Lung Track Summaries:
The Evolution of Lung Support Devices
Regulatory considerations in Lung Transplantation

Sangeeta M. Bhorade, MD
Professor of Medicine
Northwestern University
ECMO as a Bridge to Transplant Should be Exempt from 1 Year Mortality Outcomes in Lung Transplant

Charles Hoopes  MD versus Duane Davis, MD MBA
“... hospitals have become more risk averse based on these metrics with concerns about treating patients who are considered relatively at higher risk for survival”

“... providing the optimal treatment option for patients with end-stage organ disease may place programs at higher risk for punitive regulatory consequences”

“... metrics should be applicable to assess performance ... and most importantly directly align with what is in the best interest of the patient population”

Approved by the AST Executive Committee on April 4, 2017
The "curve of downshifting risk"... surgical innovation and behavior

Stewart and Stevenson (2011) Circ
“ECMO risk prediction has two key goals ... (1) prospectively stratify the outcome risk and (2) measure risk-adjusted ECMO performance across all patients.”

“Across these objectives, the different indications for ECMO, modalities, and characteristics of the infrastructure and practice patterns all matter. Accordingly, the ideal model would be customized along those dimensions, be constructed in large datasets and successfully validated in external datasets.”
Balance between doing the right thing and doing the thing right

Figure 3: The right balance in adjusting program-specific outcomes for risk. “Too much” adjustment could forgive centers for performing futile transplants and wasting organs. “Not enough” adjustment could discourage centers from performing transplants in suitable high-risk candidates, and/or accepting high-risk donors.
Ex Vivo Lung Perfusion is an Essential Tool for Donor Optimization

Shaf Keshavjee MD and Thomas Egan MD, MSc
EVLP Provides the Opportunity to Test Questionable Organs

- Different threshold 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
- A stable lung on EVLP will work after transplant
- Use more lungs SAFELY (no more “adventures” with “marginal lungs”
Decision Making - Experience

You cannot make a chicken out of a fried egg!!

- Experienced team can make the decision together with the more junior team that went on recovery.
Donor with High PAP and PE: Significant Improvement of Pulmonary Hemodynamics after Treatment on EVLP

Diagnosis

Treatment

Response monitoring
EVLP Provides the Opportunity to Repair Donor Lungs

EVLP Treatment Strategies

- Perfusion
- Gene Therapy
- Cell Therapy
- Inhaled Gases
- Drugs
- Immuno-cloaking
- Biological
EVLP Impact on lung donor pool

- multiple publications attest to ↑ use of lungs after EVLP
- most of these lungs would not have been used
- most reports show equivalent early and late mortality
- does EVLP “recondition” lungs?
- if bad lungs become better, shouldn’t good lungs become even better?
Does EVLP make lungs better?

- lit search: human ex vivo lung perfusion
- 307 citations back to 1988 – some irrelevant
- not one citation showed better lung function or survival with EVLP alone
Conclusions

- **EVLP is a useful tool to help evaluate lungs**
  - absolutely necessary for uDCDD lungs
- **EVLP will probably be very useful to treat lungs**
- currently there is no evidence that EVLP should be performed on every set of lungs
The Regulatory Imperative – Impact on the Practice of Lung Transplant

Christopher Wigfield MD
Examples of the regulatory imperative

1. *identify accountability*
2. *be enforceable*
3. *be easy to understand*
4. *have broad public support*
5. *be balanced and avoid knee-jerk reactions*
6. *reconcile contradictory policy objectives*
7. *balance risks, costs and benefits*
8. *avoid unintended consequences*
9. *be relevant to current conditions*

“was it allocated or complicated?”
Regulatory realities- Redefining Benefit of Lung Transplant in the Current Era

Gundeep Dhillon MD, MS
Since LAS implementation...

- Decreased number of wait list patients and waiting list time per patient
- Decreased waiting list mortality, initially, now increasing
- Recipient Characteristics Shift
  - Older patients
  - Sicker Patients
  - Group D / ILD recipient favored
- High LAS scores associated with increased post-transplant mortality
- But, No change in overall survival at 1 year
But ...

- Long-term survival appears to have worsened
- Increased resource utilization
- Indirect evidence of increased morbidity
Survival Benefit of Lung Transplantation in the Modern Era of Lung Allocation

David M. Vock¹, Michael T. Durheim²,³, Wayne M. Tsuang⁴, C. Ashley Finlen Copeland³, Anastasios A. Tsiatis⁵, Marie Davidian⁵, Megan L. Neely²,⁶, David J. Lederer⁷, and Scott M. Palmer²,³
Summary

• Implementation of LAS shifted the organs towards older & sicker patients

• Concurrent increase in regulatory pressures, probably led to:
  • Increased focus on 1-year survival
  • Worsening long term outcomes
  • Increased resource utilization to maintain 1-year outcomes

• Risk aversion leading to decreased number of transplants in the higher LAS groups
Cell Free DNA and Other Immune Monitoring Techniques in Lung Transplantation – Are We There Yet?

David Neujahr MD
Key Points (are these technologies ready for prime time?)

Dad, are we there yet?

NO!
When will new technologies be “there”?

• Cell free DNA is a technology without a well formulated question...yet
  • Artifact of using an existing technology for a separate purpose
  • Longitudinal studies are key

• Viral next-gen sequencing
  • Needs to be paired with other measures to be informative
  • Cost needs to come down

• Microvesicles/Exosomes
  • Too early to tell, but hot topic
  • Lots of abstracts at ATC!
Controlled Donation after Determination of Circulatory Death (cDCDD- Improving yield

Michael Smith MD
Improving Lung DCD Yield
Summary

• DCD is an important resource to narrow donor shortage
• Controlled DCD criteria are similar to DBD
• Outcomes for Controlled DCD are comparable to DBD
• Challenges
  • Restricted donor/pt management
  • Alleviate “dry run” cost allocation issues
  • Graft risks
    • Aspiration
    • Prolonged WIT
  • EVLP for extended criteria controlled DCD
• Consider expansion of uncontrolled DCD programs
  • EVLP likely to improve outcomes
Xeno Lung Transplantation - The Path Forward

Agnes Azimzadeh PhD
The Path Forward

• Combine TBM and EPCR
• Evaluate TFPI
• Humanize pig vWF
• Target cellular adhesion pathways (selectins, CD11b/CD18/Mac-1 integrin)
• Target macrophages (clodronate liposomes, ASGR1, SIRP1a)
• Target sialidases
Extracorporeal Lung Support-A Bridge too far?

Jonathon D’Cunha MD
ECMO

- Any patient with refractory hypoxemia or hypercapnia despite optimal ventilatory support and adjunctive medical management

- Often referred to as “bridge” therapy

- Bridge to what:
  - Recovery
  - Transplant
Summary

• ECMO is a viable and dynamic option for failing patients

• Patients should be carefully selected
  • Center volume
  • Pulmonary Hypertension
  • Other Organ failure
  • Sensitization
  • Re-tx
Major Take Message

Timely implementation of ECMO translates to greatest benefit
The Artificial Lung- Can it be realized?

William Federspiel PhD
The Natural Lung Versus an Artificial Lung

Nature’s Technology

The natural lung is a remarkable organ for gas exchange

“A” vs “V”

A ~ 140 m²
A/V ~ 2900 cm⁻¹
δ ~ 1 μm
VO₂ ~ 210 - 3200 ml/min

“Our” Technology

Hollow Fiber Membrane Modules

A ~ 2.5 m²
A/V ~ 28 cm⁻¹
δ ~ 10-30 μm
VO₂ ~ 150 - 250 ml/min

Alveolar-Capillary Microvascular Units
Current Artificial Lungs: ECMO Devices

MAQUET GETINGE GROUP

CARdioHELP System
The world’s smallest portable heart-lung support system.

AVALON ELITE® Bi-Caval Dual Lumen Catheter

Medical Devices Laboratory
McGowan Institute of Regenerative Medicine
A Comprehensive Solution: ModELAS*

*Modular Extracorporeal Lung Assist System: “wearable” lung assist for adults and children

<table>
<thead>
<tr>
<th>Function</th>
<th>Blood Flowrate</th>
<th>Clinical Goal</th>
<th>Clinical Market (NA/EU)</th>
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<tbody>
<tr>
<td><strong>P-ModELAS</strong></td>
<td><strong>Pediatric O₂ supply and CO₂ removal</strong></td>
<td>1-2.5 Liters/min</td>
<td>Bridge to recovery (acute) or transplant (chronic)</td>
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<tr>
<td><strong>A-ModELAS</strong></td>
<td><strong>Adult O₂ supply and CO₂ removal</strong></td>
<td>2-3.5 Liters/min</td>
<td>Bridge to recovery (severe ARDS) or transplant (chronic)</td>
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<tr>
<td><strong>A,P-ModELAS ECCO2R</strong></td>
<td><strong>Minimally invasive CO₂ removal (respiratory dialysis)</strong></td>
<td>200-500 mL/min</td>
<td>Bridge to recovery (ARDS, AE-COPD)</td>
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Medical Devices Laboratory
McGowan Institute of Regenerative Medicine
Conclusion: It can be realized but ...  
We are about 20-30 years behind VAD technology

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<tr>
<th></th>
<th>VADs</th>
<th>Artificial Lungs</th>
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<tbody>
<tr>
<td>Implantable working unit</td>
<td>Yes</td>
<td>No Extracorporeal</td>
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<tr>
<td>Reliability</td>
<td>Years</td>
<td>Days-Months</td>
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<tr>
<td>Destination Therapy</td>
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<tr>
<td>Hemocompatibility</td>
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<td>Challenge</td>
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<td></td>
<td>~ cm² contact area</td>
<td>~ m² contact area</td>
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<td>Technology Platform</td>
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