

Strategy Evolves for Improving Liver Allocation

BY ROXANNE NELSON
Contributing Writer

SEATTLE — The introduction of “MELD/PELD” 3 years ago was a start, but the liver allocation system is continually undergoing adjustments and refinements in an effort to improve outcomes, said Michael R. Lucey, M.D., at the annual meeting of the American Transplant Congress.

The Model for End-Stage Liver Disease (MELD) and Pediatric End-Stage Liver Disease (PELD) are numeric scales that in 2002 replaced the former system used for liver allocation. Both scores are based on a patient’s risk of dying while waiting for a liver transplant, and both use objective and verifiable medical data. The higher the MELD or PELD score, the greater the risk of dying from liver disease.

The MELD score uses a mathematical formula based on serum creatinine levels, bilirubin levels, and international normalized ratio. A patient’s score can range from 6 to 40. In the event of a liver becoming available to two patients with the same MELD score and blood type, time on the waiting list becomes the deciding factor. In the first year of utilizing MELD scores, the median score of patients who received livers was 18 to 20, with a few

spikes to 24 and 27, said Dr. Lucey.

Before the implementation of the MELD/PELD system, there were large disparities in waiting times across geographic regions, as well as difficulties in prioritizing patients.

While the situation has improved, there are still regional variations, said Dr. Lucey, chief of gastroenterology and hepatology at the University of Wisconsin, Madison.

“We have 11 regions and there are regional variations in mean MELD scores, from a high point of 27 to low point of 20,” he said.

In some organ procurement organizations (OPOs), no patients with a MELD of less than 10 received a transplant. Yet in others, as many as 17 or 18 patients whose MELD score was below 10 received a liver transplant.

“So the MELD system demonstrates that not only are there regional variations, but variations between OPOs,” said Dr. Lucey at the meeting, which was cosponsored by the American Society of Transplantation and the American Society

of Transplant Surgeons.

One analysis showed that the size of the OPO was associated with how the MELD score was implemented.

It found a significant disparity in MELD scores in liver transplant recipients in small versus large OPOs. Fewer transplant recipients in small OPOs had severe liver disease, as evidenced by MELD scores below 24, he said.

“The smaller OPOs tend to transplant patients who are less severely ill,” said Dr. Lucey.

“There are distinct practices across the country and between OPOs, [although] one of the priorities of MELD was to make geographic distinctions less important in organ allocation.”

This disparity, he added, does not reflect the stated goals of the current allocation policy, which is to distribute livers according to a patient’s medical need, rather than to keep organs in the local procurement area.

Patients awaiting livers used to be ranked as status 1, 2A, 2B, and 3, according to the severity of their current disease.

Before the MELD/PELD system, large disparities existed in waiting times across geographic regions and there were difficulties in prioritizing patients.

The status 1 category has remained in place as the highest priority for receiving an organ and is not affected by the MELD or PELD scores.

A high number of pediatric patients were being transplanted at stage 1 before PELD, with half of them at status 1 and 23% at status 1 by exception.

“But since PELD, there has been a minor reduction in the total number of status 1 transplants, but an increase in those getting status 1 transplants by exception,” said Dr. Lucey. “This calls for a review.”

Another issue is that more than half of the transplant candidates are listed with PELD scores of less than 10, and many such patients are being transplanted. It is important to find out what this means, he explained.

“Status 1 has been redefined for PELD, and we will have to see if stricter rules to define status 1 have had an impact—and an impact that we want,” he said.

MELD and PELD have made it easier to audit the practice of liver transplantation, Dr. Lucey concluded.

“They facilitate data-driven changes in policy and practice and, finally, allow for subsequent auditing after the changes are made, with continuing revisions as appear appropriate.” ■

Hepatic Encephalopathy Treatments Remain Unproven

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

CAMBRIDGE, MD. — Two existing medications—an antibiotic and a hypoglycemic agent—may add some strength to the poorly outfitted armamentarium for hepatic encephalopathy, Steve Solga, M.D., said at a hepatobiliary update sponsored by Johns Hopkins University.

The altered brain function of hepatic encephalopathy appears to be related to increased ammonia levels in the blood, although controversy remains on this issue. Intestinal dysmotility, common in cirrhosis, causes an overgrowth of urease-positive bacteria and increased nitrogen absorption. The impaired liver is unable to process this extra load, so ammonia levels increase.

Generally, treatment is aimed at decreasing ammonia production and absorption; neomycin and lactulose are the most common therapies. Neomycin directly decreases the gut flora, whereas lactulose decreases gut bacteria load by promoting elimination and tilts the bacterial balance toward nonammoniogenic types.

The problem, Dr. Solga said, is that while lactulose is safe, it is not as effective in resolving symptoms as is neomycin. But neomycin may not be safe for many patients.

“Some literature suggests that long-term use is associated with irreversible ototoxicity and nephrotoxicity, and that it shouldn’t be given for longer than 2 weeks

for hepatic encephalopathy in patients with preexisting renal impairment.”

Importantly, neither treatment has been adequately studied in well-designed randomized trials, he added.

Rifaximin, another poorly absorbed antibiotic often used for “traveler’s diarrhea,” is being studied for use in hepatic encephalopathy.

“Most of the trials indicate that safety is relatively well established, but we don’t have solid efficacy data yet for hepatic encephalopathy,” he said.

However, according to a 2005 review of 15 studies, rifaximin was at least as effective as lactulose and neomycin in improving neurologic symptoms and reducing blood ammonia levels (*Rev. Gastroenterol. Disord.* 2005;5[*suppl.* 1]:10-8).

The hypoglycemic agent acarbose might have some benefit for hepatic encephalopathy patients who are diabetic, he added. The drug promotes the growth of saccharolytic bacteria.

An Italian study of 107 patients found that acarbose significantly decreased blood ammonia and improved intellectual function, while controlling blood sugar (*Clin. Gastroenterol. Hepatol.* 2005;3:184-91).

Finally, gut flora therapy, in the form of either prebiotics or probiotics, has potential. However, this treatment is still in its infancy. There are also regulatory issues to contend with, inasmuch as it remains unclear whether probiotics are drugs or supplements. ■

Treatment Options Underutilized In Hepatocellular Carcinoma

BY TIMOTHY F. KIRN
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CHICAGO — Only 13% of U.S. patients who are diagnosed with hepatocellular carcinoma receive potentially curative therapy, Hashem B. El-Serag, M.D., said at the annual Digestive Disease Week.

Moreover, only one-third of those patients with single lesions get potentially curative therapy, according to Dr. El-Serag of Baylor College of Medicine, Houston.

In other countries, potentially curative therapy appears to be used at much higher rates: 40% of all hepatocellular carcinoma patients in a series from Barcelona received such therapy as did 30% of all patients aged over 75 years in Italy.

“There is significant underutilization of potentially curative therapy, even among those with favorable clinical features,” said Dr. El-Serag.

He and his colleagues examined data for a nationwide cancer registry. This registry is now linked to Medicare data. “The reasons for this observation need to be examined and corrected,” Dr. El-Serag said.

Dr. El-Serag’s study included data from 2,963 patients with hepatocellular carcinoma who were diagnosed between 1992 and 1999 and who were entered into any 1 of 11 different regional cancer registries.

In addition to the 13% of patients

who received potentially curative therapy, 4% received transarterial chemoablation and 35% received systemic chemotherapy or radiotherapy. The other 48% of the patients received no treatment at all.

The study found that age and ethnicity affected which patients received potentially curative therapy.

Among those aged 65-74 years, the rate of the use of potentially curative therapy was 17%, and among racial groups, Asian people had the highest rate of potentially curative therapy—24%—because they had more single and small tumors.

But neither of those characteristics had as strong an influence on rate as did the region where the cancer was diagnosed, Dr. El-Serag said, although he did not identify which regions had the highest or lowest rates.

The rates of attempted therapy did increase over time in the study, but this improvement was not dramatic, he added. For example, between 1992 and 1995, 53% of patients received no treatment. But the rate fell to 43% between 1996 and 1999.

Many physicians have had too dismal a view of the prognosis of hepatocellular carcinoma, and that perception does not appear to have changed much between 1999 and the present, Dr. El-Serag said. Specifically, the majority of physicians still do not know that liver transplantation is an option for liver cancer, he added. ■