Acute pulmonary failure...failure of gas exchange (hypoxia and/or hypercarbia), failure of perfusion, mechanical loss of airway...and potential rescue therapies...

Mechanical ventilation
- Noninvasive ventilation
- Permissive hypercarbia
- High frequency ventilation
- Prone position ventilation
- Intraotracheal pulmonary ventilation (ITPV)

Pharmacologic therapies
- Nitric oxide
- Partial liquid ventilation
- Surfactant therapy

Surgical therapies
- Extracorporeal gas exchange
  - ECMO
  - Intrascular gas exchange (IVOX)
  - Extracorporeal CO2 removal (ECCO2R)
  - Arteriovenous CO2 removal (AVCO2R)
  - Total artificial lung
- Atrial septostomy (+/- ECMO)
- Thromboembolectomy (+/- ECMO)
- "Emergent" pulmonary transplant (+/- ECMO bridge)

Extracorporeal membrane oxygenation (ECMO/ECLS): epidemiology and outcomes
University of California San Francisco 2002 to 2010 (N=100)

- Wean from ECMO 78%
- Survival to discharge 68%
- Complications 18% minor, 4% major

Pulmonary transplant from an ECMO bridge ... the UCSF experience ('03 to '10)

- 30 yr male (CF, redo) hypoxia/acidosis (mixed) dead (14 mo), sepsis/BO
- 60 yr male (scleroderma) hypoxia/TV failure withdrawal of support
- 46 yr male (FF) car pulm failure (PEA) alive (58 mo)
- 55 yr male (FF) cardiogenic shock (RV) alive (34 mo)
- 55 yr male (FF) cardiogenic shock (RV) alive (54 mo)
- 44 yr male (ChoNICH, ARF) hypoxia alive (42 mo)
- 7 yr male (CF) hypoxia/acidosis (mixed) alive (26 mo)
- 58 yr male (scleroderma) cardiogenic shock (RV) alive (23 mo)
- 47 yr female (tumor) cor pulm failure (PEA) alive (23 mo)
- 30 yr female (IPH) cor pulm failure (PEA) alive (16 mo)
- 58 yr male (FF) hypoxia, LV failure alive (14 mo)
- 14 yr female (IPH) cor pulm failure (PEA) alive (12 mo)
- 48 yr idiopathic IPH hypoxia alive (1 mo)
- 63 yr male (PHTN, COPD) PEA alive (2 mo)
- 50 yr male (PHTN, COPD, Anx) PEA alive (8 weeks)
- 19 yr female (PHTN, VOD) PEA alive (4 weeks)
- 23 yr female (CF) hypercarbia/hypoxia/BPF alive (3 weeks)

"Pump failure" - not primary lung failure - was the indication for mechanical support

Restrictive lung disease - hypoxia, secondary pulmonary hypertension (car pulm failure)
- Cystic fibrosis - hypercarbia and mixed respiratory/metabolic acidosis

Mechanical ventilation was a pre-terminal - and precipitating - event
1. "Ventilatory failure", problems with respiratory mechanics, hypercapnia, airway obstruction and airway loss.

42 yo chronic steroid use secondary congenital adrenal hyperplasia, acute respiratory failure, secondary inhalational petroleum exposure. Intubation c/t tracheal tear. On admission pH 6.9, Pco2 146 mmHg, PaO2 322 mmHg, HCO3 27 on THAM. hypercarbic respiratory failure.

The problem – and clinical implications - of defining acute pulmonary failure...

2. "Respiratory failure", problems with gas exchange, hypoxia, membrane dysfunction and V/Q mismatch (intrapulmonary shunt)

The definition of the syndrome was clarified by a 1992 American-European Consensus Conference. The term "Acute Lung Injury" has been used as an umbrella term for hypoxic respiratory failure, a severe version of which is "Acute Respiratory Distress Syndrome" (ARDS).

- Bilateral pulmonary infiltrates on chest x-ray
- Pulmonary Capillary Wedge Pressure <18mmHg
- PaO2/FiO2 <300 = ALI
- PaO2/FiO2 <200 = ARDS

Although not strictly part of the definition, there is widespread airway collapse (low lung volumes), surfactant deficiency and reduced lung compliance.


3. "Pump failure", problems with perfusion, RV failure (pulmonary hypertension, LV failure)

52 yo male with severe COPD, stridor, and three month history of progressive hemoptysis, now "massive" hemoptysis.

4. Complicated airway management...

Rescue therapies for acute pulmonary failure. WTSA 2010
The problem – and clinical implications – of defining acute pulmonary failure...

5. Acute exacerbation of chronic, progressive disease...

52 yo interstitial lung disease (pulmonary fibrosis), hypoxia (DLCO < 20% predicted), hypercapnea (PCO2 > 50 mmHg), and secondary pulmonary hypertension (PAS > 80 mmHg)

Intubation...subsequent PEA arrest

Extra-pulmonary gas exchange

Historical context
- oxygenators, biological and mechanical

Application (why are you doing this and what do you want)
- moratorium of decision ... "rapid deployment ECMO" (RDE)
- bridge to recovery ... "traditional ECMO"
- bridge to transplant ... "walking ECMO" (pumpless extracorporeal lung assist, PECLA)
- destination therapy ... "artificial lung"

Deployment (how do we do it and when do we try)...
- central vs. peripheral, venovenous vs. venoarterial, PA to LA, RA to PA, RA to Ao, pumpless extra-corporeal lung assist (PECLA)

Problems (general, device specific, and evolving)

3 October 1930...

"at 8 AM respirations ceased and the blood pressure could not be obtained. Within 6 min and 30 sec Dr. Churchill opened the chest, incised the pulmonary artery, extracted a large pulmonary embolus, and closed the incised wound..."

"the idea occurred to me if it were possible to remove continuously some of the blue blood from the patient’s swollen veins, put oxygen into the blood and allow carbon dioxide to escape from it, and then to inject continuously the now red blood back into the patient’s arteries, we might have saved her life. We would have bypassed the obstructing embolus and performed part of the work of the patient’s heart and lungs outside the body."

JH Gibbon

Gibbon JH Jr. The maintenance of life during experimental occlusion of the pulmonary artery followed by survival. Surg Gynecol Obstet 1939;69:204


1953 Cecilia Bovalis (closure of ASD)

Rescue therapies for acute pulmonary failure. WTSA 2010

Gibbon-IBM II "screen oxygenator"
Silicone-coated microporous polypropylene is generally advocated as the best clinically available complex membrane and is widely used not only for cardiopulmonary bypass but also for long-term extracorporeal circulation. It is biocompatible, gas permeable, and plasma nonleakage properties


"A policy of using ECMO in mature infants with severe but potentially reversible respiratory failure results in significantly improved survival without increased risk of severe disability. The benefit of ECMO for babies with diaphragmatic hernia is unclear. Further studies are needed to consider the optimal timing for introducing ECMO; to identify which infants are most likely to benefit; and to address the implications of neonatal ECMO during later childhood and adult life."


Therapeutic efficacy...

- patient population (application)
- deployment is time sensitive and case specific
- resource utilization (public health and integrated care systems)
Is ECMO standard of care in adult refractory respiratory failure?…acute pulmonary failure?

The National Institute of Clinical Excellence in the United Kingdom reviewed ECMO for adults and published a policy document in January 2004. They concluded there was insufficient evidence to support its application at that time. To this end, they recommended that ECMO should not be offered to adult patients unless they were enrolled in the CESAR trial...

The sole Australian governmental policy document on ECMO was published in 1990 by the National Health Technology Advisory Panel. This only concerned the provision of a pediatric service and made no recommendations for adult patients.

Similarly, neither the Extracorporeal Life Support Organization nor the National Institutes of Health in the United States have produced any formal stance on ECMO for adults...

"Analysis and review of trial data does not support its application; however, the body of reported cases suggests otherwise."


Extra-pulmonary gas exchange

Historical context

Application (why are you doing this and what do you want)

Deployment (how do we do it and when do we try)

Problems (general, device specific, and evolving)

Current technologies for extracorporeal gas exchange

ECMO (venovenous, veno-arterial)

Extracorporeal CO2 removal (ECCO2R)

Arteriovenous CO2 removal (AVCO2R)

Total artificial lung

Basic ECMO...

Cannulation... clinical need determines strategy

femoral vein to IJ (VV)

femoral vein to femoral artery (VA)

femoral vein and IJ to femoral artery (VA)

RA to Ao (central VA) "extracorporeal CPR" (VAD)

PA to RA, right heart bypass (VAD)

VAD dual lumen cannula (Helios)

"pumpless" arterio-venous cannulation

Membrane oxygenator (Quadrox)

Centrifugal blood pump (Centrimag vs Biomedicus)

Anticoagulation (heparin ACT "point of care" TEG)

<i>/+</i> mechanical ventilator (early trach 72 hours)

Personnel (MCS service line)
Bi-Caval Dual Lumen Cannula

I. Ambulatory “OxyRVAD” for Total Right Heart and Respiratory
Support by open thoracotomy. The “OxyRVAD” is created by commercially available components consisting of a compact low resistance gas exchange device coupled to a right ventricular axial flow anterior assist device. Through a left 4th ICS thoracotomy, the main pulmonary artery (PA) and right atrium were exposed (n = 5 sheep). The OxyRVAD was then interposed pumly from RA to PA at 3 L/min. 3/5 survived the full 2-week study, and one sacrificed day 13. Pump flow was stable at a 3 liters/min. CO2 removal was constant during the experiment at 200 ± 19 ml/min. O2 transfer was 144 ± 44 ml/min.

2. Percutaneous pump–artificial lung with Single Site venous cannulation by Wang-Zwischenberger double lumen cannula (W-Z DLC). Based in double lumen VV ECMO, the DLC is designed to be inserted from the jugular vein traversing the SVC-RA-IVC. The drainage lumen has a wide open end placed in the IVC for the lower body venous drainage and a side opening in SVC for upper body venous drainage. The infusion lumen opens towards the tricuspid valve in the RA.

56 yo idiopathic pulmonary fibrosis, uncomplicated bilateral lung tx March ’08 Dec. ’08 Trichosporon pneumonia, progressive SOB secondary to post-infectious oblitative bronchiolitis. Profound hypoxia with effort, non-ambulatory on high flow O2 (ICU), listed for redo lung transplant

Stress ECHO (exercise, supine bicycle)

- Pre VV ECMO
  - 6 min 13 sec, max 10 watts
  - sats 84% on 6L NC with max exercise
  - exercise d/c’d secondary SOB (pH 7.32)
  - PASP 60 - RA with peak exercise (PVTI 13)
  - Rest: shortness of breath, 1st DVT

- Ambulatory exercise, secondary to hypoxia
- Subjective recovery time “hours”

- Post VV ECMO
  - 9 min, max 50 watts
  - sats 87% on RA with max exercise, 98% on 4L (Stage 3)
  - exercise d/c’d secondary fatigue
  - PASP 45 - RA with peak exercise (PVTI 10)
  - Rest: shortness of breath

- Ambulatory on treadmill
- Subjective recovery time “minutes”

*More fibrinolysis, less thrombocytopenia
This is ECMO?

"walking ECMO", dual lumen VV (hypoxia, CO2 secondary BOS... to redo BLTx)

"ambulatory right heart bypass", PA to LA cannulation (RV failure, hypoxia, PHTN s/p PEA... to BLTx)

"walking bypass", RA to Ao cannulation (RV failure, hypoxia, PHTN s/p PEA... to BLTx)

"pumpless extracorporeal lung assist" (pECLA), PA to LA cannulation (RV failure, hypoxia... to Tx)

Goal: adequate LV preload and systemic cardiac output, no end organ ischemia
Criteria: norepi<0.04 ucg/kg/min, PaO2>60mmHg in an ambulatory patient
Pump driven, regulate LV preload and RV afterload (flows 1.5 to 4.5 L/min)
Alternative cannulation: RA to PA (thromboemboli, anticoagulation, and intrathoracic pressure)

Ambulatory right heart bypass", for pulmonary hypertension and secondary RV failure, hypoxia

"Ambulatory right heart bypass", for pulmonary hypertension and secondary RV failure, hypoxia

"pumpless extracorporeal lung assist" (pECLA), native RV perfusion across low resistance oxygenator and pulmonary vascular bed (in series)
flows between 1.6 and 2.3 L/min (PVR dependent)

Acute exacerbation of chronic, progressive disease (interstitial lung disease).

"50% of patients die in a relatively acute manner with progressive symptoms of less than one month's duration: the extent of restrictive physiology is a poor predictor of mortality"

Kim et al. (2005) Chest 127:171

"acute exacerbations" or an "accelerated phase of rapid clinical decline"... characterized the clinical course of IPF and is associated with a poor prognosis: a consensus definition should be developed and the etiology, risk factors, pathogenesis, treatment, and predictors need to be studied.


Is there a role for ECMO in progressive, lethal lung disease...?
A management algorithm "acute" idiopathic pulmonary fibrosis — two observations

- intubation/mechanical ventilation pre—terminal event ...
- secondary pulmonary hypertension was "common" and "unpredictable" ...

Algorithm strategy ...

I. tx ineligible — palliative care

II. age > 55 yr, tx eligible — mechanical ventilation: 6 transplanted, 5 deaths "waiting"

III. age < 55 yr, tx eligible

permissive hypercapnea (pH 7.2)
pO2 < 60 mmHg
SBP < 90 mmHg (norepi/milrinone vs epinephrine)
ECHO "cor pulmonale", nitric oxide
21 day "non-functional" exclusion paralytics?

VA ECMO for end organ injury (10 patients)

Pulmonary transplant from an ECMO bridge — the UCSF experience ('03 to '10)

<table>
<thead>
<tr>
<th>Age</th>
<th>Diagnosis</th>
<th>ARDS/1</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 yo</td>
<td>CF, redo</td>
<td>hypoxia/acidosis (mixed)</td>
<td>dead (14 mo), sepsis/BO</td>
</tr>
<tr>
<td>37 yo</td>
<td>IPF</td>
<td>hypoxia/RF failure</td>
<td>withdrawal of support</td>
</tr>
<tr>
<td>46 yo</td>
<td>IPF</td>
<td>cor pulmonale (PEA)</td>
<td>alive (38 mo)</td>
</tr>
<tr>
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<td>IPF</td>
<td>cardiogenic shock (RV)</td>
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</tr>
<tr>
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<td>IPF</td>
<td>cardiogenic shock (RV)</td>
<td>alive (38 mo)</td>
</tr>
<tr>
<td>24 yo</td>
<td>(Homan Rich, AIP)</td>
<td>hypoxia</td>
<td>alive (38 mo)</td>
</tr>
<tr>
<td>29 yo</td>
<td>(CF)</td>
<td>hypoxia/acidosis (mixed)</td>
<td>alive (26 mo)</td>
</tr>
<tr>
<td>58 yo</td>
<td>(scleroderma)</td>
<td>cor pulmonale (PEA)</td>
<td>alive (32 mo)</td>
</tr>
<tr>
<td>47 yo</td>
<td>(sarcoid)</td>
<td>cor pulmonale (PEA)</td>
<td>withdrawal of support</td>
</tr>
<tr>
<td>59 yo</td>
<td>(IPF)</td>
<td>cor pulmonale (PEA)</td>
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<td>cor pulmonale (PEA)</td>
<td>alive (12 mo)</td>
</tr>
<tr>
<td>63 yo</td>
<td>(PHTN, COPD)</td>
<td>hypoxia</td>
<td>alive (12 mo)</td>
</tr>
<tr>
<td>60 yo</td>
<td>(PHTN, COPD, AcoS)</td>
<td>PEA</td>
<td>alive (3 weeks)</td>
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<td>hypercarbia/hypoxia/BPF</td>
<td>alive (3 weeks)</td>
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"Pump failure" — not primary lung failure — was the indication for mechanical support
restrictive lung disease — hypoxia, secondary pulmonary hypertension (cor pulmonale)
cystic fibrosis — hypercapnea and mixed respiratory/metabolic acidosis

Mechanical ventilation was a pre-terminal — and precipitating — event

PROGRESSION OF ARTIFICIAL LUNGS FROM DESIGN TO CLINIC

- choice of gas exchange fiber
- geometry of the blood path
- resistance to blood flow
- device compliance
- avoidance of air embolism
- use of various pumps, both integral and auxiliary

Adoption of artificial lungs depends on the design of clinical studies that establish the most effective circumstances in which to use these devices. Defining the most effective time to introduce a device, minimizing the risks of cannulation, and determining whether combined circulatory and gas exchange support is necessary should define subsequent clinical trials.

*Ambulatory bridge to transplant

*Randomization of early ECMO/NIPPV vs conventional mechanical ventilation