Low Plasma Adiponectin Levels Are Associated With Increased Hepatic Lipase Activity In Vivo

Response to Schneider et al.

Recently, close attention has been given to the relationships between plasma adiponectin levels and lipolytic enzymes such as hepatic lipase and lipoprotein lipase activities in an effort to understand the possible mechanism of hyperlipidemia in low adiponectin. The cross-sectional study by Schneider et al. (1) has concluded that postheparin plasma hepatic lipase activity inversely associated with plasma adiponectin levels, independent of insulin resistance represented by homeostasis model assessment of insulin resistance and inflammation. In a separate issue of Diabetes Care, the same group also concluded that postheparin plasma lipoprotein lipase activity is positively associated with plasma adiponectin levels, independent of insulin resistance and inflammation (2). We believe they have overgeneralized in terms of populations and race regarding the independence of the observed associations. In fact, in our study of Japanese hyperlipidemic men, we also found that postheparin plasma hepatic lipase activity is inversely and lipoprotein lipase activity positively associated with plasma adiponectin levels in univariate analysis, which is quite similar to their findings up to this point. However, in our study these associations did not persist after adjustment for age, BMI, and homeostasis model assessment of insulin resistance (3). Although we recognize that the sample size of our study subjects was smaller than theirs, the possible factors contributing to this inconsistency could be due to the different genetic background between Western and Japanese populations. Plus their study subjects had much higher BMI and fasting insulin levels in either non-diabetic or diabetic subjects than ours. We presume that their findings on the independence of the association of hepatic lipase or lipoprotein lipase activities to plasma adiponectin from insulin resistance and inflammation may be limited to certain populations. Further studies are needed to clarify this point in other populations.

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Response to Kobayashi et al.

We thank Kobayashi et al. (1) for their interest in our work on the relationship between adiponectin and human plasma lipases (2,3). These authors raise the question of whether differences in genetic background, BMI, or insulin levels of the studied populations could help to explain the differences with regard to statistical significance between their and our results. Although we exclusively studied Caucasian subjects, other authors have recently reported an independent influence of adiponectin on hepatic lipase activity in Chinese and African-American populations (4,5). Therefore, the genetic background does not appear to play a major role in the association of adiponectin and hepatic lipase. However, we cannot rule out that the association may be different in a Japanese population. This could be due to the fact that the T-allele frequency of the functional −514C/T polymorphism in the hepatic lipase promoter has been reported to be much higher in Japanese than in Caucasian subjects (6). In
addition, population-based studies do not as yet consider factors such as adiponectin’s oligomer composition and possible resistance to its action, which may contribute to variances of the results among different subject cohorts. The association between adiponectin and lipoprotein lipase activity still awaits further clarification in populations other than Caucasians.

We performed additional analyses of our data regarding a potential influence of BMI and/or insulin levels on the association of adiponectin and hepatic lipase. When we divided the patients into groups below or above the median BMI and insulin levels, respectively, we observed no significant difference with regard to the association of adiponectin with hepatic lipase (nondiabetic male coronary artery disease subjects: BMI $\geq 27.4$ kg/m$^2$, $n = 115$, $r = -0.29$, $P < 0.01$; BMI $< 27.4$ kg/m$^2$, $n = 91$, $r = -0.28$, $P < 0.01$; insulin $< 21$ µU/ml, $n = 131$, $r = -0.36$, $P < 0.01$; insulin $> 21$ µU/ml, $n = 75$, $r = -0.2$, $P = 0.1$; similar results were seen in the diabetic subjects). Therefore, differences in BMI and insulin levels between the studied populations are unlikely to be the cause of divergent results. We believe that the difference in statistical significance of the results of our studies and that of Kobayashi et al. (7) is likely due to the larger sample size in our studies.

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