Ethics and Advocacy in the Modern Era of Pediatric Liver Transplantation in the United States

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Disclosure

• In the past 12 months, I have had no relevant financial relationships with the manufacturers of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity

Learning Objectives

Upon completion of this session, the participants will:

1) Have a better understanding of the ethical principles behind prioritizing children in deceased liver allocation
2) Be able to employ potential strategies for advocating on behalf of children in the deceased liver allocation system
3) Have a improved understanding of the ethical issues that surround anonymous altruistic living donor liver donation
Case

Introduction

Liver transplant = definitive treatment for:
- childhood end-stage liver disease
- metabolic disease
- certain liver malignancies
- Excellent patient and graft survival
  > 95% at 1 year post transplant

Additional Disclosure Slide

• I am not an ethicist
• I am a transplant hepatologist
• I am on the pediatric committee of UNOS
• I chair the education committee of SPLIT

Graphic from Johns Hopkins Gastroenterology and Hepatology
History of Allocation in the United States

<table>
<thead>
<tr>
<th>1980s</th>
<th>1990s</th>
<th>1998</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal communication</td>
<td>Wait time</td>
<td>Final Rule Issued</td>
</tr>
</tbody>
</table>

- **1998—Final Rule**

- **Mandate:**
  - Allocate in order of medical urgency
  - Minimize the role of waiting time
  - Avoid futile transplantation
  - Decrease inter-transplant center variance
  - Broader geographic distribution


Figure X-1. Comparison of Original MELD and OPTN/UNOS MELD PELD Equations

Original MELD
\[
MELD = 0.957 \times \text{LN} \left( \text{creatinine} \right) + 0.378 \times \text{LN} \left( \text{bilirubin} \right) + 1.12 \times \text{LN} \left( \text{INR} \right) + 0.643 \times \text{LN} \left( \text{cause of cirrhosis} \right)
\]

OPTN/UNOS MELD
\[
MELD = 0.957 \times \text{LN} \left( \text{creatinine} \right) + 0.378 \times \text{LN} \left( \text{bilirubin} \right) + 1.12 \times \text{LN} \left( \text{INR} \right) + 0.643 \times \text{LN} \left( \text{cause of cirrhosis} \right)
\]

PELD
\[
PELD = 0.435 \times \text{age} + 1.287 \times \log \left( \text{albumin} \right) + 0.480 \times \log \left( \text{bilirubin} \right) + 
(1.957 \times \log \left( \text{INR} \right) + (0.857 \times \text{growth failure}^*)
\]

*Chronic liver disease = 1, all others = 0
**Values < 1 are truncated to 1
***Age < 1 year = 1, all others = 0
****Values > 2 standard deviations from the mean = 1, all others = 0

Implementation of MELD


Adult Waitlist mortality

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients at start of year</td>
<td>14956</td>
<td>15360</td>
<td>15428</td>
</tr>
<tr>
<td>Removed for Transplant</td>
<td>5659</td>
<td>5726</td>
<td>5660</td>
</tr>
<tr>
<td>Removed for death or deterioration</td>
<td>2820</td>
<td>2988</td>
<td>3002</td>
</tr>
</tbody>
</table>

*Mortality rates ranging 18-20% per year
Pediatric Waitlist mortality

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients at start of year</th>
<th>Removed for Transplant</th>
<th>Removed for death or deterioration</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>701</td>
<td>564</td>
<td>75</td>
</tr>
<tr>
<td>2011</td>
<td>666</td>
<td>539</td>
<td>45</td>
</tr>
<tr>
<td>2012</td>
<td>655</td>
<td>528</td>
<td>54</td>
</tr>
</tbody>
</table>

*Mortality rates ranging 7-11% per year

PELD Exception Scores

- Applications can be made by clinicians on behalf of their patients to the Regional Review Board (RRB) for additional exception points
- This is arbitrary and unstandardized
- Opens the system up to unfair application

Prediction rates for exception requests by region
US Exception Requests in pediatric pts with chronic liver disease

Exception requests were associated with higher calculated MELD/PELD, younger age, and White race.

Exception status was associated with a 3-fold higher hazard ratio of transplantation.


The Tragedy of the Commons

Number of patients added to the liver waitlist per year

UNOS OPTN Data
Simon Horslen. July 2014

Special Ethical Considerations in the Allocation of Human Organs to Pediatric Candidates

- UNOS Pediatric Transplantation and Ethics Committees
- Provide guidance about how organ allocation policies should address pediatric patient needs
- Justifications for pediatric priority in organ allocation

Ethical Principles of Pediatric Organ Allocation, OPTN
Declaration of the Rights of the Child

Whereas the child, by reason of his physical and mental immaturity, needs special safeguards and care, including legal protection …

Whereas mankind owes to the child the best it has to give …

The child shall enjoy special protection, and shall be given opportunities and facilities, by law and by other means, to enable him to develop physically, mentally, morally, spiritually, and socially in a healthy and normal manner …

In the enactment of laws for this purpose, the best interests of the child shall be the paramount consideration.

1959, United Nations General Assembly

Prudential Lifespan Account

• Children with end-stage organ failure have time-limited opportunity for growth and development and may suffer lifelong consequences if not expeditiously transplanted

• How each individual would want to invest resources across one life with goal to make a life go as well as possible

Prudential Lifespan Account

![Diagram of lifespan stages: Birth, Childhood, Adolescence, Young Adulthood, Middle Age, Retirement, Schooling, Physical development, Social development, Having and raising children, Career development.]

If you are investing in a lifespan, where are you going to put your dollars?
Fair Innings

- Every individual deserves to experience a full life
- Children will die prematurely, denying opportunities in adulthood to complete education, establish career, have a family

Maximin Principle

- Maximizing the minimum benefit to the least advantaged, or giving priority to the most disadvantaged groups
- Give the most benefit to the least-advantaged members of society
Maximin Principle

Society’s institutional arrangement is just insofar as it improves the lot of the worst-off group.

Priority in reducing the gaps between the worst off and the rest of the population.

• Pediatric candidates are disadvantaged
  • small size
  • developing anatomy
  • lack of availability of life-sustaining therapies
Utility Considerations

Pediatric liver recipients have a better patient and graft survival than adult recipients


How do we invoke change on behalf of children?

- Alternatives should be fair, equitable, and improve pediatric waitlist outcomes without affecting the adult waitlist
How do we invoke change on behalf of children?

International experience

• Brazil
  • Pts < 12 years of age allocation score = (calculated PELD)x3
  • 6x increase in split liver transplantation and decreased waiting time


• Eurotransplant
  • “Pediatric MELD” score assigned < 12 years of age, point score corresponding to 35% 3-month wait-list mortality, upgraded by a 15% increase every 90 days
  • 12-16 yrs age given a score corresponding to a 15% 3 month waitlist mortality, upgraded by 10% every 90 days


Discussion

Case #2

• Twins, adopted, both with end-stage liver disease from Alagille syndrome
• Only the father is a match/suitable candidate
• Desperate, they go to the media to plead for an anonymous altruistic living donor
Case #2

Overview: Living Donor Liver Transplantation

Pros
- Controlled setting, decreased ischemia time
- In related individuals, may improve tolerance of graft
- In areas facing critical shortage, may be the only choice

Cons
- Psychiatric complications
- Health related quality of life
- Physical complications (donor complication rate 40%, biliary complication rate 10.6%, Incision infection rate 5.8%, 0.2% donor mortality)
- Psychosocial health: costs, family impact

Anonymous living liver donation

Living liver donation from genetically and emotionally related donors is effective and accepted life-saving therapy for escalating number of patients with end-stage liver disease

Donor complication rates ~40%, 10x risk of mortality (0.28%) of kidneys

Anonymous altruistic donation

In emotionally or genetically related donors, we expect, particularly in pediatrics, that the donor will be better off after surgery than before because of the benefit to the recipient.

This assurance does not exist in anonymous donation.

What do providers think about anonymous altruistic donation?

Most participants (caregivers, coordinators) were either wary of or opposed to altruistic stranger donation.

"It's nice to be nice to other people but it's a strange thing. For me, it's difficult to understand... at this moment, I wouldn't consider it really."

Source:

Table 1: Reasons for accepting LALDs

<table>
<thead>
<tr>
<th>Reason for accepting LALDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. History of altruistic behavior (i.e. must &quot;walk the talk&quot;).</td>
</tr>
<tr>
<td>2. High level of motivation to donate.</td>
</tr>
<tr>
<td>3. Logical rationale for donation.</td>
</tr>
<tr>
<td>4. Altruistically motivated.</td>
</tr>
<tr>
<td>5. No expectation of secondary benefit (e.g. media or public attention, compensation, atonement).</td>
</tr>
<tr>
<td>6. Voluntary informed consent is obtained.</td>
</tr>
<tr>
<td>7. No evidence of increased risk of negative psychiatric or psychosocial outcomes.</td>
</tr>
<tr>
<td>8. Willingness to maintain confidentiality.</td>
</tr>
<tr>
<td>9. Family support of donor's decision to donate anonymously.</td>
</tr>
<tr>
<td>10. Understanding and acceptance of standard organ allocation criteria.</td>
</tr>
</tbody>
</table>

Source:
How effective are media campaigns?

- Over 5 years—1000 potential donors initiated call, majority do not respond to calls or fail to complete required questionnaire
- Only 29 people submitted appropriate documentation, passed screening and underwent further eval in a 5 year period
- 17 terminated, leaving 12
  - 7 patient decisions
  - 5 medical concerns
  - 4 anatomical unsuitability
  - 2 breach of anonymity
Evaluation of anonymous living donors

- Need for protection of donor and recipient
- Rigorous requirements:
  - Past history of altruistic acts
  - Logical rationale for donation understandable to the team
  - No major psychiatric or psychosocial issues
  - Strong social supports
  - Must be willing to maintain confidentiality of patient information
  - No expectation of unacceptable secondary benefit such as media or public attention or illegal compensation
  - Must remain anonymous to recipient for at least 6 months
- Left lateral segment donation preferred due to surgical risk