COMMENTS AND RESPONSES

Prevalence of Nonalcoholic Fatty Liver Disease and Its Association With Cardiovascular Disease Among Type 2 Diabetic Patients

Response to Schindhelm, Heine, and Diamant

We appreciate the comments by Schindhelm et al. (1) regarding our recent article reporting the prevalence of nonalcoholic fatty liver disease (NAFLD) and its association with cardiovascular disease (CVD) in a type 2 diabetic population (2). In that study, we found that NAFLD is extremely common in type 2 diabetes and is associated with a higher frequency of manifest CVD. The prevalence of NAFLD was 69.5% among participants, and NAFLD was the most common cause (81.5%) of hepatic steatosis on ultrasound. In contrast, the frequency of hepatic steatosis likely due to other nonalcoholic secondary causes (e.g., medications or viral hepatitis) was low (~3%).

In that study, serum alanine aminotransferase (ALT) concentrations (odds ratio 1.46 [95% CI 1.2–2.5]) and other liver enzymes were found to be significantly associated with prevalent CVD in univariate regression analysis (data not shown in the article). These associations were only slightly attenuated after adjustment for sex, age, smoking, diabetes duration, A1C, and LDL cholesterol. However, none of the liver enzymes were independently associated with prevalent CVD after further adjustment for the metabolic syndrome and/or ultrasound-diagnosed NAFLD.

Although the ALT determination may be of limited use in clinical settings because of its low specificity and sensitivity (especially in type 2 diabetic patients, as confirmed in our study, where ~85% of our patients with diagnosed NAFLD had serum ALT levels within the referenge range), we agree with the clinical suggestion that even mild elevations of ALT or other liver enzymes, in combination with clinical features suggestive of the metabolic syndrome (overweight/obesity, high triglycerides, low HDL cholesterol, and hypertension), should prompt the clinicians to initiate further diagnostic work-up for detecting the presence or absence of NAFLD in patients without type 2 diabetes. Conversely, as most type 2 diabetic patients are likely to have a form of NAFLD and as previous studies have shown that type 2 diabetes is a strong predictor of progressive NAFLD (3), we believe that an ultrasound examination of the liver is mandatory in this high-risk population and that consideration should also be given to referring most patients with type 2 diabetes to a hepatologist for further evaluation and treatment. This will be particularly important once an effective treatment for nonalcoholic steatohepatitis has been established and better noninvasive methods for assessing disease severity validated.

There is now growing evidence suggesting that the identification of NAFLD may help in CVD risk prediction (2,4–6). Patients diagnosed with NAFLD should be treated on many levels; they should be candidates not only for treatment of their liver disease but also for treatment of underlying CVD risk factors (including also insulin resistance, which plays a key role in NAFLD pathogenesis), as many patients with NAFLD will have major CVD events and die of CVD before the development of liver disease.

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