MELD-Based Liver Allocation: Who Is Underserved?

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ABSTRACT

Deceased-donor livers are a scarce, lifesaving resource. For patients whose lives depend upon liver transplantation, policies for prioritizing allograft allocation are of ultimate importance. In the current paradigm, donor livers are allocated on the basis of medical urgency. Thus, the onus is on the transplant community to redefine the allocation system continuously so that livers are targeted to patients who need them most. The current model for end-stage liver disease (MELD)-based allocation system works well, accurately predicting short-term mortality for the majority (83 to 87%) of waitlisted candidates. However, there are patients with liver diseases whose survival is dependent upon factors other than the severity of the liver disease and who may not manifest derangements in their MELD parameters. Such patients may be underserved by current MELD policies. This article reviews the development of MELD and the MELD-based liver allocation system and addresses issues relevant to whether this system may be improved.

KEYWORDS: MELD, liver transplantation, allocation, exceptions, public policy

DEVELOPMENT OF MELD

The original MELD score was developed, and subsequently validated, in populations of cirrhotic patients undergoing elective transjugular intrahepatic portosystemic shunt (TIPS) procedures.1 Using Cox proportional hazards regression modeling, serum total bilirubin, serum creatinine, the international normalized ratio for prothrombin time (INR), and etiology of liver disease were found to be strong predictors of 3-month survival after TIPS. Complications of portal hypertension, such as ascites, hepatic encephalopathy, variceal bleeding, and spontaneous bacterial peritonitis, did not improve overall accuracy in predicting 3-month mortality and therefore were not included in the MELD score.

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model. This may be explained by the fact that these portal hypertensive complications are more likely to be associated with advanced liver disease, which is adequately assessed by the MELD score laboratory parameters alone. Because of clinical challenges that may arise in trying to accurately categorize liver disease etiology for individual patients and also so as not to give an unfair advantage to one particular population of patients over another, disease etiology was ultimately excluded from the final model. Therefore, the current version of MELD is described by the following formula:

$$3.8 \log_e \text{serum bilirubin (mg/dL)} + 11.2 \log_e \text{INR} + 9.6 \log_e \text{serum creatinine (mg/dL)} + 6.4$$

Using this equation, the predicted risk of mortality increases logarithmically with increasing MELD score. MELD is a continuous scoring system and, although according to this formula scores can range from negative values to positive infinity, in its current application by the United Network for Organ Sharing (UNOS), any laboratory values less than 1.0 are set to 1.0. This was done to prevent the generation of negative MELD scores. Also, to avoid an unfair advantage to patients with intrinsic renal disease, the maximum serum creatinine level is set to 4.0 mg/dL, which is also the value that is automatically assigned to patients receiving dialysis. The upper limit of MELD is capped at 40 points by UNOS, and therefore MELD scores for prioritization of organ allocation for liver transplantation are rounded to the nearest integer and range between 6 and 40 points.

The MELD score has now been demonstrated to be a very useful prognostic indicator of 3-month mortality in a wide spectrum of chronic liver disease patients, with concordance (c) statistics of better than 0.8. In this context, a c-statistic of greater than 0.7 generally indicates a clinically useful test, with a c-statistic greater than 0.8 connoting excellent accuracy. Therefore, a c-statistic of 0.8 for MELD in predicting 3-month mortality may be interpreted in the following manner: 8 out of 10 times, the patient with a higher MELD score is more likely to die within 3 months than the patient with a lower MELD score.

**EVOLUTION TO A MELD-BASED ALLOCATION PROCESS FOR LIVER TRANSPLANTATION**

During the 1990s, as the number of patients awaiting liver transplantation increased in the presence of a stable number of available deceased-donor livers, the transplant community witnessed an increase in the number of patients dying while awaiting liver transplantation. During this period, urgency for transplantation was based upon the patient’s hospital status (intensive care unit (ICU), hospital ward, or ambulatory outpatients) and waiting time. However, this system was subject to bias. Patients were placed on the liver transplant list early in their disease course to accrue waiting time, and there was a potential for physicians to lower their thresholds for placing patients in higher levels of care (such as ICU status) to increase priority for transplantation. These factors weakened the usefulness of hospital status as an urgency measure and the length of time spent on the waiting list became an important, albeit unintended, deciding factor in the allocation process. However, it became apparent that time spent on the liver transplant waiting list did not correlate with risk of death on the waiting list. In 1998, because of increasing concerns regarding the disparity in liver allocation, the Department of Health and Human Services issued a mandate that there be a de-emphasis on time spent on the waiting list and that deceased-donor livers should be allocated on the basis of liver disease severity and risk of mortality while awaiting transplantation.

In response to this mandate and an investigation by the Institute of Medicine, UNOS initially adopted the Child-Turcotte-Pugh (CTP) classification system, an excellent predictor of outcome in patients with complications of portal hypertension, for use in liver transplantation prioritization. Unfortunately, this did not prove adequate for organ allocation because of its limited discriminatory capacity. The system included only four categories of liver disease severity (status 1, 2A, 2B, and 3), which resulted in numerous patients being lumped into each category. Consequently, time spent on the waiting list continued to be a major factor in the allocation process. Additional limitations of the CTP scoring system include the absence of a marker of renal function (such as serum creatinine) and also its reliance on subjective parameters such as degree of ascites and encephalopathy, the quantification of which may differ from observer to observer and which may be altered by medical interventions, such as the use of diuretics for ascites or lactulose for hepatic encephalopathy. Another potential problem with the CTP score arises from its use of prothrombin time and serum albumin levels, as there may be substantial laboratory variations in these values such that significant point changes can occur in the CTP score related to laboratory techniques alone. In addition, the CTP score has limited discriminative capability in that a patient with a serum total bilirubin of 4.0 mg/dL is assigned the same score as a patient with a serum bilirubin of 40 mg/dL, even though the survival of these two patients would be expected to be quite different.

As the liver transplantation community sought a more equitable prioritization system, the MELD score emerged as a desirable candidate for a liver disease severity scoring system. Wiesner et al demonstrated the applicability of the MELD scoring system to the organ allocation process for donor livers. This study
found that among 3437 adult patients listed for liver transplantation between 1999 and 2001, waiting list mortality was directly proportional to the MELD score at the time of listing. Mortality rates were approximately 2% and 71% for patients with MELD scores < 9 and ≥ 40, respectively. The c-statistic for MELD’s accuracy in predicting 3-month mortality on the waiting list was 0.83, compared with a c-statistic of 0.76 for the CTP score (Fig. 1).

CURRENT USE OF MELD IN ALLOCATION OF LIVERS FOR TRANSPLANTATION

In February 2002, MELD was formally adopted by UNOS as the basis for deceased-donor liver allocation for adult patients (≥ 18 years old). Under current UNOS policy, allocation of livers for transplantation is dependent upon several factors: blood type, severity of illness determined by the MELD score, the number of patients listed for liver transplantation in each region, the number of available deceased-donor livers within these regions, and geography in that donor organs are generally offered locally first, then regionally and nationally.8 When a patient is placed on the waiting list, the MELD score is used to determine that patient’s immediate need for transplantation. MELD scores are updated on a regular basis, and those who are more severely ill need to have updated MELD scores forwarded to UNOS more frequently. As an example, patients with MELD scores ≥ 25 have their scores updated on a weekly basis, whereas patients with MELD scores ≤ 10 need to have their scores updated only every 12 months. If a patient experiences an increase in MELD score, the patient’s waiting time is set to zero and the clock starts at the time of assignment of the higher new score. However, if a patient has a decline in MELD, the waiting time that had been accrued at the higher score is maintained and added to the time that will be accrued at the new, lower MELD. In the event that two patients with the same blood type awaiting liver transplantation in the same region have identical MELD scores, the time spent waiting on the liver transplant list at that score is used to break the tie. Although fulminant hepatic failure and other UNOS status 1 patients are exempt from the MELD-based prioritization process, MELD has been demonstrated to predict survival accurately in status 1 patients.9 However, according to current allocation policy, these patients are given priority above all other patients listed for liver transplantation because of the high acuity and mortality of their illness.

IMPACT OF MELD ON LIVER ALLOCATION FOR TRANSPLANTATION

The introduction of the MELD score has improved liver allocation.7 A study using data from UNOS compared outcomes of deceased-donor liver transplantation in the pre-MELD era (February 27, 2001 to February 26, 2002) and the post-MELD era (February 27, 2002 to February 26, 2003).10 In the post-MELD era, there was a 12% reduction in new patients registered on the liver transplant waiting list, particularly for patients with the lowest MELD scores. In addition, after implementation of MELD, there was an approximately 10% increase in the number of deceased-donor liver transplantations performed and a 3.5% decrease in the number of deaths on the waiting list. Patients receiving transplants were sicker, with higher MELD scores, in the post-MELD era compared with those in the pre-MELD era. Although there were initial concerns in the transplant community that adoption of the MELD scoring system could result in poorer transplant outcomes if livers were allocated to patients who were “too sick” (i.e., with high MELD scores), analysis of the UNOS data revealed that there was no significant change in 3-month patient and graft survival in the post-MELD era. The authors concluded that the new allocation system has been successful in de-emphasizing waiting time as a major factor in prioritizing patients for liver transplantation and has resulted in increased transplantation rates without concomitant increased mortality rates.10

MELD EXCEPTIONS IN LIVER TRANSPLANTATION SELECTION

Although MELD accurately predicts mortality in the majority of patients awaiting liver transplantation, some
patients with diseases of the liver have a waitlist mortality that may not be accurately represented by MELD because their prognosis is dependent upon factors other than liver disease severity. As such, these patients have potential for being underserved if allocation of deceased-donor livers for transplantation is based solely upon the calculated MELD score derived from the patients' laboratory values. In light of this, the current liver allocation policy has provisions that allow for exceptions to the calculated MELD-based scoring system as policy developers had recognized early on that it was unlikely that any scoring system would serve all potential liver transplant candidates equally well.

As demonstrated in Fig. 2, at least 20% of deceased-donor livers in 2004 were allocated to patients with liver diseases that were considered MELD exceptions. A few of these liver diseases, termed recognized exceptional diagnoses (or REDs), are formally incorporated into the current UNOS liver allocation policy, most notably hepatocellular carcinoma (HCC), but also hepatopulmonary syndrome (HPS), familial amyloid polyneuropathy (FAP), and primary oxaluria. Patients with these diseases may be assigned additional MELD points above and beyond their calculated MELD score. Indeed, patients with stage II HCC are among the recognized exceptional diagnoses or REDs. Liver transplant centers may try to seek additional MELD points. These clinical conditions are not formally accounted for in the current UNOS allocation policy and are referred to here as “nonrecognized exceptional diagnoses” or non-REDs. Liver transplant centers may choose to submit petitions to their RRB for additional MELD points for patients with non-REDs with the intention of giving the patient a score that more accurately reflects the perceived degree of medical urgency. However, unlike the situation with REDs, there are currently no guidelines for non-RED appeals. Therefore, each RRB functions autonomously and the merits of each request are considered on a case-by-case basis.

REFINEMENT OF MELD-BASED LIVER ALLOCATION: AN ONGOING ENDEAVOR

Past Efforts to Refine MELD Allocation

UNOS and the liver transplant community have demonstrated a strong commitment to improving allocation for liver transplantation so that organs are directed to patients who need them most urgently without over- or underserving any particular population of patients. Evidence-based adjustment of the allocation policy resulting in additional priority being granted to patients with HCC is an example of this commitment. In 2002, with the initial implementation of MELD-based allocation, the level of priority assigned to patients with HCC stages I and II was
overestimated, excessively favoring these patients and resulting in disproportionately low rates (4.9% for stage II HCC) of “dropout” from the liver transplant waiting list, related to either death or progression of cancer, compared to a much higher mortality rate of 46% in a comparison group of non-HCC patients. In light of these findings, the priority has been reduced for HCC patients so that the assigned number of MELD points is equivalent to the measured risk of dropout from the waiting list in these patients. In 2006, only patients with stage II HCC receive standardized priority, which is based upon an estimated 15% risk of dropout from the liver transplant waiting list at 6 months related to either death or disease progression precluding transplantation candidacy. Thus, the stage II HCC patients are assigned an exception MELD score of 22 with progressive increase every 3 months equivalent to a 10% mortality risk. Patients with stage I HCC no longer qualify for assignment of an exceptional MELD score.

Another example of refinement of the MELD-based allocation system is the Share MELD 15 policy. This policy, implemented in 2005, broadened the distribution area, from local to regional, for an available deceased-donor liver for candidates with a MELD score ≥ 15. Previously, a donor liver would be offered regionally only to candidates who were listed as status 1. Otherwise, the liver would remain local and only if there were no available local candidates would the liver be offered regionally to non-status 1 patients. However, according to the Share MELD 15 policy, the donor liver is first offered to local and then regional status 1 candidates. If no status 1 recipients are identified, the liver is offered to local candidates with MELD ≥ 15 and subsequently offered to regional candidates with MELD ≥ 15 before being offered to local candidates with MELD < 15. This policy shift was motivated by an analysis of UNOS data demonstrating that the risk of death after liver transplantation for patients with MELD scores less than 15 was actually greater than their risk of death waiting on the list.

Although policy changes have been successfully made to the MELD-based allocation system, there have also been proposed modifications to the allocation system that have been formally evaluated, but ultimately not adopted because of a lesser degree of evidence supporting incorporation of such changes. One example of this was the concept of incorporating the change in MELD score over time, or Delta MELD, into the liver allocation scheme. Although intuitively the idea of including Delta MELD in the allocation system seemed very reasonable, further analyses suggested that adoption of the Delta MELD concept would probably not have a substantial effect on either the distribution of liver allografts or waiting list mortality.

Future Opportunities for Refinement of MELD-Based Allocation

POTENTIAL GEOGRAPHIC DISPARITIES

The transplant community has identified further room for improvement in MELD-based allocation. One area targeted for consideration is broader geographic sharing of available liver grafts. Trotter and Osgood reported significant disparity in rates of transplantation among organ procurement organizations (OPOs), which are organizations accountable for the retrieval, preservation, and transportation of liver allografts for transplantation within a defined local area. This study comparing small OPOs (< 100 candidates listed) with large OPOs (≥ 100 candidates listed) found that despite similar distributions of MELD scores, candidates listed in small OPOs had a 2.5-fold higher rate of transplantation per year listed than candidates in larger OPOs (Fig. 3). Although the death rates per year listed on the wait list in small and large OPOs were similar, patients in large OPOs required higher MELD scores to receive a transplant. The authors concluded that broader sharing across OPOs may improve these disparate transplantation rates. In fact, two studies have reported that regional sharing for UNOS status 1 patients was associated with a reduction in waitlist mortality. Although regional sharing across OPOs occurs in some parts of the United States, this practice is not widespread for non-status 1 candidates and whether or not broader sharing would improve waitlist mortality in non-status 1 candidates.

Figure 3 Model for end-stage liver disease (MELD) score distribution in transplant recipients: small (< 100 candidates listed) versus large (≥ 100 candidates listed) organ procurement organizations (OPOs). (Reprinted with permission from Trotter and Osgood. Copyright © 2004. American Medical Association. All rights reserved.)
using MELD to assess priority is unknown. Disadvantages of broader sharing could include more complicated logistics, potential for higher costs, and increased cold ischemic time, which may lead to increased rates of graft dysfunction.19

Another geographic disparity in MELD-based allocation is the regional variation in the use and practice patterns of RRBs. One of the primary charges of RRBs is to review petitions for additional priority for transplantation of non-REDs. In a study examining national practice patterns of RRBs from February 2002 through August 2003, the distribution of petitions for non-REDs per region varied significantly (range 0.7 to 8.3%), as did the RRB rates for granting approval of requests for MELD upgrades (range 28% to 75%) and the proportion of patients receiving transplants with MELD upgrades (range 2.1% to 31%).20 Although the overall proportion of liver transplantsations performed in patients with non-REDs is small, it is notable that this proportion increased from 6% of all recipients in 2002 to 8% in 2004 (Fig. 2).20 The varied practice patterns of RRBs have a large effect on the likelihood of transplantation being performed in petitioned patients. Inaccurate overestimation of the appropriate priority and number of exceptional MELD points that should be assigned to individual patients by the RRB may excessively favor candidates with exceptions (Fig. 4). Indeed, persistent overassignment of MELD exceptions may ultimately lead to overall higher MELD scores required for transplantation (Fig. 5).

Two proposed solutions to these issues are the development of a national review board and the establishment of standardized guidelines, similar to those that currently exist for HCC and other REDs, for granting and assigning exceptional MELD scores.21,22 Incorporation of a national review board system may decrease the regional disparities in the review process. Yet one important concern raised is that the volume of petitions for review by a national review board would be very large, even if limited to non-RED petitions, which may result in undue delay in prospective review. Indeed, Rodriguez-Luna et al found that over an 18-month period (February 2002 through August 2003) there were 3281

Figure 4 Mean MELD scores for nonrecognized exceptional diagnosis (non-REDs) petitions in the different UNOS regions. Black bars: candidates listed with laboratory (standard) MELD scores. Gray bars: MELD requested by petition. White bars: MELD score at time of transplantation. (Reprinted with permission from Rodriguez-Luna et al.)

Figure 5 Impact of upgrade in MELD score on liver transplantation rate by UNOS region. The bars represent the number of liver transplantations performed divided by the number of patients listed in that region. Black bars: Proportion with laboratory (standard) MELD scores. Gray bars: Proportion with recognized exceptional diagnosis (RED) petitions. White bars: Proportion with nonrecognized exceptional diagnosis (non-RED) petitions. (Reprinted with permission from Rodriguez-Luna et al.)
Table 1 Most Common Justifications Cited by Centers in Their Petitions to Regional Review Boards for MELD Score Adjustments

<table>
<thead>
<tr>
<th>Diagnostic Categories</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>171</td>
<td>21</td>
</tr>
<tr>
<td>Portal hypertensive bleeding</td>
<td>72</td>
<td>9</td>
</tr>
<tr>
<td>Regional agreement</td>
<td>62</td>
<td>7</td>
</tr>
<tr>
<td>Other</td>
<td>54</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>827</td>
<td>100</td>
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Adapted with permission from Rodriguez-Luna et al.21

petitions submitted to all national RRBs of which 827 were non-RED petitions and, therefore, required prospective review by the RRB to assign an exceptional MELD score.21 There was a wide range of justifications for non-RED petitions (Table 1). Standardized national guidelines for some of the more commonly cited clinical entities leading to requests for MELD exceptions would probably help to streamline the review process, minimize prospective review delays, and promote consistency and fairness in the process of deciding which patients should be assigned additional MELD points. The UNOS Liver and Intestinal Transplantation Committee has recognized the potential value of such guidelines and submitted a draft of proposals addressing these issues for public comment.22 These proposals have been drafted for a variety of clinical conditions, such as ascites, using the available scientific data regarding estimated mortality risk associated with these conditions.22 Quality-of-life measures are not identified as a targeted outcome measure, as the focus is on using objective and evidence-based estimates of mortality.

ARE SOME PATIENTS WITH PORTAL HYPERTENSIVE COMPLICATIONS UNDERSERVED?

Manifestations of portal hypertension are among the most commonly cited non-REDs presented to RRBs for consideration of additional priority. In the study by Rodriguez-Luna et al, portal hypertensive complications, namely ascites, encephalopathy, portal hypertensive bleeding, and hepatic hydrothorax, accounted for 48% of non-RED petitions21 (Table 1). It is interesting to note that the leading two justifications, ascites and encephalopathy, for seeking additional priority in this study are no longer factored into prioritization for liver transplantation since the shift was made from a CTP-based to a MELD-based allocation system.23 Although previous studies have demonstrated that inclusion of portal hypertensive complications, such as ascites, add little prognostic value to the MELD score,2,24 more recent single-center studies have reported that persistent ascites, particularly in candidates with MELD scores less than 21, may be associated with an increased mortality risk that is not accounted for by MELD alone.25,26 There are a few possible explanations for the seemingly contradictory findings, including the fact that more detailed statistical analyses were performed in the latter studies. In addition, the latter studies were single center, and the variability inherent in the assessment of degree of ascites may have been less at a single center than the variability likely to be present across a multicenter study. This issue serves to emphasize the importance of trying to identify objective measurements for use in organ allocation. With respect to this, serum sodium has shown promise as an objective marker of persistent ascites. Hyponatremia is associated with portal hypertension,27,28 ascites,29,30 and increased waitlist mortality, even after adjusting for MELD score.25,31–33

Other portal hypertensive complications, such as hepatic hydrothorax, have been less well studied as predictors of waitlist mortality. Hepatic encephalopathy, although an independent predictor of mortality in liver disease34 and perhaps of waitlist mortality under the CTP allocation scheme,35 does not, based upon the available evidence, clearly add prognostic value to the MELD score in predicting waitlist mortality. A study performed after the adoption of the MELD-based allocation system reported shorter durations from the time of registration on the waiting list until transplantation for patients with hepatic encephalopathy and also a smaller proportion of patients with severe encephalopathy at the time of transplantation.36 Finally, patients with the other notorious complication of chronic liver disease, namely portal hypertensive bleeding, have not been demonstrated to be underserved by the MELD-based allocation system. Indeed, both MELD and total serum bilirubin have been shown to be strong predictors of 6-week and 1-year mortality after variceal bleeding.37,38 Overall, complications of portal hypertension are the most common justifications for petitions for additional priority presented to RRBs. However, with the exception of candidates with severe ascites and MELD scores less than 21, there is little or no evidence that these complications are associated with excess waitlist mortality beyond that which is already predicted by MELD.

NON-PORTAL HYPERTENSIVE COMPLICATIONS: UNDERSERVED OR OVERSERVED?

Candidates with non-portal hypertensive complications of liver disease account for over 50% of non-RED petitions submitted to RRBs. The justifications for these
petitions are varied and include complications such as malnutrition and recurrent cholangitis (Table 1). Each of these petitions for exceptional status is motivated by a bedside physician whose clinical impression is that the patient is in need of urgent liver transplantation. The role of the RRB in these situations is, in part, to take into consideration these bedside clinical impressions while ensuring that donor liver allocation is performed in a just manner so that no particular populations of patients are either under- or overserved. In the Scientific Registry of Transplant Recipients (SRTR) 2005 annual report, the 90-day waitlist mortality for non-RED petitioned candidates was 1%, quite low compared with mortality rates of 10% and 45% for candidates with standard MELD scores of 21 to 30 and >30, respectively. Rodríguez-Luna et al found that liver transplantation was significantly more likely to occur in non-RED petitioned patients compared with patients who had never been petitioned to the RRB, 60% versus 22%, respectively. This increased rate of transplantation in the non-RED petitioned group occurred regardless of whether the request was actually approved by the RRB. These findings suggest that the majority of the candidates with non-RED petitions are not underserved by the current MELD-based allocation system and, in fact, the group considered as a whole may be overserved.

Quantifying the risk of mortality or risk of dropout from the waiting list that may be reasonably attributable to specific disease manifestations is a critical step in trying to determine how much, if any, additional priority should be granted for non-RED petitions. With patients dying while awaiting liver transplantation, it is difficult to justify giving increased priority to candidates who may have intractable symptoms, such as pruritus, but who do not have increased mortality risk. Although justifications for non-RED petitions related to primary sclerosing cholangitis (PSC) were frequent (Table 1), mortality with PSC is accurately predicted by MELD and candidates with PSC have among the lowest waitlist mortality rates (96 per 1000 patient-years) of those with all indications for transplantation. Cholangiocarcinoma is often a looming concern in candidates with PSC and carries a very poor prognosis. Available clinical data indicate that liver transplantation is a successful treatment option for highly selected patients with this tumor. Therefore, it is likely that selected patients with documented cholangiocarcinoma will benefit from being given increased priority for liver transplantation.

In general, hepatic neoplasms do not manifest in derangements in the parameters of the MELD. Whether hepatic neoplasms are amenable to liver transplantation depends upon the type of lesion and the stage of disease. For neoplasms that are amenable to liver transplantation, such as certain neuroendocrine tumors, priority for a liver graft is based less upon pretransplantation mortality and more upon risk of dropout from the waiting list because of progression of the tumor to the point that there would be an unacceptable risk of post-transplantation recurrence. Similarly, highly selected candidates with portopulmonary hypertension without identifiable predictors of poor post-transplantation survival may be candidates for additional priority based upon their risk of dropout from the waiting list.

Several transplant centers now offer liver transplantation to highly selected candidates with well-controlled human immunodeficiency virus (HIV) disease, with reports of similar graft and patient survival compared with non–HIV-infected recipients. HIV-infected liver transplant candidates may have higher waitlist mortality rates than non–HIV candidates. As liver transplantation becomes more widely offered to HIV-infected candidates and these data are confirmed, additional priority for these patients may be indicated.

Patients with metabolic disorders, such as Wilson’s disease, iron overload, and hereditary hemochromatosis, appear to be well served by the current MELD-based allocation system. Additionally, patients with acute decompensation due to Wilson’s disease may be registered as status 1 on the liver transplant waiting list. Other, less common, metabolic diseases may be evaluated on a case-by-case basis by the RRBs.

**SUPPORTING AN EXPANDED DONOR LIVER POOL**

The use of live-donor and split livers holds promise for increasing the number of available allografts for liver transplantation. However, these procedures may also be associated with an increased risk of graft dysfunction, particularly if the allograft is too small for the recipient (graft/recipient weight ratio <0.8%), known as small-for-size syndrome (SFSS). Because graft dysfunction related to SFSS is a potentially very morbid event with associated high mortality, transplant recipients who subsequently develop this complication warrant consideration for MELD exception to allow timely retransplantation and a chance for survival.

**Summary**

The transition in 2002 to a MELD-based allocation system for liver transplantation exemplifies the commitment of UNOS and the liver transplant community to evidence-based efforts aimed at optimizing the means by which deceased-donor livers are distributed to patients according to their degree of medical urgency. The MELD score is an objective and robust predictor of short-term mortality in patients with chronic liver disease and serves as an excellent measure of urgency for the vast majority of liver transplant candidates. However, MELD exception policies are needed to define priority for liver transplantation in candidates with liver disease whose mortality is not accurately reflected in derangements of MELD parameters and also for patients who...
are at risk of dropping out from the waiting list, that is, patients whose disease progresses to a point at which liver transplantation is no longer an option.

In these patients who require MELD exceptions, estimates of the patient’s short-term mortality risk or risk of dropout from the waiting list are translated into MELD points, and these assigned MELD points are then used for prioritization. Although this intuitively seems very reasonable and works in the short term, it is also worthwhile pointing out that as more and more MELD exceptions are defined, patients will be assigned higher and higher MELD scores, thus raising the MELD threshold at which liver transplantation occurs for all patients registered on the waiting list. Standardized guidelines for MELD exceptions are needed to streamline the review process and to serve as benchmarks for further evaluation and refinements aimed at developing the most fair and just liver allocation system possible.

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ABBREVIATIONS
CTP  Child-Turcotte-Pugh (score)
FAP  familial amyloid polyneuropathy
HCC  hepatocellular carcinoma
HPS  hepatopulmonary syndrome
ICU  intensive care unit
INR  international normalized ratio for prothrombin time
MELD  model for end-stage liver disease
OPO  organ procurement organization
PSC  primary sclerosing cholangitis
RED  recognized exceptional diagnosis
RRB  regional review board
SFSS  small-for-size syndrome
SRTR  Scientific Registry of Transplant Recipients
TIPS  transjugular intrahepatic portosystemic shunt
UNOS  United Network for Organ Sharing

REFERENCES
11. 2004 OPTN/SRTR Annual Report. HHC/HRSA/HSB/DOT; UNOS; URREA.
20. 2005 OPTN/SRTR Annual Report. HHC/HRSA/HSB/DOT; UNOS; URREA.
allocation under the MELD system. Am J Transplant 2005; 5:2244–2247
41. Stock PG. Rapid deterioration of HIV co-infected patients waiting for liver transplantation is not predicted by MELD. Liver Transpl 2005;11:1315–1317