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Reliable biomarkers needed for early detection of liver cancer

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While biomarkers are needed to complement ultrasound in the early detection of hepatocellular carcinoma (HCC; liver cancer), neither des-gamma-carboxy prothrombin (DCP) nor the most widely used biomarker, alpha fetoprotein (AFP), is optimal, according to a new study in *Gastroenterology*, the official journal of the American Gastroenterological Association (AGA) Institute.

"Most surprising was the finding that patient demographics influenced both des-gamma-carboxy prothrombin and alpha fetoprotein values, but in opposite directions," said Anna S. Lok, MD, AGAF, of the University of Michigan Medical Center and lead author of the study. "This observation merits further investigation, as it might impact the accuracy of these biomarkers in the detection of liver cancer."

The study was conducted in 10 centers in the U.S. and funded by the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health.

Among 1,031 patients randomized in the Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis Trial, a nested case-control study of 39 HCC cases (24 early stage) and 77 matched controls was conducted to compare the performance of AFP and DCP. Testing was performed on serial serum samples collected during a 12-month period prior to the time of HCC diagnosis. Study results indicated that:

- The sensitivity and specificity of DCP at month 0 (at the time of HCC diagnosis) was 74 percent and 86 percent at a cutoff of 40 mAU/mL, and 43 percent and 100 percent at a cutoff of 150 mAU/mL.

- The sensitivity and specificity of AFP at month 0 was 61 percent and 81 percent at a cutoff of 20 ng/mL, and 22 percent and 100 percent at a cutoff of 200 ng/mL.

- At month -12 (12 months before the diagnosis of HCC), the sensitivity and specificity at the low cutoff was 43 percent and 94 percent for DCP, and 47 percent and 75 percent for AFP.

- Combining both markers increased the sensitivity to 91 percent at month 0 and 73 percent at month -12, but the specificity decreased to 74 percent and 71 percent.

DCP was not superior to AFP in the early detection of HCC in patients with advanced hepatitis C and neither AFP alone, DCP alone, nor the combination of AFP and DCP was sufficiently accurate to be used for HCC surveillance. The combination of both markers enhanced the sensitivity, indicating that these two markers are complementary. Therefore, prospective studies should be conducted to determine if combining both markers will improve the detection of early HCC and to establish the optimal cutoff values that should be used for patient recall and further testing.

"Until better serum markers are available, ultrasonography remains the preferred tool for HCC surveillance. However, reliable biomarkers to complement ultrasound may improve the detection of early HCC in clinical practice where interpretation of ultrasound is variable," added Dr. Lok; in this study, diagnosis of early HCC was triggered by surveillance ultrasound in only 58 percent of patients.

Liver cancer is the sixth most common malignancy and the third most common cause of cancer-related death worldwide. The incidence of HCC in the U.S. is increasing and is largely attributed to hepatitis C. While the survival of patients with most malignancies has improved over the last decade, five-year survival of patients with HCC has remained less than 10 percent. The poor outcome of patients with HCC is related to late detection with more than two-thirds of patients diagnosed at advanced stages of disease. A major problem with HCC surveillance is the lack of reliable biomarkers. While AFP is the most widely used biomarker for HCC surveillance, experience with DCP is limited.

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