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Statins and myocardial infarction: Type, dose, and administration time: Does it matter?

Nikolaos Papageorgiou, MD, PhD[a], *Effimia Zacharia, MD*[b], *Alexandros Briasoulis, MD, PhD*[c,*], *Emmanuel Androulakis, MD, PhD*[d], *and Dimitris Tousoulis, MD, PhD, FACC, FESC*[b]

[a]*Department of Cardiology, Barts Heart Centre, St Bartholomew's Hospital, London, United Kingdom*
[b]*1st Department of Cardiology, Hippokration Hospital, University of Athens, Athens, Greece*
[c]*Department of Cardiology, Detroit Medical Center, Wayne State University, Detroit, MI*
[d]*Department of Cardiology, John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom*

ABSTRACT

Patients with ST-elevation myocardial infarction (STEMI) constitute a vulnerable group that demands the careful assessment and application of all the up-to-date clinical and experimental knowledge, with final aim, the improvement of their prognosis. Statins are an indispensable part of the primary and secondary prevention of coronary artery disease (CAD), not only due to their strong hypolipidemic effect, but also due to their numerous pleiotropic properties that play an important role in the treatment of CAD, especially when the more vulnerable group of STEMI patients is addressed. Nevertheless, there are still issues that require further discussion and clarification, such as the type of statin, the dose of the regimen, the administration time, and the treatment duration.

Key words: Statins, STEMI, Cardiovascular outcomes.

Abbreviations: STEMI, ST-elevation myocardial infarction, CAD, coronary artery disease, CVD, cardiovascular disease, LDL, low-density lipoprotein, hs CRP, sensitivity C-reactive protein, SMCs, smooth muscle cells, AMI, acute myocardial infarction, MMPs, matrix metalloproteinases, ACS, acute coronary syndrome, NO, nitric oxide, PCI, percutaneous coronary intervention, SPECT, single positron-emission computed tomography, TIMI, thrombolysis in myocardial infarction, BNP, brain-type natriuretic peptide, FMD, flow-mediated dilatation, CIN, contrast-induced nephropathy.

Introduction

Statins have long been established as an indispensable part of the primary and secondary prevention of coronary artery disease (CAD), having strong hypolipidemic effect. Evidence suggests that statin treatment for primary prevention reduces the rate of major vascular events and the need for revascularization [1]. In a systematic review of 18 trials concerning patients with no history of cardiovascular disease (CVD), statin treatment was shown to decrease the rate of cardiovascular mortality, major vascular events, and revascularizations without causing serious adverse effects [2]. Beyond their hypolipidemic effect, though, statins have also pleiotropic properties that play an important role in the treatment of CAD (Fig.). This was nicely exemplified in JUPITER trial. Rosuvastatin administration in healthy subjects with low levels of low-density lipoprotein (LDL), but high levels of high-sensitivity C-reactive protein (hs CRP) reduced clinical hard end points to a greater extent than the reduction reported among healthy hyperlipidemic men [3].

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*Corresponding author. Tel.: +1 646 675 6700; fax: +1 313 745 2600.
E-mail address: alexbriasoulis@gmail.com (A. Briasoulis).

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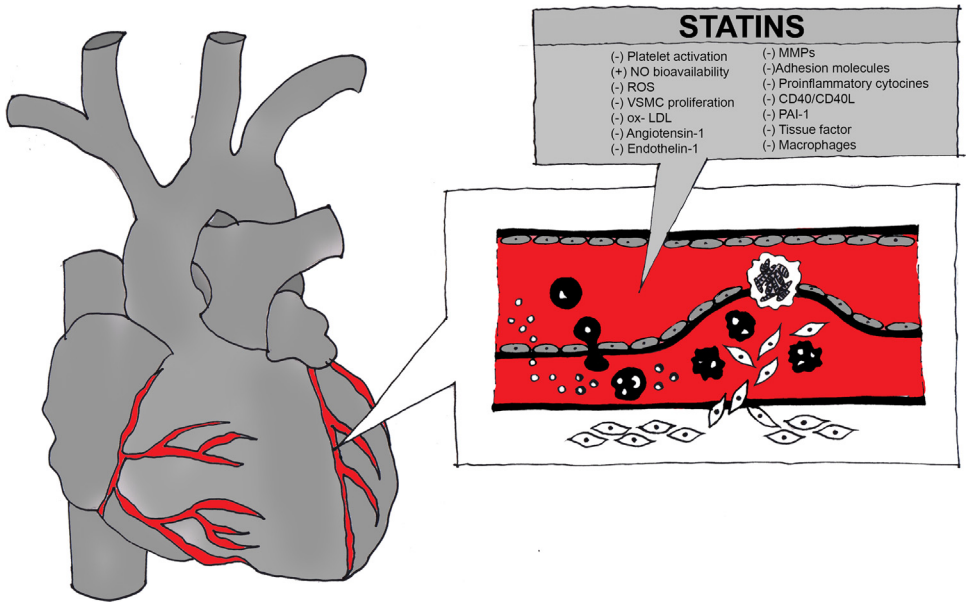

Fig – Pleiotropic effects of statins. Statins decrease the levels of proinflammatory cytokines and downregulate the expression of adhesion molecules and CD40/CD40L. Thus, not only they hinder the migration of inflammatory cells in the atherosclerotic plaque, but also they restore endothelial function, which is further enhanced by the increased bioavailability of nitric oxide (NO) and the concomitant downregulation of the potent vasoconstrictor endothelin-1. At the same time, they enhance vascular smooth muscle cells (VSMC) proliferation and prevent the matrix metalloproteinases (MMPs) activation, which results in a plaque-stabilization effect. Platelet stimulation is also reduced with statin administration, while the expression of potent procoagulants, such as tissue factor, is decreased as well. Last but not least, statins extenuate the oxidative stress and, subsequently, mitigate the low-density lipoprotein (LDL-C) oxidation.

Especially, in the context of ST-elevation myocardial infarction (STEMI), statin administration is indispensable. As a recent trial concluded, the absence of statin prescription at discharge, observed in 6% of STEMI patients, could independently predict 3-year major adverse cardiac events, major bleeding, and death [4]. Thus, the ACC/AHA and ESC/EAS guidelines have included statins in the routine management of STEMI patients [5,6]. Therefore, in the present article we will review the available data regarding to the beneficial effects of statins on the prognosis of patients with acute coronary event syndromes (ACS) and particularly of patients with STEMI.

Statin administration in patients with STEMI

In the case of an acute myocardial infarction (AMI), the fibrous cap ruptures and the underlying procoagulant core of the plaque is exposed, causing thrombus formation and sudden occlusion of the artery lumen. Inflammation has a key role, as T lymphocytes stimulate macrophages to produce matrix metalloproteinases (MMP), which degrade the fibrous cap collagen [7–9]. Statins are righteously named plaque-stabilizers, owing not only to their lipid-lowering effect but also to their pleiotropic actions. They restore the endothelial function, as they enhance the production of nitric oxide (NO) and downregulate the expression of proinflammatory cytokines and adhesion molecules. Statins also have antioxidant and angiogenic properties, while they mitigate the platelet stimulation and can, thus, limit the onset and progression of a thrombus formation [10]. Interestingly, the benefit of statin administration is evident long before their hypolipidemic action takes place [11], highlighting the importance of their administration in the short-term period after the clinical presentation in patients with an acute coronary syndrome (ACS) and in particular in patients with STEMI.

Effect of statin dose type

As a part of the changes applied in the overall management of patients with STEMI, who are undergoing primary percutaneous coronary intervention (PCI), a high-dose pre-procedural statin therapy—as opposed to the standard dose—has partially caused the decrease in mortality observed in several registries [12]. However, it is still a matter of debate if the various types of statins reduce cardiovascular mortality to a similar extent.

For rosuvastatin, recent studies are in agreement that the higher-dose regimen is more effective. Kim et al. showed that high-dose (40 mg) rosuvastatin decreased the infarct size—assessed by single positron emission computed tomography (SPECT) at a median of 3 days after primary PCI—possibly by enhancing microvascular myocardial perfusion. Pre-treated patients presented with a lower corrected thrombolysis in myocardial infarction (TIMI) frame count and a higher myocardial blush grade as opposed to controls with no statin treatment [13]. Likewise, Egede et al. [14] proved that in statin-naïve patients with STEMI the high-dose (40 mg) rosuvastatin treatment, but not the low-dose (5 mg) one, could significantly increase the endothelium-dependent