Impact and Benefits of the MELD Scoring System for Liver Allocation

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Abstract

The MELD score was described in 2000 and was employed as part of the US liver allocation policy in 2002. There were many reasons behind the decision to use the MELD score and there have been many benefits to the liver allocation system by doing so. Measuring any system used for allocation of scarce resources can be difficult, but evaluation of the justice and utility of such a system provides some framework for assessing its effectiveness. In this review, the benefits realized from the MELD-based allocation system will be assessed according to justice and utility parameters. In organ allocation, individual justice is served when patient-specific variables are used to assign waiting list priority rather than using physician-based observations or behaviors. Utility should be measured, not just in terms of patient survival after transplant, but also in terms of the overall utility of the system for assigning organs to those most in need and giving little priority to those who will be harmed or have little benefit.

The impact of adoption of this system can be measured by the number of the publications that include MELD or liver allocation in their data. The world has recognized the relative objectivity of the MELD score and the ability to communicate among widely diverse groups using this common language. Perhaps this is the most important impact of the MELD “era.”

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Key words

MELD score. Liver allocation. Survival benefit.
Introduction

There are many approaches to the allocation of scarce resources. Systems designed for prioritizing the recipients of these resources can be weighted, on the one hand, toward individual justice or, on the other hand, toward maximizing systemic utility. Thus, in the case of organ allocation, donor livers can be directed to the most deserving candidates, based on individual assessments of need, or to those candidates most likely to achieve the best outcome overall. However, implementations of systems at either end of this justice/utility spectrum necessarily carry undesirable consequences. For example, allocating donor livers purely to individuals deemed to “need the organ most” requires that some measurement of need be defined. To maintain fairness, this measure should not be subjective since other patients’ estimations of need will also be affected. Moreover, observer biases in determining need also can influence the interpretation of what is just. At the other end of the spectrum, allocating organs only to patients most likely to achieve the best outcome means that many other patients with good but not necessarily the best characteristics for success will go unserved, and potentially many more will die while waiting in such a pure utilitarian system. Patients with the best outcome also are likely to have reasonably good outcomes without the transplant, so less is gained by allocating the limited number of donor livers to patients who are going to have better outcomes whether or not they get the transplant. Moreover, for patients with stable, relatively mild liver disease, the risks of the transplant surgery and medications often are greater than the liver disease itself, making transplantation a more risky proposition than waiting until the liver disease progresses further.

In the remainder of this review, I will highlight how the model for end-stage liver disease (MELD)-based liver allocation system in the USA has provided benefit in better achieving a balance between individual justice and utility, and subsequently outline the worldwide impact that the MELD score and allocation systems based on MELD have provided.

MELD score advantages

Partly due to dissatisfaction with existing allocation systems and partly due to improved predictive models, the U.S. liver allocation system was revised in 2002 in an effort to better balance the justice and utility tradeoffs. The MELD score, originally developed to predict the risk of death in patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) procedures, was validated as a reproducible, reasonably accurate predictor of mortality in several different populations of patients with chronic liver disease. From an individual justice point of view, the MELD score offered several advantages for prioritizing waiting liver transplant candidates.

1. The components of the MELD score, three blood tests – bilirubin, international normalized ratio (INR) and creatinine – are much more objective measures directly related to a patient’s condition than many of the previously employed measures for liver disease severity. For example, encephalopathy and ascites are much more subjective measures and depend on the observer’s experience and timing of the observation. They are more specific to the observer and do not directly indicate a patient’s condition. Similarly, time on the waiting list does not define the intrinsic liver disease of the patient and is much more a function of physician practice behavior, referral to the liver transplant program, and access to healthcare in general and much less related to the severity of illness or mortality risk. In addition, location of care, often categorized as home, hospitalized, or in intensive care, is also more related to physician behavior than intrinsic patient condition. These previously employed measures of liver transplant need were much less accurate reflections
of individual justice because they are not directly derived from the individual patient and much more associated with the treating physicians’ observations and/or the system.

2. The MELD score, in defining risk of dying from liver disease, provided a much more precise and transparent measure of liver disease severity than some other measures such as time on the list or location of care delivery.

3. The MELD score is a much more continuous scale than previous categorical systems for prioritizing patients. Previous classification systems using categorical variables tended to group patients together, even though they may have had considerably different underlying clinical characteristics, different need for liver transplantation, and varying risks for death. In addition, disease severity scales such as the Child Turcotte Pugh Score imposed a “ceiling effect” on the more ill candidates since patients with bilirubin of 5 were treated the same as a bilirubin of 15 or 20. Individual justice is better served when individual patients can be discerned and separated more accurately by employing continuous measures of disease severity instead of using categorical classifications.

Because the MELD score provides a relatively simple method for risk adjustment of patient and graft survival after transplantation, the MELD score also has benefits when measuring liver transplant utility. Many investigators have documented that liver transplant results are associated with MELD score at transplantation. However, although this association is consistent, liver transplant results are also influenced by non-recipient factors such as donor characteristics or surgeon/center experience. Thus, the MELD score is not nearly as accurate for predicting posttransplant survival as it is for predicting survival without a liver transplant. Nonetheless, stratifying patients by MELD score at transplantation has provided important utilitarian observations about the entire liver transplant system when pretransplant and posttransplant survival are combined together to define liver transplant benefit. Merion, et al. measured transplant benefit and found that for patients with lower MELD scores, their projected survival was greater without a liver transplant than could be expected if they were to receive a transplant. For these patients, liver transplantation does not provide a survival benefit. On the other end of the MELD score scale, patients with the highest MELD score always received benefit, even if they receive grafts from donors with higher risks of graft failure. These observations again point out the benefits of this relatively objective, transparent disease severity scale.

The most recent liver transplant results have been published in the U.S. Organ Procurement and Transplantation Network/Scientific Registry for Transplant Recipients OPTN/SRTR annual report. Figure 1 indicates the steady decline in death rates since the U.S. liver allocation system was changed in 2002 to a MELD-based system of implementation. Figure 2 displays an equally impressive decline in time to transplantation after the allocation system was changed. These are two extremely important benefits of implementing the MELD system in the USA. Separate analyses have confirmed these results. By using a metric defining mortality risk, the MELD-based system more precisely directs organs to those most likely to die in the short term, thereby reducing the waiting
Impact of MELD score and MELD-based liver allocation

Patients have not seen any decrement in posttransplant outcome since implementing the MELD system. Figure 3 displays the most recent data for adjusted patient survival by year from the OPTN/SRTR 2007 Annual report\(^{16}\). The survival curves are virtually identical, indicating that despite using a more direct disease severity scale, liver transplant patient survival has not changed compared with allocation policy in effect prior to the MELD score system. Thus, the MELD-based liver allocation system has impacted the justice and utility of the system as described above, but it has not had an adverse impact on patient (Fig. 3) or graft (data not shown) survival rates.

The MELD model was first published in 2001\(^{2}\). In the ensuing nine years, the impact of this score can be measured by a recent MEDLINE search, using MELD as the search term in which 689 citations were retrieved. Several studies have found a close correlation between preoperative MELD score and early postoperative mortality for patients undergoing routine general surgical procedures\(^{17,18}\) and for patients undergoing hepatic resection\(^{19-21}\). One recent study stratified outcome data for patients treated with simultaneous ileoanal pouch and liver transplantation using the MELD score\(^{22}\).

In China, investigators have found that the MELD score predicts mortality for patients with decompensated hepatitis B\(^{23}\) and primary biliary cirrhosis\(^{24}\) related liver disease, and that it can be used to improve outcome prediction for patients with hepatocellular carcinoma (HCC) and cirrhosis undergoing locoregional treatments\(^{25,26}\) or waiting on the transplant list\(^{27}\). Chinese ultrasonographers have also shown that the MELD score correlated with an ultrasound-derived measure of liver disease severity\(^{28}\).

The MELD score has been correlated with many other manifestation of liver disease such as hepatic venous pressure gradient in Spain\(^{29}\), findings on MRI scans\(^{30}\), cognitive impairments\(^{31}\), brain blood flow in Italy\(^{32}\), TIPS flow velocities\(^{33}\), response to medical treatment for refractory ascites in Canada\(^{34}\), soluble vascular cell adhesion molecule-1 levels in Spain\(^{35}\), and liver disease-
related quality of life in Brazil\textsuperscript{36}. The MELD score has also been used extensively to stratify study subjects and risk adjust for outcome analyses in studies of renal failure-related mortality in cirrhotics in France\textsuperscript{37} and Spain\textsuperscript{38}, for primary hepatitis C virus (HCV) treatment\textsuperscript{39}, for treatment of HCC in Taiwan\textsuperscript{40}, for predicting sobriety and mortality in alcoholic liver disease in Sweden\textsuperscript{41}, and for evaluating outcome after treatment for severe liver failure in Singapore\textsuperscript{42}. Studies of acute liver failure have found that MELD is closely correlated with mortality risks for cases where the etiology of the acute liver failure is unknown\textsuperscript{43}, and is useful for stratifying patients treated with artificial liver support devices\textsuperscript{44}.

Outside of the liver allocation role MELD plays, many liver transplant researchers have reported transplant results in the context of MELD at the time of transplantation. A descriptive analysis of the waiting list in Iran\textsuperscript{45} stratified by candidates’ MELD scores was published in 2006. Selection of liver transplant candidates in Mexico\textsuperscript{46} and Malaysia\textsuperscript{47} using the MELD score has been described. Changes in MELD score over time have been associated with increased waiting list mortality in the USA\textsuperscript{48,49} and in Italy\textsuperscript{50}, although the most significant changes tend to occur very late in the course of disease, which limits the prognostic usefulness for this “Delta MELD” measurement\textsuperscript{49}. The MELD was shown to be a good predictor for liver transplant waiting list mortality in Romania\textsuperscript{51}. French investigators recently documented that enterobacteremia following liver transplantation is correlated with MELD score at transplant\textsuperscript{52} and there is a correlation between histopathologic findings in explanted livers after transplant and MELD score at the time of transplant\textsuperscript{53}.

Many aspects of the liver transplant waiting list have been addressed utilizing MELD. Investigators from the University of Pittsburgh reported that MELD underestimates mortality risk for HIV-infected liver transplant candidates\textsuperscript{54}. Others have shown that a competing risks approach to estimating mortality risks on the waiting list should be applied\textsuperscript{55}, and that even when these methods are used to calculate waiting list dynamics, the MELD score remains highly predictive of waiting list mortality. A recent report from France indicates that a liver allocation system incorporating some aspects of the MELD-based system from the USA resulted in reduced waiting list deaths and improved access to transplant for the sickest patients\textsuperscript{56}.

As mentioned above, lifetime benefit calculations for liver transplant patients combine pre- and post-liver transplant survival rates and stratify these by MELD score at entry to the waiting list\textsuperscript{57}. Other investigators from Austria\textsuperscript{58}, Belgium\textsuperscript{59}, and a European-wide study\textsuperscript{60} have also reported pre- and post-liver transplant survival rates stratified by MELD at waitlist entry and at transplantation\textsuperscript{61}. There are other liver transplant outcome reports from Israel\textsuperscript{62}, Lithuania\textsuperscript{63}, for primary sclerosing cholangitis in Nordic Countries\textsuperscript{64}, and for re-transplant recipients\textsuperscript{65}. Recent reports from Germany have documented an association between living donor liver transplant recipient hospital mortality and MELD score at transplantation\textsuperscript{66}.

MELD has been used to perform liver transplant recipient risk adjustment to enable calculation of an index that characterizes donors in terms of the risk of liver graft failure (Donor Risk Index)\textsuperscript{10} and to assess the outcome of using liver grafts from so-called extended criteria donors in Italy\textsuperscript{67} and in the USA\textsuperscript{68}. MELD has also been used to stratify results in a paper comparing transfusion requirements among high and low MELD patients\textsuperscript{69} and in living versus deceased donor liver transplant recipients\textsuperscript{70}, and to report an association with recurrent HCV after liver transplantation\textsuperscript{71}.

Recent investigators have found a correlation between MELD score and pretransplant dobutamine stress echo findings and these were predictive of cardiac events during or after liver transplantation surgery\textsuperscript{72}. The MELD scores also are directly related to liver
transplant costs and it is clear that the MELD-based liver allocation system has an important impact on overall transplant center costs.\textsuperscript{73}

The MELD score itself has become a useful, widely accepted tool for measuring severity of chronic and acute liver disease. The benefits are many, but in particular, despite some concerns about variations in laboratory values,\textsuperscript{74,75} MELD scores are consistent across all types of patients with chronic liver disease no matter which country or region of the world and no matter what biases a clinical observer might have in otherwise assessing liver disease severity. The recognition of the usefulness of MELD and the impact thereof are represented by the explosion of publications and the implementation of MELD-based or MELD-like liver allocation systems across the world.

References


8. *This paper provides a good summary of recent liver transplant results from the US OPTN/SSR database.*


15. Schaubel DE, Sima CS, Goodrich NP, Feng S, Merion RM. The survival benefit of deceased donor liver transplantation as a function of candidate disease severity and donor quality. Am J Transplant. 2008;8:419-25. **This paper points out that, for patients with high MELD scores, the risk of death without a transplant is much higher than the risk of any graft these patients might receive.*


17. See www.ustransplant.org


