European studies on risks of hepatocellular carcinoma

October 21 2011

Among known risk factors for hepatocellular cancer, smoking, obesity, and heavy alcohol consumption, along with chronic hepatitis B and C infection, contribute to a large share of the disease burden in Europe, according to a cohort study published online October 21 in the *Journal of the National Cancer Institute.*

While a causal link between hepatitis B and C and hepatocellular cancer has been known for a few decades, tobacco smoking, obesity, and alcohol consumption are common risk factors, albeit with lower relative risks, that also contribute to the development of the disease. In fact, there were many more Europeans with hepatocellular cancer who were smokers than carriers of hepatitis virus infections. Previous studies have not explored the contribution of each risk factor.

To determine the contribution of each of these risk factors to hepatocellular carcinoma, Dimitrios Trichopoulos, Ph.D., of the Harvard School of Public Health, and colleagues, used data from the European Prospective Investigation into Cancer and Nutrition (EPIC) study, which was established to investigate the role of biological, dietary, lifestyle and environmental factors in the etiology of cancer and other diseases in several European countries. The researchers matched 115 patients with hepatocellular carcinoma to 229 control subjects.

The researchers found that 47.6% of the cases of hepatocellular carcinoma in the cohort were associated with smoking, 20.9% with hepatitis C, 16.1% with obesity, 13.2% with hepatitis B, and 10.2% with

heavy alcohol intake. They write, "We have shown that hepatocellular carcinoma, one of the most lethal human cancers, is largely amenable to primary prevention with existing knowledge and technology," noting that "although chronic infection with HBV and/or HCV was the strongest risk factor for hepatocellular carcinoma, tobacco smoking was responsible for more cases of hepatocellular carcinoma than either or both these viruses in the population."

In an accompanying editorial, Morris Sherman, M.D., and Josep M. Llovet, M.D., of the Mount Sinai School of Medicine write that this study's results are consistent with those from other epidemiological studies, but that the numbers need to be put into context.

Specifically, the editorialists caution against giving too much importance to smoking as a risk factor of hepatocellular carcinoma, since in this cohort, smoking was present in a large proportion of the population, thereby making the attributable risk more substantial than it might have otherwise been. If fact, they point out that no studies to date support the notion that smoking is a stand-alone risk factor for liver cancer. They also stress that the study does not explore combinations of risk factors in defining disease risk. Still, the data on smoking are noteworthy, they conclude. "We should be counseling our patients who have other risk factors for hepatocellular carcinoma to quit smoking. Of course, there are many other health reasons to stop smoking. Here is one more."

A second study on hepatocellular carcinoma in this issue of the Journal confirms the association between hepatitis B and hepatocellular carcinoma among a population cohort in Greenland. However, the study also finds that the Greenlanders studied have a relatively low incidence of hepatocellular carcinoma compared to those in other parts of the world, suggesting that a more benign course of Hepatitis B infection is prevalent in Greenland and accounts for the lower incidence of hepatocellular carcinoma there.

Marlene M. Børresen, M.D., Ph.D., of the Department of Epidemiology Research at Statens Serum Institut in Copenhagen, and colleagues, looked at a population of 8879 Greenlanders enrolled in populated-based serum surveys in 1987 and in 1998, who were followed until 2010. The researchers checked them for hepatitis B status, and found that those who were HBV positive had a much higher rate of hepatocellular carcinoma than those who were HBV negative. However, they also found that the incidence of hepatocellular carcinoma was much lower in Greenland than parts of the world that had a similarly high prevalence of hepatitis B.

The authors write that this finding could be attributable to a number of factors: for example, that the infection is transmitted typically during adolescence and adulthood, whereas infection during childhood carries a stronger risk for developing hepatocellular carcinoma; and that the strains of HBV that are associated with high risk of hepatocellular carcinoma are less common in Greenland than elsewhere. Furthermore, low smoking rates and alcohol consumption in Greenland may account for the lower rates of hepatocellular carcinoma, along with the relatively young age of the cohort studied (average age at recruitment was 33.4 years, with follow-up occurring in the mid-fifties.)

In an accompanying editorial, Morris Sherman, M.D., and Josep M. Llovet, M.D., of the Mount Sinai School of Medicine concur with the authors that genotype differences may in part account for the lower prevalence of hepatocellular carcinoma amongst those with HBV. The editorialists note that in Greenland, the D and B6 genotypes of HVB are most common, and that "the incidence of hepatocellular carcinoma in people infected by genotype B6 has not been documented." They add that viral load and infection by mutants of HBV are also risk factors of hepatocellular carcinoma that this study did not investigate.