Update on MELD and Organ Allocation

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In their original article, Malinchoc et al. used the variables serum bilirubin and creatinine, international normalized ratio (INR) for prothrombin time, and the cause of the underlying liver disease to calculate a risk score for patients undergoing elective TIPS.[1] They subsequently found that these variables, which were used to calculate the model for end-stage liver disease (MELD) score, resulted in a reliable measure of mortality risk in patients with end-stage liver disease.[2] The MELD score was modified, excluding the cause of liver disease. Furthermore, when United Network for Organ Sharing/Organ Procurement and Transplantation Network (UNOS/OPTN) adopted the MELD scoring system in 2002, negative values were eliminated so patients would receive a minimum score of 6, and the upper limit for the MELD score was set at 40.

Strengths of the MELD Score

The inherent advantages of the MELD score are its ease of use, statistical validation, and the incorporation of objective and widely available laboratory tests. The positive impact after application of the MELD score was immediately evident, with a reduction in waiting-list registration, waiting-list mortality, and median waiting times and an increase in the number of patients transplanted within 30 days of listing in the first year of the post-MELD era.[3] In a seminal article by Merion et al., transplant survival was clearly observed in patients with a MELD score of at least 18, the benefit of which progressively increased with higher MELD scores.[4] On the other hand, recipients who underwent liver transplantation (LT) with a MELD score less than 15 had significantly higher 1-year mortality compared with candidates with a similar MELD score who remained on the wait list.[4]

Weaknesses of the MELD Score (Table 1)

MELD Exceptions

First, the MELD score is an urgency-based or "justice" system whereby the risk of death while on the waiting list is paramount regardless of the degree in survival benefit after LT. However, quality of life does not correlate well with severity of liver disease as measured by the MELD score. In addition, patients with hyponatremia and malnutrition are not accurately accounted for by the MELD score. Other conditions that have required additional MELD exception points include hepatocellular carcinoma, hepatopulmonary syndrome, portopulmonary hypertension, cholangiocarcinoma, and familial amyloidosis.

Serum Creatinine

Serum creatinine is not an accurate marker of renal function in cirrhosis and is influenced by muscle mass, protein dietary intake, age, ethnicity, and gender. Serum creatinine is lower in female patients because of lower muscle mass. This correlates with an increase in wait-list mortality among women by 13%[3] and a reported 30% increased risk of dropout from the waiting list because of death or becoming too sick for transplant compared with men.[6] Measurement of creatinine is also compromised because of the interference of bilirubin. This can result in a variance of up to 7 MELD points in patients with bilirubin > 23.4 mg/dL.[7]

INR

The international normalized ratio (INR), which has the largest weight in the MELD score, was found to suffer the widest variation in measurement. Likewise, a transplant candidate on systemic anticoagulation may have an artificially elevated MELD despite otherwise well-compensated disease. To adjust for this discrepancy, a MELD score

Abbreviations: INR, international normalized ratio; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; OPO, organ procurement organization; PT, prothrombin time; UNOS/OPTN, United Network for Organ Sharing/Organ Procurement and Transplantation Network.

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TABLE 1 Weaknesses of the MELD Score

Male gender bias
Weak predictor of posttransplant mortality (exclusion of donor characteristics)
Interlaboratory variability of serum creatinine, bilirubin, and INR
Serum creatinine is not reliable marker of renal function in cirrhosis
PT/INR not adapted to setting of cirrhosis
Bilirubin influenced by extrahepatic factors
Disadvantageous for candidates with low MELD and complications of cirrhosis

without INR (MELD-XI) was proposed and is awaiting further validation.[8] Standardization of the INR with a so-called iver INR has been proposed but is impractical as it requires standardization of thromboplastin use.

Recent Changes and Updates (Table 2)

Even more important than changes to the way the MELD is calculated is its use in a "match run," which determines how a liver is offered by UNOS. These changes have added several layers of complexity to the system. Livers from adult donors are allocated first to the status 1A adult, then to 1B pediatric candidates located in the same region as the donor organ.

Share 35

With the implementation of "Share 35" in June 2013—candidates with MELD scores of 35 and higher within the donor's region—offers are made within the local OPO, then regionally. Analysis of the 1-year data of the post–Share 35 era was recently performed. There was a 6.6% increase in the number of transplants performed for patients with MELD $\geq$ 35, an increase in regional sharing by 11.4%, with no impact on overall waiting-list mortality or that based on age or ethnicity, no overall change in post-transplant survival, no impact on overall liver discard rate, and similar overall import/export dynamics.

Liver-Intestine 29

At a MELD score $\geq$ 29, a combined liver/intestine offer is extended first to recipients in local OPO, followed by a nationwide offer.

Share 15

"Share 15" (national sharing of livers to candidates with MELD $\geq$ 15), candidates with MELD scores $>$ 15 are offered first to a patient within the local OPO and then regionally. Finally, UNOS offers the organ to national candidates in status 1A or 1B, national candidates with scores greater than 15, candidates with scores less than 15 locally, regionally, then nationally.

Future Changes

Proposed Modifications (Table 3)

Over the years, numerous modifications to the MELD scoring system have been proposed. (Table 3) Of these, MELD-Na more accurately predicted drop-out rates for patients awaiting LT.

TABLE 2 Sequence of Organ Allocation From Deceased Donors

Status 1A Combined local and regional patients
Status 1B Combined local and regional patients
MELD $\geq$ 35 by descending MELD score; local candidates ranked above regional candidates at each score
MELD 29-34 Local patients
MELD $\geq$ 29 Local then national liver-intestine patients
MELD 15-28 Local patients
MELD 15-34 Regional patients
National status 1A patients
National status 1B patients
National patients with MELD $\geq$ 15
Local patients with MELD $<$ 15
Regional patients with MELD $<$ 15

TABLE 3 Proposed Modifications of MELD Score

MELD-Derived Models [Reference]	Modification
MELD-Na [Biggins et al, 2006]	Serum sodium incorporated into standard MELD
Updated ("reweighted") MELD (Sharma et al, 2008)	Assigning lower weight to serum creatinine and INR with higher weight to bilirubin
MESO [Huo et al, 2007]	MELD to serum sodium ratio
MELD-AS [Heuman et al, 2004]	Presence of ascites incorporated in standard MELD
Integrated MELD (iMELD) [Luca et al, 2007]	Serum sodium and age incorporated into standard MELD
UK end-stage liver disease (UKELD) [Barber et al, 2007]	Similar to MELD-Na
MELD-XI [Heuman et al, 2007]	MELD without INR
Delta (Δ) MELD [Hou et al, 2005]	Changes in MELD over time
MELD-gender [Cholangitas et al, 2007]	Gender incorporated into standard MELD

MELD-Na Score

In liver transplant candidates, serum sodium is associated with mortality independent of MELD score, particularly for those with low serum sodium levels.[9] There is an increase in mortality by 5% for each millimole decrease in serum sodium between 125 and 140 mmol/L.[7] It has been shown by several investigators that incorporating sodium into the MELD score increases its predictive accuracy,[10] especially for patients with ascites.[8] Specifically, it was shown that 7% of waiting-list deaths could be averted using MELD-Na score over standard MELD score.[9] Supported by these findings, the OPTN committee proposed (OPTN policy 3.6.1) to add serum sodium to the MELD score equation as follows:

$$\text{MELD-Na} = \text{MELD} + 1.32 \times (137 - \text{Na}) - [0.033 \times \text{MELD} \times (137 - \text{Na})]$$

Region Redistricting

To reduce geographic disparity, waitlist deaths and variation in MELD scores at transplant and to minimize

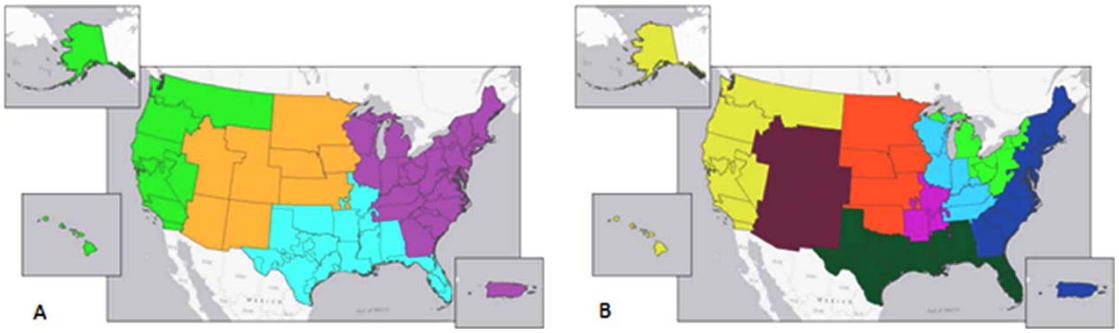

Figure 1 Proposed redistricting maps of four district models (A) and eight district models (B). The images are reproduced with permission from UNOS/OPTN. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

undesirable effects such as increases in organ preservation time, cost related to organ preservation and transplant, and organ discards, OPTN leadership has presented a concept paper supporting the restructuring of the current 11 UNOS regional format to 4 or 8 "districts". (Figure 1) The mathematical models used to generate the redistricting plans were limited by a set of parameters – the districts should be contiguous with a minimum of 6 transplant centers per district, maximum of 3 hours medial travel time between donation service areas (DSAs) in the same district, and the number of waitlist deaths under redistricting must not be statistically significantly higher than current system.[11] Changes to the liver allograft distribution system in the US continue to be discussed by the transplant community.

Conclusion

The MELD score effectively prioritizes liver allocation by estimating the risk of death in patients who are on the liver transplant list with improved liver transplant wait-list survival. [Kamath] Although various modifications have been proposed, the MELD remains the standard for liver transplantation LT allocation and distribution. It may not be long before MELD-Na becomes the new standard by which to predict mortality in patients with end-stage liver disease. A controversial proposal of liver redistricting will be a source of public debate in the months to come. ■

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