Adherence to Statin Therapy in Elderly Patients After Hospitalization for Coronary Revascularization

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Low levels of statin adherence have been documented in patients with coronary artery disease (CAD), but whether coronary revascularization is associated with improved adherence rates has yet to be evaluated. We identified all Medicare beneficiaries enrolled in 2 statewide pharmacy assistance programs who were ≥65 years old, who had been hospitalized for CAD from 1995 through 2004, and who had been prescribed statin therapy within 90 days of discharge (n = 13,130). Statin adherence was measured based on the proportion of days covered with statin therapy after hospital discharge, and full adherence was defined as proportion of days covered ≥80%. Statin adherence was compared in patients with CAD treated with medical therapy (n = 3,714), percutaneous coronary intervention (n = 6,309), or coronary artery bypass graft surgery (n = 3,107). Statin adherence significantly increased over the period of the study from 70.5% to 75.4% (p <0.0001). After hospitalization for CAD, patients treated with percutaneous coronary intervention and coronary artery bypass graft surgery had full adherence rates of 70.6% and 70.2%, respectively. Full adherence rates were significantly lower for patients treated with coronary revascularization compared to patients treated with medical therapy (79.4%, p <0.0001). Independent predictors of higher statin adherence included treatment with medical therapy, later year of hospital admission, white race, previous statin use, and use of other cardiac medications after CAD hospitalization (p <0.01 for all comparisons). In conclusion, in patients receiving invasive coronary treatment, statin adherence remains suboptimal, despite strong evidence supporting their use. Given the health and economic consequences of nonadherence, these findings highlight the need for developing cost-effective strategies to improve medication adherence after coronary revascularization. **© 2011 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2011;107: 1409–1414)**

Substantial attention has been focused on increasing statin prescription rates in hospital and at time of discharge for patients with coronary artery disease (CAD). Conversely, less interest has been paid to understanding and improving postdischarge adherence to these medications. Long-term studies of patients with CAD treated primarily with medical therapy have noted disappointingly low rates of adherence, ranging from 50% to 85% at 1 year to 45% to 50% at 5 years after statin initiation.[1–3] However, no studies have assessed adherence to statin therapy in patients with high-risk CAD treated with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Mechanically revascularized patients may be more adherent to preventive therapies given patient perceptions of the severity of their illness. Alternatively, after undergoing PCI or CABG, patients may have fewer ischemic symptoms and believe that subsequent preventive therapies are unnecessary. Therefore, the goal of this study was to compare adherence to statin therapy in patients hospitalized with CAD treated with coronary revascularization or medical therapy.

Methods

We assembled a cohort of Medicare beneficiaries with CAD by linking Medicare files describing all clinical encounters to complete medication-use data from the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE) and the New Jersey Pharmaceutical Assistance to the Aged and Disabled (PAAD) programs. During the period studied, PACE and PAAD provided prescription drug benefits to lower middle-income Medicare beneficiaries ≥65 years of age whose yearly earnings were above the threshold to qualify them for Medicaid. Participants paid copayments of $5 through $10 per prescription without any deductibles. The programs covered all medications that required a prescription and did not restrict which medications could be prescribed (i.e., the programs did not use formularies, preferred drug lists, or previous authorization programs). Data from PACE, PAAD, and Medicare was assembled into a relational database consisting of claims for all filled prescriptions and hospital and clinical characteristics for the patients in our cohort. These data sources have been used extensively to study population-based medication use.[4,5] All traceable patient-specific identifying factors were transformed into anonymous coded study numbers to pro-

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doi:10.1016/j.amjcard.2011.01.013

Table 1
Baseline characteristics

Characteristics	Medical Therapy (n = 3,714)	PCI (n = 6,309)	CABG (n = 3,107)
Patient characteristics			
Age (years), mean ± SD	79.5 ± 6.9	75.9 ± 6.0	75.1 ± 5.3*
Women	77.4%	73.3%	68.4%*
White	91.9%	90.0%	91.6%*
Previous myocardial infarction	14.9%	21.3%	38.0%*
Previous percutaneous coronary intervention	4.4%	2.1%	6.8%*
Previous coronary artery bypass graft surgery	0.8%	1.0%	0%*
Heart failure	64.1%	33.4%	45.2%*
Stroke	7.8%	4.7%	6.0%*
Peripheral vascular disease	5.5%	5.2%	5.2%
Hypertension	84.7%	89.0%	91.1%*
Diabetes mellitus	48.3%	42.2%	49.8%*
Chronic kidney disease	34.1%	22.6%	26.3%*
Prehospital medication use (1 year)			
Total number of medications, mean ± SD	11.2 ± 7.6	11.0 ± 7.1	11.5 ± 8.1*
Previous statin	58.6%	59.5%	66.8%*
Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker	61.4%	50.8%	51.8%*
Clopidogrel	23.3%	54.7%	19.5%*
β Blocker	68.1%	66.2%	72.6%*
Calcium channel blocker	51.6%	50.7%	51.7%
Digoxin	13.7%	8.2%	13.4%*
Diuretics	13.5%	11.8%	10.8%*
Fibrate	3.5%	3.5%	4.5%*
Nitrates	67.2%	63.1%	60.4%*
Warfarin	9.4%	6.9%	7.4%*
Posthospital medication use (30 days)			
Total number of medications, mean ± SD	6.0 ± 4.2	5.6 ± 3.8	5.6 ± 4.3*
Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker	44.8%	38.8%	31.4%*
Clopidogrel	22.1%	53.0%	9.3%*
β Blocker	56.0%	56.0%	57.4%
Calcium channel blocker	22.9%	27.6%	16.2%*
Digoxin	9.7%	5.4%	15.5%*
Diuretics	5.1%	4.8%	3.5%*
Fibrate	0.8%	1.3%	1.1%
Nitrates	57.1%	45.8%	11.7%*
Warfarin	8.0%	5.5%	8.0%*
Posthospital statin type			
Atorvastatin	30.5%	36.7%	33.9%*
Fluvastatin	2.5%	2.9%	2.6%
Lovastatin	8.1%	6.4%	6.8%
Pravastatin	13.4%	13.3%	13.8%
Rosuvastatin	0.3%	1.0%	0.4%
Simvastatin	45.2%	39.7%	42.5%
Hospital characteristics			
Teaching hospital	48.8%	70.1%	76.5%*
Length of stay (days), mean ± SD	6.8 ± 3.8	4.4 ± 4.3	10.0 ± 5.1*

* $p < 0.05$.

tect subjects' privacy. This study was approved by the institutional review board of the Brigham and Women's Hospital, Boston, Massachusetts.

We included all patients who were discharged alive from the hospital after admission for active CAD from January 1, 1995 through December 31, 2004. This included patients who were treated with medical therapy after myocardial infarction or unstable angina (*International Classification of Disease, Ninth Revision*, codes 410.01 to 410.91 or 411), patients who underwent PCI (codes 36.01 to 36.09), and patients who underwent CABG (codes 36.1x or 36.2x). Validation studies have demonstrated that these codes have a specificity of ≥96% for the diagnosis of CAD.[6,7] We used a hierarchical approach to define the 3 subgroups in this study. Patients admitted with active CAD who underwent CABG during the index hospitalization were assigned to the CABG subgroup, regardless of whether they received PCI. Patients with CAD who underwent PCI (but not CABG) during the index admission were allocated to the PCI subgroup. All other patients with CAD were classified as those treated with medical therapy. Because our focus was adherence to statin therapy during follow-up after CAD hospitalization, only patients who filled a statin prescription within 90 days of hospital discharge were included. The date of the

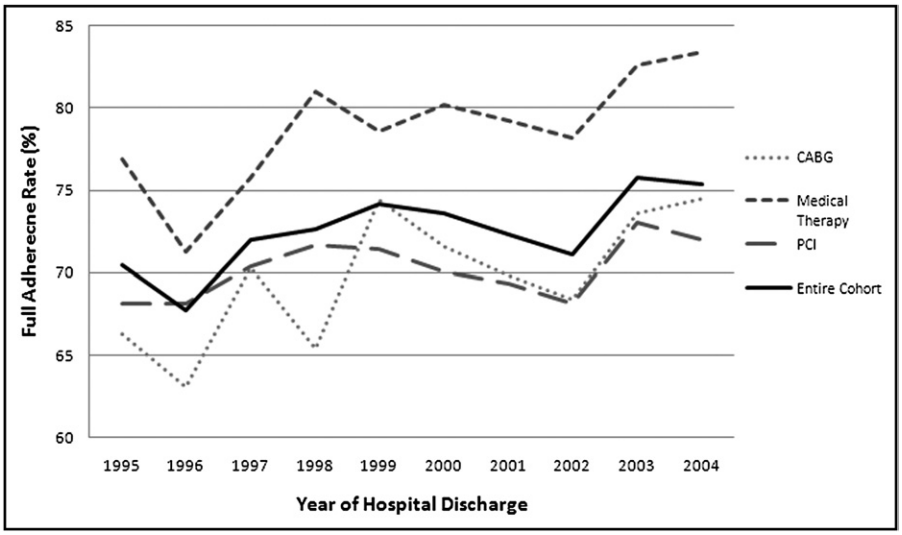

Figure 1. During the period of the study, rates of full adherence significantly increased for the entire cohort *(solid black line)* and within the coronary artery bypass grafting *(dotted line)* and medical therapy *(upper dashed black line)* subgroups individually. There was a nonsignificant trend for increased adherence over time for the percutaneous coronary intervention *(lower dashed gray line)* subgroup.

first statin prescription fill after hospital discharge was defined as the index date for each patient (i.e., start of follow-up). Follow-up terminated on December 31, 2005. We excluded patients who died during the index hospitalization and patients who were not active users of either drug benefit program.

We determined patient co-morbidities 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 hospitalization, gender, race, length of hospital stay, previous myocardial infarction or acute coronary syndrome, hypertension, diabetes mellitus, congestive heart failure, stroke, peripheral vascular disease, previous CABG, previous PCI, and chronic kidney disease. We assessed whether each patient used any statin in the 1-year period before the index CAD hospitalization. We also determined the total number of generic medications prescribed and use of the following specific medications in the 1-year period before and 30 days after CAD hospitalization: angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, β blockers, calcium channel blockers, clopidogrel, fibrates, diuretics, nitrates, digoxin, and warfarin. Hospitals accredited by the Association of American Medical Colleges were classified as teaching hospitals. All other hospitals were classified as nonteaching hospitals.

We measured statin adherence using the proportion of days that patients had medication available to them after hospital discharge. This widely used measurement, proportion of days covered, was calculated by dividing the number of days of medication supplied between the first and last statin prescriptions during the study period (numerator) by the number of days between these 2 prescriptions plus the accumulated days supplied from the last prescription (denominator).[8] We defined patients as being "fully adherent" if their proportion of days covered was $\geq$80%. We then compared rates of full statin adherence between patients admitted to hospital for CAD who were treated with medical therapy, PCI, or CABG using Fisher's exact test. Baseline characteristics of patients treated with medical therapy, PCI, or CABG were compared using Student's *t* tests, Fisher's exact tests, or chi-square tests, as appropriate. Statistical significance was defined as a p value <0.05. Trends in average yearly full adherence were compared among the 3 subgroups using analysis of variance.

Multivariable logistic regression analysis was used to identify predictors of statin full adherence for the entire cohort. Indicator terms for the 3 subgroups were included in the models. To adjust for important clinical covariates, the following factors were also incorporated in the models: age, gender, race, year of index hospitalization, treatment in a teaching hospital, history of peripheral vascular disease, congestive heart failure, previous stroke, previous myocardial infarction, diabetes mellitus, statin use in the 1-year period before hospital admission, number of generic medications used in the 1-year period before hospital admission, and cardiac medication use (β blocker, angiotensin-converting enzyme inhibitor, or angiotensin II receptor blocker) within 30 days after hospital discharge. We then repeated our analysis to test whether statin adherence differed if we included only new statin users (i.e., those patients who did not fill a statin prescription in the 1-year period before their index hospitalization, n = 5,120). Odds ratios are reported with 95% confidence intervals. All analyses were performed using SAS 8.2 (SAS Institute, Cary, North Carolina).

Results

Our cohort consisted of 13,130 patients admitted to hospital with CAD who were treated with medical therapy (n = 3,714), PCI (n = 6,309), or CABG (n = 3,107). Mean age of the cohort was 76.7 $\pm$ 6.1 years, and 73.3% of patients were women (Table 1). Patients treated with CABG were significantly younger, had a higher incidence of diabetes mellitus, and were more likely to have previously received

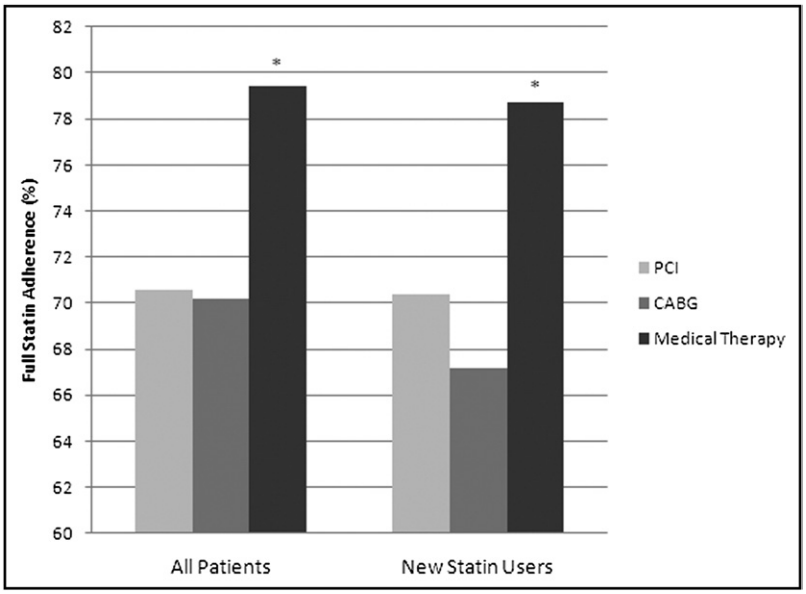

Figure 2. Patients treated with medical therapy *(black bars)* had significantly higher full statin adherence rates after hospitalization for coronary artery disease (*p <0.0001) compared to patients treated with coronary artery bypass grafting *(dark gray bars)* or percutaneous coronary intervention *(light gray bars)*.

Table 2
Predictors of full statin adherence (proportion of days covered >80%) after hospitalization for coronary artery disease for entire cohort and for new statin users

Characteristics	Entire Cohort (n = 13,130)		New Statin Users (n = 5,120)	
	OR	95% CI	OR	95% CI
Coronary artery bypass vs medical therapy alone	0.68	0.60–0.77*	0.66	0.54–0.80*
Percutaneous coronary intervention vs medical therapy alone	0.70	0.64–0.78*	0.76	0.64–0.89*
Patient characteristics				
Patient age (per additional year)	1.02	1.01–1.03*	1.02	1.01–1.03*
Male gender	1.06	0.96–1.15	0.96	0.83–1.10
White race	2.04	1.80–2.31*	1.82	1.48–2.23*
Diabetes mellitus	1.08	0.99–1.17	1.03	0.90–1.17
Peripheral vascular disease	1.05	0.88–1.26	0.92	0.67–1.26
Congestive heart failure	1.16	1.06–1.26*	1.30	1.13–1.48*
Stroke	1.09	0.92–1.29	1.21	0.90–1.62
Previous myocardial infarction	1.04	0.94–1.14	0.96	0.81–1.12
Hospital characteristics				
Teaching hospital	1.05	0.96–1.14	1.06	0.93–1.22
Year of admission (per additional year)	1.02	1.01–1.04*	1.02	1.00–1.05*
Preoperative medications				
Prehospital statin use	1.13	1.04–1.23*	—	—
Number of prehospital medications (per additional medication)	0.99	0.99–1.00	1.00	0.98–1.01
Postoperative medications				
Posthospital β-blocker use	1.13	1.04–1.22*	1.25	1.10–1.42*
Posthospital angiotensin-converting enzyme inhibitor or angiotensin II receptor use	1.22	1.12–1.33*	1.18	1.03–1.34*

* p <0.05.
CI = confidence interval; OR = odds ratio.

statin therapy (p <0.05 for all comparisons). Patients treated with medical therapy were more likely to have a history of stroke (p <0.05). Patients treated with PCI had a high rate of clopidogrel use before hospitalization (i.e., clopidogrel prescription before elective PCI).

During the period of the study, rates of full adherence significantly increased (Figure 1) from 70.5% to 75.4% for the entire cohort (p <0.0001) and within the CABG and medical therapy subgroups individually (p <0.01 for the 2 comparisons). For the PCI subgroup, there was a nonsignificant trend of increased adherence over time (p = 0.15). After hospitalization for CAD, patients treated with PCI and CABG had full adherence rates of 70.6% and 70.2%, respectively (Figure 2). Full adherence rates were significantly lower for patients treated with coronary revascularization compared to patients treated with medical therapy

(79.4%, p <0.0001). Similar results were obtained when the cohort was limited to new statin users only, with full adherence rates significantly lower in patients treated with PCI (70.4%) and CABG (67.2%) compared to patients treated with medical therapy (78.7%, p <0.0001).

Multivariable logistic analysis was performed to identify independent predictors of statin full adherence for the entire cohort (Table 2). Factors independently associated with higher statin adherence included later year of hospital admission, older patient age, white race, history of congestive heart failure, previous statin use, and cardiac medication use (β blocker, angiotensin-converting enzyme inhibitor, or angiotensin II receptor blocker) within 30 days after hospital discharge (p <0.01 for all comparisons). Compared to medical therapy alone, treatment with CABG or PCI independently predicted lower statin adherence after hospitalization for CAD, even after controlling for other factors influencing adherence (p <0.0001 for the 2 comparisons). Similar results were obtained when analysis was restricted to new statin users only (Table 2).

Discussion

Numerous studies have demonstrated that statins decrease the risk of recurrent cardiovascular events and improve survival in patients with CAD.[4,9] As 1 of the safest classes of drugs ever developed, statins are recommended as preventive therapy for all patients with CAD even after coronary revascularization.[10] Because of the health and economic benefits associated with their use, considerable attention has been placed on implementing quality-improvement initiatives to increase use of statins in hospital and at time of discharge.[11–13] Long-term adherence to statin therapy has been the subject of less investigation, especially for patients undergoing coronary revascularization.

In this study of 13,130 patients discharged after hospitalization for CAD, we compared statin adherence during outpatient follow-up between patients treated with PCI or CABG and those receiving medical therapy alone. Compared to patients treated with medical therapy, we found that adherence to statin therapy was significantly lower in patients treated with percutaneous or surgical revascularization. Even in new statin users, statin adherence was lower after invasive coronary treatment.

This is the first study to compare adherence rates across treatment methods for patients with acute CAD. Adherence to statin therapy is clearly a complex process, affected by a variety of factors including perceptions and understanding of disease burden.[14] Given the invasive nature of percutaneous and surgical revascularization, we hypothesized that these patients would have exhibited the greatest health-conscious behavior and would have had the highest levels of statin adherence over the course of follow-up. In contrast, the lower adherence rates that we found in patients treated with PCI and CABG may be a reflection of less symptom recurrence and therefore less perceived need for medical therapy after coronary revascularization.

More generally, our analysis demonstrates suboptimal rates of statin adherence for all patients with acute coronary disease, regardless of the treatment method that they receive. Our estimates are consistent with those found by previous investigators.[1–3,15,16] Long-term adherence with lipid-lowering therapy has been estimated at 50% to 85% at 1 year, 40% to 77% at 2 to 3 years, and 45% to 50% 5 years after statin initiation.[1–3,15,16] In a study of 31,750 patients with CAD treated at Duke University, Newby et al[1] noted that self-reported consistent use of lipid-lowering therapy over the course of follow-up was only 44%. Low statin adherence is associated with poor long-term outcomes, with a 30% to 80% increased risk of recurrent cardiovascular events and all-cause mortality.[1,17,18] In addition, greater adherence should prevent costly clinical events, and the resultant cost savings may more than offset the added costs of increased medication consumption.[19] Thus, given the health and economic consequences of nonadherence, the development of cost-effective strategies to improve medication adherence after CAD hospitalization should be a clear priority, particularly after coronary revascularization.

Several methods for improving long-term statin adherence have been promoted in the literature including early physician follow-up, use of frequent lipid level monitoring, and enrollment in cardiac rehabilitation and patient education programs.[14,20,21] Patients who undergo outpatient physician follow-up within 1 month after hospital discharge for myocardial infarction have significantly higher rates of statin use 6 months later.[22] Moreover, financial barriers are well known to negatively affect statin adherence including lower income and higher insurance copayments, and eliminating them may improve cardiovascular outcomes and decrease overall health spending.[2,16,23,24] These factors likely explain the high long-term adherence rates observed in clinical trials evaluating the aggressive use of medical therapy for treatment of CAD[25,26] because patients in these settings are actively engaged with health care professionals and generally receive their medications for free.

Previous research has identified factors that predict improved adherence to statin therapy. Similar to the present study, white race has repeatedly been shown to be independently associated with higher statin adherence compared to African-American patients.[1,2] Concomitant treatment with other cardiac medications including β blocker and angiotensin-converting enzyme inhibitor therapy has also been linked with improved statin adherence. This may relate to patients having already accepted long-term treatment with other medications and are therefore more inclined to accept statin therapy.[1,27] Efforts to decrease disparities in care should include adherence as a focus.

Our results should be interpreted in the context of several limitations. First, as in other studies of adherence, we restricted our attention to adherence in patients who initiated treatment after hospital discharge. Some patients do not fill even a first prescription after hospital discharge and were not considered by our analysis.[28] Second, we studied elderly patients and predominantly women enrolled in Medicare and the PACE and PAAD prescription drug benefit plans and thus our results may not necessarily be generalizable to other groups of patients. Because determinants of adherence likely differ among patient cohorts and health care arrangements, our findings should be confirmed in other populations. Payment-related reasons for low adherence may be more prominent in other cohorts comprised of patients who have lower incomes, who are less educated, or who lack

drug insurance. Further, the administrative data we used do not contain detailed clinical information such as cholesterol levels, symptom recurrence, or quality-of-life information. From our database, we were unable to differentiate patient nonadherence from physician nonprescription, and it is impossible to ascertain with full certainty whether a patient is actually taking or "adhering to" a medication. We did not evaluate the impact of socioeconomic status or exposure to health care professionals on statin adherence because this has been the subject of several previous research studies.[2,14,16,20–23] Third, we estimated adherence to statins using a prescription-based proportion of days covered. Although there are a multitude of other instruments to assess adherence, some with finer resolution, there is no gold standard.[14] Our measurement of adherence is consistent with those used in other studies,[1–3,15,16] is not subject to recall bias,[29] and has been shown to correlate with pill counts.[30]

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