

Scoring Method Foretells Outcome of Liver Cancer

BY ALICIA AULT
Contributing Writer

CHICAGO — Perioperative mortality and long-term survival of patients with cirrhosis and hepatocellular carcinoma can be predicted using the Model for End-Stage Liver Disease, said Swee Teh, M.D., at the annual meeting of the Society for Surgery of the Alimentary Tract.

Typically, the Child-Turcotte-Pugh score is used most often to predict survival in patients being considered for resection, said Dr. Teh. He and his colleagues at the Mayo Clinic, Rochester, Minn., wanted to determine if the Model for End-Stage Liver Disease (MELD) score could predict perioperative mortality.

The MELD was developed by the United Network for Organ Sharing as a means of ranking patients waiting for a liver transplant and was used regularly starting in early 2002. Scores range from 6 (less ill) to 40 (gravely ill) and rely on three lab tests: bilirubin, international normalized ratio of prothrombin time, and creatinine.

Dr. Teh and his colleagues reviewed the charts of all patients who had a resection for hepatocellular carcinoma between January 1993 and December 2003, and analyzed perioperative mortality and long-term survival, applying both the Child-Turcotte-Pugh and MELD scores. Child-Turcotte-Pugh scores are categorized by three groups: the least sick patients are in class A and have 5-6 points; the moderately ill are in class B, with 7-9 points; and the more severely ill are in class C, with 10-15 points.

There were 82 patients with both cirrhosis and hepatocellular carcinoma (62 male and 20 female). The mean age was 62.1 years for all patients. Overall, 32% of the patients were stage I; 26%, stage II; and 42%, stage III.

The Child-Turcotte-Pugh score for the patients ranged from 5 to 9. Thirty-seven patients had a MELD score of less than 8, and 45 had a MELD of greater than 9 (with a range of 9-15).

The higher MELD scores tended to be associated with greater resection and lower survival. Fifty-nine of the patients had a minor resection, defined as less than three segments (29 had a MELD of less than 8, and 30 had a MELD of greater than 9); and 23 patients had a resection of more than four segments (with 8 having a MELD of 8 or less and 15 with a MELD of 9 or more).

There were 13 perioperative deaths. There appeared to be no correlation between the Child-Turcotte-Pugh score and death during surgery, said Dr. Teh. But all 13 patients who died had a MELD score greater than 9, he said.

'MELD is predictive not only of perioperative mortality but also of survival' and is 'more predictive than the Child-Turcotte-Pugh' score.

At 30 days post resection, none of the patients with a MELD of less than 8 had died, compared with 29% of those with a MELD of greater than 9. The differences between the scores continued to be significant at 1, 3, and 5 years, at which point there was 51% survival among patients with a MELD of less than 8, and 24% among those with a MELD of greater than 9.

Dr. Teh said that because the study appeared to show that MELD is a strong predictor of perioperative mortality and long-term survival, his group recommends resection in patients with scores of less than 8 and organ transplants in those with a 9 or higher score.

Kevin Behrns, M.D., of the University of North Carolina at Chapel Hill, who discussed the paper at the meeting, said Dr. Teh's work showed that "MELD is predictive not only of perioperative mortality but also of survival" and that it is "more predictive than the Child-Turcotte-Pugh" score. ■

Avoid Surgery in Cases of Severe Hepatitis, Advanced Cirrhosis

BY MICHELE G. SULLIVAN
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CAMBRIDGE, MD. — The increased risk of mortality in patients who undergo surgery for serious liver disease is reason to postpone an operation until the disorder responds to treatment or resolves, Adrian Reuben, M.B., said at a hepatobiliary update sponsored by Johns Hopkins University.

"Surgery is contraindicated in those with acute hepatitis—especially alcoholic hepatitis—and severe chronic hepatitis and advanced cirrhosis," said Dr. Reuben of the Medical University of South Carolina, Charleston.

"In cardiac surgery, patients with Child-Turcotte-Pugh [CTP] Class A scores do well, but for anyone with CTP Class B or C, surgery may be prohibitively dangerous," he said.

Patients with severe liver disease are more susceptible to infection, which aggravates vasodilation and exacerbates the hyperdynamic circulation.

"This can precipitate hepatorenal syndrome or convert existing hepatorenal syndrome from stage II to stage I," he explained.

Other reasons for adverse outcomes include concomitant renal dysfunction; reduced hepatic drug metabolism; poor nutrition, which is common in those with advanced liver disease; and ascites. Ascites carries the risks of infection, poor wound closure, and dehiscence, and it impairs respiration.

Mortality risk is much greater in patients with cirrhosis and increases steadily with higher CTP score.

Dr. Reuben reviewed five studies of abdominal surgery in patients with cirrhosis conducted from 1984 to 2004. Among a total of 391 patients, overall mortality ranged from 16% to 28%, with a range of 8%-19% for elective surgery and 32%-50% for emergency surgery. Rates were much lower among those with CTP Class A (3%-10%) than those with CTP Class C (55%-100%).

Other variables predictive of mortality

in these studies were encephalopathy, ascites, infection, coagulopathy (high international normalized ratio [INR]), high creatinine, and gastrointestinal and pulmonary operations.

The risk of postsurgical mortality is increased in both viral and alcoholic hepatitis. "With acute viral hepatitis, the increased risk is about 10%-15%. With alcoholic hepatitis, it's vastly increased: 55%-100%," Dr. Reuben said.

"You must also be very aware of alcoholic hepatitis; sometimes it mimics acute cholangitis," he added.

An increased mortality risk has also been associated with nonalcoholic fatty liver disease (NAFLD). A 1998 study that looked at hepatic resection for cancer showed a 3% mortality rate for those with nonfatty livers. Mortality increased to 7% for those with mild NAFLD and to 14% for those with moderate to severe disease (*J. Gastrointest. Surg.* 1998; 2:292-8).

Biliary tract surgery is also risky for the cirrhotic patient. Only those with very low scores (less than 8) on the Model for End-Stage Liver Disease (MELD) scale are at minimal or no risk. Laparoscopic surgery is recommended for cirrhotic patients, because it reduces blood loss, postoperative complications, anesthetic and surgical times, and length of hospital stay.

Arthroplasties are also dangerous for the patient with cirrhosis, he said, with combined mortality and complication rates increasing with liver disease severity. The rates are about 11% in those with CTP Class A disease, almost 50% among those with CTP Class B, and 100% in those with CTP Class C.

If surgery is necessary in patients with cirrhosis, all nephrotoxic drugs should be avoided, and opiates should be limited. Opiates can cause sedation and lead to constipation, a contributing factor to hepatic encephalopathy.

Cirrhotic patients undergoing transurethral prostatectomy had a 7% mortality rate, compared with 2% in controls, he said. ■

Hepatic Encephalopathy Treatments Remain Unproven

BY MICHELE G. SULLIVAN
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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.

But according to a 2005 review of 15 studies, rifaximin was at least as effective as lactulose and neomycin in improving neurologic symptoms and in reducing blood ammonia levels (*Rev. Gastro-*

enterol. 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 sacrolytic 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. ■