Paradoxical association between lipid levels and incident atrial fibrillation according to statin usage

H.J. Ahn¹, S.R. Lee¹, E.K. Choi¹, S.W. Lee², K.D. Han³, S. Kwon¹, S. Oh¹, L.I.P. Gregory⁴

¹Seoul National University Hospital, Seoul, Korea (Republic of); ²Department of Medical Statistics, College of Medicine, Catholic University, Seoul, Korea (Republic of); ³Department of Statistics and Actuarial Science, Soongsil University, Seoul, Korea (Republic of); ⁴University of Liverpool, Liverpool Centre for Cardiovascular Science, Liverpool, United Kingdom

Funding Acknowledgement: Type of funding sources: None.

Background: In epidemiology studies, a higher level of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) is associated with a lower risk of atrial fibrillation (AF). Statin use might exert possible confounding effects in the paradoxical relationship; however, the inverse link between AF and cholesterol level that distinguishes statin users from non-users has not been evaluated.

Objective: We investigated the epidemiological relationships of TC–AF and LDL-C–AF in statin users and non-users, respectively.

Methods: From the Korean National Health Insurance Service database, we included 9,778,014 adults who underwent a health examination in 2009 and had no prior AF history. The levels of TC and LDL-C at the health exam were categorized in quartile (Q) and decile (D) values of the total study population. The study population was grouped into statin users and non-users, and TC–AF and LDL-C–AF relationships were evaluated.

Results: 867,336 (8.9%) were on statin use among the total population. Statin users showed higher TC level (208.4±55.6 vs. 194.1±39.5 mg/dL, \( p < 0.001 \)) and LDL-C level (123.0±102.2 vs. 121.3±226.3, \( p < 0.001 \)) compared to non-users. Inverse associations of TC–AF and LDL-C–AF were observed; higher levels of TC and LDL-C were associated with a lower risk of AF. The hazard ratios (HR) and 95% confidence intervals (CI) were 0.797 (0.786–0.809) for the highest quartile of TC (Q₄, TC ≥ 218) and 0.832 (0.82–0.843) for the highest quartile of LDL-C (Q₄, LDL-C ≥ 135) when adjusted by age, sex, lifestyle behaviors, comorbidities, and low-income status. Statin users exhibited higher AF incidence rate than non-statin users, but the association in statin users generally tracked that seen among non-statin users demonstrating similar HR in Q₄ of TC [0.812 (0.790–0.835)] for statin users and 0.812 (0.798–0.826) for non-statin users] and LDL-C [0.842 (0.819–0.865) for statin users and 0.849 (0.835–0.863) for non-statin users].

Conclusion: The paradoxical relationship between lipid levels (TC and LDL-C) and incident AF remained consistent both in statin users and non-users. Further research is required to investigate an underlying mechanism for the cholesterol paradox of AF which still seems evident despite the pleiotropic effects of statin.