Lipid Factors as Predictors of Coronary Disease

To the Editor:

We read the report by Levine et al. (1) demonstrating that plasma lipoprotein(a) (Lp(a)) concentrations are inversely correlated to triglyceride concentrations in patients undergoing coronaryography. In a recent study, we measured Lp(a) concentrations in the plasma of 280 patients (229 men, 61 women), ages 31 to 66 years and hospitalized in Cardiology for bypass surgery. We used the Laurell (2) electroimmunodiffusion technique (standard serum, and polyclonal anti-Lp(a) antibody from ImmunoFrance). We performed in parallel enzymatic assays of total cholesterol and triglycerides (CHOD-PAP and GPO-PAP methods, both from Boehringer Mannheim, Mannheim, Germany), and an immunonephelometric assay of apolipoproteins (apo) A-I and B (protocol and reagents from Behring, Marburg, Germany). Severity of coronary atheroma was determined by coronaryographic analysis according to an extent score proposed by Moise et al. (3). Table 1 lists the results of univariate correlation between Lp(a), other lipids, and lipoproteins and coronary lesion score. Because Lp(a) was not normally distributed, we performed logarithmic transformation of this variable. A significant correlation appeared between Lp(a) and age, cholesterol, and apo B, as well as between extent score, age, cholesterol, and apo B. No correlation appeared between plasma Lp(a) and triglyceride concentrations, nor between the severity of coronary disease and triglyceride concentration.

The triglyceride titration technique was the same in both studies. Only the Lp(a) measurement technique was different, Levine et al. using an immunoturbidimetric assay. However, Lp(a) has several isoforms and this variation in particle size may influence the concentration results in such a technique.

We therefore think that as long as the measurement method is not independent of the molecule size variation, no biological relationship can be assumed.

References

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The authors of the report in question respond:

To the Editor:

Ruelland et al. question whether immunoturbidimetry can recover lipoprotein(a) (Lp(a)) polymorphs equivalently, yet they provide no data demonstrating equivalent recovery of polymorphs by electroimmunoassay (EIA). The authors are apparently assuming that molecular size polymorphism is a problem only for assays based on light scattering. The failure of an ELISA method (Immuno, Heidelberg, Germany) to recover Lp(a) morphs equivalently was recently reported at the Second International Conference on Lp(a) (1). Albers and Marcovina reported the same problem with an ELISA assay utilizing apolipoprotein B detection (2). These studies suggest that this is not a method-specific problem.

There are at least two reasons why a particular immunonassay system may not be able to recover the polymorphic forms of Lp(a). The first is that the different polymorphs differ in the number and kind of epitopes. The second is that the fraction of Lp(a) associated with triglyceride-rich lipoproteins (e.g., very-low-density lipoprotein, ~25.0–75.0 nm diameter) vs cholesterol-rich low-density lipoprotein (~17.0–26.0 nm) varies between subjects. Ruelland et al. also failed to take into account the fact that the distribution of Lp(a) polymorphisms and plasma values varies among ethnic groups. It is unlikely that the ethnic mix of our population in New York City matched the of theirs in Rennes. This may account, in part, for the lack of a relationship between triglycerides and Lp(a) in their population.

The interference of triglycerides with each assay method for Lp(a) must be determined. Walek et al. (3) demonstrated that triglyceride-rich particles in hypertriglyceridemic samples (triglycerides >4.00 g/L) interfere with Lp(a) determination by radial immunodiffusion (RID), EIA, and ELISA. Ruelland et al. have not addressed interference by triglycerides in their method, nor have they indicated the triglyceride distribution range in their patient population. They have also not indicated whether their patients were fasting; this is an important consideration for studies relating triglycerides to disease.

We have previously published data showing no interference by triglycerides up to 4.36 g/L in the immunoturbidimetric assay (4). Only one sample in our study was higher (4.70 g/L). Finally, Ruelland et al. are apparently unaware of three other reports.