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Reply

Microalbuminuria and nonalcoholic fatty liver disease

To the Editor:

We appreciate the comments about our work, which investigated the relationship between microalbuminuria and the severity of liver histopathology in a sample of nondiabetic patients with nonalcoholic fatty liver disease (NAFLD). An important finding of our cross-sectional study was the independent association between microalbuminuria and higher fibrosis scores after adjustment for age, sex, and homeostasis model assessment of insulin resistance values.

First, the authors suspected that prediabetes could have confounded the observed relationship. Of the 87 patients with NAFLD in our study, 25 were found to have prediabetes according to the results of the oral glucose tolerance test. Of the 25 NAFLD patients with prediabetes, 2 (8%) were found to have microalbuminuria. In contrast, microalbuminuria was found in 12 (19.3%) of the 62 NAFLD patients with normoglycemia. This difference did not reach statistical significance according to the Fisher exact test ($P = .33$). The results of this analysis indicated that prediabetes was evenly distributed according to the levels of microalbuminuria and was unlikely to influence the main conclusions. Second, it was argued that the association between microalbuminuria and liver fibrosis could have been confounded by hypertension, dyslipidemia, and other components of the metabolic syndrome. To address these concerns, we have performed a forward stepwise regression analysis with liver fibrosis scores as the dependent variable and age, sex, body mass index, waist circumference, systolic blood pressure, diastolic blood pressure, triglycerides, high-density lipoprotein cholesterol, aspartate aminotransferase, alanine aminotransferase, homeostasis model assessment of insulin resistance, ferritin, and microalbuminuria (as a continuous variable) as predictors. Of note, results showed that microalbuminuria was the only independent predictor of the fibrosis score ($\beta = .29$, $P < .05$) even when all these variables were forced into the model. These results clearly indicate that our findings were not confounded by other potential metabolic factors. In our study, 32 patients (36.8%) with NAFLD had the metabolic syndrome. Again, the association between microalbuminuria and liver fibrosis did not change when the model was adjusted for age, sex, and the metabolic syndrome ($\beta = .27$, $P < .05$). Finally, the authors argued that all abnormal urinary albumin excretion test results should be confirmed in 2 of 3 samples collected over a 3- to 6-month period because of the known day-to-day variability. Although controversy still exists regarding the type of urine specimen to be used to evaluate microalbuminuria, we acknowledge that the lack of confirmation of microalbuminuria over a 3- to 6-month period may be a potential caveat of our study. However, as the authors themselves state, assessment of albumin excretion rate in timed urine collections (24 hours or overnight) is clinically valuable and remains the most direct measure of urinary albumin excretion. Taken together, the additional analyses clearly confirm that microalbuminuria is an independent predictor of liver fibrosis scores in our patients with NAFLD even after allowance for the construct of metabolic risk factor clustering.

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