Alanine Aminotransferase Is Associated With Metabolic Syndrome Independently of Insulin Resistance

To the Editor:

Yun et al in an elegant study showed (in 28,456 subjects who visited Health Promotion Centres in Korea) that serum alanine aminotransferase (ALT) activity was significantly associated with metabolic syndrome (MetS) independently of insulin resistance (IR).¹ Some comments may be of interest.

Others^{2,3} have not confirmed that the relationship between serum ALT activity and MetS is independent of IR. Zhang et al concluded that liver enzymes, especially ALT, were significantly associated with IR (by clamp assessment) and that individual liver enzymes may have different relationships with the components of MetS.⁴ These discrepancies with the results of Yun et al may relate to differences in population characteristics (including ethnicity) and methods used to assess IR. However, the other studies²⁻⁴ were not powered by as large a number of participants as in the Yun et al study.

The findings of Yun et al provide a link between serum ALT activity and vascular risk (as represented by MetS). Indeed, there is evidence that abnormal liver function tests (LFTs) are associated with a greater risk of vascular events.⁵ We recently showed that in patients with coronary heart disease (CHD), those with abnormal LFTs had a greater risk of vascular events and a greater benefit from treatment with statins when compared with those who had normal LFTs.⁵ The results from Yun et al also suggest an indirect link between serum ALT activity and the risk of developing type 2 diabetes (as represented by MetS). For example, γ -glutamyl-transferase (GGT) and ALT were associated with incident diabetes in another study⁶ in which GGT was the strongest predictor of diabetes after fasting hyperglycemia. This latter finding leads us to enquire if Yun et al considered relationships with LFTs other than ALT.

Another interesting association has been suggested between MetS, ALT activity and serum uric acid (SUA) levels. A higher SUA level was associated with greater mean serum ALT and GGT activities in a study based on the first National Health and Nutrition Examination Survey (NHANES I).⁷ We also reported significant correlations between SUA and ALT ($r=0.21$, $P=0.002$), as well as between SUA and GGT ($r=0.39$, $P<0.001$), in patients ($n=437$) with CHD and slightly abnormal LFTs.⁸ In contrast, no significant associations between SUA levels and LFTs were observed in those patients with normal LFTs ($n=1,163$).⁸ These findings lead us to ask if Yun et al had access to SUA levels.

It is crucial to better understand the links between ALT activity (as well as that of other LFTs) and vascular risk.

There is also a need to establish if normalizing LFTs (possible surrogate markers for non-alcoholic fatty liver disease) is associated with a clinically relevant vascular risk reduction.⁹

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