr>
<td>≥60</td>
<td>-3</td>
</tr>
<tr>
<td>Immunocompromised status*</td>
<td>-2</td>
</tr>
<tr>
<td>Mechanical ventilation prior to initiation of ECMO</td>
<td></td>
</tr>
<tr>
<td>&lt;48 h</td>
<td>3</td>
</tr>
<tr>
<td>48 h to 7 d</td>
<td>1</td>
</tr>
<tr>
<td>&gt;7 d</td>
<td>0</td>
</tr>
<tr>
<td>Acute respiratory diagnosis group (select only one)</td>
<td></td>
</tr>
<tr>
<td>Viral pneumonia</td>
<td>3</td>
</tr>
<tr>
<td>Bacterial pneumonia</td>
<td>3</td>
</tr>
<tr>
<td>Asthma</td>
<td>11</td>
</tr>
<tr>
<td>Trauma and burn</td>
<td>3</td>
</tr>
<tr>
<td>Aspiration pneumonitis</td>
<td>5</td>
</tr>
<tr>
<td>Other acute respiratory diagnoses</td>
<td>1</td>
</tr>
<tr>
<td>Nonrespiratory and chronic respiratory diagnoses</td>
<td>0</td>
</tr>
<tr>
<td>Central nervous system dysfunction†</td>
<td>-7</td>
</tr>
<tr>
<td>Acute associated (nonpulmonary) infection‡</td>
<td>-3</td>
</tr>
<tr>
<td>Neuromuscular blockade agents before ECMO</td>
<td>1</td>
</tr>
<tr>
<td>Nitric oxide use before ECMO</td>
<td>-1</td>
</tr>
<tr>
<td>Bicarbonate infusion before ECMO</td>
<td>-2</td>
</tr>
<tr>
<td>Cardiac arrest before ECMO</td>
<td>-2</td>
</tr>
<tr>
<td>$P_{aCO_2}$, mm Hg</td>
<td></td>
</tr>
<tr>
<td>&lt;75</td>
<td>0</td>
</tr>
<tr>
<td>≥75</td>
<td>-1</td>
</tr>
<tr>
<td>Peak inspiratory pressure, cm H$_2$O</td>
<td></td>
</tr>
<tr>
<td>&lt;42</td>
<td>0</td>
</tr>
<tr>
<td>≥42</td>
<td>-1</td>
</tr>
<tr>
<td>Total score</td>
<td>-22 to 15</td>
</tr>
</tbody>
</table>

Schmidt et al, AJRCCM 2014
Respiratory ECMO survival prediction (RESP)

Derived from ELSO Registry (n = 2355) 2000 to 2012

<table>
<thead>
<tr>
<th>Total RESP Score</th>
<th>Risk Class</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥6</td>
<td>I</td>
<td>92%</td>
</tr>
<tr>
<td>3 to 5</td>
<td>II</td>
<td>76%</td>
</tr>
<tr>
<td>−1 to 2</td>
<td>III</td>
<td>57%</td>
</tr>
<tr>
<td>−5 to −2</td>
<td>IV</td>
<td>33%</td>
</tr>
<tr>
<td>≤−6</td>
<td>V</td>
<td>18%</td>
</tr>
</tbody>
</table>
ECCO2 REMOVAL / RESPIRATORY DIALYSIS
ECCO2 removal

• Technique providing artificial respiratory support by removal of CO2 from blood through an extracorporeal gas exchanger

• Feature of other ECLS

• Low flow VV or AV devices – provide CO2 removal without oxygenation
History

• 1976 - Kolobow and Gattinoni explored the possibility of treating severe respiratory failure using low frequency PPV alongside ECCO2 removal in sheep
• 1986 – first clinical study on V-V ECCO2 removal by Gattinoni et al
• 1997 – first clinical study on A-V ECCO2 removal
Inhibition of cell membrane repair
Suppression of innate immunity & host defence
Uncoupling of RV & pulmonary circulation – RV failure
Increase in intracranial pressure
Depression of myocardial contractility

Morimont et al, Critical Care 2015, 19 : 117
Benefits of ECCO2R

- Decreases the detrimental effects of hypercapnia
- Better oxygenation
  - Increases the alveolar O2 concentration in accordance with the alveolar gas equation
  - By removing CO2, ECCO2R allows ventilation strategies that are focused on oxygenation rather than CO2 elimination
- "Rest lung" concept

*Morimont et al, Critical Care 2015, 19:117*
Benefits of ECCO2R

• COPD
  Obviates the need of intubation & IMV
  Facilitates withdrawal of IMV & extubation

• Weaning from MV
• Bridge to lung transplantation

Morelli et al, Intensive Care Med 2017, 43 : 519-30
In ARDS...

- Decreases the ventilator induced lung injury (VILI) by allowing to ventilate the lung at low volumes and pressures
- Allows to continue low tidal volume ventilation (< 6 ml/kg IBW)
- Upto 50 % reduction in MV can be obtained while maintaining normocarbia

*Morimont et al, Critical Care 2015, 19 : 117*
*Morelli et al, Intensive Care Med 2017, 43 : 519-30*
In ARDS...
V – V ECCO2
A – V ECCO2

Pumpless device
MAP of at least 70 mm Hg
AV pressure gradient ≥ 60 mm Hg
Low resistance circuits

Higher cardiac index > 3 L/min / m²
A proportion of CO doesn’t affect the peripheral perfusion

Presence of hemodynamic instability / heart failure limits the use of such devices
Various devices

- The Pump-Assisted Lung Protection (PALP) (Maquet, Rastatt, Germany)
- The iLA Activve® (Novalung, Germany)
- The Hemolung® system (Alung Technologies, Pittsburgh, USA)
- The Decap® system (Hemodec, Salerno, Italy)
Complications of ECCO2 R

• Similar to ECMO
• Earlier had more complications in v/o large cannulas, complex circuits, high anticoagulation requirements
• A-V devices – Limb ischemia (ensure that the internal diameter of the artery is 1.5 times the external diameter of the cannula)
• V-V devices – thrombosis of the circuit
Evidence in ARDS

• Randomized controlled trial in 1994
• 40 patients of severe ARDS
• LFPPV - ECCO2 (21) vs conv MV (19)
• 30 day mortality
• No difference in survival in both \{14/21 (66.6\%) vs 11/19 (57.9\%)\}
• 30% patients had severe hemorrhage

Morris et al, Am J Respir Crit Care Med 1994; 149:295-305
Evidence in ARDS

• The high mortality of ECCO$_2$R in the early use were likely to be due to the complex extracorporeal systems with high flow resistances and large surface areas

• Use of occlusive roller pumps (high haemolysis rate)

• Less biocompatible membrane requiring high anticoagulation levels

• MV was in the pre-ARDSNet era and employed high tidal volumes and peak pressures

*Morris et al, Am J Respir Crit Care Med 1994; 149:295-305*
## Evidence in ARDS

### Tidal Volume Lower than 6 ml/kg Enhances Lung Protection

<table>
<thead>
<tr>
<th>Participants</th>
<th>Prospective study among 32 patients of ARDS who were ventilated ARDS protocol for atleast 72 hrs</th>
</tr>
</thead>
</table>
| Intervention | 10 patients $28 \leq P_{plat} \leq 30 \text{ cm } H2O$ were placed on V-V ECCO2 device and progressive reduction in VT  
VT was reduced from $6.3 \pm 0.2$ to $4.2 \pm 0.3$ ml/kg, and $P_{plat}$ decreased from $29.1 \pm 1.2$ to $25.0 \pm 1.2$ cm H2O ($P < 0.001$)  
PEEP was increased to attenuate the reduction of P/F ratio  
CT scan & BAL cytokine analysis was done before & after 72 hrs |
| Results      | $33.6 \pm 6.3\%$ reduction of $P_{aco2}$ (from $73.6 \pm 1.1$ to $48.5 \pm 6.3$ mmHg) sufficient to normalize arterial pH (from $7.20 \pm 0.02$ to $7.38 \pm 0.04$)  
Decrease in poorly aerated & hyper inflated areas of lungs on CT  
BAL cytokines concentration significant reduction was seen |

Terragni et al, Anaesthesiology 2009; 111:826–35
Evidence in ARDS

- Use of VT lower than 6 ml/kg PBW was a/w significant reduction of inflammatory and morphological markers of VILI
- Only observational study
- No control group of patients who received usual care without Lower ARDSNet/Carbon Dioxide Removal

Terragni et al, Anaesthesiology 2009; 111:826–35
## Evidence in ARDS

<table>
<thead>
<tr>
<th>LTV (3ml/kg) + AV ECCO2R Vs conventional LPV, XTRAVENT study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
</tr>
<tr>
<td>79 patients of moderate/severe ARDS after 24 hrs stabilisation period</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td>Randomized to receive a low VT ventilation (3 ml/kg) + ECCO2 [or] ARDSNet strategy (6 ml/kg)</td>
</tr>
<tr>
<td>PEEP following ARDSNet “high-PEEP/FIO2” table</td>
</tr>
<tr>
<td>RR 10–25/min with an I: E ratio of 1:1</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
</tr>
<tr>
<td>28-days and 60-days ventilator-free days (VFD)</td>
</tr>
<tr>
<td><strong>Results</strong></td>
</tr>
<tr>
<td>VFD’s within 60 days were not different between the study group (33.2 ± 20) and the control group (29.2 ± 21, p = 0.469)</td>
</tr>
<tr>
<td>Mortality rate did not differ between groups</td>
</tr>
</tbody>
</table>

# Evidence in ARDS

<table>
<thead>
<tr>
<th></th>
<th>Av ECCO2-R (n = 40)</th>
<th>Control (n = 39)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>VFD _28 days</td>
<td>10.0 ± 8</td>
<td>9.3 ± 9</td>
<td>0.779</td>
</tr>
<tr>
<td>VFD _60 days</td>
<td>33.2 ± 20</td>
<td>29.2 ± 21</td>
<td>0.469</td>
</tr>
<tr>
<td>LOS ICU (d)</td>
<td>31.3 ± 23</td>
<td>22.9 ± 11</td>
<td>0.144</td>
</tr>
<tr>
<td>LOS hospital (d)</td>
<td>46.7 ± 33</td>
<td>35.1 ± 17</td>
<td>0.113</td>
</tr>
<tr>
<td>In hospital mortality</td>
<td>7/40 (17.5 %)</td>
<td>6/39 (15.4 %)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Evidence in ARDS

• In a post hoc analysis, ARDS patients who were more hypoxemic (P/F < 150) at baseline and who were treated with the low VT strategy had a significantly shorter ventilation period (28.2 ± 16.4 Vs 40.9 ± 12.8, p=0.033)

• No survival benefit was seen with LTV + ECCO2R
### Evidence in ARDS

Fanelli et al, Critical Care (2016) 20:36

<table>
<thead>
<tr>
<th>Participants</th>
<th>Prospective study among 15 patients of moderate ARDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>VT was gradually reduced from 6 to a min value of 4 mL/kg by 0.5 mL/kg every 30 min &amp; PEEP was increased to target a Pplat between 23 and 25 cmH2O. If arterial pH was &lt;7.25 with PaCO2 &gt;60 mmHg, despite an increase in RR up to 35/min, ECCO2R device was switched on.</td>
</tr>
<tr>
<td>Results</td>
<td>Initial reduction in VT, without ECCO2R resulted in significant respiratory acidosis (pH &lt;7.25) in all. Significant reduction in Pplat from 27.7 ± 1.6 to 23.9 ± 1 cmH2O. Mortality at 28 days was 47 %, which was expected. 1/3 rd required either proning or ECMO for refractory hypoxia.</td>
</tr>
</tbody>
</table>
Evidence in ARDS

• Systematic review
• 14 studies with 495 patients (two RCTs and 12 observational studies)
• No survival benefit seen in both RCTs
• More ventilator free days in P/F < 150 (Xtravent study)
• No difference in ICU LOS

Fitzgerald et al, Critical Care 2014, 18 : 22
Evidence in ARDS

• All the studies showed reductions in tidal volume, peak inspiratory pressure, arterial partial pressure of carbon dioxide and increase in arterial pH

• Increased transfusion requirements were seen in couple of studies

• Lack of robust data supporting the use of these devices and their cost effectiveness

Fitzgerald et al, Critical Care 2014, 18 : 22
Awaited…

- SUPERNOVA trial, ECCO2 removal combined with ultra low tidal volume MV in ARDS
- EOLIA trial (ongoing RCT, France), ECMO vs conventional MV for moderate to severe ARDS
Take home message

• Requires early & careful selection of patients with reversible disease and without significant comorbidities
• Rescue therapy for patients with severe ARDS
• Evidence of benefit in H1 N1 related ARDS
• VV ECMO – therapy of choice in ARDS
• ECCO2 R therapeutic adjunct in moderate to severe ARDS