Ex vivo Lung Perfusion is an Essential Tool for Donor Optimization

Debate: Pro

AST CEOT Meeting
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Disclosure

• Founding Partner:
  • Perfusix Canada Inc. (CSO)
  • Perfusix USA Inc. (Lung Bioengineering /UT)
  • XOR Labs Toronto Inc. (CSO)

• XVIVO Perfusion – Research support and clinical trial
• United Therapeutics – Research support and clinical trial
• Xenios/Fresenius – Research support and investor in XOR
Caution: All “EVLP” is not the same!

• Further disclosure and clarification
• EVLP with the **Toronto Technique** is a standard of practice at Toronto General Hospital
• The comments and claims that I will make are based on our research experience in the development of the **Toronto EVLP Technique** and on our CLINICAL experience of over 386 EVLP cases
• There are other systems and techniques out there that I cannot speak to as I have no experience with other than reported outcomes
The Problem

• Utilization of donor lungs in the USA is still only 20%
• Outcomes of lung transplantation are variable
• Many usable lungs are declined
• Varying levels of expertise and experience in decision makers regarding accept or not
• Donor Optimization = optimal utilization + optimal outcomes
• 10 reasons why EVLP is an essential tool for donor optimization
1. EVLP Provides the Opportunity to Test Questionable Organs

- Different thresholds of comfort to accept a “non-perfect” organ
- Retrieval by “unknown” retrieval surgeon
- If you are not sure/ not comfortable – check it out on EVLP
- Use more lungs SAFELY (the era of “adventures” with “marginal lungs” is over)
- A stable lung on EVLP will work after transplant
Decision Making - Experience

- Experienced team can make the decision together with the more junior team that went on recovery.

You cannot make a chicken out of a fried egg!!
If you are not sure about a donor lung…

• Bring it home
• Put it on EVLP and check it out
• Easy!
2. EVLP Provides the Opportunity to Further Assess, Improve and Optimize Injured Donor Lungs

- Pulmonary edema
- Inflammation
- Infection
- Pulmonary embolism
Resolution of pulmonary edema during EVLP

Donor P/F 230

Recipient P/F 420
Donor with High PAP and PE: Significant Improvement of Pulmonary Hemodynamics after Treatment on EVLP

Diagnosis

Treatment

Response monitoring
Waiting List, Transplants and Donors
(All Organs-Ontario)
Source: TGLN 1995 – 2017

Number of Patients
3. EVLP Creates the Opportunity to Develop New Sources of Organs

- DCD – donation after cardiac death
- Non-Perfused Organ Donors (NPODS)
- Hepatitis C infected organs

![HCV viral load graph](graph.png)
DCD Utilization Statistics

• DCD – source of many donor lungs
• DCD – has some potential increased risks:
  • Aspiration AFTER extubation
  • Shock lung with prolonged agonal hypotension
• DCD lungs are not being used in the US
Lung Quality and Utilization in Controlled Donation after Circulatory Determination of Death Donors within the United States

Joshua J Mooney, MD¹, Haley Hedlin, PhD¹, Paul K Mohabir, MD¹, Rodrigo Vazquez, MD², John Nguyen, RN³, Richard Ha, MD⁴, Peter Chiu, MD⁴, Kapilkumar Patel, MD¹, Martin R. Zamora, MD⁵, David Weill, MD¹, Mark R Nicolls, MD¹, and Gundeep S Dhillon, MD¹

• SRTR data: DNDD utilization rate in USA is 21%
• DCDD utilization rate in USA is 2.1%
• DCDD rate in Canada and Australia and Europe 28%

Increasing lung transplant center expertise and commitment to eDCDD procurement along with minimizing the impact of aborted runs through the use of technologies such as EVLP are needed to improve U.S. eDCDD lung utilization.
Should All DCD Lungs be Treated with EVLP?

Avoid surprises…

DCD, rapid arrest after WLST, “no concerns” straight to transplant
DCD Lung Transplantation: Standard of Care

15-30% of transplants from DCDs


### Table 1: Characteristics of DCD Practices in Participating Centers

<table>
<thead>
<tr>
<th>Center</th>
<th>Transplants 2012 to 2014 (n)</th>
<th>Percentage of Transplants from DCD (%)</th>
<th>Use of heparin pre-mortem</th>
<th>Use of Bronchoscopy Pre-mortem</th>
<th>Selective use of EVLP</th>
<th>Stand-off period</th>
<th>Maximum time allowed for WLS T to arrest</th>
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<tbody>
<tr>
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<td>352</td>
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<td>Yes</td>
<td>Yes</td>
<td>5 min</td>
<td>60 min</td>
</tr>
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</table>

DCD, donation after circulatory death donor; EVLP, ex vivo lung perfusion; WLS, withdrawal of life support therapy.

<sup>a</sup>When allowed by donor hospital.
4. EVLP Allows Significant Prolongation of Preservation Time

- At TGH we routinely transplant lungs over 12h preservation time
- Patients can remain at home – further distances
- Don’t need to call in patient until donor assessment is complete (even more important in DCD as 40-50% don’t arrest)
- No need to rush in difficult cases worrying about ischemic time
- More transplants can occur in the daytime – teams can sleep → better performance, lower costs, allow program volume escalation without team burnout
Towards Elective Lung Transplantation: Outcome of Transplantation of Lungs Preserved More Than 12h

5. EVLP Improves transplant logistics

Time for manpower and operating room logistical planning (for lung and other organs as well as other OR activity)
6. EVLP Provides Time for Improved Allocation

- Allows time for organ allocation when decline occurs at the last minute by original accepting team
- Will allow time for advanced organ matching: epitope based HLA matching
So, I’ve told you that EVLP is essential for donor lung optimization and utilization....
Where is the proof?
Toronto Lung Transplant Program Annual Growth

1991-2017

- **2000-2006**: Plateau
  - Mean 93.5
  - ~100% increase
  - **ECD era**

- **2006-2011**: Plateau
  - Mean 93.5
  - **EVLP era**

- **2012-2016**: 70% increase

**Year**
- 1991: 27
- 1992: 27
- 1993: 25
- 1994: 24
- 1995: 25
- 1996: 24
- 1997: 25
- 1998: 24
- 1999: 25
- 2000: 33
- 2001: 50
- 2002: 59
- 2003: 54
- 2004: 64
- 2005: 68
- 2006: 87
- 2007: 163
- 2008: 104
- 2009: 102
- 2010: 104
- 2011: 116
- 2012: 133
- 2013: 115
- 2014: 122
- 2015: 145
- 2016: 170
- 2017: 170

**Number of LTx**
- 0
- 50
- 100
- 150
- 200
EVLP & Lung Transplant Activity / Year

1983 - 2017

Total EVLP performed to-date (N=252)
Operative (30d) Mortality Rate
(Avg 3% past 5 yr)

Rate %: # death within 30-d post-op / # Tx within Calendar year
Operative (30d) Mortality by Year
1983 – 2017

THIS is donor optimization!
We should aspire to creating organs that are BETTER than the state in which we found them…
7. EVLP Provides the Opportunity to Repair Donor Lungs

EVLP Treatment Strategies

- Perfusion
- Gene Therapy
- Cell Therapy
- Immuno-cloaking
- Inhaled Gases
- Drugs
- Biological
8. EVLP Will Prepare You for The Future

• Management of donor organs today has essentially not changed since the inception of transplant

• Processes are highly inefficient

• Assessment - imprecise

• Allocation systems - inefficient, ineffective and challenging

• Significant logistical challenges

• Resource intense - inefficient and expensive use of transportation, people and ORs etc.

• We need to accelerate evolution of processes of organ management and transplantation as a whole…
9. EVLP will enable specialization of organ management in specialized centers: a lesson from the history of blood transfusion.

Unprocessed whole blood transfusion in the battlefield

Processed blood transfusion in individual hospitals

Standardized, centralized collection, processing, storage, distribution

Control quality - SOP’s, infection control, shelf life, inventory, distribution, tracking, safety standards

Optimized utilization

Separation of components for specific patient needs (RBC, platelets, plasma, cryo etc.)

Management of Blood Products – The Evolutionary Path

Ability to scale up, achieve cost and utilization efficiencies
10 Key Reasons Why EVLP is an Essential Tool for Donor Optimization

1. EVLP provides the opportunity to test questionable organs, improve utilization
2. EVLP provides the opportunity to further assess, improve and optimize injured donor lungs, improve outcomes
3. EVLP creates the opportunity to develop new sources of organs
4. EVLP allows significant prolongation of preservation time
5. EVLP improves transplant logistics – performance and cost
10 Key Reasons Why EVLP is an Essential Tool for Donor Optimization

6. EVLP provides time for improved allocation
7. EVLP provides the opportunity to repair donor lungs
8. EVLP will prepare you for the future - engineered organs with superior, predictable function and outcomes
9. EVLP will enable specialization and scaling of organ management processes in specialized organ repair centers
10. I have just shown you it’s possible!
The Toronto Lung Transplant Program