Increased Lipoprotein (a) and familial hypercholesterolemia: a dangerous combination. Data from a 12-year follow-up study

I. Andrikou1, K. Grigoriou1, I. Dima1, I. Skoumas1, K. Tsioufis1, C. Vlachopoulos1

1Hippokration General Hospital, Athens Medical School, Athens, Greece

Funding Acknowledgements: None.

Background: Lipoprotein (a) [Lp(a)] is a molecule characterized by very increased atherogenicity. Mounting evidence support the causal link between high Lp(a) concentration and atherosclerotic cardiovascular (CV) disease in the general population.

Purpose: The role of Lp (a) in specific categories of patients at high CV risk, such as patients with familial hypercholesterolaemia (FH), is also of special importance. The aim of our study was to investigate the prognostic role of Lp (a) regarding major adverse CV outcomes in subjects with heterozygous FH.

Methods: 155 patients from the outpatient lipid clinic of our hospital (56 males, mean age 41.2 ± 14.2 years, 26% smokers, 16% with diabetes mellitus), without history of CV disease, who fulfilled the FH criteria participated in the study. Participants were evaluated for a mean follow-up period of 12.4 ± 7.1 years with at least one annual visit. Venous blood samples were obtained at baseline in all patients for the determination of plasma glucose, lipid profile and levels of Lp(a). All subjects were on lipid-lowering medication during the follow-up period. The endpoint of our study was the composite of major CV events (coronary artery disease events and stroke).

Results: The incidence of the composite endpoint of major CV events during the follow-up period was 9% (n=14). In the total population, the mean baseline Lp (a) levels were 34.9 ± 33.7 mg/dl, while 42% had increased Lp (a) levels ≥ 30 mg/dl. The group of FH patients with new-onset CV disease had higher levels of Lp(a) at baseline compared to those without new-onset CV disease (48.1 ± 37.3 vs 33.6 ± 33.1 mg/dl, p=0.01). Also, those with new-onset CV disease had higher percentage of increased Lp(a) levels (≥ 30 mg/dl) at baseline compared to those without development of CV disease (71% vs 39%, p=0.02). Multiple Cox regression analysis revealed that during the follow-up period independent predictors of major adverse CV events were: increased baseline Lp(a) levels (≥ 30 mg/dl) (HR 5.61, 95% CI 1.51-10.92, p=0.01), male sex (HR 8.11, 95% CI 2.02-12.48, p<0.01), baseline low-density cholesterol levels (HR 1.01, 95% CI 1.00-1.02, p=0.04) and the presence of hypertension at baseline (HR 3.59, 95% CI 1.03-12.49, p=0.04), after adjustment for confounding factors.

Conclusions: In patients with FH, increased baseline Lp(a) is an independent predictor of adverse CV events, after a 12-year follow-up period. FH patients with Lp (a) levels ≥ 30 mg/dl have an almost 5-fold greater CV risk compared to those with lower Lp (a) levels. It seems that Lp (a) reclassifies the already increased CV risk of FH subjects into an even higher level.