Organ allocation for liver transplantation: Is MELD the answer? North American experience

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March 1998: US Department of Health and Human Services issues its “Final Rule”

- Required changes in transplantation:
  - “Sickest first” priority
  - Objective listing criteria
  - Reducing geographic disparities
The Mayo TIPS Model


- Studied 231 patients undergoing TIPS for variceal bleeding (75%) or ascites (25%)
- Outcomes at 90 days
  - 70 deaths
  - 7 transplanted (censored)
- Multivariate analysis with Cox regression identified 4 predictors of 90 day mortality: bilirubin (B), INR, creatinine (Cr) and etiology (Et) = non-cholestatic non-alcoholic.
- The resulting model:
  \[ \text{Ln (Cr)} \times 9.57 + \text{Ln (B)} \times 3.78 + \text{Ln (INR)} \times 11.20 + \text{(Et)} \times 6.43 \]
From Mayo TIPS model to MELD

- Validated as a predictor of general cirrhotic survival

- Modified to simplify application in the transplant setting:
  - Give 6.4 points regardless of etiology
  - Set minimum values of 1 for bilirubin, creatinine and INR
  - Set maximum value of 4 for creatinine
  - Set creatinine to 4 for patients on dialysis
  - Round to nearest whole number

- Became basis for organ allocation for LT in US 2/27/02
Consequences of MELD based LT

Year-end active wait list
New listings
Transplants

Source: SRTR 2006 annual report and data tables www.ustransplant.org
Trends in waiting time

Source: SRTR 2006 annual report and data tables www.ustransplant.org
Consequences of MELD based LT:

Trends in pretransplant waiting list mortality

Source: SRTR 2006 annual report and data tables www.ustransplant.org
One year mortality following OLT as a function of MELD

Source: SRTR 2006 annual report and data tables
www.ustransplant.org
Consequences of MELD based LT: Trends in post transplant mortality

<table>
<thead>
<tr>
<th>Year</th>
<th>One Year Mortality (%)</th>
<th>Source: SRTR 2006 annual report and data tables <a href="http://www.ustransplant.org">www.ustransplant.org</a></th>
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Trends in mortality: confounding factors unrelated to MELD

- **Better outcome**
  - Increasing organ availability
  - Increasing transplantation for hepatocellular carcinoma
  - Better patient selection
  - Technical improvements

- **Worse outcome**
  - Increased recipient age
  - Increased use of extended criteria livers
Continued evolution of MELD-based organ allocation in the U.S.

- **2004** Reduced priority for hepatocellular carcinoma
- **2005** “Share 15” – regional sharing to avoid transplant at MELD < 15
- **2006** MESSAGE conference to address MELD exceptions
Is MELD the answer?

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<th>Pro</th>
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<td>Rationally derived</td>
<td>Based on a nonrepresentative small sample; ? recalibrate</td>
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<td>Simple</td>
<td>Could be simpler (baseline =0, eliminate logarithms?)</td>
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<td>Accurate</td>
<td>Poor discriminator at lower end of scale; fails to capture risk associated with ascites and hyponatremia</td>
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<td>Objective</td>
<td>Affected by factors unrelated to severity of cirrhosis</td>
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MELD vs. CTP score

Status 2 (CTP class C; n=3437)

Note also CTP curve as shown is inconsistent with reported area under curve

Wiesner et al, 2003; Gastro 124:91-6

Status 2 and 3 (CTP B&C; n=6958)

Heuman & Mihas, 2003
Gastro 125: 992-3
Resistant ascites (R) and hyponatremia (H) are independent predictors of pretransplant mortality for patients with MELD < 21.

MELD-AS (supplemented with 4.5 points each for uncontrolled ascites and low sodium) was a better predictor of 180 day preLT mortality than MELD or CTP.

Hepatology 40:802-10, 2004
Factors unrelated to cirrhosis severity that can affect MELD scores

- **Minor (1-5 points)**
  - Lab variations in INR determination
  - Gilbert’s syndrome
  - Prerenal azotemia (overdiuresis)

- **Major (5 – 15 points)**
  - Oral anticoagulant therapy
  - Acute biliary tract obstruction
  - Intrinsic renal disease
Dealing with MELD distortions: oral anticoagulation

Cohort: 554 cirrhotic veterans referred for OLT prior to 12/1/03. Using logistic regression, we developed a 90 day survival model incorporating Ln (bilirubin) and Ln (creatinine), omitting INR and normalized to same range as MELD

\[ M\text{ELD-}X_{\text{INR}} = 5.1 \ln (Bili) + 11.8 \ln (Cr) + 9.4 \]

Validation:

Holdout – 278 veterans referred after 12/1/03
Independent – UNOS wait list 11/1/01
Noncholestatic
Cholestatic

Heuman et al, 2007; Liver Transpl 13:30-7
Conclusion

- MELD is an answer, but not the answer.

- MELD based organ allocation
  - has met the Final Rule requirements
  - effect on pre or post-transplant mortality unclear

- MELD could be improved by
  - recalibration and simplification
  - inclusion of additional independent risk factors
  - exclusion of nonhepatic influences
Everything should be made as simple as possible, but not simpler.

- Albert Einstein