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3 May 2020
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Use of ECMO and Cardiopulmonary Bypass in Lung Transplantation

A. Sasha Krupnick
Surgical Director of Lung Transplantation
University of Virginia/University of Maryland as of July 2020
Disclosures

• I’m a surgeon (don’t ask complicated questions)

• Courier Therapeutics (no relation to current topic)
Outline

• Lung Transplantation
  • History and current data of lung transplantation
  • Limitations of the filed
  • Pre-operative use of extracorporeal oxygenation
  • Selective vs Elective vs. Emergent use of extracorporeal oxygenation /circulatory support intraoperatively
  • Pre-operative use of extracorporeal oxygenation/ circulatory support
History of Human Lung Transplantation

James Hardy 1918-2003

First human lung transplant on June 11, 1963
Immunosuppression: thymic irradiation, azathioprine and prednisone

Patient died 3 weeks after due to renal failure

This event was overshadowed by death of civil rights advocate Medgar Evers
1964-First heart transplant in man/primate to human
Modern Era of Lung Transplantation

1963-1978 - 38 lung or heart/lung transplants performed-none left the hospital

1983 – University of Toronto: single lung TX; Success
1983 – University of Toronto: double lung TX; success
1989 – Washington University: bilateral sequential lung TX
NUMBER OF LUNG TRANSPLANTS REPORTED BY YEAR AND PROCEDURE TYPE

NOTE: This figure includes only the lung transplants that are reported to the ISHLT Transplant Registry. As such, this should not be construed as representing changes in the number of lung transplants performed worldwide.
Solid Organ Survival

- Heart
- Liver
- Kidney
- Pancreas
- Intestine
- Lung

Graph showing the survival rates of different solid organs over time after transplant.
Use of ECMO as Bridge to Lung Transplantation

- 2005-LAS (Lung Allocation Score) System;
- 2017-Donation Service Area (DSA) as the first level of distribution with a 250 nautical mile circle around the donor hospital.
Use of ECMO as Bridge to Lung Transplantation

Effect of the lung allocation score on lung transplantation in the United States

Thomas M. Egan, MD, MSc, and Leah B. Edwards, PhD

The Journal of Heart and Lung Transplantation, Vol 35, No 4, April 2016
Use of ECMO as Bridge to Lung Transplantation

1987-2008

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mechanical ventilation (n = 586)</th>
<th>ECMO (n = 51)</th>
<th>Unsupported (n = 15,297)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD or 15th/50th/85th</td>
<td>Mean ± SD or 15th/50th/85th</td>
<td>Mean ± SD or 15th/50th/85th</td>
</tr>
<tr>
<td></td>
<td>85th percentiles</td>
<td>85th percentiles</td>
<td>85th percentiles</td>
</tr>
<tr>
<td>Recipient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>38 ± 21</td>
<td>39 ± 22</td>
<td>48 ± 14</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23 ± 5.3</td>
<td>25 ± 4.9</td>
<td>24 ± 4.8</td>
</tr>
</tbody>
</table>

Should lung transplantation be performed for patients on mechanical respiratory support? The US experience

David P. Maze, MD,¹ Lucy Thami, MS,¹ Edward R. Norwick, MD, MS,¹ Sudhak C. Morby, MD, PhD,¹
Gina R. Peterson, MD, PhD,¹ and Eugene H. Blackstone, MD²

The Journal of Thoracic and Cardiovascular Surgery • Volume 139, Number 3
Use of ECMO as Bridge to Lung Transplantation
1987-2008

### Table 1
Recipient condition at the time of transplant

<table>
<thead>
<tr>
<th>Variable</th>
<th>2010</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical condition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalized in ICU</td>
<td>150</td>
<td>276</td>
</tr>
<tr>
<td>Hospitalized not in ICU</td>
<td>148</td>
<td>242</td>
</tr>
<tr>
<td>Not hospitalized</td>
<td>1487</td>
<td>1530</td>
</tr>
<tr>
<td>Hospitalization unknown</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td><strong>Vent/ECMO at transplant</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vent + ECMO</td>
<td>22</td>
<td>63</td>
</tr>
<tr>
<td>Vent only</td>
<td>130</td>
<td>64</td>
</tr>
<tr>
<td>ECMO only</td>
<td>7</td>
<td>33</td>
</tr>
<tr>
<td>Neither</td>
<td>1626</td>
<td>1895</td>
</tr>
</tbody>
</table>

### Abbreviation:
ICU, intensive care unit.
Use of ECMO as Bridge to Lung Transplantation

**Absolute contraindications**
Contraindications for the use of ECMO as a bridge to lung transplantation are as follows:

1. Ineligibility for lung transplant
2. Refractory bacteremia or septic shock
3. Irreversible multiorgan damage (other than lungs)
4. Severe arterial occlusive disease
5. Contraindications to systemic anticoagulation
6. Uncontrolled metastatic disease or other terminal illness that is not otherwise treatable with lung transplant
7. Acute intracerebral hemorrhage or stroke
Use of ECMO as Bridge to Lung Transplantation
Use of ECMO as Bridge to Lung Transplantation

The “Sport Model”: Extracorporeal Membrane Oxygenation Using the Subclavian Artery

Mauer Biscotti, MD, and Matthew Bacchetta, MD

© 2014 by The Society of Thoracic Surgeons

Fig 1. Hemashield graft and subclavian artery anastomosis shown during an operation. The arrows indicate the orientation of the patient as labeled.

Fig 2. “Sport model” configuration. RA indicates right atrial electrocardiographic lead.
Use of ECMO as Bridge to Lung Transplantation

**Figure 1.** Kaplan–Meier curves comparing survival between patients with and without ECMO bridge to lung transplantation according to years: 2000 to 2002 (A), 2003 to 2005 (B), 2006 to 2008 (C), and 2009 to 2011 (D). ECMO, Extracorporeal membrane oxygenation.
Use of ECMO as Bridge to Lung Transplantation

### Table 3
Summary of recent studies reviewing 1-year survival outcomes of ECMO bridging conditional on receiving a lung transplant after ECMO

<table>
<thead>
<tr>
<th>Single Center Studies</th>
<th>Number of Patients</th>
<th>1-y Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lang et al, 2012</td>
<td>34</td>
<td>63%</td>
</tr>
<tr>
<td>Shafii et al, 2012</td>
<td>19</td>
<td>79%</td>
</tr>
<tr>
<td>Weig et al, 2013</td>
<td>26</td>
<td>54%</td>
</tr>
<tr>
<td>Crotti et al, 2013</td>
<td>22</td>
<td>79%</td>
</tr>
<tr>
<td>Lafarge et al, 2013</td>
<td>36</td>
<td>60%</td>
</tr>
<tr>
<td>Inci et al, 2015</td>
<td>26</td>
<td>68%</td>
</tr>
<tr>
<td>Biscotti et al, 2017</td>
<td>40</td>
<td>92%</td>
</tr>
</tbody>
</table>
Use of ECMO as Bridge to Lung Transplantation

<table>
<thead>
<tr>
<th>Box 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factors that affect posttransplant survival in patients on ECMO support</td>
</tr>
</tbody>
</table>

Favorable factors

- Age less than 50 years
- Normal or marginally elevated total bilirubin
- Normal or mildly elevated pulmonary artery pressures
- Less than 14-day duration on ECMO
- Low SOFA score (<6)
- Noninvasive ventilation
- Ability to participate in physical therapy (i.e., “awake ECMO”)

Unfavorable factors

- Age greater than 60 years
- Total bilirubin greater than 3
- Severe pulmonary hypertension
- Prolonged ECMO (>14 days)
- Prolonged mechanical ventilation
- Prolonged immobility on ECMO
- SOFA score greater than 9
- Major bleeding, infectious complications, or end-organ perfusion
- Complications on ECMO
- Retransplant with a retransplant interval less than 1 year

Abbreviations: ECMO, extracorporeal membrane oxygenation; SOFA, sequential organ failure assessment.

Adapted from Loor G, Simpson L, Parulekar A. Bridging to lung transplantation with extracorporeal circulatory support: when or when not? J Thorac Dis 2017;9:3352–61; with permission.
Use of ECMO as Bridge to Lung Transplantation

Box 1
Factors that affect posttransplant survival in patients on ECMO support

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<tr>
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</tr>
<tr>
<td>Normal or mildly elevated pulmonary artery pressures</td>
</tr>
</tbody>
</table>

Two fundamental questions are important when deciding to place a patient on ECMO:

I. Is this patient a potential candidate for a lung transplant?

II. Is the prognosis reasonable for surviving to transplant and having quality of life and survival after transplant?

- Prolonged ECMO (>14 days)
- Prolonged mechanical ventilation
- Prolonged immobility on ECMO
- SOFA score greater than 9
- Major bleeding, infectious complications, or end-organ perfusion
- Complications on ECMO
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Intraoperative Circulatory Support for Lung Transplantation

- No extracorporeal support
- Partial support
- Full support
Intraoperative Circulatory Support for Lung Transplantation

Globally, interoperative use of mechanical circulatory/ventilatory support for lung transplantation ranges from 30 to 50% with variations between centers regarding type of device and timing.

**Off Pump-Pros:** no heparin, no risk of cannulation, circuit activation of inflammatory mediators

**Off Pump-Cons:** hemodynamic instability during dissection, poor oxygenation due to single lung ventilation of bad lung, after implantation the new lung gets 100% of the blood flow right away.

**ECMO vs. full CPB:** use of pump suction for tough dissection, different degree of anticoagulation, full vs partial support
Intraoperative Circulatory Support for Lung Transplantation

In God we trust; all others must bring data. W. Edwards Deming

Early days prior to LAS-most COPD patients

Cardiopulmonary bypass for bilateral sequential lung transplantation in patients with chronic obstructive pulmonary disease without adverse effect on lung function or clinical outcome

Wilson Y. Sotsu, MD

The Journal of Thoracic and Cardiovascular Surgery • August 2002
Intraoperative Circulatory Support for Lung Transplantation

Intraoperative extracorporeal membrane oxygenation and the possibility of postoperative prolongation improve survival in bilateral lung transplantation

Kounal Hoetzenecker, MD, PhD, Stefan Schwarz, MD, Moritz Muckenhuber, MD, Alberto Bonazzo, MD, Florian Freistatier, PhD, Thomas Schwenger, MD, PhD, Oriolya Bata, MD, Peter Jakob, MD, Negar Ahmadi, MD, Gabriella Muraköy, MD, Helmut Prosch, MD, Helmut Hager, MD, Georg Roth, MD, György Lang, MD, PhD, Shahrokh Tadjavi, MD, and Walter Klepetko, MD.

The Journal of Thoracic and Cardiovascular Surgery • Volume 155, Number 5
Intraoperative Circulatory Support for Lung Transplantation

UVA Protocol
- elective central ECMO for all cases
- hep 50U/kg with goal of ACT180-220
- analyzing data now
Postoperative Circulatory Support for Lung Transplantation

- Non-optimal donor lung
- Ex-vivo lung perfusion
- Ischemic injury
- Intraoperative ECMO
  - Lung protective ventilation
  - Controlled reperfusion
- Reperfusion damage
- Prolonged postoperative ECMO
  - Lung protective ventilation
  - Bypass pulmonary blood flow

- Severe PGD
- Need for unplanned ECMO
- Additional damage
- Need for aggressive ventilation and catecholamines
Table 3 Published case series on secondary ECMO implant after lung transplantation

<table>
<thead>
<tr>
<th>Study</th>
<th>N patients</th>
<th>Survival</th>
<th>Weaned patients</th>
<th>Time ECMO-weaning (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meyers et al., 2000</td>
<td>12 (2.7)</td>
<td>–</td>
<td>8 (66.6)</td>
<td>4.2 (mean)</td>
</tr>
<tr>
<td>Dahlberg et al., 2004</td>
<td>16 (9.3)</td>
<td>46% at 2 years</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Oto et al., 2004</td>
<td>10 (2.1)</td>
<td>–</td>
<td>4 (40.0)</td>
<td>4 (mean)</td>
</tr>
<tr>
<td>Mason et al., 2006</td>
<td>22 (4.0)</td>
<td>41% at 1 year ¹</td>
<td>–</td>
<td>4 (median)</td>
</tr>
<tr>
<td>Fischer et al., 2007</td>
<td>151</td>
<td>42% at hospital discharge</td>
<td>–</td>
<td>6 (mean)</td>
</tr>
<tr>
<td>Bermudez et al., 2009</td>
<td>58 (7.6)</td>
<td>40% at 1 year</td>
<td>39 (57.2)</td>
<td>5.5 (mean)</td>
</tr>
<tr>
<td>Hartwig et al., 2012</td>
<td>28 (8.0)</td>
<td>64% at 1 year</td>
<td>27 (96.4)</td>
<td>3.6 (mean)</td>
</tr>
<tr>
<td>Marcaccio et al., 2012</td>
<td>24</td>
<td>25% at hospital discharge</td>
<td>14 (58.3)</td>
<td>4.5 (median)</td>
</tr>
<tr>
<td>Mulvhill et al., 2018</td>
<td>107 (5.1)</td>
<td>62% at 6 months</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Values are reported as n (%). ¹ survival was 41% at 1 year in patients with early graft failure and acute rejection and only 3% in patients with sepsis and pneumonia.
Postoperative Circulatory Support for Lung Transplantation

Table 3: Published case series on score

<table>
<thead>
<tr>
<th>Study</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meyers et al., 2000 (84)</td>
<td></td>
</tr>
<tr>
<td>Dahlberg et al., 2004 (85)</td>
<td></td>
</tr>
<tr>
<td>Oto et al., 2004 (86)</td>
<td></td>
</tr>
<tr>
<td>Mason et al., 2006 (67)</td>
<td></td>
</tr>
<tr>
<td>Fischer et al., 2007 (68)</td>
<td></td>
</tr>
<tr>
<td>Bermudez et al., 2009 (69)</td>
<td></td>
</tr>
<tr>
<td>Hartwig et al., 2012 (15)</td>
<td></td>
</tr>
<tr>
<td>Marasco et al., 2012 (70)</td>
<td></td>
</tr>
<tr>
<td>Mulvihill et al., 2018 (71)</td>
<td></td>
</tr>
</tbody>
</table>

Values are reported as n (%). 1, survi with sepsis and pneumonia.

**FIGURE 4.** Intraoperative extracorporeal membrane oxygenation (intraOp ECMO) and patients not undergoing ECMO were matched to balance pretreatment characteristics using propensity score matching. Patients who were supported by ECMO had better survival compared with patients not undergoing ECMO, although this was not statistically significant. ECMO, Extracorporeal membrane oxygenation; intraOp, intraoperative.
Postoperative Circulatory Support for Lung Transplantation

- Total number of LTx during the study period (n=722) → Patients excluded from the analysis (n=140)
- Number of LTx meeting the inclusion criteria (n=582)

- n=116
  - Transplantation w/o ECMO
  - group I

- n=466
  - Pre-emptive central v/a ECMO after opening the chest
  - ECMO flow 50% of cardiac output
  - After Implantation - decannulation and recirculation of ECMO
  - Two measurements - after decannulation and after closure of chest
    - PO2/FIO2 < 100 in one of the two measurements or
      - mPAP > 2/3 of mSAP or
      - clear trend of worsening between the two time points or
      - Primary pulmonary hypertension recipients
    - no
      - no postOp ECMO
        - n=343
        - group II
    - yes
      - Prolongation of ECMO (v/a femoro-femoral)
        - n=123
        - group III
Summary

Lung transplantation is evolving as a therapy for end stage lung failure

Intraoperative circulatory support gaining favor as we transplant sicker patients (anecdotal data supports this)

Post Operative support when used rationally can improve survival