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Editorial commentary: The pleiotropic effect of statins on the atherosclerotic plaque and coronary heart disease

Antonis I. Sakellarios, PhD*, Dimitrios I. Fotiadis, PhD

Unit of Medical Technology and Intelligent Information Systems, University of Ioannina and Dept. of Biomedical Research, Institute of Molecular Biology and Biotechnology, Forth, GR 45110, Ioannina, Greece

In this issue of Trends in Cardiovascular Medicine, Almeida and Budoff present many perspectives on the role of statins on atherosclerotic plaque with the main aim of highlighting the changes in atherosclerotic plaque in terms of plaque regression, stabilization and their pleiotropic effects. Statins are considered one of the main lipid-lowering strategies for primary and secondary prevention of coronary heart disease (CHD) [1]. In fact, it has been demonstrated in many clinical trials that lipid-lowering using statins may reduce the risk of cardiovascular event. In this article, several types of statins are presented that have different rates of absorption and solubility, but all reduce the serum LDL concentration in a non-linear way.

The most interesting part of the article is the summary of the pleiotropic effect of statins. In particular, statins may play a significant role by plaque stabilization, decreasing oxidative stress, improving vascular tone, reducing platelet aggregation and also exerting anti-inflammatory effects. It is expected that the pleiotropic effect of statins impacts the atherosclerotic plaque in many different aspects [2]. More specifically, the overall effect of statins to reduce the atherosclerotic plaque is presented in detail. That conclusion is supported by many studies especially based on invasive imaging of coronary arteries. Additionally, it is demonstrated that different doses of statins may have significantly different outcomes. This effect of statins on plaque progression and especially on its reduction must be considered in current practices of CHD risk stratification [3,4] even in current risk scores or in future computational modeling approaches based on machine learning or biomechanics [5].

Another effect of statins in CHD is that they promote plaque stabilization. Indeed, statins modify plaque composition by transforming lipid or soft tissue into much more dense plaques such as calcified plaque. The authors of those articles attempt to explain the biological mechanism of this effect, assuming that specific macrophage types are responsible for the plaque stabilization, an argument that it is agreement with experimental studies. Additionally, one of the most significant effects of statins is the stabilization of vulnerable and high risk plaques, when these are defined in terms of the thin fibrous cap. Those articles conclude that statins increase fibrous cap thickness, thus providing stabilization of the plaque and reducing the risk of plaque rupture, results supported by large clinical trials [6,7].

Finally, the article presents the role of statins in the reduction of inflammation. Indeed, many trials demonstrated that statins reduce the inflammatory markers in serum. Despite the fact that the biochemical underlying mechanisms are not clear yet, the authors present their hypothesis based on the results of clinical trials or other imaging studies.

There is no doubt that statins have a pleiotropic effect on cardiovascular disease and atherosclerotic plaque. Preventive strategies require rapid lowering of serum cholesterol and statins are considered cornerstones to this aim. Statins reduce lipids; nonetheless their effect is much more incremental for the cardiovascular status of the patient. The most important results of statin medication is that inflammation reduction alters plaque composition in terms of stabilization and eventually reduces the risk of plaque rupture [8–10]. On the other hand, there is also the hypothesis that statins may be more effective at the early stages of the disease rather than during the more progressed stages of CHD, where the evolution or the vulnerability may be affected by other factors such as biomechanical e.g. endothelial shear stress [11]. For this reason, the guidelines propose initiating statin therapy as an earlier intervention in CHD, since it is expected to have long-term impact on the heavy burden of cardiovascular disease [12].

In recent years, more agents such as proprotein convertase/subtilisin kexin type 9 (PCSK9) inhibitors or some even more innovative [13,14] are becoming available for lipid-lowering and inflammation reduction. However, the cost-effectiveness of each approach must be proven and statins will still have a leading role in the preventive strategies of CHD and atherosclerotic plaque management [15].

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* Corresponding author: Antonis I. Sakellarios, PhD, Unit of Medical Technology and Intelligent Information Systems, University of Ioannina and Dept. of Biomedical Research, Institute of Molecular Biology and Biotechnology, Forth GR 451 10 Ioannina, Greece.

E-mail address: ansakel13@gmail.com (A.I. Sakellarios).

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