Risk of Primary and Recurrent Acute Myocardial Infarction From Lipoprotein(a)—I

Numerous studies in newborns, infants, children, adults, parents and grandparents have conclusively demonstrated that serum levels of lipoprotein(a) [Lp(a)] are largely genetically determined, with full expression of the Lp(a) gene in the first year of life. Serum levels of Lp(a) increase twofold between the first week and 8.5 months of age to reach stable, life-long levels (1). Lp(a) levels at 8.5 months of age are not different from parental values and are closely correlated with that of the affected parent (1). Lp(a) levels in children 8 to 12 years old are highly correlated with premature coronary artery disease (CAD) and "coronary history score" in grandparents (2). Parents of male children with Lp(a) levels >25 mg/dl have a 2.5-fold higher incidence of myocardial infarction (MI) (3). I therefore disagree with the conclusion of Kinley et al. (4) from the Australian Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) study that elevated serum levels of Lp(a) may be the effect of advanced atherosclerosis and MI rather than the cause. The results from two other MONICA centers appear to provide insights into the paradoxically higher Lp(a) levels in patients without than with recurrent MI. In the Scottish MONICA study (5), compared with age-matched men, the fatality rates for MI in women were 14% higher after admission to the hospital and 22% higher after admission to coronary care, yet the case fatality rates at 28 days were identical (men 49.8%; women 49.6%). Women had more shock and syncope and had a worse prognosis in the hospital only because an equivalent number of men had died suddenly before reaching the hospital. Prehospital death accounted for 74% of deaths in men compared with only 65% in women (5). The New Zealand MONICA study (6) also had similar results, with identical 28-day case fatality rates in both men and women. The higher case fatality rate after hospital admission was compensated by a lower prehospital CAD case fatality in women. A higher rate of death after MI in patients with high levels of Lp(a) is highly plausible, as discussed later.

In a study (7) of 79 Swedish men who survived an MI before the age of 45, reinfarction occurred within 3 years in 16 and was fatal in 9 (56%). Lp(a) levels were highly correlated with the coronary stenosis score as well as the recurrence of MI. Mean Lp(a) levels were twofold higher in patients without and fourfold higher in those with recurrent MI than in the control population. In a British study of 266 patients followed up for 965 days after an acute MI, elevated levels of Lp(a) were an independent risk factor for cardiac mortality, with a relative risk of 2.16 on multivariant analysis (8). Those patients with Lp(a) levels >30 mg/dl had a significantly higher cardiac mortality rate (29.8% vs. 18.6%, p = 0.05) than those with Lp(a) levels <30 mg/dl.

Patients with higher levels of Lp(a) in the present study (4) indeed had advanced coronary atherosclerosis disease, a powerful prognostic factor for cardiac morbidity and mortality, including out of hospital deaths (9). Others (10,11) have also reported significant correlation of Lp(a) levels with the extent, severity and rapid angiographic progression of CAD (12), all of which are highly predictive of the development of clinical coronary events and mortality after an MI (13). Thus, the exclusion of patients who died outside the hospital in the study by Kinley et al. (4) may have biased their results and conclusions.

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Risk of Primary and Recurrent Acute Myocardial Infarction From Lipoprotein(a)—II

Kinlay et al. (1) have shown, as have others, that a high lipoprotein(a) [Lp(a)] concentration is a significant but weak predictor of myocardial infarction risk. In contrast, in a recent prospective cross-sectional study

Table 1. Independent Predictors ($p < 0.01$) of Coronary Artery Disease Score in White or Indo-Asian Patients Ranked in Order of Explanatory Value (contribution to cumulative adjusted r^2)*

Metabolic Variable	Cumulative r^2 Value
White patients (n = 102)	
Lp(a)	0.24
Fasting insulin	0.38
Total cholesterol	0.45
Triglycerides	0.50
Indo-Asian patients (n = 102)	
Lp(a)	0.21
Total cholesterol	0.35
Fasting insulin	0.41
HDL cholesterol	0.45

*Data from Shaukat et al. (2). HDL = high density lipoprotein; Lp(a) = lipoprotein(a).