MELD—good for many, not as good for others ... at least for now

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Since its introduction in early 2002 as the prioritization system utilized by the United Network for Organ Sharing (UNOS) for patients on liver transplant waiting lists in the United States, the model for end stage liver disease (MELD) [1–3] has been extensively validated over time as a very sensitive predictor of pre-transplant mortality. Part of the success of the MELD system has been the foresight of UNOS to continuously reexamine MELD and be open to modifying it, so as to address inequities that might favor or prejudice certain patient groups. This is in fulfillment of the “final rule” of the organ procurement and transplantation network (OPTN) ensuring that all patients have as equal access to transplantation as possible [4]. For instance, in the early days of MELD, patients with small hepatocellular carcinoma (HCC) were given priority on the transplant waiting list (T1 lesions) and patients meeting the current T2 criteria were given higher priority than they currently have. T1 listing was done away with and patients with T2 criteria were assigned lower MELD scores when analysis suggested that patients with HCC were being given too much priority on the list and that non-HCC patients might be suffering the consequences of less access to organs and higher death rates on the waiting list [5, 6]. There are now specific disease states that allow patients to receive additional MELD priority scores, such as hepatopulmonary syndrome, portopulmonary hypertension, and familial amyloidosis [7]. Realization that patients with low MELD scores having hyponatremia are more likely to die on the waiting list has spurred ongoing research to assess whether an adjusted MELD score in this setting would be warranted [8]. Even patients having certain cholangiocarcinomas are

now given priority in the waiting list because research has demonstrated appreciable survival with aggressive treatment protocols [9].

The success of MELD has captured the interest of the transplant community outside of the United States, and it has now been adopted by many other countries [10–13]. MELD has also been shown to have utility in predicting outcome in patients suffering from acute liver failure, alcoholic hepatitis, and in patients with chronic liver disease undergoing surgery or experiencing traumatic injury [14–18]. To date, however, it has not been shown to reliably predict post-liver transplant mortality. In listed patients with small changes in MELD score (delta MELD), there can be appreciable changes in pre-transplant mortality, although studies do not convincingly show this to be a strong predictor for having a bad outcome [19, 20].

In the issue of *Hepatology International*, Badr Al-Freah and colleagues [21] reviewed the results of an analysis of patients listed between 1998 and 2005 at the New Zealand Liver Transplant Unit with retrospective calculation of the MELD score at the time of listing and subsequently at the time of transplantation. They took into account prioritization points for HCC and studied 264 patients. Typically, patients in Australia and New Zealand are prioritized to transplantation when they are Child’s Class C and have had complications of portal hypertension, with hospitalized patients being further prioritized. The investigators found that MELD scores at transplant as well as delta MELD scores did not correlate with 3- and 12-month post-transplant mortality. The authors concluded that the MELD allocation system would not be helpful in New Zealand, which has a single transplant center and organ procurement organization, and I am in agreement with this. Their results are not surprising in light of the fact that median waiting time prior to transplantation was 72 days and the MELD

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score at listing (unadjusted for HCC) was 15 with only 20 % of patients having a MELD score >20. The program achieved an outstanding 1-year survival rate of 94 %. Patients were listed for HCC if they met University of California, San Francisco (UCSF) criteria [22] or Milan criteria [23] and were assigned 24 points instead of 22. There was no real delta MELD, not unexpected since the waiting time was short. Of the total patients, 15 % ($n = 38$) were delisted with 23.7 % dying of sepsis/multi-organ failure and tumor progression in 14 (36.8 %). A 15 % waiting list death rate seems somewhat high in light of the overall comparatively low MELD scores with which the patients were listed. Death from infection in decompensated cirrhotic patients is not unusual, however, and if one excluded the large number of patients dying from HCC progression, the number of patients dying on their waiting list was under 10 %.

Some data which the investigators did not provide and that which would have been helpful in further critically examining their results and trying to extrapolate them to the current MELD system of the United States are as follows: the specifics of the actual MELD score (i.e., how many patients had renal failure or were on hemodialysis); were patients with HCC actively being treated with loco-regional therapy while on the list or did they initially have HCC fulfilling UCSF criteria and were then downstaged into fulfilling Milan criteria; what were the miscellaneous diagnoses for listing (28 % of the patients); and finally what were the causes of death of the patients dying during the first year after the transplant. No information is provided on the donor organs with regard to length of cold ischemia time and donor age, both of which can affect post-liver transplant outcome. The majority of organs presumably were procured locally and had short ischemic times, and the program could probably be more selective in matching recipient and donor. One-third of patients were listed for accepted MELD exceptions but the authors do not specify what the indications were and how many MELD points were allotted. Their patient population is very different from that seen in Europe and the United States with many more patients having hepatitis B, their use of the UCSF criteria in an overall lower percentage of HCC patients being listed for transplant, and overall lower MELD scores and shorter waiting times for all listed patients. Thus, their results are not really applicable to the current transplant environment faced by the majority of liver transplant programs relying on deceased donor organs at a time of organ donor scarcity. Further, data on the comparative successes of the other programs in the Australasian system would also be of interest.

Despite these methodological shortcomings and comparative disparities in demographics, I believe that the results of Badr Al-Freah and colleagues are a clarion

example of ideally how transplant prioritization and allocation of organs could work. The Australasian system is unit-based with donors obtained from their own procurement unit first offered to that particular transplant center and offered out only on a strict rotating basis when not accepted by that program. Their overall number of patients on liver transplant lists is small and patients are thus effectively managed by transplant physicians who have close relationships with their patients and knowledge of their medical histories, thus allowing the physicians to detect subtle changes in their patients' conditions. I am sure that these close relationships, which we all strive for but often are unable to achieve because of the sheer number of patients flooding United States and European transplant centers, translate into better patient satisfaction and post-transplant compliance.

Currently, in the United States, there are geographic disparities in liver allocation with some regions of the country being able to transplant livers in patients having MELD scores of 20 and some regions of the country being able to transplant livers in patients with MELD scores closer to 30. This is having a clear negative impact on waiting list mortality and post-liver transplant patient and graft survival in many centers, despite the innovative and skillful techniques of the liver transplant surgeons having to place more extended donor organs into sicker patients. Unfortunately, there may be no light at the end of the tunnel as the number of patients developing decompensated liver disease and HCC is expected to increase well into the future. Hopefully, calls for changing the current liver allocation in the United States will not fall on deaf ears and changes can be instituted that take advantage of a broader geographic donor sharing.

I agree with Badr Al-Freah and colleagues in that New Zealand currently does not require MELD to achieve excellent post-transplant survival of their patients. Their waiting list mortality would be just as outstanding as their post-transplant survival if patients were listed with Milan criteria staging of their HCC rather than UCSF criteria. However, as the number of patients increases on their waiting list and the need and demand for transplantation soars in New Zealand, the time-tested benefits of MELD will need to be reassessed.

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