CME The Impact of Postoperative Discontinuation or Continuation of Chronic Statin Therapy on Cardiac Outcome After Major Vascular Surgery

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BACKGROUND: Statins reduce cardiac morbidity in nonsurgical populations, and may benefit surgical patients. We sought to examine cardiac outcome in patients who continued, compared with those who discontinued, statin therapy after major vascular surgery.

METHODS: Prospectively collected data were examined for an association between statin therapy and perioperative cardiac morbidity in patients undergoing infrarenal aortic surgery. Between January 2001 and December 2003, there were no guidelines for perioperative continuation of statins (discontinuation group, $n = 491$). From January 2004, guidelines were instituted whereby statin therapy was continued starting as soon as possible after surgery (continuation group, $n = 178$). The occurrence of cardiac myonecrosis (defined as an increase of cardiac troponin I more than the 99th percentile or 0.2 ng/mL) was analyzed. Intra-cohort (propensity score) and extra-cohort (Lee score) adjustments of the risk were performed.

RESULTS: The median delay between surgery and resumption of statin therapy was 4 days and 1 day in the discontinuation and continuation groups ($P < 0.001$), respectively. Using propensity score matching for likelihood of preoperative treatment, the odds ratio associated with chronic statin treatment to predict myonecrosis for patients with versus without early postoperative statin resumption (continuation versus discontinuation groups) was 0.38 and 2.1 (relative risk reduction of 5.4; 95% confidence interval: 1.2–25.3, $P < 0.001$), respectively. The odds ratio after adjustment for the Lee score was 0.38 in the continuation group and 2.1 in the discontinuation group (relative reduction of 5.5; 95% confidence interval: 1.2–26.0, $P < 0.001$). Postoperative statin withdrawal (>4 days) was an independent predictor of postoperative myonecrosis (OR 2.9, 95% confidence interval 1.6–5.5).

CONCLUSIONS: Discontinuation of statin therapy after major vascular surgery is associated with an increased postoperative cardiac risk, suggesting that statin therapy should be resumed early after major vascular surgery.

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Major vascular surgery is associated with a mortality rate of up to a 5% 30-day mortality rate, mainly because of adverse cardiac events, including myocardial infarction (1). Apart from β-adrenergic blockers (2,3), there are few drugs available which can decrease the risks for perioperative cardiac complications. Treatment with 3-hydroxymethylglutaryl coenzyme A reductase inhibitors, or statins, is increasingly used in patients with cardiovascular disease. In addition to their lipid decreasing properties, statins have other well described vascular effects, including antioxidant, antiinflammatory (4), plaque-stabilizing actions, as well as effects that improve endothelial function and reduce platelet aggregation (5,6). Treatment with statin drugs has been shown to reduce myocardial infarction and stroke in primary and secondary prevention studies (7). Other data have suggested a benefit for surgical patients treated with statins when compared with patients not receiving this therapy (8–11). Nevertheless, in many patients statins are discontinued in the immediate perioperative period because of the concerns about impaired gastrointestinal absorption and severe rhabdomyolysis (12).

During a survey of our vascular surgery database, we observed that patients chronically treated with statins had a surprisingly increased level of cardiac risk, despite multivariate risk adjustment, in contrast with previous reports from others groups (9,11). Because statins are given orally, statin withdrawal for

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several days has been a common practice in the management of our patients after major abdominal vascular surgery. After the publication of clinical and experimental reports describing adverse effects associated with statin withdrawal (13–17), we modified our therapeutic approach to continue statin therapy during the immediate postoperative period.

In the present study, we evaluated the effect on postoperative cardiac morbidity of our past practice (stopping statins) and compared it with our amended practice (resumption of statins immediately after surgery). We therefore tested the hypotheses that withdrawal of statins during the postoperative period is associated with an increased cardiac risk after major vascular surgery.

METHODS

Patient Characteristics

The Pitié-Salpêtrière Vascular Surgical Register is a comprehensive database, recorded prospectively which contains clinical and surgical characteristics of all patients undergoing vascular surgery at our institution since 1984 (18,19). A systematic audit by one of the authors (MB) allowed verification of the accuracy in data coding. For this study, we included all patients who underwent infrarenal aortic reconstructive surgery or endoprosthetic procedures (aneurysm or occlusive disease of the aorta) from January 2001 to December 2004. Patients undergoing emergency surgery were excluded. The study was approved by our institutional ethics committee (Comité Consultatif de Protection des Personnes se Prêtant à la Recherche Biomédicale Pitié-Salpêtrière, Paris, France). Because data were collected while patients were receiving standard clinical care, the requirement for written informed consent was waived.

Perioperative Management

All patients were screened in accordance with the recommendations of the American College of Cardiology/American Heart Association Task Force (20). In patients with poor or nonevaluable functional capacity, unstable coronary artery disease, or with a positive noninvasive myocardial stress test, coronary angiography was performed. A percutaneous coronary procedure was performed at the same time as catheterization if technically feasible; if not, coronary artery bypass graft was considered (19). Patients undergoing percutaneous coronary procedures received one or more bare metal stents and were treated with clopidogrel for 4 wk and aspirin indefinitely. Aortic surgery was conducted after a 4-wk delay and after discontinuing aspirin for 1 wk (19). Surgery was performed under general anesthesia, with IV propofol, sufentanil, and atracurium, as previously described (18,19).

Postoperatively, patients were transferred to the postanesthesia care unit (PACU). Postoperative hypertension (systolic arterial blood pressure more than 30% of baseline value) was treated by an IV bolus of nicardipine 1 mg followed by continuous IV administration, or by clonidine (150 μg IV or subcutaneously). Tachycardia (heart rate more than 80 bpm) was treated with IV β-adrenergic receptor blocking drugs (e.g., esmolol or atenolol). The target heart rate was 70 bpm. Postoperative analgesia included IV morphine followed by subcutaneous morphine administration, as previously described (21). All patients received subcutaneous low molecular weight heparin (enoxaparin 40 mg daily) after the operation until postoperative day 30. β-Blockers were resumed the evening after surgery for patients receiving this therapy before surgery. In patients with documented and previously treated coronary artery disease, aspirin was reintroduced on postoperative day 1.

Blood was obtained for measurement of cardiac troponin I (cTnI) in all patients on arrival to the PACU, and on the first, second, and third postoperative days. This measurement was performed using an immunoenzymofluorometric assay on a Stratus autoanalyser (Dade-Behring, Paris LA Défense, France). An electrocardiogram was performed on arrival into the PACU, and on the first, second, and third postoperative days, and after the third day if there were clinical abnormalities and/or if there were increased cTnI values.

Perioperative Administration of Statins

Patients not chronically treated with a statin drug during either study period were considered as controls, and they did not receive the treatment perioperatively. During the first period (discontinuation group), from January 2001 to December 2003, no specific guidelines were followed regarding postoperative statin readministration. Restarting statins was not considered as important as resuming β-adrenergic blockers and/or antiplatelet therapy. Statin treatment frequently occurred only after the initial postoperative period after return to the surgical ward. From January 2004 (continuation group), strict guidelines were implemented to continue statins up to the evening before surgery with resumption of treatment on the first postoperative day either orally or via a nasogastric tube. The administration of statin drugs during the postoperative period was verified by examination of the nursing records during the two study periods. Perioperative management was the same for all patients during both periods of the study, except for the readministration of statins.

End Points

Postoperative cardiac myonecrosis was defined as an abnormal cTnI value at any time during the postoperative period (18,22,23). The cutoff used during the study period to define normality was 0.2 ng/mL, a value above the 99th percentile for our laboratory (23). Death was defined as death from any cause occurring

during hospitalization and/or within 30 days after surgery.

Statistical Analysis

Data are expressed as mean ± SD. Comparison of two means was performed using the Student's *t*-test. Because this study was not randomized and because patients receiving statins preoperatively had a different perioperative risk than those who did not, we performed a separate multivariate risk adjustment to analyze the perioperative risk associated with statin treatment, in both the discontinuation and continuation groups. Two different methods (intra-cohort and extra-cohort adjustment) were considered, as previously described (19).

Intra-Cohort Adjustment

For each patient, a propensity score (24), indicating the likelihood of receiving statin drugs, was calculated with a forward stepwise conditional multivariate logistic regression, where all perioperative predictors identified in the univariate analysis were included in this analysis. End points were compared globally using the Mantel–Haenszel test.

Extra-Cohort Adjustment

We chose the risk index from Lee et al. (25) in which one point is assigned to each of the following characteristics: high-risk type of surgery, known ischemic heart disease, history of congestive heart failure, history of cerebrovascular disease, diabetes mellitus, and renal failure. This index effectively combines the clinical cardiac risk into one variable. Subsequently, the prognostic value of this risk index and the additional prognostic value of chronic statin therapy were analyzed by logistic regression.

Finally, we pooled patients receiving statins from the discontinuation and continuation groups and determined the best threshold (which minimized the distance to the ideal point, i.e., sensitivity = specificity = 1) of the delay to postoperative statin administration in predicting cardiac myonecrosis, using the receiver operating curve (ROC). The area under the ROC curve and its 95% confidence interval (CI) was calculated.

The adjusted postoperative risk associated with statin withdrawal was determined by a backward stepwise logistic regression using preoperative and intraoperative variables that are associated with poor prognosis (18,19). In the discontinuation group, several patients received statin drugs in the first postoperative days, whereas in the continuation group some patients had no statin treatment by postoperative day seven. Those patients could have induced a bias into the group analyses. The aims of this complimentary analysis were first to delete this potential bias, second to delete the potential historical bias induced by the design of the study.

Calibration and discrimination of the logistic models were assessed using the Hosmer–Lemeshow statistics (26) and c-statistic, respectively. Internal validation was also performed using the jack knife method and the proportion of patients appropriately classified was required to be more than 75% (data not shown).

We calculated the number of patients required in the continuation group as follows: Assuming an α risk of 0.05 and a β risk of 0.20, we estimated that the odds ratio (OR) of myonecrosis associated with statin administration in the discontinuation group was 2.0 and that the percentage of patients treated with statins was 50%. We calculated that at least 165 patients should be included to detect a reduction of this OR to 0.5, indicating a relative reduction of 4.

Patients with lost data were excluded. All statistical comparisons were two-tailed and a P value of <0.05 was considered significant. Statistical analysis was performed using SPSS version 13 software (SPSS Inc., Chicago, IL).

RESULTS

Data were reviewed from 491 patients in the discontinuation group and 178 patients in the continuation group. During the two periods, 294 patients (44%) were chronically treated with statins (simvastatin: 40%; pravastatin 34%; atorvastatin 24%; fluvastatin 2%). Statins were more frequently used in the continuation group (51% vs 41%, $P = 0.02$). Table 1 describes the patients' main clinical characteristics.

The delay between surgery and restarting statin drugs could not be precisely determined in 26 patients, of which 23 (5%) were in the discontinuation and 3 (2%) were in the continuation group. These 29 patients were excluded from analysis.

The median delay for resuming statin therapy was 4 days (95% CI: 3.7–4.3 days) in the discontinuation and 1 day (95% CI: 0.7–1.3 days) in the continuation group ($P < 0.001$) (Fig. 1). When preoperatively treated with statins, 22% of the patients received statins on postoperative day 1 in the discontinuation group vs 70% in the continuation group ($P < 0.001$) (Fig. 1).

Intra-Group Risk Adjustments

Variables significantly associated with chronic statin treatment were used to construct a propensity score (age, coronary artery disease, renal failure, diabetes, and hypertension) for the likelihood of receiving statins before surgery. The Hosmer–Lemeshow statistic value for this model was 5.9 ($P = 0.65$) and the c-statistic was 0.73. After adjustment for the propensity score, the OR associated with chronic statin treatment for predicting postoperative cardiac myonecrosis was 2.1 (95% CI: 1.1–3.8, $P < 0.03$) in the discontinuation group and 0.38 (95% CI: 0.15–0.98 $P < 0.04$) in the continuation group (Table 2), indicating a relative reduction of the OR of 5.4 (95% CI: 1.2–25.3, $P < 0.001$) between the two periods. No significant difference was found

Table 1. Patient Characteristics During the Two Study Periods

Variables	Discontinuation group		Continuation group	
	Control (N = 289)	Statin (N = 202)	Control (N = 86)	Statin (N = 92)
Patient characteristics				
Age (yr)	68 ± 11	67 ± 11	68 ± 11	66 ± 10
Male	254 (88)	184 (91)	76 (88)	81 (88)
Previous myocardial infarction	40 (14)	58 (29)*	7 (8)	16 (17)*
Previous myocardial revascularisation	31 (11)	57 (28)*	16 (19)	32 (35)*
CABG	15 (5)	32 (16)*	9 (10)	12 (13)
PCI	16 (6)	25 (12)*	7 (8)	20 (22)*
Coronary artery disease	70 (24)	120 (59)*	22 (26)	50 (54)*
Cardiac failure	13 (4)	14 (7)	7 (8)	4 (4)
Hypertension	147 (51)	135 (67)*	49 (57)	63 (68)
Diabetes	31 (11)	30 (15)	3 (3)	14 (15)*
Renal failure	31 (11)	39 (19)*	13 (15)	18 (20)
Preoperative hemodialysis	3 (1)	1 (1)	1 (1)	3 (3)
COPD	126 (44)	76 (38)	34 (40)	41 (45)
Respiratory failure	48 (17)	20 (10)*	11 (13)	6 (7)
Patient chronic treatment				
Nitroglycerin	25 (9)	32 (16)*	5 (6)	14 (15)*
β-blockers	67 (23)	92 (46)*	29 (34)	46 (50)*
ACEI or ARA	81 (28)	96 (48)*	17 (20)	37 (40)*
Surgery characteristics				
Aneurysm	208 (72)	144 (71)	62 (72)	62 (67)
Endoprothetic procedure	102 (35)	62 (31)	29 (34)	31 (34)
Reintervention (any type)	34 (12)	15 (7)	12 (14)	8 (9)
Packed red blood cells >3 units	46 (16)	39 (19)	21 (24)	12 (13)
Outcome				
Cardiac myonecrosis	22 (8)	33 (16)*	15 (17)†	11 (12)
Elevated cTnI >1.5 ng/mL	10 (3)	10 (5)	7 (8)	4 (4)
Death	8 (3)	8 (4)	3 (3)	2 (2)

Data are mean ± SD, or number (percentage).

ACEI = Angiotensin converting enzyme inhibitors; ARA = angiotensin-II receptor antagonists; COPD = chronic obstructive pulmonary disease; CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; Renal failure was defined as a preoperative creatinine value >120 μmol/L; and cardiac myonecrosis as cardiactroponin I (cTnI) >0.20 ng/mL.

* $P < 0.05$ vs control in each group; † $P < 0.05$ vs discontinuation group with statin or control.

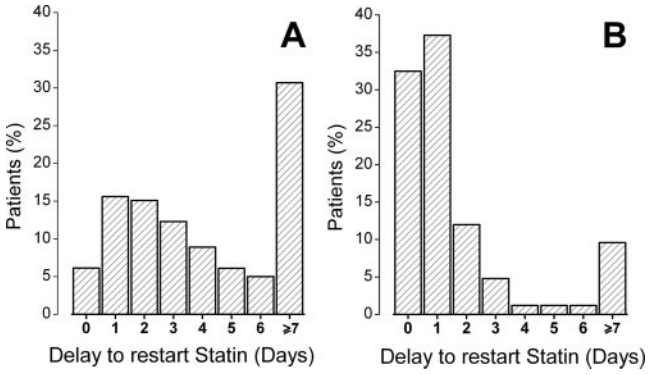

Figure 1. Distribution of the delay between surgery and restarting of statins in the discontinuation group (n = 491, Panel A) and continuation group (n = 178, Panel B).

in operative mortality between control patients and patients receiving preoperative statins for either the discontinuation or the continuation group (Table 2).

Extra-Group Risk Adjustment

The OR associated with statins in predicting postoperative cardiac myonecrosis after adjustment for the Lee risk index was 2.1 (95% CI: 1.2–3.9, $P < 0.04$) in the discontinuation group and 0.38 (95% CI: 0.15–0.98; $P < 0.05$) in the continuation group (Table 3), indicating a relative reduction of the OR of 5.5 (95% CI: 1.2–26.0, $P < 0.001$) between the two periods. No significant difference was found for death (Table 3).

Pooled Analysis

All patients who received statins during the two study periods (n = 262 with a known delay) were thus pooled. The threshold for the delay between surgery and restarting statins to predict increased postoperative cardiac myonecrosis determined by ROC curve analysis was 4 days. The area under the ROC curve was 0.65 (95% CI: 0.55–0.75).

We used this pooled population of patients treated with statins (n = 262) to perform logistic regressions to predict postoperative cardiac myonecrosis. The readministration of statins with an early delay (≤4 days) was compared with restarting statins with a prolonged delay (>4 days, statin withdraw) after surgery. Six variables were found to be independent predictors of myonecrosis: age, known coronary artery disease, open surgery for aneurysm, need for re-operation (any type in the days after aortic surgery), the number of blood units transfused, and statin withdrawal (Table 4). The Hosmer–Lemeshow statistic was 5.1 (P = 0.74) and the c-statistic was 0.81. The OR associated with a prolonged delay between surgery and restarting of statins

Table 2. Intra-Cohort Risk Adjustment Using the Propensity Score Analysis in Patients with or Without Chronic Statin Treatment in the Two Study Periods

Propensity score quartiles	1	2	3	4	*P* value	OR statins (95% CI)	Relative reduction of OR statins
Discontinuation group							
Number of patients					—		
Control	104 (36)	88 (30)	59 (20)	38 (13)		—	—
Statins	23 (11)	31 (15)	65 (32)	83 (41)			
Propensity score							
Control	0.19 ± 0.04	0.33 ± 0.04	0.49 ± 0.06	0.70 ± 0.06	0.73	—	—
Statins	0.20 ± 0.03	0.22 ± 0.04	0.52 ± 0.06	0.73 ± 0.0			
Cardiac myonecrosis							
Control	7 (7)	4 (4)	6 (10)	5(13)	0.02	2.1	—
Statins	4 (17)	5 (16)	9 (14)	15 (18)		(1.1–3.8)	
Death							
Control	1 (1)	1 (1)	2 (3)	4 (10)	0.59	1.4	
Statins	0 (0)	1 (3)	2 (3)	5 (6)		(0.5–3.9)	—
Continuation group							
Number of patients							
Control	30 (35)	28 (33)	17 (20)	11 (12)	—	—	—
Statins	10 (11)	20 (22)	27 (29)	35 (38)			
Propensity score							
Control	0.20 ± 0.03	0.32 ± 0.04	0.50 ± 0.06	0.73 ± 0.0	0.67	—	—
Statins	0.22 ± 0.03	0.33 ± 0.04	0.51 ± 0.07	0.73 ± 0.0			
Cardiac myonecrosis							
Control	5 (17)	2 (7)	2 (12)	6 (54)	0.04	0.38	5.4
Statins	1 (10)	1 (5)	1 (4)	8 (23)		(0.15–0.98)	(1.2–25.3)
Death							
Control	0 (0)	2 (7)	0 (0)	1 (9)	0.27	0.48	2.9
Statins	0 (0)	0 (0)	0 (0)	2 (6)		(0.07–3.51)	(0.1–55.7)

P value refers to global comparison between control and statins; NS = not significant.

Table 3. Extra-Cohort Risk Adjustment Using the Lee Score in Patients with or Without Chronic Statin Treatment in the Two Study Periods

Lee score	1	2	3	>4	*P* value	OR statins (95% CI)	Relative reduction of OR statins
Discontinuation group							
Number of patients							
Control	94 (69)	121 (62)	51 (49)	23 (42)	—	—	—
Statins	43 (31)	75 (38)	52 (51)	32 (58)			
Cardiac myonecrosis							
Control	5 (5)	10 (8)	5 (10)	2 (9)	0.01	2.1	—
Statins	4 (9)	9 (12)	13 (25)	7 (22)		(1.2–3.9)	
Death							
Control	1 (1)	3 (3)	1 (2)	3 (13)	0.78	1.1	—
Statins	1 (2)	2 (3)	3 (6)	2 (6)		(0.4–3.1)	
Continuation group							
Number of patients							
Control	48 (65)	28 (36)	8 (42)	2 (25)	—	—	—
Statins	26 (35)	49 (64)	11 (58)	6 (75)			
Cardiac myonecrosis							
Control	5 (10)	3 (11)	6 (75)	1 (50)	0.04	0.38	5.5
Statins	1 (4)	5 (10)	2 (18)	3 (50)		(0.15–0.98)	(1.2–26.0)
Death							
Control	0 (0)	1 (4)	2 (25)	0 (0)	0.32	0.39	2.8
Statins	0 (0)	1 (2)	1 (9)	0 (0)		(0.05–2.57)	(0.2–62.6)

P value refers to global comparison between control and statins; NS = not significant.

was 2.9 (95% CI: 1.5–5.6; $P = 0.001$). Interruption of more than 4 days of chronic treatment with statins was associated with a 2.9-fold increase in the postoperative rate of postoperative cardiac myonecrosis.

DISCUSSION

Our study suggests that postoperative withdrawal of statins from patients undergoing surgical or

Table 4. Independent Variables Associated with Postoperative Cardiac Myonecrosis in Patients Chronically Treated with Statins Regardless of the Period of Study Where Delay Between Surgery and Restarting of Statins was Known ($N = 262$)

Variables	Odds ratio (95% confidence interval)	P value
Obliterative vascular disease	1.8 (1.1–3.2)	0.04
Coronary artery disease	1.8 (1.1–3.2)	0.03
Age >75 yr	2.0 (1.1–3.7)	0.03
Statins withdrawal = 4 days	2.9 (1.6–5.5)	0.001
Reintervention (any type)	3.7 (1.9–7.1)	<0.001
PRBC >3 units	4.1 (2.4–7.2)	<0.001

PRBC = Packed red blood cell units.

percutaneous treatment of infrarenal aneurysms is associated with higher risk for cardiac morbidity. We found that, in patients treated with statins before surgery, a delay of restarting this therapy by more than 4 days was associated with a higher risk of cardiac myonecrosis.

The effect of withdrawal of statin treatment has been examined in nonsurgical patients (13,15,27,28). In stable cardiac patients, it appears that discontinuation of statins is not associated with an extensive increased risk of acute myocardial injury (28). However, an accumulation of evidence suggests an adverse effect of statin withdrawal in patients with acute coronary artery syndromes. An almost three-fold higher risk for cardiac death or recurrent myocardial infarction was observed to be associated with statin withdrawal (13) during the initial 72 h after admission for acute myocardial infarction. More recently, a retrospective study showed that patients who discontinued statins during hospitalization for acute coronary syndromes had an approximately two-fold increase in hospital death rate (15). Furthermore, in these studies, statin withdrawal was associated with a higher rate of cardiac complications when compared with patients who had never been treated with statins. Other data have suggested potential deleterious effects of statin withdrawal in patients with sepsis (27) or after coronary artery bypass surgery (29).

Although the mechanisms by which statin withdrawal might contribute to adverse cardiac outcomes is not clear, several possible explanations have been proposed (16,30). Endothelial dysfunction is predictive of cardiac events (31) and statins significantly improve endothelium-mediated responses in patients with coronary artery disease (5). Improvement in endothelial function is lost within 1 day of cessation of statin therapy and endothelial-dependent blood flow even returns to below baseline values (14,32). Other protective effects of statin drugs on inflammatory processes, platelet aggregation, oxidant stress and, perhaps, antiapoptotic effects might have further harmful consequences when these drugs are abruptly withdrawn during an acute event with known stimulatory effects on these injurious pathways (33,34).

The deleterious effects of statin drug withdrawal thus appear most marked in patients with acute, rather than chronic, manifestations of coronary artery disease. The perioperative period is associated with many factors that increase the risk for myocardial injury, including activation of the sympathetic nervous system as well as inflammatory and thrombotic pathways (35). Thus, any benefits of continuation of statin treatment might be particularly beneficial to surgical patients at risk for myocardial injury. In this study we used propensity matching for the likelihood of preoperative statin treatment to adjust for factors that might have differentially contributed to this therapy during the two different periods of this study. After adjusting for propensity score, we found that statin therapy before surgery was significantly associated with risk for myonecrosis in the discontinuation group (OR 2.1, 95% CI 1.1; 3.8, $P < 0.03$). In contrast, statin therapy in the continuation group was associated with a significant risk reduction for myonecrosis (OR 0.38, 95% CI 0.15; 0.98, $P < 0.04$). These findings persisted after adjusting for risk of cardiac events using the Lee cardiac risk index (25). Finally, we pooled data from both study epochs to group patients based on whether statin therapy was resumed early versus late after surgery. Based on multivariate logistic regression analysis we found that resuming statin therapy <4 days after vascular surgery was an independent risk factor for postoperative myonecrosis.

Our results are in accordance with other reports in high-risk surgical patients (7,36,37). Although given for its lipid-decreasing effects, Poldermans et al. (11) observed that patients treated with statins before vascular surgery had 4.5-fold less perioperative mortality than control patients (7). More recently, in a retrospective study of 780,591 patients who underwent noncardiac surgery, Lindenauer et al. (9) observed that perioperative treatment with statins reduced the risk of postoperative death compared with patients not receiving this treatment. Because this study considered patients who did not receive statins on postoperative day 1 as being untreated, a deleterious effect of statin withdrawal may have contributed to the observed beneficial effect. In a retrospective study conducted in 1163 patients undergoing vascular surgery, O'Neil-Callahan et al. (10) observed a reduction of a postoperative composite end point (including death, myocardial infarction, ischemia, congestive heart failure, and ventricular tachyarrhythmias) in patients treated with statin. Finally, in a prospective, placebo-controlled, randomized study, Durazzo et al. (8) demonstrated that short-term treatment with atorvastatin 20 mg before vascular surgery significantly reduced the incidence of a composite end points, including death from cardiac cause, nonfatal myocardial infarction, unstable angina, and stroke.

Some limitations to our study, in addition to the retrospective study design, deserve consideration. In

the discontinuation group, preoperative statin treatment identified a group of patients at higher risk for perioperative cardiac morbidity than the continuation group. We cannot exclude that these differences contributed to our results. Late resumption of statin therapy might have been even more marked in this subset of patients. It is thus possible that factors other than statin treatments that were not included in our analysis might have contributed to the outcomes we observed. Treatment with β-adrenergic blockers, aspirin, and angiotensin enzyme inhibitors before surgery were not different between the groups, but we cannot exclude the benefit from these therapies after surgery as there was no protocol dictating these treatments. We did not have strict treatment algorithms for perioperative care, although general guidelines were in place. Nevertheless, the risk adjustment techniques used in our study should have limited possible bias, and these drugs were not significant predictors of cardiac myonecrosis. Indeed, we found no significant differences during the two study periods, except for statin administration (Table 1). Although we did not observe a benefit of statin therapy on operative mortality, the power of our study was not sufficient to exclude this possibility. Our primary end point of myonecrosis is clinically relevant, and has been found to strongly correlate with duration of hospitalization and death (18,38). We did not measure plasma statin levels and we do not know how well these drugs were absorbed when given orally or via a nasogastric tube early in the postoperative period. Pharmacokinetic studies are required to determine the optimal perioperative strategy of statins administration.

In conclusion, withdrawal of statins after major vascular surgery is associated with an increased risk for postoperative myonecrosis, whereas early resumption of treatment is associated with a cardiac protective effect. These data appear to confirm growing experimental and clinical data in nonsurgical patients concerning the deleterious cardiac effects of statin withdrawal.

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