Mechanical Support of the Right Heart and Pumpless Lung Assist Device: Potential Uses as a Bridge to Lung Transplantation

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Surgery for pre-capillary pulmonary hypertension

- Pulmonary endarterectomy
- Lung and heart-lung transplantation
- Mechanical support as a bridge to recovery or to transplantation
Number of lung transplantation and pulmonary endarterectomy per year in Toronto

Pulmonary Endarterectomy Program
2005 - 2010 (March)

• 63 patients referred for CTEPH
  ➢ 40 patients underwent pulmonary endarterectomy
    • 37 elective, 3 emergency
  ➢ 23 patients did not have surgery because of:
    – Distal disease (n=10)
    – Absence of PH at rest (n=7)
    – Significant co-morbidities (n=4)
    – Patient refused surgery (n=1)
    – Death before surgery (n=1)

Toronto Lung Transplant & Pulmonary Endarterectomy Programs

Toronto Pulmonary Endarterectomy Program
Survival after elective pulmonary endarterectomy
2005 - 2010 (March)

Lung Transplant Program
Indications for Transplantation 1983-2010 (March)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive Disease</td>
<td>348</td>
<td>(32 %)</td>
</tr>
<tr>
<td>Interstitial Disease</td>
<td>315</td>
<td>(29 %)</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>255</td>
<td>(23 %)</td>
</tr>
<tr>
<td>PAH</td>
<td>72</td>
<td>(7 %)</td>
</tr>
<tr>
<td>Eisenmenger’s</td>
<td>31</td>
<td>(3 %)</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>9</td>
<td>(1 %)</td>
</tr>
<tr>
<td>Re-transplant</td>
<td>32</td>
<td>(3 %)</td>
</tr>
<tr>
<td>Other</td>
<td>25</td>
<td>(2 %)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1087</strong></td>
<td></td>
</tr>
</tbody>
</table>
Indications for Transplantation (Adults)
1983 – 2010 (March)

- COPD/Emphysema: 32%
- Cystic Fibrosis: 22%
- PAH: 10%
- ILD/IPF: 30%
- Re-Tx: 3%
- Other: 3%

N=1046 (96.2 %)

Toronto Lung Transplant Program

Indications for Transplantation (Peds)
1983 – 2010 (March)

- PAH: 24%
- CF: 60%
- Obstructive Disease: 8%
- ILD: 3%
- RE-Tx: 5%

N=41 (3.8 %)

Toronto Lung Transplant Program
Overall survival after lung transplantation
1983 – 2010 (March)

- 56% survival at 2 years
- 39% survival at 5 years
- Median survival: 6.8 years

Toronto Lung Transplant Program

Lung transplantation for PAH
2005 - 2010 (March)

- 158 PAH patients referred for lung transplantation
- 49 listed and 44 transplanted
  - 32 bilateral transplant
  - 12 heart-lung transplant
- Indications for transplantation
  - 21 idiopathic PAH
  - 8 Eisenmenger’s syndrome
  - 12 connective tissue disorders (scleroderma, lupus)
  - 3 CTEPH

Toronto Lung Transplant Program
Survival after lung transplantation for PAH
2005 - 2010 (March)

Toronto Lung Transplant Program

Waiting List, Transplants and Donors
(All Organs-Ontario)

Source: TGLN 1991-2009
Lung transplant waiting list mortality

- Pulmonary Arterial Hypertension
- Cystic Fibrosis
- Idiopathc Pulmonary Fibrosis
Death on waiting list before and after implementation of Lung Allocation Score in the US (UNOS data 2002-08)

Methods to bridge PH patients to lung transplantation

- High flow $O_2$
- Mechanical ventilation
- Inotropic support
- Artificial lung
Conventional ECMO

Novalung®

- membrane ventilator
- NovaPort low resistance cannula
- Blood in / out (symmetrical)
- gas inlet
- gas outlet
Novalung Technical Data

- Gas exchange by diffusion across a plasma tight membrane
- Low resistance (6mmHg at 1.5L/min)
- Heparin coated surface (ACT 120 - 140s)
- Low shear stress (blood trauma)
- Surface area = 1.3 m$^2$
- Blood flow = 0.5 – 4.5L/min
- Filling volume = 250 ml saline

Novalung
Pumpless Mode – Femoral Artery to Femoral Vein
Bridge to lung transplantation with the novel pumpless interventional lung assist device Novalung

Stefan Fischer, MD, MSc,Andre R. Sinner, MD, Tobias Welte, MD, Markus M. Hoepner, MD, Anna Meyer, MD, Verena Teissmann, MD, Bernhard Gehrsitz, MD, Jann Gottlob, MD, Axel Rennhack, MD, and Martin Staubli, MD

Background: Worsening of lung failure in patients awaiting lung transplantation may lead to ventilator-refractory hypercapnia and respiratory acidosis. Most transplant centers consider posttransplantation extracorporeal membrane oxygenation as a combination therapy for lung transplantation because of the poor outcomes. We, for the first time, applied the novel pumpless interventional lung assist Novalung for bridge to lung transplantation in patients with severe ventilator-refractory hypercapnia. We report on our initial experience.

Methods: Between March 2003 and March 2005, 176 lung transplantations were performed, of which 60% were high urgency lung transplantations. Twelve of the high urgency recipients had severe ventilator-refractory hypercapnia and respiratory acidosis. These patients were connected to the novel pumpless interventional lung assist Novalung for bridge to lung transplantation.

Initial Experience with Novalung as a Bridge to Lung Transplantation – Hannover Medical School

- N = 12 patients
- Patients with refractory respiratory failure
  - Hypercapnia and acidosis despite maximal conventional ventilation
- Placed on Novalung as a bridge to transplant → AV pumpless mode
- ACT 160-180 sec (Bolus of 10,000 IU + continuous infusion)
Initial Experience with Novalung as a Bridge to Lung Transplantation – Hannover Medical School

- 3 pts required change of the device due to clotting (ACT<150sec)
- 10/12 patients successfully bridged to transplantation
- 8/10 survived lung transplant
- Cause of death: Multi-organ Failure
  - (2 prior to, 2 after LTx)
Novalung
Veno - Arterial (ECMO) mode

Novalung
Veno – venous mode
Novalung PA to LA
Bridge to Lung Transplant for PAH Patients
“Oxygenating right-to-left shunt”

PA-LA pumpless Novalung provides:
1) Unloading the right ventricle
2) Oxygenation

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PA-LA Novalung Bridge to transplant

- Severe PH with hemodynamic instability due to RV failure (failed medical treatment and inotropic support)
- VA ECMO inserted under local anesthesia through femoral vessels to stabilize the patient
- Induction of anesthesia
- Sternotomy and insertion of LA and PA cannulas
- VA ECMO weaned
- Drainage and sternotomy closure
Chest x-ray before insertion of PA-LA Novalung

Chest x-ray after PA – LA Novalung

Novalung Flow = 2.5 -2.8L/min
Novalung PA-LA: Bridge to lung transplant

Novalung PA-LA: Bridge to lung transplant
Pediatric PA-LA Novalung
Bridge to Lung Transplant (patient with PVOD)

Pre-Novalung

Post-Novalung

Patient with PVOD after Novalung bridge to lung transplant.
6 months later, December 2008
World Transplant Games 2009
Silver medal

Overall ECMO + Novalung Experience/Year
2000 – 2010 (March)
Novalung: Bridge to transplant 2006 - 2009 (n=11)

- ECLS mode:
  - A-V (n=3), V-A (n=3), V-V (n=1), PA-LA (n=4)

- Indications:
  - PAH (n=4), IPF (n=3), CF (n=2), Other (n=2)

- Bridge to transplant 100% (11/11)
Survival after Novalung as bridge to transplant
2006 - 2010 (March)

Impact of aggressive pre-transplant management on waiting list mortality in iPAH patients

- 23% waiting list mortality in 1998-2005 vs 0% since 2006

* PA-LA Novalung
Conclusions

• Lung transplantation is an important option for PAH patients

• Mortality on the waiting list remains a major problem, particularly for PAH patients

• Aggressive pre-transplant management can help to reduce waiting list mortality in PAH patients

• Novalung is a safe and valuable option to bridge PAH patients to lung transplantation
Thank you

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