We appreciated hearing from Feminò et al regarding our recently published paper on the association between lipid profile and risk of atrial fibrillation (AF) in the Niigata Preventive Medicine Study.1 It has been suggested that high cholesterol levels are associated with a low risk of AF,2,3 and recent findings in our1 and other studies4 that decreased levels of total cholesterol and low-density lipoprotein (LDL) cholesterol were associated with the increased risk of AF further support the hypothesis. However, the mechanism underlying the inverse association of cholesterol levels with the risk of AF is unclear and difficult to explain. In the editorial accompanying our paper, 3 mechanisms were suggested: age, thyroid dysfunction, and inflammation.5 Furthermore, because the role of chronic infection, which is one of the most frequent events associated with an inflammatory process, has been suggested in the pathogenesis of AF,6,7 Feminò et al have indicated that chronic infection may decrease the cholesterol levels and thus increase the risk of AF. In fact, herpes simplex virus infection has been associated with increased risk of developing AF,8 but neither Helicobacter pylori nor Chlamydia pneumoniae has been associated with the prevalence of AF, although elevated levels of C-reactive protein were associated with AF in the same cohort.9

In our study, the association of LDL cholesterol level with the risk of AF was relatively weak compared with that of the HDL cholesterol level and was not significant in subgroups, suggesting that LDL cholesterol is not a central player in the pathogenesis of AF. However, AF is a heterogeneous disorder and thus there is still a possibility that LDL cholesterol has a role to play. Actually, although randomized trials and a meta-analysis have failed to show the effects of lipid-lowering therapy on prevention of AF,10,11 statin therapy was effective in patients with elevated levels of high-sensitivity C-reactive protein, but not of LDL cholesterol, in a recent randomized study.12 To elucidate the mechanism of the cholesterol paradox in AF, further studies including appropriate populations are needed.

References

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