

Serum fibrosis markers correlate with liver fibrosis stage in patients with advanced chronic hep C

March 3 2008

A prospective study of patients with advanced chronic hepatitis C (CHC) revealed that a 3-variable model of serum fibrosis markers, including serum HA, TIMP-1 and platelet count, could identify cirrhosis with better accuracy than other published models. These findings are in the March issue of *Hepatology*, a journal published by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases (AASLD).

Liver biopsy is currently considered the best way to assess the stage and severity of chronic liver disease. However, it is limited by sampling error, understaging and variability in interpretation. Also, because of its risks, inconvenience and costs, it isn't practical to use to follow disease progression and treatment effects. As a result, researchers have been trying to develop less invasive tests that can accurately predict disease stage and fibrosis progression.

Researchers led by Robert Fontana of the University of Michigan Medical School examined a panel of serum fibrosis markers along with routine laboratory tests for their ability to estimate cirrhosis in a cohort of patients with advanced hepatitis C. They included 513 patients enrolled in the HALT-C trial, a prospective multi-center NIH study of extended peginterferon therapy for patients with hepatitis C and advanced fibrosis who were non-responders to prior antiviral therapy.

Fontana and his colleagues aimed to determine the utility of a panel of serum fibrosis markers including serum PIIINP, TIMP-1, HA, and YKL-40 in estimating initial disease stage in the subjects by comparing the markers with each patient's Ishak fibrosis score from liver biopsy. They also examined the relationship between the serum fibrosis markers and hepatic collagen content as measured by computerized morphometry.

“On univariate analysis, nearly all of the tested variables were independent predictors of cirrhosis,” the authors report. They then conducted multivariate analyses and created a model that included TIMP-1, log HA and platelet count. “The 3-variable model was significantly better than any of the individual serum fibrosis markers alone in estimating the presence of cirrhosis,” they write. The model had an area under the receiver operating curve of 0.81 and was better at predicting cirrhosis than other published models.

The model would have correctly categorized 153 HALT-C patients as having a low likelihood of cirrhosis with 86% accuracy. An additional 146 subjects would have been categorized as having a high likelihood of cirrhosis with 73 % accuracy.

The serum fibrosis markers also correlated with the collagen content of biopsy samples, however not as closely as they did with the Ishak fibrosis scores. This suggests that the serum fibrosis markers more closely reflect the pattern of fibrosis determined by standard light microscopy than the quantity of hepatic collagen determined by computerized morphometry.

The study was limited by the unique nature of the HALT-C patient population and by the fact that the models were not tested in an external validation cohort. Still, the researchers conclude, “on multivariate analysis, a 3-variable model consisting of TIMP-1, HA, and platelet

count distinguished patients with non-cirrhotic CHC from those with cirrhosis. Also, this new model performed significantly better than other models based on routine laboratory tests, suggesting that serum fibrosis markers provide useful, incremental information in estimating disease stage in CHC.”

Source: Wiley

Citation: Serum fibrosis markers correlate with liver fibrosis stage in patients with advanced chronic hep C (2008, March 3) retrieved 19 April 2024 from <https://medicalxpress.com/news/2008-03-serum-fibrosis-markers-liver-stage.html>

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