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Statins Reduce Incidence of Early Perioperative Complications and Length of in-Hospital Stay after Coronary Artery Bypass Graft Surgery

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Abstract

Background: Coronary artery bypass grafting (CABG) is associated with several perioperative complications that may significantly prolong length of in-hospital stay, increase costs and provide worse long term outcome. The 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase inhibitors, or statins, exert anti-inflammatory and vascular protective effects. We hypothesized that pre-operatory statin therapy may reduce incidence of early perioperative complications and length of in-hospital stay following CABG.

Methods: We retrospectively enrolled 103 patients (age 67±3; 18 females), who underwent CABG. Patients were allocated into 2 groups: 57 patients on statin therapy prior to CABG (St Group) and 46 patients not on statin therapy (n-St group). Demographic and clinical features, pre-operative medications use and the incidence of early adverse postoperative events were collected. Pre-operative risk of death using the European System for Cardiac Operative Risk Evaluation (EuroSCORE) was also calculated. The primary end-point was the composite of early complications occurring after surgery, including infections, bleedings, sustained ventricular and supra-ventricular tachyarrhythmias, cardiogenic shock, myocardial infarction and mortality. As secondary end-points single perioperative complications were considered. In-hospital stay length was also evaluated.

Results: Clinical features, cholesterol levels and EuroSCORE were similar between two groups. Statin therapy and EuroSCORE emerged as predictors of the composite adverse outcome. n-St patients had a significant higher rate of early complications if compared with St patients: the primary endpoint occurred in 18 St patients (31%) versus 25 (54%) non-St patients (p=0.019). Multivariate analysis confirmed pre-operative statin therapy and EuroSCORE as independent predictors of the primary endpoint (OR=0.307, 95% CI=0.123-0.766, p=0.011 and OR= 2.114, 95% CI= 1.213- 4.407, p= 0.002 respectively) showing a protective role of the statin therapy.

The incidence of secondary end-points did not differ significantly between the groups, while in-hospital stay was longer in n-St group if compared with St group (7.7±3,9 days vs 5,6±1,8 days; p=0,001).

Conclusion: Our data suggest that statin therapy may reduce early perioperative complications after coronary artery bypass grafting. This effect is independent from cholesterol basal levels, thus supporting pre-operative statin use in patients undergoing CABG.

Keywords: Statins; CABG; Prevention

Abbreviations: CABG: Coronary Artery Bypass Grafting; HMG-CoA: 3-hydroxy-3-methylglutaryl-CoA; MI: Myocardial Infarction; ICU: Intensive Care Unit; EuroSCORE: European System for Cardiac Operative Risk Evaluation; UTI: Urinary Tract Infection; BP: Blood Pressure; LBBB: Left Bundle Branch Block; CPR: C-Reactive Protein; SAA: Serum Amyloid A

Introduction

Despite the improvements in the surgical technologies, coronary artery bypass grafting (CABG) associated mortality is a considerable medical and socioeconomic problem, with estimates ranging as high as 2% to 4%. Moreover, perioperative major cardiovascular events including myocardial infarction (MI), major bleeding, atrial fibrillation, stroke, renal failure, infections, need for inotropic support may significantly prolong length of stay in Intensive Care Unit (ICU) with increased costs and severe long term complications [1].

Statins, inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A reductase, are powerful inhibitors of cholesterol biosynthesis. Beyond their lipid-lowering actions, statins are known to exert multiple pleiotropic effects including improvement of endothelial function, plaque stabilization, decrease of inflammatory markers, and attenuation of myocardial ischaemia-reperfusion injury that can offer direct organ protection and contribute to improve clinical outcome in the early postoperative course [2-4].

Long-term lipid-lowering therapy with statins prevents progression of atherosclerotic coronary artery and vein graft disease [5]. Statins were found to be associated with a reduced incidence of perioperative mortality in patients undergoing major non-cardiac vascular surgery [6,7]. However, in patients undergoing cardiac surgery results are conflicting [8-12].

Powell et al observed that in patients undergoing first-time isolated CABG, pre-operative use of lipid-lowering therapy was associated with improved survival to hospital discharge [8]. Retrospective cohort studies, moreover, showed that statins pre-operative therapy was associated with a significant reduction in the risk of 30-day mortality

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and morbidity [9-10]. On the other hand, large observational studies failed to demonstrated a beneficial effect of pre-operative statin use on in-hospital mortality or major morbidity following cardiac surgery [11,12].

In view of the limited clarity of available data, we conducted an observational retrospective cohort study of consecutive patients undergoing primary CABG surgery to determine if statins could reduce early post-CABG mortality and decrease the incidence of major postoperative adverse events in ICU (Figure 1).

Materials and Methods

Study design

A retrospective cohort study of all consecutive patients (age 67±3; 18 females) undergoing primary isolated on-pump CABG surgery from January 1, 2008, to April 30, 2008 at our Institution was performed. Patients with history of atrial arrhythmias (atrial flutter, fibrillation, and supraventricular tachycardia) as well as combined CABG and valve or other cardiac surgery (eg, atrial septal defect repair, ventricular aneurysm resection) were excluded from the analysis. Patients were classified into 2 groups: patients receiving pre-operative lipid-lowering therapy and patients not receiving pre-operative lipid-lowering therapy at admission. Patients were considered as taking statins if on treatment with this class of drugs continuously from at least 1 month before CABG surgery. Commercially available statins screened for in this study included simvastatin, atorvastatin, and rosuvastatin.

Data collection

Patients' demographic variables, pre-operative risk factors, co-morbid conditions, pre-operative medications use (including statin therapy, ACE-inhibitors, β-blockers and aspirin) and the incidence of adverse perioperative events, in the first 7 post-CABG days, were collected.

For each patient, the pre-operative risk of death using the European System for Cardiac Operative Risk Evaluation (EuroSCORE) [13] was also calculated.

The primary end-point was the composite of early complications occurring after surgery during stay in ICU and in Sub-Intensive Care Unit. Measured adverse outcomes included: postoperative infections;

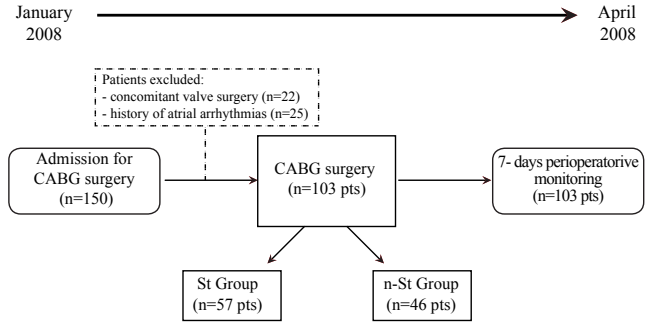

Figure 1: Flow-chart of the study. From January 2008 to April 2008, 150 consecutive patients, undergoing primary isolated on-pump CABG surgery, were enrolled. 25 patients with history of atrial arrhythmias and 22 patients undergoing concomitant valve surgery were excluded from the analysis. Finally, 103 patients, divided into two groups on the basis of statin medication, were included in our study and anamnestic and clinical data were collected. All patients were followed for 7 days after surgery to assess the incidence of perioperative adverse events.

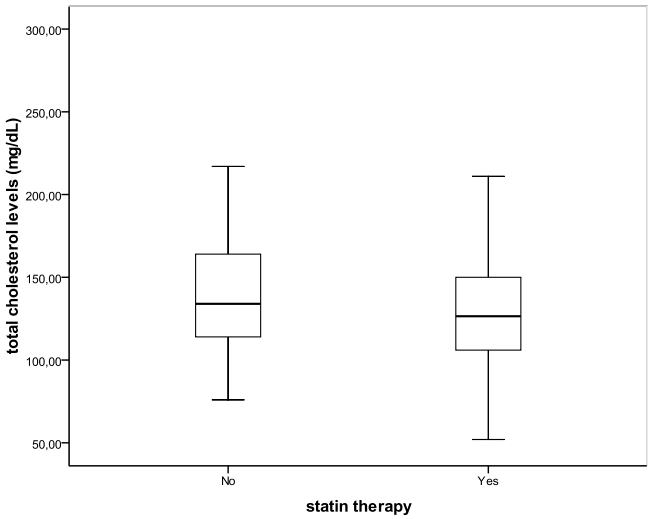

Figure 2: Comparison of cholesterol levels between St and n-St patients.

reoperation for bleedings; sustained ventricular and supra-ventricular tachyarrhythmias requiring medical treatment or DC shock, including atrial fibrillation; cardiogenic shock needing inotropic support; Myocardial Infarction (MI) and mortality. A diagnosis of postoperative infection was made if one of the following occurred: pneumonia, deep sternal wound infection, sepsis, Urinay Tract Infection (UTI) with bacteremia. A diagnosis of cardiogenic shock was made if systolic blood pressure (BP) was < 70 mmHg or cardiac index was < 2.2 L/min/m^2, needing for inotropic support (including Intra-Aortic Balloon Pump counterpulsation, adrenaline or dobutamine infusion). According to current guidelines, a diagnosis of MI was made if there was elevation of troponin greater than 5 x 99th percentile URL plus either new pathological Q waves or new LBBB, or angiographically documented new graft or native coronary artery occlusion, or imaging evidence of new loss of viable myocardium [14]. As secondary end-points single perioperative complications were considered. In-hospital stay duration was also evaluated.

Statistical analysis

According to current literature [15], for sample size calculation we hypothesized a 20% risk reduction of composite adverse outcome in patients on statin therapy. On the basis of a mean number of 150 isolated CABG interventions performed in our Cardiac Surgery ward in a four- months period, we calculated a sample size of about 50 patients for each subgroup in order to detect a statistically significant difference between the two groups with a 95% power and a type I error of 0.05. Comparison among groups for discrete categorical variables was carried out by determining chi^2 statistic, using Fisher's exact test as appropriate. Continuous variables not normally distributed were presented as median and interquartile range (IQR) and compared by Mann-Whitney U-test. Predictors of combined outcome were assessed using a stepwise multivariate logistic regression model to estimate the odds ratio (OR) and corresponding 95% confidence interval (95% CI). Univariate analysis was performed including demographic variables, cardiovascular risk factors and relevant co-morbidities, known to be related to adverse outcome on the basis of current evidence. Variables showing statistical differences at p≤0.20 were included into a multivariate backward binary logistic regression model. Finally p < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 17.0 software (SPSS Inc, Chicago, IL, USA).

	St group (n=57)	n-St group (n=46)	*p* value
Age (years), median ± IQR	64.98±7.74	66.65±8.65	0.26
Gender, male; n (%)	48 (85.7)	34 (74.5)	0.076
Cholesterol levels (mg/dl), median ± IQR	134.46±48.01	139.89±36	0.18
Diabetes, n (%)	13 (23.2)	15 (32)	0.22
Previous MI, n (%)	29 (51.8)	30 (63.8)	0.15
Smoke habit, n (%)	33 (58.9)	23 (48.9)	0.21
Familiy history of CAD, n (%)	20 (35.7)	7 (14.9)	**0.014**
Hypertension, n (%)	46 (82.1)	39 (83)	0.56
Three-vessels disease, n (%)	47 (84)	39 (83)	0.55
Cerebrovascular disease, n (%)	4 (7.1)	2 (4.3)	0.43
Pulmunary disease, n (%)	9 (16.1)	7 (14.9)	0.55
Renal failure, n (%)	1 (1.8)	1 (2.1)	0.7
EuroSCORE, median ± IQR	3.35 (1.33-39)	3.14 (1.21-37)	0.571
β-blockers, n (%)	50 (87)	38 (83)	0.62
ACE-Is, n (%)	51 (90)	41 (89)	0.85
ARBs, n (%)	13 (23)	14 (32)	0.22
Aspirin, n (%)	54 (95)	44 (96)	0.81

IQR= interquartile range; n= number.
ACE-I = angiotensin converting enzyme inhibitor;
ARB= angiotensin receptor blocker.

Table 1: Clinical and Biochemical Baseline Characteristics of the study population.

	Univariate analysis			*Multivariate analysis*		
	OR	**95%CI**	***p* value**	**OR**	**95%CI**	***p* value**
Age, years	1.053	1.000-1.110	0.052	1.047	0.990-1.107	0.111
Gender, male	0.728	0.287-1.847	0.504			
Cholesterol levels	1.643	0.181-2.346	0.911			
Diabetes	0.571	0.229-1.425	0.23			
Previous MI	1.062	0.481-2.346	0.861			
Smoke habit	0.801	0.365-1.759	0.58			
Family history of CAD	1.161	0.479-2.817	0.741			
Hypertension	0.667	0.240-1.850	0.436			
Three-vessels disease	3.204	0.917-11.196	0.068	3.534	0.937-13.31	0.062
Cerebrovascular disease	0.262	0.029-2.327	0.229			
Pulmunary disease	2.727	0.907-8.200	0.074	2.782	0.817-9.476	0.102
Renal failure	1.405	0.085-23.099	0.812			
EuroSCORE	2.327	1.513-4.505	**0.009**	2.114	1.2134.407	**0.002**
Statin therapy	0.388	0.173-0.867	**0.021**	0.307	0.123-0.766	**0.011**
β-blocker therapy	0.694	0.279-1.428	0.293			
ACE-Is therapy	0.791	0.365-1.759	0.597			
ARBs therapy	0.813	0.458-1.916	0.642			
Aspirin therapy	0.846	0.367-2.435	0.857			

Table 2: Predictors of primary endpoint at univariate and multivariate analysis.

	St group (n=57)	n-St group (n=46)	*p* value
Primary End-Point	18 (31%)	25 (54%)	**0.019**
In-Hospital infections	1 (1.7%)	3 (6.5%)	ns
Bleeding	1 (1.7%)	2 (4%)	ns
VTs	4 (7%)	4 (9%)	ns
AF/ other SVTs	11 (24%)	12 (21%)	ns
Inotropic support	1 (1.7%)	3 (6.5%)	ns
MI	0 (0%)	0 (0%)	ns
Mortality	0 (0%)	1 (2%)	ns
In-Hospital Stay (days)	5,6±1,8	7.7±3,9	**0.001**

VTs= Ventricular Tachyarrhythmias ; AF= atrial fibrillation ; SVT= Supra-Ventricular Tachyarrhythmias

Table 3: Perioperative complications of St and n-St patients.

Results

A total of 150 patients undergoing primary on-pump CABG surgery were screened. According to the prespecified exclusion criteria, 22 patients were excluded for concomitant valve surgery and 25 for history of atrial arrhythmias. We finally enrolled 103 consecutive patients (age 67±3; 18 females), classified into 2 groups: patients

receiving pre-operative lipid-lowering therapy (St, n=57, 55%) and patients not receiving pre-operative lipid-lowering therapy (n-St, n=46, 45%) on admission. The pre-operative characteristics of study population are summarized in Table 1. Among St Patients, 27 were on atorvastatin (mean dose 11, 42 mg/day), 27 on simvastatin (16,66 mg/day) and 3 on rosuvastatin (mean dose 5 mg/day). No significantly statistical differences were observed between groups with respect to age, gender, presence of diabetes, history of myocardial infarction, smoke habit, hypertension, presence of three-vessel disease, cerebrovascular and pulmonary disease, renal failure, and EuroSCORE. Only a higher prevalence of family history of coronary artery disease was observed in St group. Of note, the cholesterol levels were similar between St- and non-St patients (Figure 2).

At univariate analysis, only statin therapy and EuroSCORE emerged as predictors of the composite adverse outcome. Age, presence of-three vessels disease and history of pulmonary disease showed a weak trend for statistical significance.

Multivariate analysis confirmed pre-operative statin therapy and EuroSCORE as independent predictors of the primary endpoint (OR=0.307, 95% CI=0.123-0.766, p=0.011 and OR= 2.114, 95% CI= 1.213- 4.407, p= 0.002 respectively) (Table 2). n-St patients had a significant higher rate of early complications if compared with St patients: the primary endpoint occurred in 18 St patients (31%) versus 25 (54%) non-St patients (p=0,019) (Table 3). The incidence of secondary end-points did not differ significantly between the groups. Of note, in-hospital stay was longer in n-St group if compared with St group (7.7±3,9 days vs 5,6±1,8 days; p=0,001).

Discussion

Despite progress in surgical techniques, cardiac surgical morbidity and mortality is still a problem of significant medical and socioeconomic significance. Our study suggests that pre-operative statin therapy may reduce the occurrence of perioperative adverse events after CABG.

We studied retrospectively a population of 103 patients, all of whom had undergone primary CABG surgery, of whom 57 on statin therapy (St group) and 46 not (n-St group). In our population, pre-operative statin therapy and EuroSCORE emerged as the only predictors of early post-CABG complications and of in-hospital stay duration. Of note, pre-operative statin therapy had a beneficial effect on outcome which was independent of cholesterol levels.

Statins exert their primary effect on cholesterol metabolism reducing cholesterol levels. Long-term statin administration in ambulatory patient populations with hypercholesterolemia has been previously associated with a reduced risk of adverse cardiovascular events, including death, MI, stroke, and renal dysfunction [16]. Furthermore, many randomized clinical trials have shown a beneficial effect of long-term statin administration in primary and secondary prevention of adverse cardiovascular outcomes even in patients with mild hypercholesterolemia and with normal total and low-density lipoprotein cholesterol levels [17,18]. All these data strongly support the use of statins for primary and secondary prevention of coronary artery disease, as recommended by current guidelines.

Moreover, statin therapy has been shown to exert an early beneficial effect on outcome in patients undergoing percutaneous coronary interventions [19-21].

Recent evidence suggests that pre-operative statin therapy in patients undergoing non-cardiac surgery improves the post-operative outcome by reducing adverse cardiovascular events and all-cause mortality [6,7]. However, in patients undergoing cardiac surgery, results are conflicting.

Some studies failed to show a beneficial effect of statins on perioperative adverse events after CABG, while others suggest that pre-operative statin therapy may reduce the occurrence of these end-points [8-12].

Our data are largely consistent with those of recently published meta-analysis [15,22] on the topic, that have demonstrated a substantial improvement in early clinical outcome for statins pretreated patients undergoing cardiac surgery, in particular reducing the short-term mortality and the incidence of atrial fibrillation and stroke.

Although the exact mechanisms linking pre-operative statin therapy with reduced cardiac surgical mortality are unclear in the present study, we can hypothesize that this finding may be due, more than to their lipid lowering effect, to their pleiotropic, anti-inflammatory effects. A significant increase in inflammatory markers, including C-reactive protein (CRP), serum amyloid A (SAA), TNF-α, IL-6, has been shown during by-pass circulation, suggesting an activation of inflammation during the procedure [23]. Furthermore, statins have consistently been demonstrated to decrease inflammation in both in vitro and in vivo. Statins have been shown to be protective against tissue injury in multiple models of ischemia/reperfusion, including heart, lung, brain, kidney, and gut. In patients with acute coronary syndromes or idiopathic dilated cardiomyopathy, statin therapy has been shown to reduce serum inflammatory marker levels, including CRP, SAA, tumor necrosis factor-α, interleukin-6, and brain natriuretic peptide [24-26]. Indeed, data from JUPITER trial [27] suggest that in apparently healthy subjects, CRP screening might be an effective method to identify subjects who are more or less likely to benefit from statin therapy for cardiovascular risk reduction, regardless of cholesterol levels. Taken together these findings may represent the theoretical framework for the reduction in perioperative complications observed in our study.

Our study has several limitations. First of all, it is an observational retrospective study, with inability to control all confounding factors such dosage of statin therapy. Second, the small sample size probably influenced the results concerning the secondary end-points. Third, we can only speculate about the mechanism underlying the beneficial effect of statins; it might be due to their inflammatory properties but we failed to collect blood samples to measure inflammatory biomarkers levels in order to assess differences between groups.

Conclusions

Our study, despite the limitations discussed above, demonstrates that statin therapy may reduce early perioperative complications after CABG and that this effect is independent from cholesterol levels, thus supporting pre-operative statin use in patients undergoing CABG. However, larger prospective studies are needed to investigate this important and interesting topic.

References

1. Anthony A, Sendelbach S (2007) Postoperative complications of coronary artery bypass grafting surgery. Crit Care Nurs Clin North Am 19: 403-415.

2. Lazar HL, Bao Y, Zhang Y, Bernard SA (2003) Pretreatment with statins enhances myocardial protection during coronary revascularization. J Thorac Cardiovasc Surg 125: 1037-1042.

3. Martínez-Comendador JM, Alvarez JR, Mosquera I, Sierra J, Adrio B, et al. (2009) Preoperative statin treatment reduces systemic inflammatory response and myocardial damage in cardiac surgery. Eur J Cardiothorac Surg 36: 998-1005.

4. Dereli Y, Ege E, Kurban S, Narin C, Sarigül A, et al. (2008) Pre-operative atorvastatin therapy to decrease the systemic inflammatory response after coronary artery bypass grafting. J Int Med Res 36: 1248-1254.

5. Knatterud GL, Rosenberg Y, Campeau L, Geller NL, Hunninghake DB, et al. (2000) Long-term effects on clinical outcomes of aggressive lowering of low-density lipoprotein cholesterol levels and low-dose anticoagulation in the post coronary artery bypass graft trial. Post CABG Investigators. Circulation 102: 157-165.

6. Poldermans D, Bax JJ, Kertai MD, Krenning B, Westerhout CM, et al. (2003) Statins are associated with a reduced incidence of perioperative mortality in patients undergoing major noncardiac vascular surgery. Circulation 107: 1848-1851.

7. O'Neil-Callahan K, Katsimaglis G, Tepper MR, Ryan J, Mosby C, et al. (2005) Statins decrease perioperative cardiac complications in patients undergoing noncardiac vascular surgery. J Am Coll Cardiol 45: 336-342.

8. Powell BD, Bybee KA, Valeti U, Thomas RJ, Kopecky SL, et al. (2007) Influence of preoperative lipid-lowering therapy on postoperative outcome in patients undergoing coronary artery bypass grafting. Am J Cardiol 99: 785-789.

9. Clark LL, Ikonomidis JS, Crawford FA jr, Crumblej A III, Kratz JM, et al. (2006) Preoperative statin treatment is associated with reduced postoperative ,mortality and morbidity in patients undergoing cardiac surgery: an 8-year retrospective cohort study. J Thorac Cardiovasc Surg 131: 679-685.

10. Pan W, Pintar T, Anton J, Lee VV, Vaughn WK, (2004) Statins are associated with a reduced incidence of perioperative mortality after coronary artery bypass graft surgery. Circulation 110: II45-49.

11. Ali IS, Buth KJ (2005) Preoperative statin use and outcomes following cardiac surgery. Int J Cardiol 103: 12-18.

12. Subramaniam K, Koch CG, Bashour A, O'Connor M, Xu M, et al. (2008) Preoperative statin intake and morbid events after isolated coronary artery bypass grafting. J Clin Anesth 20: 4-11.

13. Nashef SA, Roques F, Hammil BG, Peterson ED, Michel P, et al. (2002) EuroSCORE Project Group Validation of European System for Cardiac Operative Risk Evaluation (EuroSCORE) in North American cardiac surgery. Eur J Cardiothoracic surgery 22: 101-105.

14. Thygesen K, Alpert JS, White HD; Joint ESC/ACCF/AHA/WHF (2007) Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. Eur Heart J 28: 2525-2538.

15. Liakopoulos OJ, Choi YH, Haldenwang PL, Strauch J, Wittwer T, et al. (2008) Impact of preoperative statin therapy on adverse postoperative outcomes in patients undergoing cardiac surgery: a meta-analysis of over 30 000 patients. Eur Heart J 29: 1548-1559.

16. Shepherd J, Cobbe SM, Ford I, Isles CG, Lorimer AR, et al. (1995) Prevention of Coronary Heart Disease with Pravastatin in Men with Hypercholesterolemia. N Engl J Med 333: 1301-1308.

17. Downs JR, Clearfield M, Weis S, Whitney E, Shapiro DR, et al. (1998) Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. AirForce/Texas Coronary Atherosclerosis Prevention Study. JAMA 279: 1615-1622.

18. Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, et al. (1996) The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. N Engl J Med 335: 1001-1009.

19. Chan AW, Bhatt DL, Chew DP, Quinn MJ, Moliterno DJ, et al. (2002) Early and Sustained Survival Benefit Associated with Statin Therapy at the time of Percutaneous Coronary Intervention. Circulation 105: 691-696.

20. Serruys PW, Foley DP, Jackson G, Bonner H, Macaya C, et al. (1999) A randomized placebo- controlled trial of fluvastatin for prevention of restenosis after successful coronary balloon angioplasty: Final results of the fluvastatin angiographic restenosis (FLARE) trial. Eur Heart J 20: 58-69.

21. Herrmann J, Lerman A, Baumgart D, Volbracht L, Schulz R, et al. (2002) Preprocedural Statin Medication Reduces the Extent of Periprocedural Non-Q-Wave Myocardial Infarction. Circulation 106: 2180-2183.

22. Winchester DE, Xuerong W, Xie L, Bavry AA (2010) Evidence of Pre-Procedural Statin Therapy: a Meta-Analysis of Randomized Trials. J Am Coll Cardiol 56: 1099-1109.

23. Gaudino M, Nasso G, Zamparelli R, Andreotti F, Burzotta F, et al. (2002) Inflammatory and fibrinolytic activation after coronary artery bypass with extracorporeal circulation. Ital Heart J Suppl 3: 646-651.

24. Kinlay S, Schwartz GG, Olsson AG, Rifai N, Leslie SJ, et al. (2003) Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering Study Investigators. High-dose atorvastatin enhances the decline in inflammatory markers in patients with acute coronary syndromes in the MIRACL study. Circulation 108: 1560 –1566.

25. Brown WV (2003) Benefits of statin therapy in patients with special risks: coronary bypass surgery, stable coronary disease, and acute coronary syndromes. Clin Cardiol 26: III13–III18.

26. Node K, Fujita M, Kitakaze M, Hori M, Liao JK (2003) Short-term statin therapy improves cardiac function and symptoms in patients with idiopathic dilated cardiomyopathy. Circulation 108: 839–843.

27. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM Jr, et al. (2008) JUPITER Study Group. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 359: 2195-2207.