Studies of patients with cirrhosis uncover limitations in liver cancer screening

December 1 2011

Two studies available in the December issue of *Hepatology*, a journal of the American Association for the Study of Liver Diseases, have uncovered limitations in screening for primary liver cancer, also known as hepatocellular carcinoma (HCC). The first study found that, if given the choice during a clinical trial, most patients with cirrhosis prefer surveillance over the possibility of non-screening, therefore making a randomized study of HCC screening not feasible. A second study determined that ultrasonographic screening at three monthly versus six monthly intervals did not improve the detection of small liver cancers.

Medical evidence reports HCC to be the sixth most common cancer and the third most common cause of cancer death worldwide, with 90% of all cases in western countries attributed to chronic liver diseases, typically at the cirrhosis stage. The National Cancer Institute estimates that more than 26,000 cases and close to 20,000 deaths from liver and bile duct cancer occurred in the U.S. in 2011. Clinical guidelines recommend routine screening for HCC, but the efficacy and optimal intervals for testing are strongly debated by experts.

In the first study, researchers led by Professor Jacob George from the University of Sydney and Westmead Hospital in Australia, examined the feasibility of undertaking a randomized controlled trial of HCC surveillance in patients with cirrhosis. The screening program included ultrasonography every six months and alpha-fetoprotein testing every three months. Of the 205 participants with cirrhosis who received information outlining the risks and benefits of surveillance for liver

cancer, 99.5% declined randomization, with 88% electing for a non-randomized screening program.

"While a randomized controlled trial is ideal to assess the success of a cancer surveillance program, we found that patients with cirrhosis declined randomization due to possible allocation to a non-screening group," explains Professor George. "Since HCC screening in cirrhotic patients is routine practice for a majority of clinicians, it is impossible to assign patients to a genuine control group. However, further prospective studies that compare individual screening strategies are warranted." In a survey of 40 gastroenterologists of the Sydney Liver Group, the authors found that 74% routinely screen cirrhotic patients despite believing that screening did not increase patient survival (37%) or that the surveillance was cost-effective (66%).

One such liver cancer screening strategy was investigated by a team of French and Belgian researchers led by Professor Jean-Claude Trinchet with the Hôpital Jean Verdier in Bondy, France. The team conducted a multicentre trial with 1278 cirrhotic patients who received ultrasonographic screening at either three-month or six-month intervals. Their results indicated that cirrhosis resulted from excessive alcohol use in 39% of participants, 44% from hepatitis C virus (HCV), and 13% from hepatitis B virus (HBV). During the study period from July 2000 to July 2009, researchers detected at least one focal lesion in 28% of patients, but confirmed small HCC (less than 30 mm) in only 10% of participants.

Dr. Trinchet said, "Our study found that ultrasonographic surveillance performed every three months detects more small focal lesions than screening at six-month intervals. However, more frequent screening did not improve the detection of liver cancer at an earlier stage." The authors note that detection of small tumors were more likely missed in patients with HCV or who abuse alcohol and suggest the limitations of current

diagnostic procedures may explain their negative findings. Again, further investigations of screening methods and diagnostic procedures are needed to improve the outcomes in those at risk for developing liver cancer.

More information: "Feasibility of Conducting a Randomized Control Trial for Liver Cancer Screening: Is a Randomized Controlled Trial for Liver Cancer Screening Feasible or Still Needed?" H. Poustchi, GC Farrell, SI Strasser, AU Lee, GW McCaughan and J George. *Hepatology*; August 24, 2011.DOI: 10.1002/hep.24581

"Ultrasonographic Surveillance of Hepatocellular Carcinoma in Cirrhosis: A Randomized Trial Comparing 3- and 6-month Periodicities." Jean-Claude Trinchet, Cendrine Chaffaut, Valérie Bourcier, Françoise Degos, Jean Henrion, Hélène Fontaine, Dominique Roulot, Ariane Mallat, Sophie Hillaire, Paul Cales, Isabelle Ollivier, Jean-Pierre Vinel, Philippe Mathurin, Jean-Pierre Bronowicki, Valérie Vilgrain, Gisèle N'kontchou, Michel Beaugrand and Sylvie Chevret. *Hepatology*; September 6, 2011. DOI: 10.1002/hep.24545

Provided by Wiley