Patterns and predictors of statin use after coronary artery bypass graft surgery

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Objectives: The benefits of statin therapy for patients with coronary artery disease have been well documented, including those occurring after coronary artery bypass graft surgery. The purposes of this study were to assess statin prescription rates in patients who have undergone coronary artery bypass graft surgery and to identify the determinants of postoperative statin administration.

Methods: A retrospective cohort of 9284 Medicare patients aged 65 years or older who underwent coronary artery bypass graft surgery (1995–2004) was assembled by using linked hospital and pharmacy claims data. Rates of statin use after hospital discharge were calculated, and predictors of postoperative statin use were identified by using generalized estimating equations.

Results: Overall, 35.9% of patients received statins within 90 days of coronary artery bypass graft surgery discharge. Use of statins within 90 days after coronary artery bypass graft surgery steadily improved during the study period, from 13.1% in 1995 to 60.9% in 2004. Patient factors independently associated with an increase in postoperative statin therapy included preoperative statin use (odds ratio, 7.69), later year of operation (odds ratio, 1.22 per additional year), and additional postoperative medications (odds ratio, 1.16 per additional medication). Factors independently associated with a decrease in postoperative statin therapy included peripheral vascular disease (odds ratio, 0.60), diabetes mellitus (odds ratio, 0.67), stroke (odds ratio, 0.77), and older age (odds ratio, 0.96 per additional year). Surgeon and hospital characteristics were not independently associated with postoperative statin use.

Conclusions: Statins are considerably underused after coronary artery bypass graft surgery, although recent prescription rates are increasing. Patterns of use do not appear to correlate with coronary artery disease risk. These findings highlight the need for targeted quality improvement initiatives to increase the rate of statin administration to this at-risk population.

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Although coronary artery bypass graft (CABG) surgery effectively treats ischemic heart disease, the long-term results after CABG surgery are compromised by the progression of atherosclerosis in native coronary arteries and saphenous vein bypass grafts.^{1,2} Only 60% of vein grafts remain patent 10 years after surgical intervention, and 50% of those that are patent have clinically important stenosis.^{1,2} Accordingly, patients after CABG surgery are at high risk for subsequent ischemic events, including death, myocardial infarction, and stroke.^{1,2}

Clinical trials have consistently demonstrated that statins reduce the risk of recurrent cardiovascular events and improve survival in patients with coronary artery disease (CAD), including survival in patients after CABG surgery.^{3–5} In the largest study involving patients after surgical revascularization, treatment with 40 to 80 mg of lovastatin daily reduced low-density lipoprotein (LDL) cholesterol levels to less than

Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CAD	= coronary artery disease
CI	= confidence interval
GEE	= generalized estimating equation
LDL	= low-density lipoprotein
OR	= odds ratio
PAAD	= New Jersey Pharmaceutical Assistance to the Aged and Disabled
PACE	= Pennsylvania Pharmaceutical Assistance Contract for the Elderly

100 mg/dL and significantly reduced the progression of post-operative vein graft disease compared with moderate cholesterol treatment with 2.5 to 5 mg of lovastatin daily.⁵

The American Heart Association/American College of Cardiology Secondary Prevention Clinical Guidelines⁶ and the National Cholesterol Education Program Adult Treatment Panel III Guidelines^{7,8} currently recommend treatment to achieve LDL levels of less than 100 mg/dL for patients with documented atherosclerotic vascular disease, including patients after CABG surgery. Because less than 7% of patients with atherosclerosis are able to achieve LDL levels of less than 100 mg/dL with diet and exercise regimens^{9,10} in the absence of severe contraindications, essentially all patients after CABG surgery are candidates for long-term postoperative statin therapy.¹¹ Whether patients undergoing CABG surgery actually receive statins after the operation is largely unknown. Therefore we sought to assess the rate of statin use among patients discharged from the hospital after CABG surgery and to identify the determinants of statin use in this population.

Materials and Methods**Setting and Design**

We assembled a retrospective cohort of Medicare patients who underwent CABG surgery by linking Medicare files to data from the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE) and the New Jersey Pharmaceutical Assistance to the Aged and Disabled (PAAD) programs. Both PACE and PAAD provide prescription drug benefits to lower middle-income individuals aged 65 years or older whose yearly earnings are above the threshold to qualify them for Medicaid. Participants pay copayments of between \$5 and \$10 per prescription without any deductibles. The programs cover all medications that require a prescription and do not restrict which medications can be prescribed (ie, the programs do not use formularies, preferred drug lists, or prior authorization programs).

Data from PACE, PAAD, and Medicare were incorporated into a relational database consisting of data for all filled prescriptions, procedures, physician encounters, hospitalizations, long-term care admissions, and deaths for the patients in this cohort. These data sources have been used extensively to study population-based

health outcomes.^{12,13} All traceable person-specific identifying factors were transformed into anonymous, coded study numbers to protect subjects' privacy. This study was approved by the institutional review board of the Brigham and Women's Hospital.

Cohort

We included patients who were discharged from the hospital after undergoing CABG surgery (International Classification of Diseases–Ninth Revision 36.1x or 36.2x) between January 1, 1995, and December 31, 2004. We excluded patients who died within 90 days after surgical intervention, patients who were not active users of either drug benefit program, and patients who received prescriptions for cerivastatin since this drug was withdrawn from the market. The date of discharge from the hospital after CABG was considered as the index date for the study analysis.

Statin Use

We assessed statin prescription rates (ie, prescriptions that were filled) in the 1-year period before CABG surgery, as well as within 90 days, 180 days, and 365 days after the CABG discharge date. Patients were classified into drug and dose categories based on their statin prescription data before and after surgical intervention. "High-intensity statins" were those that would be expected to decrease LDL cholesterol levels by greater than 40% (atorvastatin, >10 mg; lovastatin, >40 mg; rosuvastatin, >5 mg; simvastatin, >40 mg). All other statin drug-dose combinations were considered "low-intensity statins" (atorvastatin, ≤10 mg; lovastatin, ≤40 mg; rosuvastatin, ≤5 mg; simvastatin, ≤40 mg; any dose of fluvastatin; any dose of pravastatin).^{8,14}

Patient Covariates

We determined patient comorbidities by searching physician service claims and hospitalization records for relevant diagnostic codes in the 1-year period before the index date. In this manner the following characteristics were identified: age at index date, year of operation, sex, race, length of hospital stay, previous myocardial infarction or acute coronary syndrome, hypertension, diabetes mellitus, congestive heart failure, stroke, peripheral vascular disease, previous CABG surgery, previous percutaneous coronary intervention, chronic kidney disease, and chronic obstructive pulmonary disease. We also determined the use of the following concurrent medications in the 1-year period before and 90 days after CABG surgery: angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, β -blockers, calcium-channel blockers, fibrates, diuretics, nitrates, digoxin, warfarin, and clopidogrel.

Hospital and Surgeon Covariates

We identified the hospital and surgeon for each CABG procedure. Hospitals that were accredited with the Association of American Medical Colleges were classified as teaching hospitals. All other hospitals were classified as nonteaching hospitals. We classified the "operating surgeon" as the cardiac, cardiothoracic, or thoracic surgeon who submitted a claim for CABG on the date of surgical intervention using Medicare Part B claims. Records containing invalid provider identification numbers were excluded from further analysis. If 2 or more surgeons were identified for an individual patient, then we defined the most responsible surgeon as the

surgeon that submitted the most claims for that specific patient after surgical intervention. The annualized volume of Medicare patients undergoing CABG surgery treated by each surgeon was estimated by dividing the total number of Medicare patients undergoing CABG surgery for each surgeon during the study time period by the number of years that each surgeon treated 1 or more patients. Surgeons were ranked in order of annualized volume and were then categorized into high-, medium-, and low-volume surgeon tertiles of equal size. The annual volume of the hospital from which each patient was discharged was determined in a similar manner as for surgeon volume, and high-, medium-, and low-volume hospital tertiles were subsequently created.

Statistical Analysis

Our primary outcome was the rate of statin prescriptions that were filled within 90 days after CABG discharge. We compared statin users and nonusers using unpaired 2-sided Student *t* tests, Fisher exact tests, or χ^2 trend tests, as appropriate. Independent predictors of postoperative statin use within 90 days after CABG discharge were identified by using generalized estimating equations (GEEs) with clustering at the surgeon level. Factors of clinical relevance thought to affect postoperative statin rates were incorporated into the GEE analysis, including age, sex, race, year of operation, number of postoperative medications, peripheral vascular disease, preoperative stroke, recent myocardial infarction or acute coronary syndrome, hypertension, diabetes mellitus, preoperative statin use, teaching hospital, hospital volume, and surgeon volume. Odds ratios (ORs) are presented with 95% confidence intervals (CIs). All analyses were performed with SAS version 8.2 software (SAS Institute, Cary, NC).

Sensitivity Analysis

Additional analyses were performed for confirmatory purposes, including the use of interaction terms in the GEE analyses and the removal of patients from the cohort who required long-term care after surgical intervention. Other methods of categorization (instead of tertiles) were used to further evaluate associations between surgeon and hospital volume and postoperative statin use.

Results

Patient Cohort

Our cohort consisted of 9284 patients who underwent CABG surgery between 1995 and 2004. The mean age of the cohort was 75.7 ± 5.5 years, and 64.3% of patients were women. Preoperatively, the incidence of diabetes mellitus was 48.1%, the incidence of stroke was 15.7%, and the incidence of peripheral vascular disease was 6.0%. The majority of patients underwent CABG surgery at teaching hospitals (77.3%), with 89.7% undergoing operations at high-volume hospitals and 80.5% undergoing operations by high-volume surgeons. The mean length of stay after CABG surgery was 11.1 ± 7.2 days.

Statin Prescription Rates

During the 1-year period before CABG surgery, 37.3% of patients received a statin prescription (low-intensity statins,

Figure 1. Statin prescription rates before and after coronary artery bypass grafting (CABG) surgery. Prescription rates decreased slightly from before surgical intervention to 90 days after surgical intervention but then steadily increased to 1 year after CABG surgery.

30.8%; high-intensity statins, 6.5%). In contrast, only 35.9% of patients undergoing CABG surgery were prescribed statins within 90 days after the CABG procedure (low-intensity statins, 30.3%; high-intensity statins, 5.6%). Of the patients who received preoperative statin therapy, only 67.4% of these patients received postoperative statins. Statin administration rates were low among all patient subgroups, including those with diabetes mellitus, cerebrovascular disease, or peripheral vascular disease (statin rates of 37.5%, 33.1%, and 32.3%, respectively). In comparison with statin use, 57.3% of patients received β -blockers after surgical intervention, 36.3% received angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, 21.1% received calcium-channel blockers, 19.3% received digoxin, 17.8% received nitrates, 14.8% received warfarin, 8.0% received clopidogrel, 5.0% received diuretics, and 1.6% received fibrate therapy.

Statin prescription rates increased with duration of time after surgical intervention, from 35.9% to 42.0% to 48.1% within 90, 180, and 365 days after CABG discharge, respectively (Figure 1). Statin prescription rates also increased substantially with each additional year in the study, with a low of 13.1% in 1995 to a maximum of 60.9% in 2004 (Figure 2). The most common statins used after surgical intervention included simvastatin (15.7%) and atorvastatin (12.7%). Fewer patients were prescribed pravastatin (4.6%), lovastatin (2.0%), fluvastatin (0.9%), and rosuvastatin (0.1%).

Predictors of Statin Use

Table 1 describes the characteristics of the patients who did and did not receive statins within 90 days after CABG discharge. Statin users were more likely to have received

Figure 2. Statin prescription rates within 90 days after coronary artery bypass grafting (CABG) surgery stratified by year of operation. Statin prescription rates steadily increased each year of the study.

preoperative statins than nonusers ($P < .0001$). Postoperative statin users were also more likely to have taken other cardiac medications both before and after surgical intervention (all $P < .05$). Although statin users were more likely to be female and have diabetes mellitus, nonstatin users were more likely to be older, have longer hospital stays, and have other comorbidities (stroke, congestive heart failure, and chronic obstructive pulmonary disease; all $P < .05$). Statin users were more likely to have had operations in recent years, although nonstatin users were more likely to have had operations at teaching hospitals ($P = .10$) and at high-volume hospitals ($P = .01$).

After adjusting for patient-, surgeon-, and hospital-related characteristics, the strongest predictor of postoperative statin therapy was preoperative statin use (OR, 7.69; 95% CI, 6.81–8.68; $P < .0001$; Table 2). Later year of operation (OR, 1.22 per additional year; 95% CI, 1.19–1.25; $P < .0001$) and additional postoperative medications (OR, 1.16 per additional medication; 95% CI, 1.15–1.18; $P < .0001$) also independently predicted postoperative statin use. Factors associated with a reduction in postoperative statin use included a history of peripheral vascular disease (OR, 0.60; 95% CI, 0.48–0.75; $P < .0001$), diabetes mellitus (OR, 0.67; 95% CI, 0.59–0.75; $P < .0001$), preoperative stroke (OR, 0.77; 95% CI, 0.67–0.90; $P = .0006$), and older age (OR, 0.96 per additional year; 95% CI, 0.95–0.97; $P < .0001$). Surgeon and hospital characteristics were not independently associated with postoperative statin use. Sensitivity analyses yielded nearly identical results to those presented.

TABLE 1. Baseline characteristics for patients treated with and without statins 90 days after CABG discharge

Characteristic	Nonstatin users (n = 7121)	Statin users (n = 3474)
Demographics		
Age, mean $\pm$ SD	75.9 $\pm$ 5.5	75.2 $\pm$ 5.4*
Female sex, %	62.4	67.8*
White race, %	92.6	91.8
Comorbid conditions, %		
Prior myocardial infarction	16.0	13.4*
Congestive heart failure	52.6	47.4*
Stroke	16.4	14.4*
Peripheral vascular disease	6.4	5.4
Hypertension	87.6	91.9*
Diabetes	46.9	50.2*
Chronic kidney disease	27.2	27.2
Chronic obstructive pulmonary disease	32.5	28.8*
Previous CABG	0.1	0.4*
Previous stent/PTCA	9.0	9.9
Preoperative medication use, %		
Prior statin	19.0	70.0*
ACE inhibitor or angiotensin II receptor blocker	35.7	51.8*
Clopidogrel	8.2	19.4*
β -Blocker	47.8	71.6*
Calcium-channel blocker	43.8	50.5*
Digoxin	13.8	16.8*
Diuretics	6.5	10.1*
Fibrate	3.4	4.0
Nitrates	47.6	59.5*
Warfarin	10.2	11.7*
Postoperative medication use, %		
ACE inhibitor or angiotensin II receptor blocker	29.4	48.6*
Clopidogrel	4.1	14.7*
β -Blocker	46.0	77.2*
Calcium-channel blocker	18.8	25.0*
Digoxin	17.8	21.9*
Diuretics	3.7	7.3*
Fibrate	1.6	1.5
Nitrates	16.4	20.4*
Warfarin	14.3	15.6
Hospital characteristics		
Teaching hospital, %	77.9	76.4
Annual volume of hospital, %		
High (≥ 54 patients/y)	90.2	88.8
Medium (3-53 patients/y)	9.2	10.8*
Low (≤ 2 patients/y)	0.7	0.4
Annual volume of surgeon, %		
High (≥ 20 patients/y)	80.5	80.4
Medium (3-19 patients/y)	17.1	17.5
Low (≤ 3 patients/y)	2.3	2.1
Length of stay, mean $\pm$ SD	11.8 $\pm$ 7.2	10.1 $\pm$ 5.0*

CABG, Coronary artery bypass grafting; SD, standard deviation; PTCA, percutaneous transluminal coronary angioplasty; ACE, angiotensin-converting enzyme. * $P < .05$.

TABLE 2. Multivariable predictors of postoperative statin use

Characteristic	Adjusted odds ratio (95% confidence interval)
Increased statin use	
Preoperative statin use	7.69 (6.81–8.68)
Year of operation (per additional year)	1.22 (1.19–1.25)
Postoperative medications (per additional medication)	1.16 (1.15–1.18)
Decreased statin use	
Peripheral vascular disease	0.60 (0.48–0.75)
Diabetes mellitus	0.67 (0.59–0.75)
Stroke	0.77 (0.67–0.90)
Patient age (per additional year)	0.96 (0.95–0.97)
Nonsignificant factors	
Male sex	1.05 (0.95–1.16)
White race	0.99 (0.82–1.20)
Prior myocardial infarction	0.98 (0.84–1.13)
Hypertension	1.00 (0.83–1.20)
Teaching hospital	1.01 (0.86–1.19)
Medium-volume vs low-volume hospital	1.49 (0.78–2.87)
High-volume vs low-volume hospital	1.52 (0.79–2.91)
Medium-volume vs low-volume surgeon	0.93 (0.62–1.38)
High-volume vs low-volume surgeon	0.98 (0.67–1.44)

Discussion

Clinical trials have consistently demonstrated that statins reduce the risk of recurrent cardiovascular events and improve survival across a wide range of cholesterol levels in patients with CAD.³ The benefits of statin treatment appear to be applicable to men and women, as well as to older and younger patients.³ As one of the safest classes of drugs ever developed,¹⁵ statins are recommended as preventive therapy for patients with CAD, even after surgical revascularization.^{7,16} Given the weight of the evidence and the fact that statins have been shown to reduce saphenous vein graft disease,^{4,5,17} in the absence of serious contraindications, effectively all patients after CABG surgery should be prescribed long-term statin therapy.⁶⁻⁸ In contrast, we observed that (1) overall, only 37.3% of patients received statin therapy before CABG surgery, and even fewer patients (35.9%) were prescribed statins within 90 days postoperatively; (2) although rates of statin prescriptions have increased substantially over time, they still remain suboptimal; and (3) patients with risk factors for future vascular events, such as diabetes mellitus and history of stroke, were the least likely to receive statins.

As the largest study to date to have evaluated medical therapy after CABG surgery, the results of this research confirm those of smaller cohort studies that have docu-

mented low statin prescription rates after CABG surgery.^{18,19} Most recently, in a study of 320 patients undergoing CABG surgery, the use of antilipid agents was 55% at admission, 57% at CABG discharge, and 76% at 12 months after surgical intervention.²⁰ Likewise, in a study of evidence-based preventive therapies in 31,750 Duke University patients, Newby and colleagues²¹ reported the consistent use of lipid-lowering therapy in only 44% of patients with CAD (treated with medical, percutaneous, or surgical therapy). Similar to the current study, Newby and colleagues²¹ also reported that the use of lipid-lowering agents increased over time, with 63% of patients taking lipid-lowering therapy in 2002 compared with approximately 25% in 1995. The results our cohort and that from Duke²¹ both identified older age as a predictor of lower statin use, despite the fact that the elderly derive more absolute benefit from statins as a consequence of their high baseline risk of cardiovascular disease.^{3,22}

In addition to advanced age, patients with other cardiac risk factors paradoxically received less preventive statin therapy after surgical intervention compared with that received by patients without these risk factors. A history of peripheral vascular disease, diabetes mellitus, and stroke were all independently associated with a reduction in postoperative statin prescription rates. Patients with these risk factors could benefit the most from statin therapy.^{3,21} This finding is analogous to the results reported by Lee and associates²³ regarding the underuse of angiotensin-converting enzyme inhibitors and β -blockers in patients with heart failure at the greatest risk of death. Physician belief that patients with comorbidities will experience less benefit and greater harm from statin therapy is one potential explanation for this treatment-risk paradox. Alternatively, physicians might be less attentive to preventive therapy when caring for patients with multiple concurrent conditions, or they might be less inclined to prescribe medications to patients thought unlikely to adhere to treatment.^{23,24}

The strongest factor associated with the administration of postoperative statin therapy in our cohort was the use of preoperative statins. As a consequence, encouraging appropriate preoperative statin use might be an effective strategy to increase postoperative use. Moreover, preoperative statin use reduces the incidence of adverse cardiovascular events after CABG surgery.^{25,26} Still, only 67% of patients who received preoperative statins were prescribed statins after surgical intervention in this study, suggesting that preventive statin therapy is being forgotten or disregarded after CABG surgery.

Overall, too few patients are being prescribed statins after CABG surgery, and this study highlights the need for targeted quality improvement initiatives focusing on the prescription habits of cardiac surgeons and cardiologists. Several researchers have explored approaches to improving these treatment gaps in cardiovascular care and preven-

tion.^{22,27} Audit with feedback on performance is one important method that can be used to achieve this goal among patients after CABG surgery and should be explored further.²⁰ Moreover, recent randomized controlled trials have demonstrated that, compared with usual care, the addition of electronic information systems (electronic medical record reminders and automated voice message reminders) or the use of integrated team care models (pharmacy team outreach groups and transition coaches) might improve medication administration and therapeutic monitoring after hospital discharge.^{28,29}

Through the use of a large database and robust statistical methods, we believe that our study provides the best current evaluation of statin administration after CABG surgery. However, our results should be interpreted in the context of several limitations.

First, this research focused specifically on elderly patients enrolled in Medicare and the PACE and PAAD prescription drug benefit plans. Because the average age of patients undergoing CABG surgery in this cohort was 75.7 years and 64.7% of patients were female, our results might not be generalizable to patients with other demographic or clinical characteristics.

Second, the administrative data used does not contain detailed clinical information, such as cholesterol levels, or the reasons for physicians' prescription choices. For example, statins might have preferentially been prescribed to patients with higher baseline cholesterol levels. Moreover, it is possible that patients who filled their statin prescriptions in this study might not have actually ingested the medications. That said, it is generally agreed that the rate of prescriptions being filled by patients well approximates their actual consumption.³⁰

Finally, it is impossible to differentiate patient noncompliance in filling a prescription from physician nonprescription in our data.

In summary, much progress has been made in the evaluation of preventive therapies, and yet many patients do not receive the medical therapies that can improve their outcomes. This study illustrates that statins are considerably underused after CABG surgery. However, their use has increased in recent years. These findings highlight the need for targeted quality improvement initiatives to further increase the rate of statin administration to this at-risk population.

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