Statins May Reduce Hepatocellular Carcinoma Risk

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WASHINGTON — The use of statins may reduce the risk of hepatocellular carcinoma by half, according to the results of a case-control study of more than 6,500 U.S. veterans.

"Statin use may be associated with a 40%-50% risk reduction of HCC," said Dr. Hashem El-Serag, chief of gastroenterology and hepatology at Baylor College of Medicine in Houston, at the annual Digestive Disease Week.

Although there have been a number of experimental studies indicating a potential cancer-reducing effect for statins, there has been little epidemiologic evidence for a protective effect of statins against HCC.

Dr. El-Serag and his colleagues performed a nested, case-control study within a large cohort of Veterans Affairs patients who were newly diagnosed with diabetes between 1997 and 2002. Health records for these patients have been linked to the VA pharmacy benefits data. VA health records were also linked with Medicare records for patients 65 years and older.

Cases were defined as patients with incident HCC, identified by ICD-9 codes indicative of the disease. Control patients were identified among patients in the diabetes cohort, who did not have a diagnosis of HCC by the time of cancer diagnosis in a corresponding case.

Case patients were matched with four control patients based on age, gender, and incidence density, which allows for matching of the duration and timing of the potential exposure period between cases and controls. In all, 1,303 case patients with HCC were identified. They were matched with 5,212 control patients.

The main exposure was statin filled prescriptions prior to the index date (the date of HCC diagnosis) or the corresponding date for the control patients. All statins on the VA formulary were included. Simvastatin was the most commonly used during the study period.

The unadjusted odds ratio for the association of HCC and any statin was 0.45, and the adjusted odds ratio was 0.63.

"On average there's a 55% reduction in the risk among those prescribed statins compared to those without statins," said Dr. El-Serag, who is also gastrointestinal section chief at the Michael E. DeBakey VA Medical Center in Houston.

Duration of statin use did not appear to affect the reduction in HCC risk associated with statin use. The exclusion of statin use within 1 year of HCC diagnosis produced similar results. Likewise, the use of simvastatin alone does not appear to affect the association.

The researchers assessed confounding by presence of liver disease, because patients with liver disease are less likely to receive statins. Liver disease was broadly defined from codes indicative of mere elevation of liver function tests to those indicative of cirrhosis. However, no actual laboratory results were available from the database.

Patients with liver disease had an odds ratio for HCC of 0.53 and those without liver disease had an odds ratio of 0.63. "If you adjust for liver disease, the odds ratios lessen a little bit or the association is attenuated, but again you have approximately a 40% reduction in the risk," Dr. El-Serag said.

To assess confounding by indication, they also examined the association between HCC and nonstatin cholesterol-lowering medications and triglyceride-lowering medications. However, there were no significant associations between HCC and use of nonstatin cholesterol-lowering or triglyceride-lowering prescription drugs.

The researchers also performed a chart validation study to verify exposure and case-control status. To do this, they identified 9 case patients and 95 control patients who had visits to the local VA facility. "We found 100% agreement between the presence or absence of a filled statin prescription in the database as compared with the record," Dr. El-Serag said.

They also found a 100% negative predictive value, meaning that patients without an ICD-9 code for HCC were correctly identified as control patients. The positive predictive value was 89%, meaning that 89% of patients had HCC in their medical record.

Dr. El-Serag reported that the study was funded by a grant from the American College of Gastroenterology. ■