

Scoring Method Identifies Nonalcoholic Fatty Liver

BY MARY ANN MOON

Researchers have developed a simple scoring method to identify nonalcoholic fatty liver disease using easily available clinical and laboratory data, Dr. Anna Kotronen and her colleagues reported.

The authors also devised an equation containing the same variables as this NAFLD liver fat score that can be used to estimate a patient's individual liver fat content as a percentage.

"To our knowledge, the NAFLD liver fat score and equation are the first simple tools allowing prediction of NAFLD and liver fat in humans based on routinely available data," said Dr. Kotronen of the University of Helsinki and her associates (*Gastroenterology* 2009; June 12 [doi:10.1053/j.gastro.2009.06.005]).

The prevalence of NAFLD is estimated to be 20%-30% in the general population, and up to 75% among obese people. Liver function abnormalities are both insensitive and nonspecific markers of the disorder, and the best method for measuring liver fat content—proton magnetic resonance spectroscopy, or 1H-MRS—often is not available in general practice.

The investigators devised their scoring method by characterizing 313 subjects whose liver fat content had been measured using 1H-MRS, and identifying which variables independently predicted NAFLD. They then tested the validity of the method in another 157

subjects who also underwent 1H-MRS.

A total of 359 of the study subjects did not have diabetes, and 111 had type 2 diabetes but had no other known disease except obesity.

The variables of interest were presence of the metabolic syndrome; increased levels of fasting serum insulin, fasting plasma glucose, fasting serum aspartate aminotransferase (AST), and alanine aminotransferase (ALT); and a decreased AST/ALT ratio. The scoring method assigns numerical values to each of these variables and can be calculated online.

The resulting score, if higher than -0.640, predicted NAFLD with a sensitivity of 86% and a specificity of 71%. In the validation group, a cutoff score of -0.640 or higher predicted NAFLD with a sensitivity of 84% and a specificity of 69%.

The data also were used to create a liver fat equation to predict an individual patient's liver fat percentage.

When clinicians use this score to discover which patients with type 2 diabetes have NAFLD, they can better select antihyperglycemic drugs. For example, PPAR-gamma (peroxisome proliferator-activated receptor-gamma) agonists, also known as thiazolidinediones, are known to decrease liver fat content by approximately half, and they also significantly reduce hepatic inflammation, ballooning necrosis, and, possibly, fibrosis in patients who have nonalcoholic steatohepatitis.

No financial conflicts of interest were reported. ■

OTC Analgesics Unrelated to Decompensation in Cirrhosis

BY MARY ANN MOON

Over-the-counter analgesics may not contribute to acute liver decompensation or worsen existing decompensation in patients with cirrhosis, Dr. Sakib Karim Khalid and his colleagues reported.

These hepatotoxic agents—specifically, acetaminophen and NSAIDs such as aspirin, ibuprofen, naproxen, and sulindac—have been suspected of causing acute hepatic decompensation or of worsening the condition of an already decompensated patient with cirrhosis, but prospective data are lacking.

Dr. Khalid of Yale University, New Haven, Conn., and his associates performed a case-control study in which 91 consecutive cirrhosis patients hospitalized for acute hepatic decompensation were compared with two groups of control subjects to determine whether use of over-the-counter analgesics during the preceding 30 days could account for the decompensation.

The study was supported in part by Ortho-McNeil Pharmaceuticals Inc.

Acute hepatic decompensation was characterized by variceal hemorrhage, new or worsening ascites, encephalopathy, jaundice, spontaneous bacterial peritonitis, spontaneous bacteremia, or renal dysfunction, they said (*Clin. Gastroenterol. Hepatol.* 2009 Apr 24. [doi:10.1016/j.cgh.2009.04.015]).

One control group comprised 153 cir-

rhosis patients who were not hospitalized; the other comprised 89 patients without cirrhosis who were hospitalized for reasons unrelated to liver failure.

The researchers expected to find that patients with acute hepatic decompensation had taken more OTC analgesics than either control group, but "our results actually show that a lower proportion of patients with cirrhosis use OTC analgesics in general, and that an even lower proportion... had used them in the preceding month," they wrote.

Only 32 cirrhosis patients with acute liver failure (35%) reported using any OTC analgesics during the preceding 30 days, compared with 80 cirrhotic controls (52%) and 62 noncirrhotic controls (70%). In particular, acetaminophen "was used by only one-fifth of the cirrhotic cases," was used at daily doses that were equivalent to those used by cirrhotic control subjects, and was never used at a dose that exceeded the therapeutic dose of 4 g/day.

These results suggest that OTC analgesics "do not contribute to acute hepatic decompensation in cirrhosis," Dr. Khalid and his colleagues wrote.

Specifically, "acetaminophen at a maximal daily dose of 3 g/day (for up to 2 days) or at a daily dose of 1 g/day (for up to 25 days) does not appear to be associated with acute hepatic decompensation," they said.

No financial conflicts other than the study sponsorship were reported. ■

Breath Test Appears to Predict Liver Decompensation Risk

BY MICHELE G. SULLIVAN

CHICAGO — A noninvasive breath test that measures exhaled ¹³C-methacetin can accurately predict the risk of liver decompensation within up to 2 years.

With more confirmatory research, the test "could be used to give transplant priority to patients who are at risk of imminent decompensation, or to determine whether a cirrhotic patient has enough liver reserve to undergo a hepatic resection or other surgery," Dr. Gadi Lalazar said at a press briefing at the annual Digestive Disease Week.

Currently, the Model for End-Stage Liver Disease (MELD) and Child-Pugh scores are the best ways to evaluate hepatic reserve in patients with chronic liver disease, said Dr. Lalazar of Hebrew University-Hadassah Medical Center, Jerusalem. But the scoring systems aren't foolproof. "MELD's main predictive power is only for up to 90 days, and we often see patients with similar MELD scores and very different disease courses—some will decompensate and die and some will not."

The breath test is administered with a portable machine (Breath ID, manufactured by Exalenz Bioscience Ltd.). Patients fast for 8 hours before the test,

then drink 150 mL of water containing 75 mg of methacetin. They wear a nasal cannula while hooked to the machine, which continuously collects and analyzes their breath for 60 minutes.

Methacetin is metabolized solely by healthy hepatocytes, Dr. Lalazar said. He described the process in a paper published earlier this year (*World J. Gastro.* 2009;15:966-72).

Preliminary studies found that the test reliably distinguished between early cirrhotic and noncirrhotic patients with 95% sensitivity and 97% specificity.

Dr. Lalazar and his colleagues examined the test's ability to predict death from liver failure over a 2-year period in a cohort of 575 patients with chronic liver disease. The patients' mean age was 48 years; 209 of them had cirrhosis. The mean MELD score at baseline was 9. Most of the group (67%) had

hepatitis C infection. Patients were divided into risk groups according to their breath test results: low risk (342 patients), moderate risk (135), and high risk (98).

There were 25 deaths in the entire cohort over the 2-year follow-up period. When analyzed by the breath test risk levels, most of the deaths occurred in the high-risk group (15% of that group). Deaths occurred in 6% of the moderate-risk group and in 1% of the low-risk group. The relationship of death to risk group was consistent at every time point in the study. (See chart.)

The investigators then examined the

rate of death in the subgroup of cirrhotic patients. The breath test identified 42 patients as low risk, 83 patients as moderate risk, and 84 as having a high risk. At 2 years, there was 1 death in the low-risk group, 7 in the moderate-risk group, and 14 in the high-risk group.

The machine is now being analyzed in a phase III U.S. trial for the detection of cirrhosis in patients with chronic liver disease (clinicaltrials.gov identification number NCT00736840).

Dr. Lalazar said he had no financial interest in the company or any other potential conflict regarding the study. ■

Chronic Liver Disease Patients Stratified by Breath Test

Overall survival (n = 575)

Risk group	3 months	6 months	12 months	18 months	24 months
Low	100%	100%	100%	99%	99%
Moderate	98%	98%	96%	90%	90%
High	96%	91%	79%	79%	73%

Survival among cirrhosis patients (n = 209)

Low	100%	97%	97%	97%	97%
Moderate	97%	97%	89%	85%	85%
High	95%	91%	78%	78%	70%

Source: Dr. Lalazar