MELD System: Past and Present

Patrick S. Kamath, MD
Mayo Clinic College of Medicine
Division of Gastroenterology and Hepatology
MELD for Liver Transplantation: Outline

• What is the MELD Score?
• Why was liver allocation changed to the MELD-based system in the US?
• How is MELD used for organ allocation?
• How has MELD impacted liver transplantation?
What is the MELD?
Model for End-Stage Liver Disease (MELD)

- Mathematical survival model
- MELD score estimates risk of 3 month mortality
- Uses 3 easily obtained laboratory values:
  - Serum total bilirubin
  - Serum creatinine
  - INR for prothrombin time
MELD Equation

MELD = (0.957 x log(creatinine) + 0.378 x log(bilirubin) + 1.12 x log(INR) + 0.643) x 10

## Sample MELD Scores

<table>
<thead>
<tr>
<th>INR</th>
<th>Bilirubin</th>
<th>Creatinine</th>
<th>MELD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>1</td>
<td>19</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>3</td>
<td>33</td>
</tr>
<tr>
<td>Score</td>
<td>3 Month Mortality Risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>80%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
• Why was liver allocation changed to the MELD-based system in the United States?
Liver Transplantation: Who Needs it Most? (Justice)

- The patient most at risk of dying needs the transplant the most

- But how do you decide who is most at risk of dying?

- (Utility = Who will benefit the most)
The collision of philosophies
Treat sickest first, or give livers to the less ill?

You had one factory with a lot of raw material. Now you’ve got a lot of factories but you haven’t got a lot more raw material, so they’re all competing for the raw material.”

Peering at a smiling self-portrait of her daughter, Kathy Miller questions the death of Katy, 21, who participated in a special trial for liver transplant patients at the University of Pittsburgh Medical Center.
Problems with Previous Allocation Scheme

- Patients (18,000) prioritized based on 3 categories
- Fewer than 100 Status 1 (highest)
- 2B class: >10,000 patients
- Waiting time became main determinant
- ICU patients higher priority
Final Rule Mandate: DHSS March 2000

• Priority for organ allocation should be established on objective, measurable, clinical criteria

• Waiting time must be de-emphasized

• Patients should be rank ordered on the liver list according to predicted mortality
### Deceased Donor Liver Allocation
February 2002 Changes

<table>
<thead>
<tr>
<th>OLD UNOS POLICY</th>
<th>NEW UNOS POLICY</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Local, regional, national</td>
<td>• Local, regional, national</td>
</tr>
<tr>
<td>• Medical status →</td>
<td>• Probability of death</td>
</tr>
<tr>
<td>• Waiting time →</td>
<td>• No waiting time</td>
</tr>
<tr>
<td>• Regional sharing for status 1</td>
<td>• Regional sharing for status 1</td>
</tr>
<tr>
<td>• Status 2A for ICU →</td>
<td>• No preference for ICU patients</td>
</tr>
</tbody>
</table>

\[\text{Old UNOS Policy} \rightarrow \text{New UNOS Policy}\]
• How is the MELD used for organ allocation?
MELD and Liver Allocation

• Fulminant hepatic failure highest priority

• Highest MELD score determines priority amongst patients with cirrhosis and same blood type

• Waiting time used only to break ties at identical MELD scores

• MELD scores updated at regular intervals
MELD/PELD Allocation Scheme
Initiated on February 27, 2002

- What impact has MELD had on the waiting list?
- What are the MELD scores of patients on the waiting list, dying or transplanted?
- What effect does MELD have on deaths on the waiting list?
- What effect does it have on liver transplant outcomes?
3-Month Mortality Based on Listing MELD Score

Gastroenterology; 2003
# MELD Score and Risk of Death Waiting for Liver Transplant

<table>
<thead>
<tr>
<th>MELD</th>
<th>RR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>0.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>11-20</td>
<td>1.0</td>
<td>------</td>
</tr>
<tr>
<td>21-30</td>
<td>8.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>31-40</td>
<td>35.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
90-Day Cadaveric Transplantation Rate
Isolated Liver Only *

Caudaveric Transplant Rate (%)

MELD: Lab

6-10: 1.6
11-20: 7.5
21-25: 31.2
26-30: 50.1
31-40: 66.5
All: 8.9
• How has MELD impacted liver transplantation?
National Effect of MELD Recipients in ICU at Time of Transplant

Based on OPTN data as of April 11, 2003

p < 0.00001

Pre-MELD (1/01-2/02)
Post-MELD (4/02-1/03)
### Comparison of Two Eras and the Impact of MELD

<table>
<thead>
<tr>
<th></th>
<th>Era 1</th>
<th>Era 2</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2/28/01 - 8/28/01)</td>
<td>(2/28/02 - 8/28/02)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New listings</td>
<td>5697</td>
<td>4746</td>
<td></td>
</tr>
<tr>
<td>Cadaver transplant</td>
<td>2358</td>
<td>2478</td>
<td></td>
</tr>
<tr>
<td>Living donor transplant</td>
<td>250</td>
<td>187</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Mean MELD at transplant</td>
<td>11.4</td>
<td>22.1</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Retransplant</td>
<td>86</td>
<td>81</td>
<td>p ns</td>
</tr>
<tr>
<td>HCC</td>
<td>8.8%</td>
<td>21.7%</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Liver/kidney</td>
<td>1.1%</td>
<td>2.1%</td>
<td>p ns</td>
</tr>
</tbody>
</table>
Waiting List

Has there been a reduction in Mortality?
Deaths on UNOS Liver Waiting List

Years
- 95
- 96
- 97
- 98
- 99
- 00
- 01
- 02
- 03
- 04
- 05
- 06

Deaths
- 0
- 500
- 1000
- 1500
- 2000
- 2500

MELD
- 838
- 994
- 1185
- 1435
- 1858
- 1922
- 2046
- 1897
- 1838
- 1734
- 1687
- 1593
Deceased Donor System

Median Time to Transplant (TT) for New Liver Waiting List Registrations, 2002-2006

Source: 2007 OPTN/SRTR Annual Report, Table 1.5.
Waitlist and Transplant Activity for Liver, 1997-2006

Source: OPTN/SRTR Annual Report Tables 1.3, 1.6, 1.7
The 2005 SRTR Report on the State of Transplantation

The Scientific Registry of Transplant Recipients

Since 2001, the gap between the number of liver transplants and the number of wait-listed liver candidates has shrunk by nearly a third.

- Number of active waiting list patients at year-end
- Number of liver transplants per year

2001 gap = 9,727
2004 gap = 6,576
MELD Transplantation Era

Are traditionally disadvantaged groups less disadvantaged?
Cadaveric Transplants Per 1000 Patient-years On The Liver Waiting List

Ethnicity

<table>
<thead>
<tr>
<th>Candidate Ethnicity</th>
<th>Era 1</th>
<th>Era 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>270.4</td>
<td>291.4</td>
</tr>
<tr>
<td>Black</td>
<td>308.8</td>
<td>385.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>264.4</td>
<td>279.4</td>
</tr>
<tr>
<td>Asian</td>
<td>231.4</td>
<td>330.5</td>
</tr>
</tbody>
</table>
MELD Transplantation Era

Has post transplant survival changed?
Post-Transplant Graft Survival

Percent Surviving

Days

Era 1

Era 2

0 20 40 60 80 100
Post-Transplant Patient Survival

Percent Surviving vs. Days

Era 1
Era 2
Mortality Reduction with MELD System

- Fewer deaths on transplant list
- Shorter time to transplant
- Fewer removals from wait list
- No change in survival
MELD and Transplant Benefit

• Is there a MELD score which determines survival benefit with liver transplantation?
Mortality Rates by MELD: “Transplant Benefit”

- HR=3.6, P<0.001
- HR=2.3, P<0.001
- HR=1.2, P=0.41
- HR=0.6, P<0.001
- HR=0.3, P<0.001
- HR=0.2, P<0.001
- HR=0.1, P<0.001
- HR=0.0, P<0.001

Mortality rate per 1000 patients

HR=hazard ratio
Dr. Steven Rudich
Transplant surgeon,
University of Cincinnati

With a MELD of 15, your one-year survival is practically 100 percent. Your one-year survival with a MELD of even 17 or 18, my friend, is pretty damn good.”

Dr. John Fung
Chairman of surgery,
The Cleveland Clinic

(The Share 15 policy) was a way to show that with a score of less than 15, you didn’t get any benefits from transplantation.”
Transplanting TOO SOON

Dr. A. Joseph Tector, chief of transplantation at Clarian Health in Indianapolis, prepares a donor liver for transplantation into a 53-year-old hepatitis C patient with a MELD score of 18. Clarian has a statistically higher-than-expected one-year success rate for grafts, and 89 percent of its patients are alive a year after transplant. This patient survived the transplant surgery.
Terry Masker
Died June 20
after two liver
transplants

MELD Score
predicts mortality
(graphic below)

Why did we let
them kill me?"

Terry Masker’s
MELD score was
11 at the time
of his first
transplant.
COURTESY OF THE MASKER FAMILY

Terry and Carol Masker celebrate Terry’s 60th birthday only weeks before he died at Strong Memorial Hospital in Rochester, N.Y.
Dr. Andreas Tzakis
Director, Miami Transplant Institute

The hospital doesn’t like (transplanting sicker patients), the insurance company doesn’t like it, the doctors don’t like it because it requires a lot of work. If you put all those things together, there’s a lot of pressure to do patients with low-MELD scores.”

Dr. Adel Bozorgzadeh
Director of transplantation, Strong Memorial Hospital, Rochester, N.Y.

"If there was a surplus of organs available in this country, I really doubt anyone would be using extended-criteria organs. What are you supposed to do? Let the patients die?"

Tzakis, director of the Miami Transplant Institute, performs a transplant at Jackson Memorial Hospital in Miami. "It’s a question of us," he said, "to help those who need us the most."
Ellen Kerber of North Huntingdon was diagnosed with primary biliary cirrhosis, an autoimmune disease which affects the liver, 15 years ago. She has a low-MELD score, and still leads an active life. Doctors say she might need a transplant, but she’s holding off as long as possible.
MELD and Resource Utilization

• Is increasing MELD score associated with increasing resource utilization?

Yes, but costs nationwide incurred in looking after patients with cirrhosis have decreased.
## MELD -based Liver Allocation

### ADVANTAGED
- High MELD score
- Renal failure, anticoagulation
- Hepatocellular carcinoma
- Special diseases: amyloidosis, oxalosis
- Special conditions: HPS

### DISADVANTAGED
- Debilitating illness with low MELD score: ascites, encephalopathy, pruritus
- Symptomatic cholestatic liver diseases, chronic graft failure
- Special conditions: PPH, foreign national patients
- Emerging indications: CCA, NET
MELD and Liver Transplantation: Summary

- Excellent predictor of pretransplant survival
- Decreased registrations
- Decreased death rate on waiting list
- Sicker patients transplanted
- Post transplant survival unchanged
- Better defining survival benefit - optimal timing
- Evidence-based decision-making
MAYO CLINIC