HCV ADVOCATE

HEPATITIS JOURNAL REVIEW

Volume 2, Issue 6
May 8, 2005

Hepatitis C

By Liz Highleyman

Diabetes Ups Liver Cancer Risk

Diabetes may increase the risk of hepatocellular carcinoma (HCC; a type of liver cancer) by as much as 3-fold, according to an article published in the April issue of *Gut*. J.A. Davila, H.B. El-Serag, and colleagues performed a retrospective analysis of data from the Surveillance, Epidemiology, and End Results/Medicare database, a large, population-based survey of cancer risk factors and outcomes. The analysis included 2,061 liver cancer patients aged 65 or older and 6,183 randomly selected control subjects without cancer. The authors found that 43% of the HCC patients were diagnosed with diabetes during the three years prior to their liver cancer diagnosis, compared with 19% of control subjects. Conversely, after adjusting for demographic factors including sex and race/ethnicity and for the presence of other conditions associated with liver cancer (chronic hepatitis B or C, alcoholic liver disease, hemochromatosis), the risk of developing HCC was three times higher among the subjects with diabetes. Looking at the subset of patients with other liver conditions, diabetes was still associated with a 2.87-fold increase in risk. By itself, chronic hepatitis C was associated with a 24-fold increase in HCC risk. Among people with both hepatitis C and diabetes, the HCC rate was about 37 times higher, suggesting that the two conditions interact synergistically to increase the likelihood of liver cancer.

In related news, J.A. Marrero and colleagues from Spain reported on a comparison of HCC prognostic staging sys-

Hepatitis Journal Review

A publication of the Hepatitis C Support Project

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tems in the April issue of *Hepatology*. The researchers studied 239 patients with liver cirrhosis and HCC between January 2000 and December 2003; nearly two-thirds (62%) had hepatitis C. After one year, 58% of the patients were still alive; the three-year survival rate was 29%. The factors most strongly associated with poor survival were diminished performance status, a MELD score greater than 10, portal vein thrombosis, and tumor size larger than 4 cm; receiving treatment was linked to increased survival. The researchers concluded that the Barcelona Clinic Liver Cancer staging system, which takes all these factors into account, "provided the best prognostic stratification" compared to six other HCC staging methods.

How Hepatitis C Affects Quality of Life

Brennan Spiegel and colleagues from the University of California at Los Angeles performed a systematic review of more than 30 published studies looking at health-related quality of life (HRQoL) among hepatitis C patients; their results appeared in the April issue of *Hepatology*. The researchers found that, overall, individuals with HCV had significantly lower SF-36 scores than HCV negative people. (The Medical Outcomes Study 36-item short-form health survey, better known as SF-36, is a common measure of health and quality of life status that takes into account factors such as pain, psychological well-being, energy level, limitations of physical and social activity, and interference with "usual role" activities.) Not surprisingly, individuals who achieved sustained virological response (SVR) after hepatitis C treatment had higher HRQoL scores than patients without SVR. However, HRQoL did not correspond to liver histology or ALT level, suggesting that quality of life in people with HCV is related to other factors besides degree of liver damage. The researchers concluded that traditional outcome measures such as ALT changes "fail to capture the full spectrum of illness related to chronic HCV." They concluded that the SF-36 vitality scale (which includes six items) can be used to obtain a better picture of quality of life in people with hepatitis C. They estimated that a score difference of 4.2 points represents the minimum clinically significant difference in HRQoL, and recommended that this measure be used to assess the benefit of treatment in everyday clinical practice and clinical trials.

Liver Transplants in the News

Orthotopic liver transplantation (OLT) appears superior to the heterotopic liver transplant (HLT) procedure, according to a case-control study published in the April issue of *Liver Transplantation*. In an orthotopic transplant¾the most common type¾the old, dysfunctional liver is removed and replaced with a new donor liver. In a heterotopic transplant, a donor liver is inserted into the abdomen but the patient's old liver is also left in place. HLT is sometimes recommended in cases of fulminant liver failure, acute liver toxicity, and other conditions in which the patient's own original liver might be expected to regenerate. In this study, the first to compare long-term survival rates after the two procedures, S. de Rave and colleagues from Rotterdam compared 17 patients with chronic liver disease receiving heterotopic transplants at Erasmus Medical Center with 34 individuals who received standard orthotopic transplants. After adjusting for various potentially confounding factors, the researchers found that one-year patient survival rates were similar for the two techniques (29% for HLT vs 26% for OLT). However, the long-term rates of graft failure and death were higher for the

HLT patients. "[T]he long-term outcome of HLT was inferior," the researchers concluded. "HLT cannot be recommended as an alternative to OLT for any of the indications we studied."

In an attempt to increase the number of donor livers available for transplant, researchers have explored using livers that are considered suboptimal for one reason or another. According to an article in the March *Archives of Surgery*, transplant success is most influenced by three factors: donor age, the length of time the liver is left on ice between procurement and transplantation (cold ischemia time, or CIT), and how urgently the recipient needs a new liver. Derek Moore and colleagues performed a retrospective review of data from 483 adult patients who underwent orthotopic liver transplantation at Vanderbilt University Medical Center between January 1991 and July 2003. They found that donor age older than 60 years, CIT of 12 hours or more, and higher United Network for Organ Sharing (UNOS) urgency status independently predicted poorer graft and patient survival. Five-year graft survival rates were 72% with liver donors younger than 60 years compared with 35% for older donors. Graft survival was 71% with CIT of less than 12 hours vs 58% with more than 12 hours. Patients with UNOS scores of 2B or 3 had a graft survival rate of 71% vs 60% among those with scores of 1 or 2A. Combing these factors, the researchers estimated that a transplant from a young donor after less than 12 hours to a UNOS status 2B or 3 patient would have a 75% chance of survival after five years, compared with just a 20% probability for a graft from an elderly donor after 12 hours to a status 1 or 2A patient. Other factors, including donor obesity, donor/recipient sex mismatch, recipient age, and cause of liver disease, were not strongly linked to survival.

Finally, the April issue of *Journal of Hepatology* featured a special forum surveying the state of knowledge about hepatitis C and liver transplantation. Articles examine topics including living donor transplants, recurrent hepatitis C after transplantation, the usefulness of MELD scores in making decisions about liver allocation, and care for hepatitis C patients on the liver waiting list.

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