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Review article

Statin therapy in the prevention of atrial fibrillation in the early postoperative period after coronary artery bypass grafting: A meta-analysis



O.L. Bockeria^{a,*}, V.A. Shvartz^a, A.A. Akhobekov^a, L.A. Glushko^a, T.G. Le^a,
A.R. Kiselev^{a,*}, M.D. Prokhorov^b, L.A. Bockeria^a

^a Department of Surgical Treatment for Interactive Pathology, Bakoulev Scientific Center for Cardiovascular Surgery, Moscow, Russia

^b Saratov Branch of the Institute of Radio Engineering and Electronics of Russian Academy of Sciences, Saratov, Russia

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ABSTRACT

Background: Postoperative atrial fibrillation (POAF) is observed in the early postoperative period in approximately every third patient after coronary artery bypass grafting (CABG). The pathogenesis of POAF is multifactorial and is not yet fully studied. In many studies, postoperative inflammatory response has been extensively investigated as a potential basic factor of POAF. It is known that statins have anti-inflammatory properties. In some studies, pre- and perioperative use of statins has shown the decrease of incidence of POAF after CABG.

Objective: We conducted meta-analysis of randomized and observational studies of efficiency of statin therapy for the prevention of POAF after CABG.

Material and methods: The meta-analysis included 15 clinical trials of statins in 9369 patients with performed CABG during the past 10 years. 5598 patients (59.75%) were taking statins and 3771 patients (40.25%) were not taking statins. The following outcomes observed in the early postoperative period were studied: incidence of POAF, total mortality rate, total stroke rate, and total rate of myocardial infarction. The duration of hospitalization and levels of inflammatory markers before and after CABG were also assessed.

Results: The statin therapy reduced the incidence of POAF after CABG (OR = 0.48, 95% CI: 0.35–0.67, $P < 0.001$). Moreover, the statin therapy decreased the total length of hospital stay and levels of inflammatory markers in the blood serum.

Conclusion: The results of our meta-analysis leave no doubt in the presence of anti-inflammatory and anti-arrhythmic effect of statin therapy. We confirmed the overall positive role of using statins before CABG for POAF prevention.

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* Corresponding authors at: 135, Rublevskoe Shosse, Moscow 121552, Russia.

E-mail addresses: soleo2003@gmail.com (O.L. Bockeria), kiselev@cardio-it.ru (A.R. Kiselev).

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Introduction

Postoperative atrial fibrillation (POAF) is a fairly common complication of coronary artery bypass grafting (CABG). The frequency of POAF in the early postoperative period is 30–45% [1,2]. POAF after CABG is the major risk factor of stroke, myocardial infarction, prolonged hospitalization, and postoperative mortality [1,2]. Basic mechanism of POAF in the early postoperative period after CABG is multifactorial and not fully studied yet. However, several etiopathogenic mechanisms are undoubted. These mechanisms include the inflammation of pericardium, elevated catecholamine levels, autonomic dysfunction, and changes of blood volume and blood pressure. The emergence of the plurality of “re-entry” loops due to the dispersion of atrial refractoriness underlies the electrophysiological mechanisms of POAF after CABG [3,4]. Thus, the patients with structural changes in the atria before the CABG are more prone to the formation of “re-entry” tracks [5]. However, it should be noted that even in patients without structural changes, the physical damage of atrial myocardium in the result of the incision or perioperative ischemia can increase their arrhythmic potential [6,7].

The evidence of the important role of inflammation in the pathogenesis of POAF has been demonstrated in several studies. In particular, it was shown that the inflammation can change the atrial refractoriness by creating the “re-entry” loops and therefore giving rise to atrial fibrillation (AF) [8,9]. It is well known that operations with the cardio-pulmonary bypass are associated with a systemic inflammatory response, which may be partially the cause of POAF. According to the results of several studies, the leukocytosis which usually occurs in the first days after surgery with cardio-pulmonary bypass is an independent predictor of POAF [10,11].

The efficiency of statin therapy in the prevention of POAF in the early postoperative period after CABG has been actively studied in recent years. It is assumed that its beneficial effect in the prevention of POAF is associated with the pleiotropic (anti-inflammatory, antioxidant, and membrane-stabilized) properties of statins [12,13]. According to the results of many studies, the statin therapy reduces the level of markers associated with inflammation after CABG and other open-heart surgery [14–16].

A lot of clinical and experimental studies are devoted to the evaluation of the effectiveness of statins in the prevention of POAF after CABG, but their results are ambiguous. Many of these studies were carried out for a small number of patients. Moreover, different doses and types of statins were used in these studies. Besides, not all of them assess the role of inflammation in the POAF causing and effect of statin therapy on the duration of hospitalization.

For the purpose of data compilation and analysis of literature, we conducted an updated meta-analysis of randomized and observational studies of the statin usage in the prevention of POAF after CABG.

Materials and methods

The search of literature was conducted over the last 10 years (from 2005 to 2014) in the following databases: MEDLINE via Pubmed, Embase, Cochrane Database, Medscape, Directory of Open Access Journals, and Russian Science Citation Index, as well as on the web-sites devoted to clinical research (Clinical Center, National Institutes of Health, ClinicalStudyResults.org, ClinicalTrials.gov, and TheHeart.org).

The search strategy included the following key words in Russian and English: atrial fibrillation, ischemic heart disease, coronary artery bypass grafting, statins, and 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors. All relevant studies were used for further analysis.

To evaluate the effectiveness of statins in the prevention of POAF after CABG we used for the meta-analysis the pro- and retrospective observational studies that included patients who have undergone the isolated CABG and examined the association of statins with POAF and other various clinical outcomes (acute cerebrovascular accident, myocardial infarction, and so on). The studies that included patients with concomitant CABG with the correction of the valve disease and/or structural defects (left ventricular aneurysm, ventricular septal defect, etc.) were excluded from the meta-analysis.

The endpoints of the study were selected as follows: the frequency of POAF, the overall mortality rate in the early postoperative period, the incidence of stroke, myocardial infarction rate, length of hospitalization, and the level of inflammatory markers before and after CABG. As a result, 5

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