Original Article

Statin therapy in the primary prevention of early atrial fibrillation after coronary artery bypass grafting

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ABSTRACT

Objective: Assessment of the role of statin therapy in the prevention of postoperative atrial fibrillation (POAF) after coronary artery bypass grafting (CABG) in patients without prior atrial fibrillation.
Methods: A retrospective analysis of 206 patients, aged 57.2 ± 7.9 years (mean $\pm$ SD), who underwent isolated CABG is carried out. All patients are divided into two groups. The first group (nSt-patients) includes the patients who did not receive statin therapy prior to CABG ($n = 82$). The second group (St-patients) includes the patients who received statin therapy prior to CABG ($n = 124$). Both groups received the statin therapy from the first day after CABG. The risk of occurrence of POAF is evaluated using the Cox-regression model.
Results: The rate of POAF was 25.6% in nSt-patients and 6.5% in St-patients ($P = 0.020$). On the 4th day after CABG, white blood cells (WBC) count was $11.0 (9.0, 13.0) \times 10^9$/mL (medians with inter-quartile ranges) in nSt-patients and $9.0 (7.6, 10.2) \times 10^9$/mL in St-patients ($P < 0.001$). The peak WBC numbers occurred on the day of POAF onset. The Cox-regression analysis shows that only two factors (statin therapy and number of grafts) had significant influence on the POAF onset. Odds ratio of POAF event prediction by statin therapy was 0.20 (95%CI: 0.08–0.51), $P < 0.001$. Each subsequent graft increased the risk of POAF in 2.1 times.
Conclusion: Statin therapy carried out prior to the CABG is an effective approach to primary prevention of POAF in early postoperative period. Statin therapy after CABG in nSt-patients does not give prophylactic effect observed in St-patients.

1. Introduction

Atrial fibrillation (AF) is the most frequent postoperative complication after cardiac surgery. Postoperative atrial fibrillation (POAF) occurs in about 65% cases.[1–3] This complication leads to prolonged hospital stay and large economic cost.[4,5]

Some researchers recommend amiodarone and beta-blockers to reduce the risk of POAF.[6–8] However, it should be noted that such preventive therapy does not seem to be safe in all patients because of side effects of these drugs, such as hypotension and bradycardia associated with beta-blockers and proarrhythmogenic effect of amiodarone.[9] It is assumed that one of the reasons of POAF may be the post-operative local and systemic inflammations.[10,11] For example, coronary artery bypass grafting (CABG) is associated with the increase of the inflammatory markers, such as C-reactive protein, leukocytes, interleukin-6, and interleukin-8.[12] Up to date, the reason of POAF remains controversial and it is actively studied by many researchers.[13] Some anti-inflammatory drugs (such as nonsteroidal anti-inflammatory drugs, glucocorticoids, colchicine, and statins) have shown promising results in the prevention of POAF.[14–17]

Statin therapy is recommended in patients with coronary heart disease (CHD), but not all patients are committed to this treatment. According to some previous studies, the statin therapy is efficient

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in prevention of AF after CABG.[18–20] However, some other studies failed to demonstrate an antiarrhythmic affect of statins after open-heart surgery.[21]

The aim of our study is to assess the role of statin therapy in primary prevention of POAF in early postoperative period after GABG.

2. Material and methods

2.1. General design of study

Design of this study was approved by the Ethics Committee (Protocol No. 9, February 7, 2014) of the Bakoulev Center for Cardiovascular Surgery (Moscow, Russia).

The data on the health status of all patients with CABG were gathered retrospectively in the Department of Surgical Treatment for Interactive Pathology, Bakoulev Scientific Center for Cardiovascular Surgery (Moscow, Russia). Informed consent was obtained from all participants.

The inclusion criteria in our study were the following:

 i) CABG performed in 2013,
ii) Age from 40 to 80 years.

The patients were not included in the study if they matched the following criteria:

   i) AF prior current CABG,
  ii) Concomitant surgery (e.g. CABG with valve repair/prosthesis, CABG with aneurysmectomy, CABG with surgical correction of ventricular septal defect, etc.),
 iii) Emergency CABG,
  iv) Severe renal failure (creatinine clearance calculated by the Cockroft–Gault formula <50 mL/min),
   v) Thyroid dysfunction (hyper- or hypofunction),
  vi) Immunosuppressive and anti-inflammatory medications for the treatment of comorbid conditions,
 vii) Cancer,
viii) Organic disorders of central nervous system,
  ix) Psychological disorders,
   x) Left ventricle ejection fraction (LVEF) <35%,
  xi) Hypo- or hyperkalemia,
 xii) Treatment with amiodarone,
xiii) Other hormonal disorders.

After selection, all patients were divided into two groups:

 i) The first group was composed of patients without statin therapy prior to CABG. We named this group as nSt-patients. Note that all these patients began to receive the statin therapy from the first day after CABG.
ii) The second group was composed of patients who received the statin therapy for at least 3 days prior to the CABG and continuously after the operation. We named this group as St-patients. The period of 3 days was defined randomly according to data in the literature. It is supposed that anti-inflammatory effect of statins begins to appear after 3 days of starting the therapy.[22] In our study, only original atorvastatin (Pfizer Inc., USA) and rosuvastatin (AstraZeneca Pharmaceuticals LP, USA) were used. We did not take into account the dose of statins.

We did not influence on taking any drugs before CABG, due to the retrospective design of our study. Scarce use of statins in ambulatory practice in patients with CHD is the challenge in many countries, including Russia. According to population-based studies in Russia, statins are prescribed to CHD patients much rarely than other necessary drugs.[23,24] Moreover, the use of statins is often short. In a few months, the patients themselves stop the statin use, motivating it by normalization of cholesterol, economic aspects, and other reasons. This fact made it possible to carry out this retrospective study.

2.2. Patients

In 2013, 415 CABGs were performed in Department of Surgical Treatment for Interactive Pathology, Bakoulev Scientific Center for Cardiovascular Surgery (Moscow, Russia). Our retrospective study includes medical records on 206 patients with CHD (173 men and 33 women), aged 57.2 ± 7.9 years (mean $\pm$ SD), who underwent isolated CABG in 2013. 209 patients were excluded from the study because of fulfillment of the above mentioned exclusion criteria. Clinical status of all included patients was confirmed by the results of clinical investigation.

Finally, we have identified 82 (40%) nSt-patients and 124 (60%) St-patients.

2.3. Data collection

Clinical data including the data of physical examinations, instrumental and laboratory investigations on all included patients were obtained during their hospital treatment in pre-, intra-, and postoperative periods. The source of patient's data is a hospital chart.

2.4. Outcomes

POAF event after CABG was the endpoint of the study. AF episode occurred in the 7-day period after CABG and lasting more than 5 min was defined as a POAF event. In accordance to the treatment protocol, all patients were under 24-h bedside electrocardiography (ECG) and blood pressure (BP) monitoring for the first 72 h after the surgery. After 72 h after the surgery, Holter monitoring of ECG was used every day until the day of discharge from the hospital.

2.5. Statistical analysis

We apply the Shapiro–Wilk test to check whether the data were approximately normally distributed. Continuous variables are reported as medians (Me) with inter-quartile ranges (Q_1, Q_3) for non-normal data or mean (M) with standard deviation (SD) for normal data. Categorical data are presented as frequencies and percentages. To compare the variables between the patients' groups we use the Mann–Whitney test. The difference between the two samples is assessed by t-test. The risk of occurrence of POAF is evaluated using the Cox-regression model. Odds ratio is used for the assessment of risk-factors. The obtained estimations are considered statistically significant if $P < 0.05$.

We used the software package Statistica 8.0 (StatSoft Inc., Tulsa, Oklahoma, USA) for statistical analysis.

3. Results

The studied groups of St-patients and nSt-patients did not differ in main anthropometric, clinical, instrumental, and laboratory characteristics in pre-, intra-, and postoperative periods. Also, there was no significant difference in the length of hospital stay. The relevant data for both groups are presented in Table 1. Significant differences between the groups are found in the rate of POAF and white blood cells (WBC) in the early postoperative period (Table 1). It should be noted that all St-patients in our study received the statin