doi: 10.5761/atcs.oa.10.01588

Original Article

Do Preoperative Statins Reduce Atrial Fibrillation after Coronary Artery Bypass Grafting?

Hiroaki Sakamoto, MD, PhD, Yasunori Watanabe, MD, PhD, and Masataka Satou, MD

Objective: Recent studies have demonstrated that statins have pleiotropic effects, including anti-inflammatory effects and atrial fibrillation (AF) preventive effects. The objective of this study was to assess the efficacy of preoperative statin therapy in preventing AF after coronary artery bypass grafting (CABG).

Methods: 221 patients underwent CABG in our hospital from 2004 to 2007. 14 patients with preoperative AF and 4 patients with concomitant valve surgery were excluded from this study. Patients were divided into two groups to examine the influence of statins: those with preoperative statin therapy (Statin group, n = 77) and those without it (Non-statin group, n = 126). In addition, patients were divided into two groups to determine the independent predictors for postoperative AF: those with postoperative AF (AF group, n = 54) and those without it (Non-AF group, n = 149). Patient data were collected and analyzed retrospectively.

Results: The overall incidence of postoperative AF was 26%. Postoperative AF was significantly lower in the Statin group compared with the Non-statin group (16% versus 33%, p = 0.005). Multivariate analysis demonstrated that independent predictors of AF development after CABG were preoperative statin therapy (odds ratio [OR] 0.327, 95% confidence interval [CI] 0.107 to 0.998, p = 0.05) and age (OR 1.058, 95% CI 1.004 to 1.116, p = 0.035).

Conclusion: Our study indicated that preoperative statin therapy seems to reduce AF development after CABG.

Key words: statin, atrial fibrillation, coronary artery bypass grafting

Introduction

Atrial fibrillation (AF) is one of the most common complications after coronary artery bypass grafting (CABG) and it occurs in 20% to 40% of patients after CABG.[1–3] Postoperative AF is likely to be troublesome because it usually occurs within a few days after surgery with unstable hemodynamics.

The relationship between ischemic heart disease and hyperlipidemia is well known, and therefore many patients with ischemic heart disease are treated concurrently for hyperlipidemia. The major drugs for the treatment of hyperlipidemia are inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase, known as statins.

Recent studies have demonstrated that statins have pleiotropic effects. Reported effects include: decreased levels of high-sensitivity C-reactive protein (CRP), decreased plaque area in coronary arteries, reduced number of cardiac events after CABG, myocardial protective effects after ischemic reperfusion injury, AF preventive effects after CABG and others.[4–8]

The objective of this study was to assess the efficacy of preoperative statin therapy in preventing AF after CABG. Also, the time-dependent change of CRP levels

Department of Cardiovascular Surgery, Hitachi General Hospital, Hitachi, Ibaraki, Japan

Received: May 12, 2010; Accepted: October 4, 2010
Corresponding author: Hiroaki Sakamoto, MD, PhD. (current affiliation) Cardiovascular Surgery, Tsukuba University Hospital, 1-1-1, Tennodai, Tsukuba, Ibaraki 305-0006, Japan
Email: sakamotoh@md.tsukuba.ac.jp

was analyzed to assess the relationship between inflammation and statins.

Patients and Methods

Patient population

Patient data were collected and analyzed retrospectively. This retrospective study was approved by the ethics committee of Hitachi General Hospital. Our committee waived the need for obtaining informed consent from each patient for this retrospective study.

From January 2004 to December 2007, 221 patients underwent CABG at Hitachi General Hospital. Fourteen patients with preoperative AF and 4 patients with concomitant valve surgery were excluded from this study. Thus, 203 patients who underwent isolated CABG were included in the study population.

Patients were divided into two groups to examine the influence of statins: those with preoperative statin therapy (Statin group, n = 77) and those without it (Non-statin group, n = 126). In addition, patients were divided into two groups to determine the independent predictors for postoperative AF: those with postoperative AF (AF group, n = 54) and those without it (Non-AF group, n = 149).

The Statin group had been administered one of the following statins for hyperlipidemia by their cardiologist before being admitted to our department: atorvastatin, pravastatin, pitavastatin, rosuvastatin, simvastatin, or fluvastatin. The type, dose, or duration of preoperative statin therapy was not uniform, because this is a retrospective study. Preoperative statins were omitted on the day of the operation and re-started from the average of 1.47 days after the operation in the Statin group. Other routine postoperative medications were aspirin, ticlopidine hydrochloride, isosorbide mononitrate, diltiazem hydrochloride, and famotidine in our hospital.

All surgeries were performed through a median sternotomy using either an on-pump or off-pump technique. Cardiopulmonary bypass (CPB) was conducted using ascending aortic cannulation and bicaval cannulation, mild hypothermia (32°C), and cold blood cardioplegic arrest. Off- pump CABG (OPCAB) was performed using a heart stabilizer.

Data collection

All patients were monitored daily with continuous electrocardiographic telemetry for a minimum of 11 days after the operation. AF was defined as episodes lasting for longer than 5 minutes, as documented by telemetry. The presence of AF was determined from clinical records.

Statistical methods

Continuous variables are presented as mean ± standard deviation and were compared between groups using a t-test. Categorical data are presented as percentages and were compared between groups using the chi-square test. First, univariate analysis was performed to examine the relationship between variables and statin therapy, and the relationship between variables and the development of postoperative AF. Then, preoperative and perioperative variables which showed univariate relation ($p < 0.25$) with postoperative AF occurrence or which were previously demonstrated to be strong, independent predictors of AF[1–3, 9, 10] were entered into a multivariate logistic regression analysis model to determine the independent predictors for postoperative AF. The time-dependent change of CRP levels was analyzed using repeated measures ANOVA. All analyses were performed using the SPSS statistical software version 17.0 for Windows (SPSS Inc., Chicago, IL, USA). A p value of less than 0.05 was considered statistically significant.

Results

The results of the univariate analysis of pre-, peri-, and postoperative variables between the Statin group and the Non-statin group are shown in **Tables 1, 2,** and **3**. Similarly, these tables show the results of univariate analysis between the AF group and the Non-AF group.

The Statin group was significantly younger compared to the Non-statin group ($p = 0.007$). The AF group was significantly older ($p = 0.001$). Regarding preoperative oral medicine, calcium blockers, angiotensin II type I receptor blockers, and beta-blockers did not appear to influence the development of postoperative AF. The usage rate of beta-blockers between the AF group and the Non-AF group was similar (24% versus 33%, $p = 0.228$) (**Table 1**).

As for perioperative factors, there were no significant differences between groups except for preoperative intra-aortic balloon pumping (IABP) usage. Preoperative IABP usage rate was significantly lower in the Statin group compared with the Non-statin group (**Table 2**).

Regarding postoperative factors, there were no significant differences between groups in postoperative ventilation time, ICU stay, and incidence of complications. Moreover, thirty-day mortality was almost the same. The

Table 1 Preoperative patient characteristics and relationship with statin use and postoperative atrial fibrillation

	Statin (n = 77)	Non-statin (n = 126)	p Value	AF (n = 54)	Non-AF (n = 149)	p Value
Age (year)	63 ± 9	67 ± 9	0.007	69 ± 8	64 ± 9	0.001
Male	55 (71%)	107 (85%)	0.020	41 (76%)	121 (81%)	0.407
Acute myocardial infarction	2 (3%)	9 (7%)	0.144	4 (7%)	7 (5%)	0.511
Unstable angina	7 (10%)	18 (14%)	0.216	10 (19%)	15 (10%)	0.107
NHYA ≥ 3, 4	1 (1%)	4 (3%)	0.652	2 (4%)	3 (2%)	0.610
Hypertension	54 (70%)	81 (64%)	0.708	35 (65%)	100 (68%)	0.238
Hyperlipidemia	77 (100%)	38 (30%)	< 0.001	25 (46%)	90 (60%)	0.082
COPD	10 (13%)	15 (12%)	0.947	5 (9%)	20 (13%)	0.538
Diabetes mellitus	42 (55%)	59 (47%)	0.615	24 (44%)	77 (52%)	0.194
Renal failure	2 (3%)	15 (12%)	0.017	8 (15%)	9 (6%)	0.037
Cerebrovascular disease	15 (19%)	42 (33%)	0.016	21 (39%)	36 (24%)	0.025
Previous cardiac surgery	1 (1%)	1 (1%)	0.999	0 (0%)	2 (1%)	0.999
CTR (%)	49 ± 5	50 ± 5	0.840	51 ± 5	49 ± 5	0.160
Medical therapy						
Statins	NA	NA		12 (22%)	65 (44%)	0.005
Calcium blockers	31 (40%)	45 (36%)	0.516	21 (39%)	55 (37%)	0.797
ARBs	30 (39%)	46 (37%)	0.726	17 (31%)	59 (40%)	0.291
Beta-blockers	31 (40%)	31 (25%)	0.019	13 (24%)	49 (33%)	0.228
Preoperative echocardiography						
EF (%)	66 ± 11	63 ± 13	0.075	65 ± 12	64 ± 13	0.931
LAD (mm)	39 ± 5	39 ± 6	0.798	39 ± 5	39 ± 6	0.664
LVDd (mm)	49 ± 6	51 ± 7	0.214	50 ± 7	50 ± 6	0.708
LVDs (mm)	31 ± 7	33 ± 9	0.158	33 ± 9	32 ± 8	0.957
Preoperative lipid levels						
LDL cholesterol (mg/dl)	108 ± 37	125 ± 31	0.001	121 ± 35	118 ± 35	0.548
HDL cholesterol (mg/dl)	44 ± 11	40 ± 10	0.023	41 ± 11	41 ± 10	0.934
Triglyceride (mg/dl)	130 ± 69	118 ± 54	0.189	114 ± 48	126 ± 63	0.201

AF, atrial fibrillation; COPD, chronic obstructive lung disease; CTR, cardiothoracic ratio; ARB, Angiotensin II type I receptor blocker; EF, ejection fraction; LAD, left atrial diameter; LVDd, left ventricular dimension at end-diastole; LVDs, left ventricular dimension at end-systole

Table 2 Perioperative variables

	Statin (n = 77)	Non-Statin (n = 126)	p Value	AF (n = 54)	Non-AF (n = 149)	p Value
Emergent	0 (0%)	6 (5%)	0.085	3 (6%)	3 (2%)	0.193
OPCAB	32 (42%)	51 (40%)	0.982	21 (39%)	62 (42%)	0.764
OPE time (min)	453 ± 110	451 ± 114	0.886	450 ± 101	452 ± 117	0.881
CPB time (min)	192 ± 39	188 ± 45	0.601	180 ± 46	193 ± 41	0.123
ACC time (min)	126 ± 31	126 ± 35	0.914	124 ± 34	127 ± 33	0.677
No. of anastomosis	2.8 ± 0.9	2.7 ± 0.9	0.759	2.8 ± 0.9	2.7 ± 0.9	0.823
BTF	15 (19%)	23 (18%)	0.849	12 (22%)	26 (17%)	0.454
IABP	1 (1%)	13 (10%)	0.019	6 (11%)	8 (5%)	0.158

AF, atrial fibrillation; OPCAB, off-pump coronary artery bypass graft; OPE, operation; CPB, cardiopulmonary bypass; ACC, aortic cross-clamp; BTF, blood transfusion; IABP, intra-aortic balloon pumping

overall incidence of postoperative AF was 26%. Postoperative AF occurred in 12 patients (16%) in the Statin group. This was significantly lower compared with 42 patients (33%) in the Non-statin group (p = 0.005). The time between surgery and AF development was significantly longer in the Statin group compared with the Non-statin group (4.4 ± 3.4 days versus 2.6 ± 1.8 days, p = 0.024) (**Table 3**).

Table 3 Postoperative variables

	Statin (n = 77)	Non-Statin (n = 126)	p Value	AF (n = 54)	Non-AF (n = 149)	p Value
Ventilation (hours)	13 ± 26	22 ± 46	0.082	23 ± 42	17 ± 39	0.352
ICU stay (days)	4 ± 2	5 ± 5	0.257	5 ± 3	5 ± 5	0.688
AF	12 (16%)	42 (33%)	0.005	NA	NA	
Onset of AF (postoperative day)	4.4 ± 3.4	2.6 ± 1.8	0.024	NA	NA	
Cerebrovascular disease	2 (3%)	3 (2%)	0.689	1 (1%)	4 (3%)	0.205
PMI	6 (8%)	14 (11%)	0.448	8 (15%)	12 (8%)	0.163
DSWI	0 (0%)	2 (2%)	0.167	0 (0%)	2 (1%)	0.695
30-day mortality	1 (1%)	1 (1%)	0.999	0 (0%)	2 (1%)	0.999
Postperative echocardiography						
EF (%)	66 ± 9	64 ± 10	0.215	67 ± 9	64 ± 10	0.060
LAD (mm)	37 ± 6	37 ± 5	0.787	38 ± 5	37 ± 5	0.363
LVDd (mm)	47 ± 6	48 ± 7	0.454	46 ± 9	48 ± 6	0.237
LVDs (mm)	30 ± 6	32 ± 6	0.135	30 ± 6	31 ± 6	0.181

AF, atrial fibrillation; PMI, perioperative myocardial infarction; DSWI, deep sternal wound infection; EF, ejection fraction; LAD, left atrial diameter; LVDd, left ventricular dimension at end-diastole; LVDs, left ventricular dimension at end-systole

Table 4 Multivariate independent predictors of postoperative atrial fibrillation

Variables	Odds ratio (95% confidence interval)	p Value
Age	1.058 (1.004–1.116)	0.035
Unstable angina	1.543 (0.346–6.886)	0.570
Hypertension	0.867 (0.336–2.235)	0.768
Hyperlipidemia	1.562 (0.580–4.210)	0.378
Diabetes mellitus	0.901 (0.411–1.976)	0.794
Renal failure	2.038 (0.551–7.536)	0.286
Cerebrovascular disease	2.004 (0.877–4.578)	0.099
CTR	0.985 (0.893–1.086)	0.762
Preoperative statins	0.327 (0.107–0.998)	0.050
Preoperative beta-blockers	0.540 (0.205–1.421)	0.212
Triglyceride	0.996 (0.988–1.004)	0.327
IABP	2.605 (0.242–28.01)	0.429
OPCAB	1.190 (0.535–2.647)	0.669
Male	1.772 (0.623–5.037)	0.283
COPD	0.909 (0.429–1.927)	0.804
EF	1.009 (0.972–1.048)	0.631

CTR, cardiothoracic ratio; IABP, intra-aortic balloon pumping; OPCAB, off-pump coronary artery bypass graft; COPD, chronic obstructive lung disease; EF, ejection fraction

According to multivariate analysis, the following variables were entered into a multivariate logistic regression analysis model: age, unstable angina, hypertension, hyperlipidemia, diabetes mellitus, renal failure, cerebrovascular disease, cardiothoracic ratio, statins, beta-blockers, triglyceride, emergent operation, intra-aortic balloon pumping, OPCAB, male sex, chronic obstructive lung disease, and ejection fraction. Preoperative statin therapy demonstrated a significant inverse relation with postoperative AF development (odds ratio [OR] 0.327, 95% confidence interval [CI] 0.107 to 0.998, p = 0.05). Also, age was an independent predictor of postoperative AF (OR 1.058, 95% CI 1.004 to 1.116, p = 0.035). Emergent operation was excluded from the analysis process by the SPSS software. The detail results are shown in **Table 4**.

As for the relation with inflammation, repeated measures ANOVA indicated that the time-dependent change of CRP levels had no significant differences between the Statin and the Non-statin groups, nor between the AF and the Non-AF groups. However, a t-test indicated that CRP levels on postoperative days 7 and 14 were significantly lower in the Statin group compared with the Non-statin group (**Table 5**).

Table 6 shows the type of statins and the incidence of

Table 5 Time-dependent change of CRP levels (mg/dl)

		Statin (n = 77)	Non-Statin (n = 126)	p Value	AF (n = 54)	Non-AF (n = 149)	p Value
Preoperative CRP		0.6 ± 2.1	1.0 ± 2.4	0.257	0.9 ± 2.0	0.8 ± 2.4	0.887
CRP of Postoperative day	1	7.6 ± 2.6	7.9 ± 3.3	0.404	7.7 ± 2.6	7.8 ± 3.2	0.883
	2	15.1 ± 5.1	15.6 ± 4.9	0.474	15.5 ± 4.6	15.4 ± 5.2	0.880
	3	10.4 ± 5.4	11.4 ± 5.4	0.231	11.2 ± 4.7	11.0 ± 5.6	0.783
	4	4.9 ± 4.3	5.8 ± 5.7	0.224	5.1 ± 4.4	5.5 ± 5.5	0.648
	7	3.9 ± 2.9	5.4 ± 4.1	0.002	5.3 ± 3.9	4.7 ± 3.7	0.309
	14	1.7 ± 1.7	2.4 ± 2.4	0.011	2.4 ± 2.3	2.1 ± 2.1	0.340
Repeated ANOVA result between groups				0.575			0.878

CRP, C-reactive protein

Table 6 Type of statins and incidence of postoperative atrial fibrillation (patients)

	Postoperative AF (+)	Postoperative AF(-)	Total
Atorvastatin	8	34	42
Pravastatin	2	16	18
Pitavastatin	2	4	6
Rosuvastatin	0	5	5
Simvastatin	0	5	5
Fluvastatin	0	1	1
Total	12	65	77

AF, atrial fibrillation

AF. Postoperative AF occurred in patients with atorvastatin, pravastatin, or pitavastatin. However, no relationship was found between the type of statins and postoperative AF, because the frequency of use of each statin was significantly different.

Discussion

Statin therapy is actively performed on many heart disease patients. Many previous studies revealed that statins had the following pleiotropic effects: anti-inflammatory effects; cardiac event preventive effects; coronary plaque regression effects; and others.[4–8] Moreover, recent studies revealed that statins had preventive effects on postoperative AF.[11–13] For example, ARMYDA-3 is the first randomized, controlled trial to evaluate the impact of preoperative statin therapy on postoperative AF.[11] In ARMYDA-3, 200 patients were randomized to either preoperative atorvastatin (40 mg/day) or placebo starting 7 days before heart surgery. As a result, preoperative atorvastatin reduced the risk of postoperative AF by 61%, with an incidence of 35% in the atorvastatin group versus 57% in the placebo group. Previous studies also revealed that beta-blocker, amiodarone, and sotalol had preventive effects on postoperative AF.[14, 15] However, these drugs have potential cardiovascular side effects, such as hypotension, bradycardia, atrioventricular block, Torsades de pointes, and others. If the preventive effects of statins on postoperative AF can be confirmed, statins would become a very useful medicine because they do not aggravate hemodynamics.

In our study, univariate and multivariate analysis revealed that preoperative statin therapy had a significant preventive effect on AF development after CABG. Moreover, even if AF occurred after CABG, preoperative statin therapy delayed the onset of the first postoperative AF. In the Statin group, AF occurrence after CABG was approximately 2 days later than in the Non-statin group. This fact is meaningful for postoperative care, as it indicates that preoperative statin therapy can avoid AF development in unstable hemodynamics immediately after surgery.

Previously, many studies of postoperative AF have been done and described that predictors of postoperative AF were advanced age, male sex, and others.[1–3] Similarly, multivariate analysis showed age was a preoperative independent predictor of postoperative AF in our study.

Amiodarone and sotalol, which had a prophylactic effect on AF, were not administered to our patients in the pre- and perioperative periods. Previous studies also

revealed that beta-blockers had AF preventive effects.[14, 15] In our study, 62 patients had been administered beta-blockers preoperatively, but there was no significant difference in preoperative beta-blocker usage between the AF and the Non-AF groups. We considered the reason was that beta-blockers were not restarted after CABG in our patients. In fact, a previous multicenter study suggested that postoperative withdrawal of beta-blockers increased the risk of AF development after CABG.[3]

Some previous reports described that patients who underwent OPCAB had lower rates of postoperative AF compared with conventional CABG.[16, 17] In contrast, other reports revealed there was no significant difference in the incidence of postoperative AF between OPCAB and conventional CABG.[12, 18] Similarly, ratio of OPCAB was 39% in the AF group versus 42% in the Non-AF group in our study. There was no significant difference. We consider that it is still controversial whether OPCAB is identified as a protective factor of postoperative AF.

Regarding the anti-inflammatory effects of statins, it has been reported that statins have the effect of reducing high-sensitivity CRP levels.[4, 5, 19] Nissen and colleagues reported that atorvastatin therapy for 18 months reduced high-sensitivity CRP levels by 36% from baseline.[4] In our study, repeated measures ANOVA revealed that the time-dependent change of CRP levels was not significantly different between the Statin and the Non-statin groups. A t-test indicated that preoperative CRP levels was not significantly different between the Statin and the Non-statin groups, but CRP levels on postoperative days 7 and 14 were significantly lower in the Statin group compared with the Non-statin group. The reason our two groups had no significant difference in preoperative CRP levels is considered to be because the dose or period of preoperative statin therapy was insufficient. In previous studies from United States and Europe, statins were administered at much higher doses than our usual dose, and were administered for more than 12 months.[4, 5, 19] Also, we considered that CRP levels immediately after CABG were almost the same between the two groups because of the effects of operative stress. And, preoperative statin therapy had potentially decreased CRP levels earlier in the Statin group compared with the Non-statin group.

The REVERSAL trial reported that intensive statin therapy (80 mg of atorvastatin orally per day) reduced progression of coronary atherosclerosis, LDL cholesterol levels, and CRP levels compared with moderate statin therapy (40 mg of pravastatin orally per day).[4, 5] Lertsburapa and colleagues reported that intensive atorvastatin therapy (more than 40 mg orally per day) resulted in the greatest reduction in postoperative AF (55% reduction) compared with moderate therapy (more than 20 mg but less than 40 mg, 43% reduction) or mild therapy (less than 20 mg, 25% reduction).[13] We therefore postulated that postoperative AF correlated with LDL cholesterol levels. As for the LDL lowering therapy by statins for prevention of cardiovascular events, "the lower, the better" is recommended. However, our study revealed that no relationship existed between the LDL levels and postoperative AF. In other words, postoperative AF is not prevented by lowering LDL. This issue must be reviewed in more detail in the future.

There are some limitations to our study. First, it is based on a retrospective analysis of our single center database and a small sample study. Second, the type, dose, or period of preoperative statins was not uniform among our patients. However, the Statin group did not have emergent cases, patients who underwent elective surgery had been admitted to our department at least 5 days before surgery. This means that the preoperative statins had been administered for at least 5 days before surgery. We did not describe in detail the data regarding the statin dosages. In our study the most frequently used was atorvastatin, which was administered at 10 mg to most patients, to a maximum of 20 mg. Other statin dosages administered were equal to or less than the equivalent of 20 mg of atorvastatin. This dose is classified as low dose in previous reports from United States and Europe. If we increase the statin dosages, the effects on preventing AF or decreasing CRP levels may become more remarkable than the current results. Finally, the present study lacked the following information: unreported or undiagnosed episodes of postoperative AF; postoperative variables such as volume overload, dose of inotropic agents, or electrolyte imbalance. We should accumulate more data and conduct further detailed research in the future.

Conclusion

In conclusion, preoperative low dose statin therapy seems to reduce AF development after CABG in our study. It seems useful that statins are routinely administered to patients undergoing elective CABG.

References

1) Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, et al. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. Circulation 1996; **94**: 390-7.
2) Zaman AG, Archbold RA, Helft G, Paul EA, Curzen NP, et al. Atrial fibrillation after coronary artery bypass surgery: a model for preoperative risk stratification. Circulation 2000; **101**: 1403-8.
3) Mathew JP, Fontes ML, Tudor IC, Ramsay J, Duke P, et al. Multicenter Study of Perioperative Ischemia Research Group. A multicenter risk index for atrial fibrillation after cardiac surgery. JAMA 2004; **291**: 1720-9.
4) Nissen SE, Tuzcu EM, Schoenhagen P, Crowe T, Sasiela WJ, et al. Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease. N Engl J Med 2005; **352**: 29-38.
5) Schoenhagen P, Tuzcu EM, Apperson-Hansen C, Wang C, Wolski K, et al. Determinants of arterial wall remodeling during lipid-lowering therapy: serial intravascular ultrasound observations from the Reversal of Atherosclerosis with Aggressive Lipid Lowering Therapy (REVERSAL) trial. Circulation 2006; **113**: 2826-34.
6) Thielmann M, Neuhauser M, Marr A, Jaeger BR, Wendt D, et al. Lipid-lowering effect of preoperative statin therapy on postoperative major adverse cardiac events after coronary artery bypass surgery. J Thorac Cardiovasc Surg 2007; **134**: 1143-9.
7) Lazar HL, Bao Y, Zhang Y, Bernard SA. Pretreatment with statins enhances myocardial protection during coronary revascularization. J Thorac Cardiovasc Surg 2003; **125**: 1037-42.
8) Mannacio VA, Iorio D, De Amicis V, Di Lello F, Musumeci F. Effect of rosuvastatin pretreatment on myocardial damage after coronary surgery: a randomized trial. J Thorac Cardiovasc Surg 2008; **136**: 1541-8.
9) Miceli A, Fino C, Fiorani B, Yeatman M, Narayan P, et al. Effects of preoperative statin treatment on the incidence of postoperative atrial fibrillation in patients undergoing coronary artery bypass grafting. Ann Thorac Surg 2009; **87**: 1853-8.
10) Hernandez F, Cohn WE, Baribeau YR, Tryzelaar JF, Charlesworth DC, et al. In-hospital outcomes of off-pump versus on-pump coronary artery bypass procedures: a multicenter experience. Ann Thorac Surg 2001; **72**: 1528-33.
11) Patti G, Chello M, Candura D, Pasceri V, D'Ambrosio A, et al. Randomized trial of atorvastatin for reduction of postoperative atrial fibrillation in patients undergoing cardiac surgery: results of the ARMYDA-3 (Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery) study. Circulation 2006; **114**: 1455-61.
12) Mariscalco G, Lorusso R, Klersy C, Ferrarese S, Tozzi M, et al. Observational study on the beneficial effect of preoperative statins in reducing atrial fibrillation after coronary surgery. Ann Thorac Surg 2007; **84**: 1158-64.
13) Lertsburapa K, White CM, Kluger J, Faheem O, Hammond J, et al. Preoperative statins for the prevention of atrial fibrillation after cardiothoracic surgery. J Thorac Cardiovasc Surg 2008; **135**: 405-11.
14) Burgess DC, Kilborn MJ, Keech AC. Interventions for prevention of post-operative atrial fibrillation and its complications after cardiac surgery: a meta-analysis. Eur Heart J 2006; **27**: 2846-57.
15) Ali IM, Sanalla AA, Clark V. Beta-blocker effects on postoperative atrial fibrillation. Eur J Cardiothorac Surg 1997; **11**: 1154-7.
16) Banach M, Rysz J, Drozdz JA, Okonski P, Misztal M, et al. Risk factors of atrial fibrillation following coronary artery bypass grafting: a preliminary report. Circ J 2006; **70**: 438-41.
17) Hu S, Zheng Z, Yuan X, Wang W, Song Y, et al. Increasing long-term major vascular events and resource consumption in patients receiving off-pump coronary artery bypass. A single-center prospective observational study. Circulation 2010; **121**: 1800-8.
18) Ishida M, Kobayashi J, Tagusari O, Bando K, Niwaya K, et al. Perioperative advantages of off-pump coronary artery bypass grafting. Circ J 2002; **66**: 795-9.
19) Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM Jr, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 2008; **359**: 2195-207.