To the Editor:

The “cholesterol paradox” in atrial fibrillation (AF) has previously been reported by several studies and confirmed in a large cohort of Japanese patients with low HDL-C, LDL-C and total cholesterol (TC) levels. In the USA also, higher levels of LDL-C and TC were recently associated with a lower incidence of AF. We appreciate, particularly, in the Editorial by Suzuki, his analysis and opinion about the pathogenesis of AF: “it would be likely that there remains the possibility that a low level of LDL-C or low TC is linked to increasing AF via the pathogenesis of enhanced inflammation”.

We believe that high levels of TC, LDL-C and HDL-C in many chronic diseases, including asthma and cardiovascular diseases, represent a protective response to microbial burden, when lipoproteins can’t bind efficiently circulating endotoxins, thus neutralizing the inflammatory effects.

Low levels of lipoproteins, particularly apolipoprotein E (ApoE), are not enough to modulate the high levels of bacterial endotoxins, and thus inflammatory potential, in migraine and ischemic events also, which occur more frequently in women.

Thus, the “cholesterol paradox in AF” could indicate a chronic inflammatory status induced by a high level of circulating endotoxins and low levels of lipoproteins. This opinion, given that age and male sex are strongly associated with AF, is in agreement with results from the Japanese Ministry of Health, Labor and Welfare Statistical Database, because increasing AF with age and male sex is associated with lower TC levels.

The “cholesterol paradox” is also present in patients with heart failure (HF), because the plasma lipoproteins can’t efficiently scavenge the high level of intestinal endotoxins, particularly statins or other lipid-lowering drugs remain controversial treatments for such patients. In a recent study, lower LDL-C levels appeared to predict less favorable outcomes in patients with HF, particularly those taking statins.

Given that ApoE and ApoA-1 protect against bacterial lipopolysaccharides and endotoxemia, we believe that lower ApoE and ApoA-1 in lipoproteins, and not the lipid moieties of the particles, could rationally explain the “cholesterol paradox”.

In addition, besides the “paradox of cholesterol”, it is necessary to consider also the “paradox of statins”, which could contribute to increased metabolic syndrome and diabetes. Infectious burden, including endotoxins, is responsible for vascular events, including stroke, metabolic syndrome and diabetes, and statins have no effect on microbial burden and bacterial endotoxins.

The “paradox” is that statins, by lowering all lipoproteins, which are part of the acute response, could imbalance the immune system and thus contribute to circulating levels of endotoxins and the systemic inflammatory status of metabolic syndrome, diabetes and cardiovascular diseases.

In conclusion, it is necessary to target plasma endotoxin lowering and not the cholesterol level. Low LDL-C and TC levels are linked to AF increasing, via the pathogenesis of enhanced inflammation by the high level of circulating endotoxins and the altered immune system response.

REFERENCES


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