Working With What We Have: Optimizing Donor Lungs and Extended Criteria

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Disclosures

None

I will not discuss the role of EVLP or DCD at length, given the other lectures on these topics.
Learning Objectives

• Review the definition and early outcomes with extended criteria donor (ECD) lungs

• Discuss recent experience and potential cautions when considering use of ECD lungs

• Identify opportunities for expanding the available donor pool moving forward
Rationale for Optimizing Donor Lungs

[Graph showing the number of people on the waiting list, transplants, and donors over years.]
### Criteria used to assess donor lung suitability, defining a “standard lung donor”

<table>
<thead>
<tr>
<th>Traditional Criteria (Standard Donor)</th>
<th>Extended Criteria (Marginal Donors)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 55 y</td>
<td>Age &gt; 70 y</td>
</tr>
<tr>
<td>Clear chest X-ray</td>
<td>Minor diffuse and moderate focal chest radiograph changes acceptable</td>
</tr>
<tr>
<td>( \text{Pao}_2 \geq 300 ) on ( \text{Fi}_2 ) = 1.0 and positive end-expiratory pressure (PEEP) 5 cm H(_2)O</td>
<td>( \text{Pao}_2/\text{Fi}_2 &lt; 300 ) mm Hg on PEEP 5 cm H(_2)O</td>
</tr>
<tr>
<td>Tobacco history &lt; 20 pack yr</td>
<td>Tobacco history &lt; 40 pack yr</td>
</tr>
<tr>
<td>Absence of chest trauma</td>
<td>Chest trauma not relevant if good pulmonary function</td>
</tr>
<tr>
<td>No history of primary pulmonary disease or active pulmonary infection</td>
<td></td>
</tr>
<tr>
<td>No evidence of aspiration/sepsis</td>
<td>Aspiration/sepsis acceptable if good, stable/improving pulmonary function</td>
</tr>
<tr>
<td>Absence of pulmonary secretions at bronchoscopy</td>
<td>Purulent secretions not relevant if good, stable/improving pulmonary function</td>
</tr>
<tr>
<td>No evidence for human immunodeficiency virus, hepatitis B, hepatitis C, or any other relevant viral disease</td>
<td></td>
</tr>
<tr>
<td>No history or evidence of malignant disease</td>
<td></td>
</tr>
<tr>
<td>ABO compatibility</td>
<td></td>
</tr>
<tr>
<td>Sputum Gram stains: absence of organisms</td>
<td></td>
</tr>
</tbody>
</table>

Liberalization of Donor Criteria May Expand the Donor Pool Without Adverse Consequence in Lung Transplantation

<table>
<thead>
<tr>
<th>Ideal donor (61)</th>
<th>Extended donor (52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47 ± 14</td>
</tr>
<tr>
<td></td>
<td>46 ± 13</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>31/30</td>
</tr>
<tr>
<td></td>
<td>17/35</td>
</tr>
<tr>
<td>Underlying diagnosis</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>26</td>
</tr>
<tr>
<td>CF</td>
<td>16</td>
</tr>
<tr>
<td>IPF</td>
<td>9</td>
</tr>
<tr>
<td>Pulm HTN</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
</tr>
<tr>
<td>Type of transplant (BLT/SLT/HLT)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31/29/1</td>
</tr>
<tr>
<td></td>
<td>30/21/1</td>
</tr>
</tbody>
</table>

No significant difference in:
- OR complications
- ICU complications
- Duration of intubation
- Hospital LOS
- Hospital survival
- FEV1 at 1 year
- Survival at 1 year

Changes in Donor Characteristics

Donor Age

Eurotransplant

Donor Lung Score

Proportion Transplanted

Article in Press. Transplant International Jan 2020
Contemporary Outcomes
With Extended Donors
Continued Successful Evolution of Extended Criteria Donor Lungs for Transplantation

Alfred Hospital, Melbourne, Aus
2012-2013 donor referrals (n=318)

129 resulting in transplant
## Outcomes

### Accepted Donors

![Graph showing donor score over time](image)

### Recipient Characteristics (n=129)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of MV support (median hours)</td>
<td>24 (4-1920)</td>
</tr>
<tr>
<td>ICU LOS (days)</td>
<td>5 (2-24)</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>22 (8-190)</td>
</tr>
<tr>
<td>Airway complications (%)</td>
<td>6</td>
</tr>
<tr>
<td>30-day survival (%)</td>
<td>97.7</td>
</tr>
<tr>
<td>1-year survival (%)</td>
<td>93.1</td>
</tr>
<tr>
<td>CLAD incidence at 1 year (%)</td>
<td>18</td>
</tr>
<tr>
<td>12-month FEV1 (% predicted)</td>
<td>79 (24-146)</td>
</tr>
</tbody>
</table>
Extended criteria donor lungs do not impact recipient outcomes in pediatric transplantation

2010 – 2016, Hanover, Germany, n=57

No Differences in:

- Post-operative Spirometry
- Freedom from CLAD Development
- Overall Survival

Recipients of extended criteria donors more often underwent atypical LVR (5 vs 0 patients)
In a multivariable model, CF recipients with a donor lung > 55 years had a 4-fold mortality risk at 1 year. Risk further increased when donor smoking (any vs none) was also considered.
Donor Smoking and Older Age Increases Morbidity and Mortality After Lung Transplantation

N=588 recipients and 484 donors
1992-2012, Copenhagen

Hazard:
Smoking 1.46 (1.15-1.86) p=0.002
Age > 55 1.84 (1.39-2.45) p<0.001

1.26 (0.99-1.61) p=0.057
1.59 (1.19-2.13) p=0.002
### Adult Lung Transplants (2005-6/2017)

**Statistically Significant Risk Factors For 1 Year Mortality**

#### Continuous Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age (years)</td>
<td>Donor age (years)</td>
</tr>
<tr>
<td>Recipient creatinine (mg/dL)</td>
<td>Recipient PVR (wood units)</td>
</tr>
<tr>
<td>Recipient FVC% predicted</td>
<td>Transplant center volume within 3 yrs</td>
</tr>
<tr>
<td>Ischemic time (hours)</td>
<td>Recipient bilirubin (mg/dl)</td>
</tr>
<tr>
<td>Donor-recipient weight difference (kg)</td>
<td>Donor-recipient height difference (cm)</td>
</tr>
</tbody>
</table>

**Note:** Interaction between height difference and procedure type was retained in the final model but was not statistically significant ($p = 0.3396$).
Donor Management
UTSA Protocol implemented 2001

33 pre-SALT vs 81 post-SALT donors

1997 – 2005

Factors Associated With Organ Improvement

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial $\text{PaO}_2/\text{FiO}_2$ $\geq 175$ vs $\text{PaO}_2/\text{FiO}_2 &lt; 175$</td>
<td>3.3</td>
</tr>
<tr>
<td>Chest radiograph without substantial infiltrates</td>
<td>1.61</td>
</tr>
<tr>
<td>Normal results from bronchoscopy</td>
<td>2.68</td>
</tr>
<tr>
<td>Lung recruitment attempted</td>
<td>1.60</td>
</tr>
</tbody>
</table>
An intensive lung donor treatment protocol does not have negative influence on other grafts: a multicentre study

6 Spanish hospitals
2013 - study period (n=165 organs)
2010-2012 - control period (n=453 organs)
Examined H,L,K,P outcomes

Lung donor management protocol

1) Apnoea test performed with ventilator (continuous positive pressure mode)
2) Mechanical ventilation with PEEP 8-10 cmH₂O and tidal volume of 6-8 ml/kg
3) Recruitment manoeuvres once per hour and after any disconnection from the ventilator
4) Bronchoscopy with bilateral bronchoalveolar lavage
5) Haemodynamics closely monitored with Picco® System, goal of ELWI <10 ml/kg (administering diuretics if necessary) and CVP (objective <8 mm Hg)
6) Methylprednisolone (15 mg/kg) after brain death declaration
7) Alveolar recruitment involved controlled ventilation (peak pressure limit of 35 mmHg) with PEEP of 18-20 cmH₂O for 1 min, and decreased 2 cmH₂O each minute; after that, we increased 50% tidal volumes for 10 breaths

Graft Survival

European Journal of Cardio-Thoracic Surgery 49 (2016) 1719-1724
Lung Focused Resuscitation at a Specialized Donor Care Facility Improves Lung Procurement Rates

**Lung Donor Candidate**
- Confirm brain death
- Transfer to SDCF to ICU
- Lung protective ventilation
  - Tidal volume 6-8 mL/kg
  - Target I:E ratio 1:1
  - PEEP 8-10 cm H₂O
  - FiO₂ 100%

**Recipient Criteria**
- Pa O₂/FiO₂ ratio < 300
- Recruitment with:
  - Increased PEEP 15 cm H₂O x 2 hours if HD stable
  - Keep peak inspiratory pressure and plateau pressure <30 mmHg

- Prior ventilation settings:
  - Pa O₂/FiO₂ ratio < 300
  - Lower FiO₂ as low as possible for SpO₂ 92-95%
  - Further assessment for lung donation

- Pa O₂/FiO₂ ratio > 300
- Recruitment with:
  - Increased PEEP 15 cm H₂O x 15-20 minutes
  - Keep peak inspiratory pressure and plateau pressure <30 mmHg

- Prior ventilation settings:
  - Pa O₂/FiO₂ ratio > 300
  - Lower FiO₂ as low as possible for SpO₂ 92-95%
  - Further assessment for lung donation
Donor Recovery Center Effect

**DONORS & ORGANS TRANSPLANTED**

<table>
<thead>
<tr>
<th>Year</th>
<th>Donors</th>
<th>Organs Transplanted</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>128</td>
<td>345</td>
</tr>
<tr>
<td>2016</td>
<td>153</td>
<td>425</td>
</tr>
<tr>
<td>2017</td>
<td>170</td>
<td>495</td>
</tr>
</tbody>
</table>

**Organs/Donor**

<table>
<thead>
<tr>
<th>Year</th>
<th>Organs/Donor</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>2.67</td>
</tr>
<tr>
<td>2016</td>
<td>2.71</td>
</tr>
<tr>
<td>2017</td>
<td>2.91</td>
</tr>
</tbody>
</table>

Air Medical Journal 37 (2018) 374–379
Opportunities for Expanding Donor Recovery
A donor PaO2 / FiO2 < 300 does not determine graft function or survival after lung transplantation

Helen Whitford, MD, FRACP, Christina E. Kure, PhD, Aimee Henriksen, RN, Jamie Hobson, RN, Greg I. Snell, MD, FRACP, Bronwyn J. Levvey, RN, Silvana F. Marasco, FRACS, PhD, Julian H. Gooi, FRACS, Adam Zimmet, FRACS, Justin Negri, FRACS, Adrian Pick, FRACS, Mark Buckland, MBBS, FANZCA, Trevor Williams, MD, FRACP, Glenn Westall, PhD, FRACP, Miranda A. Paraskeva, MBBS, MPH, Catherine Martin, PhD, David C. McGiffin, MBBS, FRACS

The Journal of Heart and Lung Transplantation 2020; 1, 53-61

Slide courtesy of David McGiffin
Lungs potentially rejected based on P/F ratio of <300 mmHg in ICU (light grey shaded areas) and operating room (dark grey shaded area).

Conclusions:

(1) adhering to a P/F ratio ≥ 300 would lead to 36% of the donor lungs being rejected

(2) a donor P/F ratio < 300 is largely driven by lower lobe atelectasis, even after lung recruitment

(3) a donor P/F ratio ≥ 300 is conservative and results in wastage of donor lungs
Transplant recipient survival stratified by donor lung P/F ratio of <300mmHg versus ≥300mmHg pre-procurement (in ICU).
Impact of the Opioid Epidemic on Lung Transplantation: Donor, Recipient, and Discard Characteristics

SRTR data 2000 - 2017

Discarded ODD allografts:
- Younger
- HCV positive
- Less cigarette smoking
- More cocaine use
- PHS increased risk

Use of drug-intoxicated donors for lung transplant: Impact on survival outcomes

UNOS Registry Data

Use of drug-intoxicated donors increased from 1.9% in 2005 to 6.2% in 2014
Heart and Lung Transplants from HCV-Infected Donors to Uninfected Recipients

Donor Baseline HCV RNA (log_{10} IU/ml)

Recipient Baseline HCV RNA (log_{10} IU/ml)

Transplantation
- Sofosbuvir-velpatasvir
- Monitoring of hepatitis C viral load, antibody levels, and liver-function tests after treatment
- Sustained virologic response 12 wk after treatment
- Sustained virologic response 24 wk after treatment

N Engl J Med 380;17 NEJM.org April 25, 2019
SRTR data, U.S. deceased organ donors
March 1, 2015 - February 28, 2018
Donor prediction model utilized
Post-Transplant Survival By Lung Donor Score

The Eurotransplant Lung Donor Score.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor age (y)</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>1</td>
</tr>
<tr>
<td>45-54</td>
<td>1</td>
</tr>
<tr>
<td>55-59</td>
<td>2</td>
</tr>
<tr>
<td>60+</td>
<td>3</td>
</tr>
<tr>
<td>Donor history</td>
<td></td>
</tr>
<tr>
<td>Compromised</td>
<td>4</td>
</tr>
<tr>
<td>Uncompromised</td>
<td>1</td>
</tr>
<tr>
<td>Smoking history</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>NA</td>
<td>1</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td></td>
</tr>
<tr>
<td>Clear</td>
<td>1</td>
</tr>
<tr>
<td>Edema</td>
<td>1</td>
</tr>
<tr>
<td>Shadow</td>
<td>2</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>1</td>
</tr>
<tr>
<td>Consolidation</td>
<td>2</td>
</tr>
<tr>
<td>NA</td>
<td>1</td>
</tr>
</tbody>
</table>

LDS = 6 (n=638)  LDS ≥ 7 (n=2415)

5-Year Survival: 69.7% vs 60.9%
P=0.007

Eurotransplant 2012-2016
N=3053

Smits. Transplant International 2020
Objective Donor Scoring System for Lung Transplantation

UNOS Dataset, 2005 – 2015, N=18,816

<table>
<thead>
<tr>
<th>Donors’ Characteristics</th>
<th>Hazard Ratio</th>
<th>p Value</th>
<th>Risk Score Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;60 years</td>
<td>1.54</td>
<td>&lt;0.001</td>
<td>2</td>
</tr>
<tr>
<td>Age 51-60 years</td>
<td>1.13</td>
<td>0.004</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.16</td>
<td>&lt;0.04</td>
<td>1</td>
</tr>
<tr>
<td>&gt;20 pack-year smoking history</td>
<td>1.11</td>
<td>0.04</td>
<td>1</td>
</tr>
<tr>
<td>African-American race</td>
<td>1.12</td>
<td>&lt;0.001</td>
<td>1</td>
</tr>
</tbody>
</table>

Low = 0
Intermediate = 1
High = ≥2

ISHLT Registry Outcomes

DCD vs DBD Survival

10-year Mortality Risk Factors

- Non-heart beating donor - Yes
- AM/tuberculosis vs COPD
- Procedure Type - Bilateral/Double
- Diagnosis - CF vs COPD
- Donor history cigs use - Yes
- Donor hypertension - Yes
- Recipient diabetes - Yes
- donor/F recip vs F donor/F recip
- Diagnosis - Sarcoidosis vs COPD
- nor CMV+/Recipient CMV - Yes
- Donor diabetes - Yes
- Non CF-bronchiectasis vs COPD
- Diagnosis - Retx vs COPD
- Hospitalized - Yes
- xient pre-transplant dialysis - Yes

Hazard ratio and 95% CI

DCD = 880
DBD = 9,537

p=0.72

Van Raemdonck JHLT 2019
Yusen ISHLT 2019
Heart or lung transplant outcomes in HIV-infected recipients

Survival for Lung Transplant Recipients

Survival curves for different groups:
- HIV Cohort
- ISHLT Control

Proportion surviving

p-value 0.665 log-rank test

Years since transplant

N at risk:
- 7
- 5
- 5
- 4
- 4
- 3
- 1
- 1

Clinical Transplantation. 2019;32:1296–1305
Regulatory Considerations

• Currently, only select donor characteristics are included in U.S. lung outcomes models
  • Blood pH, Cr, pCO2, Race, Bronchoscopy, D/R weight ratio

• Some centers may take a risk-averse approach with extended-criteria donors

Hospitals are throwing out organs and denying transplants to meet federal standards

Ethical Considerations

• Organ donation consent
  – Explicit vs. Presumed
  – Autonomy
• Extended-criteria related
  – Uncontrolled DCD
  – Where are the ECD limits?

• Utility of extended criteria lungs
• Justice of distribution
• Resolution of conflicting principles
• DBD / DCD Research
Raising Organ Donor Awareness

• Donor registration awareness and local enrollment availability (DMV, campaigns, etc)

• Use of social networks and social media to create a positive incentive for donation
  – Links to state donor registries
Variability in donor organ offer acceptance and lung transplantation survival

![Graph showing cumulative incidence of waitlist mortality over time with different acceptance rates.]

Number at risk:
- < 25%: 1871
- 25-29.9%: 2351
- 30-39.9%: 2465
- 40% or above: 1506

Time from receiving first first-rank offer (Day):
- 0: 610
- 60: 393
- 120: 285
- 180: 229
- 240: 174
- 300: 131
- 360: 142

Cumulative Incidence of Waitlist Mortality (%):
- < 25%: 20%
- 25-29.9%: 15%
- 30-39.9%: 10%
- 40% or above: 5%

Article In Press. Journal Heart Lung Transplant 2020
Summary

• Expanding the criteria for “acceptable donor lungs” has improved access to transplantation

• Donor management protocols and facilities focused on organ recovery can increase the number of available organs

• Optimizing use of lungs from HCV+, overdose, and DCD donors, along with newer technologies, has the immediate potential to expand the donor pool

• Any reduced outcome with ECD lungs has to be balanced against mortality while awaiting transplant
Thank you!