Pushing the Envelope or Beyond the Pale: Utility and the High Risk Lung Candidate

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Disclosure

No conflicts to disclose
Learning Objectives

▪ Define utility
▪ Discuss limitations in determining utility
▪ Review how LAS addresses utility
▪ Discuss utility constraints in high risk lung candidates
Would you/your center consider either patient for lung transplantation? Why or why not?

<table>
<thead>
<tr>
<th>Mr. Madison</th>
<th>Mr. Unger</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 73 years old</td>
<td>• 73 years old</td>
</tr>
<tr>
<td>• COPD, former smoker</td>
<td>• IPF</td>
</tr>
<tr>
<td>• revascularized CAD, DM, BMI 32</td>
<td>• TLC 60%, DLCO 25%</td>
</tr>
<tr>
<td>• FEV1 15%, DLCO 15%</td>
<td>• 6mwt distance 300 ft</td>
</tr>
<tr>
<td>• 6mwt distance 400</td>
<td>• Progressive decline on medical tx</td>
</tr>
<tr>
<td>• Gradual decline</td>
<td>• On supplemental oxygen 4 lpm at rest</td>
</tr>
<tr>
<td>• Requires oxygen 2LPM at rest</td>
<td></td>
</tr>
</tbody>
</table>
Would you/your center consider either patient for lung transplantation?

• **Is this patient likely to benefit from transplantation**
  – Survival benefit
    • Urgency versus post-txp survival
    • How much survival benefit
  – Other benefits
  – Information gaps

• **Other considerations**
  – Regional wait-list and organ availability
  – Center-specific criteria and risk tolerance
  – Impact on other patients
  – Patient’s autonomy
OPTN White Paper:
Ethical Principles in the Allocation of Human Organs
June 2015 Revision

“The ideal allocation would be one that simultaneously maximizes the aggregate amount of (medical) good, distributes the good justly, shows respect for persons including the autonomous decisions of persons, and is in accord with any other ethical principles that might come into play.”

• Utility
• Justice
• Respect for persons (autonomy)

Utility

1. “...maximize the expected net amount of overall good (that is, good adjusted for accompanying harms), thereby incorporating the principle of beneficence (do good) and the principle of non-maleficence (do no harm).”

2. “...factors considered in the application of the principle of utility are: 1) patient survival; 2) graft survival; 3) quality of life; 4) availability of alternative treatments; and 5) age.”

3. “Factors relevant to access to the transplant waiting list, as distinguished from medical criteria used in the equitable allocation of organs, include: ethical rules (e.g., honesty, the duty not to harm), clinical indicators (e.g., co-morbidities, cause of organ failure) and psychosocial factors (e.g., financial and social support, patient adherence).”
Utility considerations

• Listing decision vs allocation priority
• LAS
  – net transplant benefit based on transplant urgency and post-transplant survival
  – “justice” based on allocation by predicted benefit
  – factors not included in LAS are particularly relevant to certain patient populations
How we think about frontiers

Pushing the envelope

• In aeronautics, the envelope refers to all probable conditions of symmetrical maneuvering flight. Popularized by Tom Wolfe – “The Right Stuff” 1979

Beyond the pale

• A pale is the area that is enclosed and safe
• Beyond the pale originates from a 1657 poem by John Harington
  The History of Polindor and Flestella
  Ortheris goes with his beloved to a lodge for 'quiet, calm and ease', but they later “roved forth beyond the pale"
Increased risk examples

• Advanced age
• Significant comorbidities
• Re-transplantation
• Patient on advanced life support
• Pan-resistant organisms
Median survival (years): 18-34=6.5; 35-49=6.7; 50-59=5.3; 60-65=4.5; >65=3.6

All pair-wise comparisons were significant at p < 0.05 except 18-34 vs. 35-49
Lung Transplantation in Older Patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
<th>1 year survival</th>
<th>3 year survival*</th>
<th>5 year survival*</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-69</td>
<td>82</td>
<td>64</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>&gt;70</td>
<td>79</td>
<td>49</td>
<td>28</td>
<td></td>
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</table>

*P<0.001
A. Single Lung

B. Double Lung
ISHLT 2019 Registry: Age and Lung Transplantation

Hazard Ratio of 5 Year Mortality

Recipient age (years)

JHLT, 2019 Oct; 38(10)
Retransplantation

Survival (%) vs. Years

Adult/Primary (N=45,542)
Adult/First Retx (N=1,799)
Pediatric/Primary (N=1,742)
Pediatric/First Retx (N=111)

All pairwise comparisons were significant at p < 0.05 except for Adult/Primary vs. Pediatric Primary and Adult/First Retx vs. Pediatric/First Retx
ECLS Bridge to Transplant

- 71/1111 patients bridged to lung txp using ECLS.
- 10% of transplants in most recent yrs
- Mostly ILD, CF, IPAH
  Median age 38
- Awake VV ECMO
  35% extubated
- Median ECLS time
  10 days (0-95)
- 89% of patients survived to Txp.
Resistant Organisms: M. abscessus

Kavaliunaite E, Harris KA, Aurora P, Dixon G, Shingadia D, Muthialu N, Spencer H
Transpl Infect Dis. 2020 Mar 4
Resistant Organisms: M. abscessus

Hamad Y, Pilewski JM, Morrell M, D'Cunha J, Kwak EJ.
Transplant Proc. 2019 Jul - Aug;51(6)
Resistant Organisms: M. abscessus

Figure 2B: Survival after Lung Transplant

M Abscessus Group = 0

CF Group = 1
TWO CONDITIONS

SURVIVAL % vs TIME
Can we predict outcomes?

Do we know all the variables?

What outcomes are we predicting?
Summary:
Utility and High-Risk Patients

- Some high-risk patients derive substantial benefit from transplantation
- Criteria used to assess utility (benefit) are not “ideal”
- Lower limits of utility influenced by organ scarcity
- Prediction tools are imperfect
  - Small patient numbers
  - Unaccounted risks/comorbidities
  - Complexity of data