

## Abnormal Liver Function Tests and Metabolic Syndrome— Is Fatty Liver Related to Risks for Atherosclerosis beyond Obesity?

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**Key words:** fatty liver, metabolic syndrome

(*Inter Med* 48: 1573-1574, 2009)

(DOI: 10.2169/internalmedicine.48.2517)

Oda and colleagues (1) reported that elevated liver enzymes, such as alanine aminotransferase (ALT) and gamma-glutamyltransferase (GGT), are related to metabolic syndrome (MetS) in Japanese men and women. One of the main causes of abnormal liver function is fatty liver disease. Recently, it was reported that non-alcoholic fatty liver disease (NAFLD) is related to cardiovascular disease (CVD) (2-5) and to most cardiovascular risk factors, including diabetes, hypertension, hyperlipidemia, and MetS (2, 5-7). Some of the suggested biological mechanisms linking NAFLD and accelerated atherosclerosis are insulin resistance, oxidative stress, inflammation, adiponectin and other adipocytokines, and abnormal lipoprotein metabolism (8, 9).

Insulin resistance and visceral adipose tissue are the two major risk factors underlying MetS, and play a pivotal role in the development of NAFLD and atherosclerosis. These confounding factors should be considered when evaluating the relationships among NAFLD, MetS, and atherosclerosis. Some prospective studies showed that increases in liver function parameters, such as GGT (2, 3) and ALT (4), are associated with the incidence of CVD events, even after adjusting for body mass index (BMI) and other components of MetS. In contrast, in an 11-year follow-up of Australians, Adams et al (6) showed that the presence of NAFLD did not increase the risk of MetS after adjusting for baseline waist circumference and other components of MetS. McKimmie et al (10) evaluated the association between hepatic steatosis and carotid atherosclerosis in the Diabetic Heart Study, and suggested that hepatic steatosis is unlikely a direct mediator of CVD. In other epidemiological studies that evaluated the association between NAFLD and MetS or

CVD, the role of obesity was not evaluated fully, although most of those with NAFLD or elevated liver enzymes tended to have higher BMIs or waist circumferences (1, 5, 7). There is insufficient epidemiological evidence in clinical practice to determine whether NAFLD is related to MetS and CVD directly, beyond obesity and insulin resistance.

In Western countries, the prevalence of NAFLD is between 24 and 42% (11, 12), and NAFLD is widely reported to be the most common chronic liver condition. In Asian countries, NAFLD is assumed to be less common. However, the reported prevalence of NAFLD in Asian populations ranges from 5-40% and the increase in NAFLD is also an important problem in Asia (13). Recently, a prospective study in China showed that NAFLD was closely associated with the onset of metabolic disorders, even among non-obese subjects (14). Subsequently, data from lean NAFLD patients in Asia would provide insight into whether NAFLD increases the risk of MetS or CVD beyond obesity.

Patients with NAFLD are at higher risk for MetS and CVD, and thus should be monitored intensively to reduce the risk factors for atherosclerosis. However, further epidemiological studies are needed to evaluate whether the presence of NAFLD or elevated liver enzymes should be dealt with as a component of MetS, as is the case with other classical CVD risk factors.

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Received for publication May 27, 2009; Accepted for publication June 2, 2009

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