

The MELD System for Liver Allocation

Implications for Patients and Payors

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Abstract

The recent implementation of the Model for End-stage Liver Disease (MELD)/Pediatric End-stage Liver Disease (PELD) system for the allocation of cadaveric liver organs in the US represents a dramatic change in organ allocation policy. Previous allocation algorithms used a categorical stratification system, in which candidates were ranked by the length of time waiting within these strata. This resulted in the ranking of patients by time waiting on the list, not by their need for a transplant. Moreover, these previous systems had not been validated for their accuracy in predicting the severity of liver disease and did not meet the needs of the enlarging population of appropriate candidates with end-stage liver disease. The MELD was identified as a potentially more accurate measure of liver disease, and a new plan for liver allocation incorporating the MELD score and virtually eliminating waiting time was devised. Several diagnoses for which liver transplantation is indicated were identified as not being served by the MELD system, so alternative mechanisms were developed for these cases. The new allocation system went into effect on February 27, 2002. One year after implementation, there was a statistically significant increase in the number of cadaveric transplants and a slight reduction in the number of waiting list deaths compared with the previous system in the year prior to MELD.

As the system evolves and improvements are made, patients have a much more objective measure of the severity of their liver disease, which is comparable regardless of the geographic location or physician. This change to a mathematically-based system that defines the risk of death represents a change in the way patients and caregivers will think about the liver transplant list. In addition, payors now have a much more objective measure of the severity of illness and can more accurately risk-adjust their comparisons of centers and patients. The new system directs organs to sicker patients, and waiting candidates are likely to experience significant declines in their quality of life while waiting. In addition, because this new policy will result in more severely ill patients receiving transplants, the costs of care are likely to increase, although preliminary results suggest that survival rates have not changed. The change to this new, more evidence-based system is a significant paradigm shift in organ allocation policy. Patients, caregivers, and payors should also be prepared for continuous evolution of the system as more data become available.

1. Background

On February 27, 2002 a new liver allocation plan came into effect in the US. This plan represented a departure from previous liver allocation systems in several areas. The driving forces for such a change were many. The liver transplant waiting list had continued to grow exponentially while cadaveric organ donation remained static. Prior to implementing this new plan, liver allocation

was based on categorical definitions of medical severity that separated waiting candidates into four groups. The highest priority was assigned to candidates meeting the Status 1 definition. These patients either had acute liver failure or immediate non-function of a transplanted liver. The remaining status definitions were based on the Child Turcotte Pugh (CTP) score.^[1] Status 2A, 2B and 3 patients were defined according to CTP score ranges and the

1 Components of the CTP score employed in the previous liver allocation policy can be found on the United Network for Organ Sharing (UNOS)/Organ Procurement and Transplantation Network (OPTN) web site (<http://www.unos.org>).

presence or absence of complications of their liver disease. Patients meeting 2A, 2B, or 3 status definitions were prioritized within their groups by their total time waiting on the list. As waiting lists grew, the number of patients in each of these categories increased and the mix of disease severity became much more heterogeneous. Waiting time became the main discriminator for patients in these large categories and reduced the role of patients' medical condition in determining their priority on the list. Furthermore, analyses of waiting time found that there was no correlation with liver transplant candidate mortality,^[2] and a pilot allocation plan that de-emphasized waiting time reduced the number of waiting list deaths.^[3] In addition, as care of patients with end-stage liver disease (ESLD) has improved, it has become apparent that the CTP score did not adequately segregate patients with progressively abnormal laboratory tests. For example, the CTP score treats patients with serum bilirubin values of 3.5 mg/dL the same as those with serum bilirubin values of 10, 20 or 40 mg/dL. The CTP score also includes subjective clinical measures, encephalopathy and ascites, which are subject to clinical interpretation and are less objective. Furthermore, the CTP score has never been prospectively validated as a measure of disease severity or mortality for patients waiting on the liver transplant list. Faced with these deficiencies and the increasingly apparent need to address the very ill patient with ESLD (who is referred late for transplant and who has little waiting time), policy-makers developed this new allocation plan that eliminated the categorical status definitions by using a continuous disease severity scale and significantly de-emphasized waiting time as a discriminator.

The Model for End-stage Liver Disease (MELD) score^[4] was chosen as the continuous disease severity scale for adult² liver allocation for several reasons. Unlike the CTP score used in previous allocation policy, the MELD score had been rigorously tested and validated as a good predictor of mortality in a variety of groups of patients with various types and degrees of chronic liver disease.^[5] The MELD score also eliminates subjective measures that were difficult to standardize or corroborate and allows for ranges of interpretations. The new MELD-based policy ranks candidates in a continuous fashion, and waiting time is used only to rank patients with identical MELD scores.³ However, the MELD score does not serve all potential liver transplant candidates well. For some patients with diagnoses not likely to progress to a life-threatening stage but for which liver transplantation is indicated, the MELD score does not assign a high priority. Patients with early stage hepatocellular carcinoma (HCC) make up the

largest group of such candidates. Several studies have shown that liver transplantation for early stage HCC yields excellent results that are superior to resection^[6] and equal to transplantation of candidates with non-malignant diseases.^[7] Nevertheless, many candidates with favorable HCC criteria are not likely to have advanced cirrhosis. Their 'window of opportunity' does not depend on progressing to a high risk of death, but rather they have a high risk of progression beyond the favorable tumor stage. It is for this reason that, after consulting the natural history literature and constructing progression risk models, the system designers chose to allow centers to request increased priority for these candidates. Similarly, candidates with other conditions that may be associated with a risk of progression beyond a 'transplantable state', but who do not have a high risk of mortality, may also have requests made for increased priority. These requests are forwarded to Regional Review Boards (RRBs) to assess their appropriateness. This peer review mechanism enables candidates for whom the MELD system may not be appropriately prioritizing their candidacy to have access to a higher priority on the waiting list.

2. Liver Allocation Under the Model for End-stage Liver Disease System: First Year Results

After 1 year of liver allocation under the MELD system, significantly fewer patients were registered (figure 1), fewer patients had died or been removed from the list for being 'too sick', and more cadaveric liver transplants had been performed compared with the corresponding 6 months a year earlier (figure 2). When adjusted for the number of patient-years on the list, the increase in rate of cadaveric transplants was statistically significant, whereas the decrease in the pre-transplant death rate for

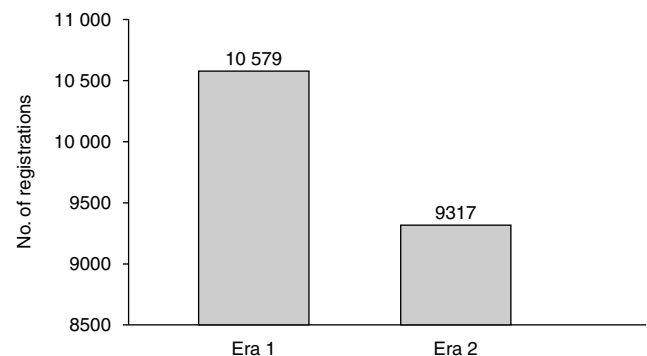


Fig. 1. Registrations for the liver transplant waiting list before the Model for End-stage Liver Disease (MELD) system (Era 1, 2/27/01–2/26/02) compared with registrations under the MELD system (Era 2, 2/27/02–2/26/03). The reduction was statistically significant by the Chi-square test ($p < 0.01$).

2 A separate risk model, called the Pediatric End-stage Liver Disease (PELD) score, was developed for pediatric liver transplant candidates. Because pediatric candidates represent less than 10% of the US liver transplant waiting list, the PELD score will not be discussed in this paper.

3 A full description of the liver allocation policy can be found at <http://www.unos.org>.

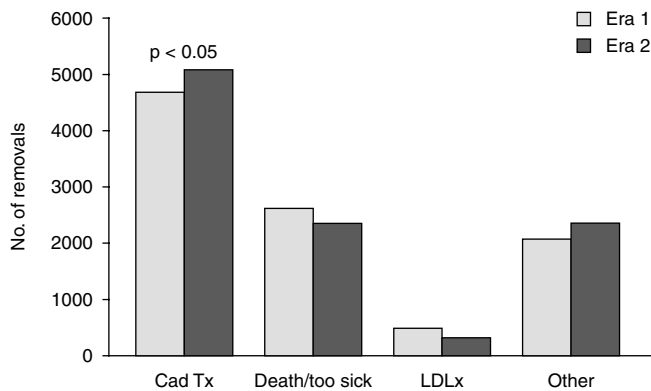


Fig. 2. Removals from the waiting list before the Model for End-stage Liver Disease (MELD) system (Era 1, 2/27/01–2/26/02) and after implementation of MELD (Era 2, 2/27/02–2/26/03). When adjusted for waiting list size, the increase in cadaveric transplants (Cad Tx) was statistically significant ($p < 0.05$). The other differences between Era 1 and Era 2 for removals for death or too sick, living donor transplants (LDLx), and other, were not statistically significant.

adult and pediatric candidates was not (figure 3). A higher proportion of transplant candidates with HCC received liver transplants under the new system (figure 4). Early survival after liver transplantation, based on reporting up to 90 days after transplantation, showed no difference under the new MELD system compared with the same 1-year period immediately prior to implementation of the MELD/PELD system (figure 5).

While these results are preliminary, they suggest that the more objective system is prioritizing candidates effectively and that organs are being directed to those most in need. The waiting list is smaller, because centers no longer face the pressure to ‘list patients early’ in order to gain waiting time. Consequently, there are fewer deaths on the waiting list overall, but when adjusted for the total size of the list, this reduction remains small and not statistically significant. After transplantation, there does not appear to be any reduction in patient survival although the results are very preliminary. Overall, the system has fewer deaths compared with the preceding year, probably due to more accurate prioritization, more cadaveric transplants, and post-transplant survival rates that are unchanged. There are many refinements and improvements that will need to be made as more experience accumulates. Indeed, this new system was meant to be a starting point from which liver allocation policy will continuously evolve.

3. Patient Implications

This new system has wide implications for patients who may be in need of liver transplantation. For patients with chronic liver disease of almost any etiology, the MELD score gives a reliable

indication of their risk of death based on simple, readily available routine laboratory tests.⁴ This enables patients and their caregivers to have an objective measure of the severity of their liver disease and follow their progress over time. In addition, patients and providers now have a standardized measure, regardless of which physician is estimating the severity of disease. This ensures that uniform standards for prioritizing patients are used across the nation. However, a given MELD score does not necessarily define a patient’s place on the list. The liver transplant waiting list is an extremely dynamic, fluid entity. Because waiting time now plays almost no role in ranking patients, new patients entering the list can easily supersede existing candidates if they have higher MELD scores. Waiting patients’ places on the list are also constantly changing due to changing laboratory values that can define higher or lower MELD scores than previously. Also, patients receive transplants and some patients develop complications or die, which results in their removal from the list. At any point in time, patients’ places on the list depend on their MELD score, the time they have been waiting at that MELD score, the number of other patients with similar or higher MELD scores, and the blood type of the donor.

The MELD score does not quantify the quality of life for a patient with chronic liver disease. Unfortunately, because of the extreme donor shortage, waiting patients usually have to experience a significant deterioration in their quality of life, corresponding to deterioration in their MELD scores. This means that most patients will suffer while waiting. However, based on the early results, the new system has reduced the chance that a waiting patient will die without a transplant even though they may be more likely to experience a reduction in their quality of life.

In the past, when liver allocation was heavily driven by waiting time, the timing of referral to a liver transplant center had a

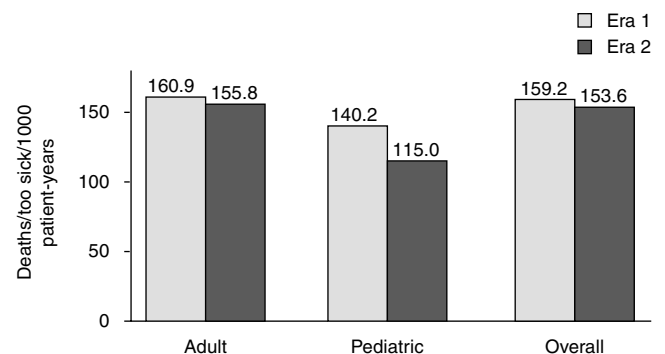


Fig. 3. Waiting list mortality rates comparing the first year (2/27/02–2/26/03, Era 2) of the Model for End-stage Liver Disease (MELD) system with the corresponding year (2/27/01–2/26/02, Era 1) in 2001. None of the differences were statistically different.

4 A ‘MELD Calculator’ is available at <http://www.unos.org>.

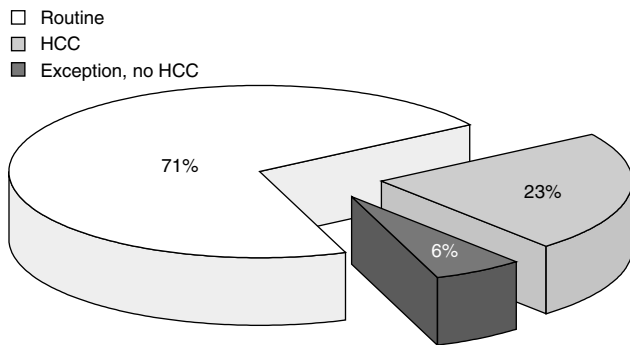


Fig. 4. Proportion of liver transplants performed for routine diagnosis, hepatocellular carcinoma (HCC) and other exceptional diagnoses under the first year of the Model for End-stage Liver Disease (MELD) system.

significant influence on the chance of receiving a transplant. Patients referred late in the course of their disease, who had not had the opportunity to gain a lot of waiting time, were at higher risk of dying while waiting, because waiting time, not severity of disease, was the main ranking criterion. The new system reduces the disadvantage assumed by patients who do not have ready access to timely medical care because the timing of their referral has little impact on their place on the list.

In addition, the increased priority for candidates with HCC has helped these patients receive timely transplants. In the past, when waiting time was the main allocation factor, candidates with HCC who waited a long time were more likely to develop later stage HCC even though they finally achieved a higher priority. This led to an increased dropout rate, which has been associated with a poorer outcome for patients with HCC in an intention-to-treat analysis of liver transplantation for HCC.^[8] The increase in transplants for HCC has not impacted on candidates without HCC, as the overall waiting list mortality rate has decreased. Longer term follow-up will be necessary to determine the full impact of such changes but, at present, liver transplant candidates with HCC seem to have improved access to transplantation without a detrimental effect on the remaining candidate pool.

4. Implications for Liver Transplant Payors

One of the most important benefits of the new liver allocation system is improvement in the objectivity of the measures by which patients are ranked. Payors now have a much more precise and consistent tool for comparing and contrasting patients and centers. The MELD score is specific for a patient, and will not change regardless of the center, region or country in which the patient resides or is listed. This will enable payors and their customers to better estimate patient and financial risks over a broad range of diseases and severities.

Because the MELD score is a better estimate of the severity of disease and will more precisely rank patients according to their severity, the system will direct more organs to sicker patients. The fact that patients going through major surgery are sicker is likely to result in increased costs of care. In a preliminary analysis of MELD scores and direct costs for 1 year of liver transplant care, a direct positive correlation was found^[9] (figure 6). Cost centers that experienced the increased costs related to higher MELD scores were those accruing dialysis care charges. This is likely to be due to the increased weight that preoperative creatinine receives in the MELD score relative to the previous allocation system. This results in more patients with compromised renal function receiving transplants, leading to increased renal dysfunction after transplant that often requires dialysis.

Payors and patients are interested in quality transplant care. The post-transplant results for patient survival are very preliminary at this time but there does not appear to be any reduction as a result of the MELD system (figure 5). Early results for other outcome measures reveal that there has been a slight reduction in the number of re-listings and re-transplants in the first year of the MELD system compared with the previous year's experience.

The new MELD system has removed waiting time as a major factor for ranking candidates. This removes the pressure in the old system to list patients early so that they could accumulate enough waiting time to get to the top of the list. As a result, minimum-listing criteria in the new system may be revised. As many as 20% of patients currently on the liver transplant list have MELD scores less than 10. These patients' mortality risks, as defined by the MELD score, are equal to, or less than, their mortality risks incurred by the transplant surgical procedure. For these patients, waiting until their disease has progressed to a higher mortality risk improves the risk-benefit of the transplantation therapy. The

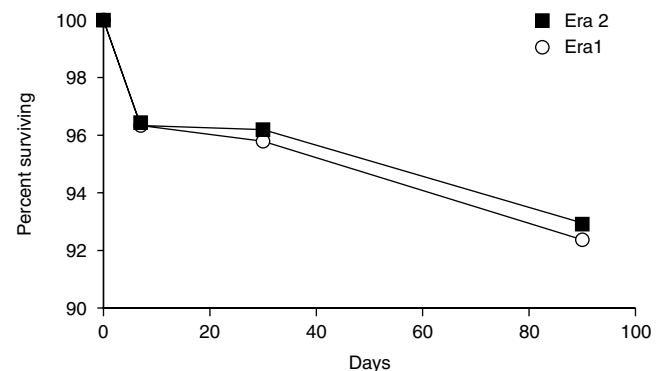


Fig. 5. Early results for post-transplant survival rates comparing 90-day survival for patients undergoing transplantation during the first 6 months prior to implementation of the Model for End-stage Liver Disease (MELD) system (Era 1) with the same period after implementation of MELD (Era 2). There was no statistical difference by log rank test ($p > 0.05$).

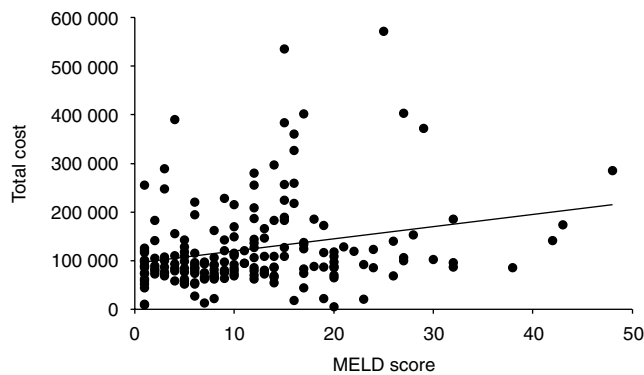


Fig. 6. Relationship between the Model for End-stage Liver Disease (MELD) score and 1-year direct costs for liver transplant care (\$US, 1999 values). $r = -0.23$, $p = 0.002$.

MELD system makes these calculations much more clear and makes it possible to adjust the minimum listing criteria based on these risks. Because some reimbursement plans define pre-transplant care as care given to patients on the waiting list, readjustment of these minimum-listing criteria could affect reimbursement schedules for payors and providers. New systems that do not utilize the minimum listing criteria for entry points may have to be defined for payors reimbursing for ESLD care.

5. Future Challenges and Conclusions

From the outset, the MELD liver allocation system was planned to be one of continuous improvement. In order to improve an evidence-based allocation system, the system should be changed as more evidence accumulates and improvements are proposed. As with all medical treatment, practice patterns change, patients and payors change and the field advances with new knowledge. Regulatory impediments that slow the ability to make these changes when the evidence warrants them will not be in the patients' best interests.

Many possible changes can be envisioned. Minimal listing requirements define that any patient with a CTP score ≥ 7 , or a patient who has had a variceal bleed in the past, qualifies for liver listing. Many of these patients with low CTP (and low MELD scores) have a 1-year survival rate in excess of that for liver transplantation. The MELD score allows patients, caregivers and payors to identify patients for whom the risk of transplant is justified. Based on this concept, the minimal listing criteria may be changed to criteria based on a risk of death, as defined by the MELD score, that is in excess of the risk of death with transplantation. Because some reimbursement plans base their reimbursement on the placement of a patient on the liver transplant list, this change may have implications for patients, payors, and physicians. One of the most important improvements in liver transplant care has been the advancement in pre-transplant care rendered by the

transplant hepatologists, which keeps these extremely complicated and ill candidates in a condition suitable for major surgery. Payors must recognize that placement on the list may not be the most important defining point on which to base reimbursement for ESLD care.

Additional model calculations will be done in the future. Potential variables for analysis include the need for dialysis treatment, mechanical ventilation, refractory ascites, and other continuous variables, such as age or post-transplant survival. Although there are no reliable models of post-transplant survival that utilize only patient-specific, pre-transplant variables, they might be developed in the future. This then would allow for a combined model that would ultimately direct the organs to those patients most likely to die without a transplant but most likely to survive with a transplant. Alternatively, MELD scores associated with high mortality but that are also associated with a low relative risk of post-transplant mortality might be used to define larger areas from which these 'ideal' recipients might potentially draw donors.

This concept of maximizing post-transplant results may require defining unacceptable success rates. Unlike most forms of medical or surgical treatment, liver transplantation cannot be offered to every individual with even a small chance of success, because the use of organs in candidates who have a very low chance of success means that another less risky candidate may potentially die because there is no organ available for that individual. This may require that the transplant community defines a MELD score for which the results are unacceptable that would effectively cause a patient to be removed from the list. This unacceptable risk may be one that many candidates are unwilling to accept. A consensus will need to be reached before such concepts are finalized into policy.

Enlarging the area from which donor organs are drawn for the patients with the highest pre-transplant mortality risk but the lowest post-transplant risks would be one way to direct more organs to the most needy patients. This also would result in the transfer of available organs from some areas of the country into others. This could have dramatic effects on the number of transplants performed at these centers and would profoundly affect patients on the waiting list and payors choosing centers based on transplant procedure volumes. Attempts at broadening sharing areas in the past have resulted in tremendous political rancor and media coverage. A computer modeling study that analyzed the effects of redrawing the distribution lines showed that larger distribution areas would result in a significant number of organs being transferred but would not result in a significant overall improvement in the number of patients undergoing transplantation and the number of life-years saved.^[10]

The future holds many challenges for liver allocation. The MELD system provides a much more objective way to approach

these challenges. Patients benefit from this much more transparent system and, because of it, payors have much better risk assessment tools available. There are many deficiencies in the MELD system and many things that still need to be addressed. Using an objective, evidence-based approach is the new paradigm for continuously improving the system for all.

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