BY LARA C. PULLEN, PHD

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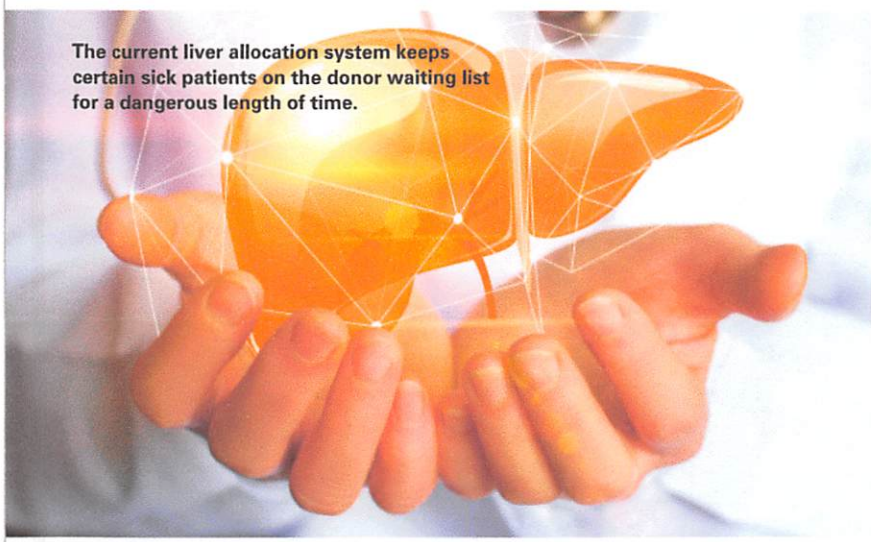
News and issues that affect organ and tissue transplantation

Liver Allocation for Rare Disease: Does the MELD Score Suffice?

Patient advocates ask whether waitlist mortality is the optimal metric for liver allocation



The current liver allocation system keeps certain sick patients on the donor waiting list for a dangerous length of time.

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On August 4, 2020, Lezlee Peterzell-Bellanich created a change.org petition asking the United Network for Organ Sharing (UNOS) to consider adding a small number of exception points to the Model End-Stage Liver Disease (MELD) scores of people suffering from late-stage primary sclerosing cholangitis (PSC) and primary biliary cirrhosis (PBC).[1] Ms. Peterzell-Bellanich had a personal stake: her husband's PSC had advanced to the point where he needed a liver transplant. However, he had become trapped in what she dubbed "MELD purgatory."

Listed MELD score ranges from 6 to 40, and predicts three-month waitlist mortality, so as to identify which candidates are likely to die without liver transplantation. Candidates can, however, receive additional points for exceptional circumstances, and the National Liver Review Board (NLRB) was established to provide efficient and equitable review of MELD exceptions. Transplant programs request a MELD exception score when they believe that the calculated MELD score, based on three laboratory parameters, for a particular candidate does not accurately reflect that individual's level of medical urgency for transplantation. The NLRB typically assigns exception points relative to the median MELD at transplant (MMaT) that reflects the score at which candidates of the same blood type and within 250 nautical miles recently accessed a deceased donor liver. A typical exception score would be MMaT – 3. For example, if the MMaT at a transplant program is 27, most exception candidates at that program will be granted a score of 24.

The transplant center acknowledged that Ms. Peterzell-Bellanich's husband's score did not adequately reflect how sick he had become, but they were unable to obtain exception points for him, a fact that confused and concerned Ms. Peterzell-Bellanich. PSC is on the list of exceptions, but her husband did not meet the specified criteria to secure additional points. "Don't you want somebody going into a transplant as strong as possible, so they have the best outcome?" she wondered.

Ms. Peterzell-Bellanich's husband did ultimately receive his liver transplant, which Shennen A. Mao, MD, performed at the Mayo Clinic in Jacksonville, Florida. A post-surgery analysis of the liver revealed a high level of dysplasia in the main bile duct that had not been evident via magnetic resonance imaging. "[For] a MELD score of 22, the condition of his liver was horrible," says Ms. Peterzell-Bellanich. Her petition seeks to enable patients like her husband to receive a liver transplant before their disease has advanced to a high-risk stage for complications. To date, it has received more than 8,000 signatures. It has also captured the attention of UNOS.

KEY POINTS

- **A patient-initiated petition has requested changes to the exception review process of the current Model End-Stage Liver Disease (MELD) scoring system; the aim is to support people with late-stage primary sclerosing cholangitis (PSC) and primary biliary cholangitis (PBC).**
- **MELD scores, a metric of waitlist mortality, may not adequately reflect a patient's health status.**
- **Transplant centers have the option to petition the National Liver Review Board (NLRB) for a policy exception if they feel a patient is not well served by the MELD score.**
- **UNOS is considering patient voices and is reviewing the medical literature to determine whether a change is justified.**

(Continued from previous page)

The creation of a NLRB was intended to create a more consistent national approach to granting exceptions which was previously reviewed on a regional basis. (The NLRB operates under the aegis of the Organ Procurement and Transplantation Network [OPTN], which in turn operates under UNOS.) The new policy outlines specific diagnoses and/or clinical conditions that would make a patient eligible for standardized exceptions. Candidates with these diagnoses or conditions are granted automatic exception points if specific criteria are met.

Thomas D. Schiano, MD, medical director of adult liver transplantation at Mt. Sinai Medical Center in New York City sits on the NLRB and reviews such exception requests. "I strongly feel for patients with PSC and PBC, the current allocation system does not do them justice," he says. Unfortunately, patients with these relatively rare conditions typically do not develop all of the usual signs of liver failure captured by the MELD score until they are extremely sick.

The Path to Change

How will Ms. Peterzell-Bellanich's petition fare? Dr. Schiano notes that "UNOS is always willing to reassess things and change things," but then adds, "I think that the likelihood that there will be changes made in the short term is quite slim." In actuality, it is the OPTN Liver and Intestinal Organ Transplantation Committee that would review published literature and outcomes data for candidates with PSC and PBC and would consider potential changes to the guidance. Julie K. Heimbach, MD, surgical director of liver transplantation at Mayo Clinic in Rochester, Minnesota, and chair of the NLRB, who has read the petition and the public comments, believes it is a lesson in "how important it is that patient voices are considered." Indeed, these voices are a driving force behind the proposed exemption rule modifications item that has been added to the next NLRB meeting agenda.

In addition, Ms. Peterzell-Bellanich's petition has prompted a review of the 5 to 10 papers that have been published on PSC and PBC and waitlist mortality, the metric by which livers are allocated, as specified by the Final Rule. Dr. Heimbach says that a cursory review of the data suggests that patients with PSC and PBC do not appear to be uniquely disadvantaged by the current system. However, if the OPTN determines upon closer review that a change to the exemption process is warranted, the proposed change will go out for public comment. Matthew Cafarella, a policy analyst at UNOS, notes that "the OPTN follows a set policy development process" and that this change to the guidance would have to go through that process, but that it would be possible to update the guidance document relatively quickly.

UNOS is fully aware that the MELD score works for most but not for all liver candidates. Matthew Prentice, manager of policy and community relations at UNOS, explains that the adoption of the MELD score was "a conscious reaction to the shortage of available organs… a conscious decision to keep mortality on the liver waiting list as low as it can be." The MELD score thus intentionally does not consider candidate quality of life before transplant or recipient outcomes after transplant.

Although the NLRB reviews specific exception requests for individual candidates, in some cases, such as in certain liver cancers that affect a large proportion of candidates, exceptions are granted without review, as long as they meet stipulated criteria. Likewise, an exception exists for PSC. However, according to Dr. Schiano, the criteria are so stringent that he has yet to have a patient qualify.

This fact prompts Ms. Peterzell-Bellanich, who is currently writing a book entitled *Second-Chance Stories*, to wonder whether the criteria can be changed for patients with PSC. Dr. Schiano points out, however, the potential difficulty in identifying clinical thresholds that apply to all patients even with the same diagnosis, because not all patients with PSC and PBC need transplants. "We always try to hold out, if possible, on sending a patient to transplantation," he acknowledges, "but once it becomes necessary, at that point I would love to get the patient transplanted without an obstacle and in a timely fashion. How we do that is the million-dollar question." The reality of liver allocation is that, in essence, advancing one group will hinder another group.

Ms. Peterzell-Bellanich also recognizes the complexity of the situation. Even as she continues to push for the granting of exceptions for patients with PSC and PBC, she has also signed up to be a UNOS ambassador, dedicating herself to helping address the overarching challenge of organ scarcity by increasing awareness of the importance of organ donation. She understands all too well the difficulties and urgent needs of families struggling with PSC/PBC as well as other medical conditions that can only be helped by a new organ. "A year is a long time in the life of someone waiting on a transplant," she says. ATI

References

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Food and Drug Administration Accepts iBox

In June, the US Food and Drug Administration (FDA) accepted the iBox Scoring System, the first universal and validated tool for predicting the risk of kidney loss, into the Center for Drug Evaluation and Research's Biomarker Qualification Program. The system can now be used as a reasonably likely surrogate endpoint for clinical trial design, which will hopefully accelerate the development and approval of novel therapies that promote long-term survival and quality of life for kidney transplant recipients.

"This is a monumental task," says Alexandre Loupy, MD, PhD, head of the Paris Transplant Group in France. "The iBox initiative is a consortium involving more than 15,000 patients from 15 clinical transplant centers internationally and 7 randomized clinical trials." The international consortium of research teams from Europe and the US created the iBox algorithm based on long-term patient data that can then be accessed during patient follow-up to generate probabilities of graft loss for as long as 10 years after patient evaluation.[1] The algorithm has been tested on more than 7,500 patients and its predictions are reliable no matter the health system, clinical situation or therapeutic intervention. ATI

Reference

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