Association of Early Follow-up After Acute Myocardial Infarction With Higher Rates of Medication Use

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Background: Early outpatient follow-up after acute myocardial infarction (AMI) is recommended in guidelines, but its relationship with the use of evidence-based therapies is unknown.

Methods: We evaluated 1516 patients hospitalized with AMI from the multicenter Prospective Registry Evaluating Outcomes After Myocardial Infarction: Events and Recovery registry. Early follow-up was defined as patient-reported visits with a primary care physician or cardiologist within 1 month after discharge. The primary outcomes were use of aspirin, β-blockers, angiotensin-converting enzyme inhibitors, and statins in eligible patients at 6 months. Multivariable analyses assessed the association between early follow-up and medication use at 6 months, adjusting for patient and clinical characteristics. Secondary analyses compared medication use at 6 months for patients receiving collaborative follow-up from a single provider versus those receiving follow-up from both provider types.

Results: Among the cohort, 34% reported no outpatient follow-up during the month following discharge. Rates of medication prescription among appropriate candidates were similar at hospital discharge for both follow-up groups. Compared with those not receiving early follow-up, those receiving early follow-up were more likely to be prescribed β-blockers (80.1% vs 71.3%; P = .001), aspirin (82.9% vs 77.1%; P = .01), or statins (75.9% vs 68.6%; P = .005) at 6 months. In multivariable analyses, a persistent relationship remained between early follow-up and β-blocker use (risk ratio, 1.08; 95% confidence interval, 1.02-1.15). In secondary analyses, statin use was higher in patients receiving collaborative follow-up (risk ratio, 1.11; 95% confidence interval, 1.01-1.22).

Conclusions: Early outpatient follow-up and collaborative follow-up after AMI is associated with higher rates of evidence-based medication use. Although further studies should assess whether this relationship is causal, these results support current guideline recommendations for follow-up after AMI.

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Quality Improvement Initiatives for acute myocardial infarction (AMI) typically focus on inpatient care, dedicating less attention to care after hospital discharge. It is known, however, that the transition from the inpatient to the outpatient setting is a critical time. Evidence suggests that contact between patients and providers (ie, physicians, nurse practitioners, and physician assistants) during this interval may be crucial for appropriate treatment modifications and recognition of errors in treatment. Early ambulatory follow-up also provides opportunities for clinical assessment, patient education, and medication review, which may in turn improve outcomes. However, little is known about the appropriate timing and type of follow-up that is necessary following hospitalization for AMI.

Current American College of Cardiology/American Heart Association guidelines recommend that patients with AMI receive follow-up within several weeks of discharge; however, the evidence to support this recommendation is limited. Although ambulatory follow-up within the year after AMI is associated with better outcomes, the impact of early follow-up, as recommended in guidelines, has not been characterized. In addition, the optimal structure of follow-up is not well defined. Several studies suggest that care by a cardiologist both during and after hos-
hospitalization results in lower mortality in patients after an AMI. Furthermore, collaborative care between primary care physicians (PCPs) and cardiologists (hereinafter, collaborative care) may be more effective than care by either alone.13–15

This study sought to determine the relationship between postdischarge follow-up within 1 month after hospitalization for AMI and the use of guideline-recommended medications at 6 months. We also assessed whether these relationships varied according to follow-up type (follow-up with only a PCP or cardiologist vs collaborative follow-up). By further characterizing the relationship between follow-up and the use of evidence-based medications after AMI hospitalization, these data could inform future guideline recommendations for AMI care and identify targets for quality improvement initiatives.

## METHODS

### STUDY POPULATION

Study participants were recruited from January 2003 to June 2004 as part of the Prospective Registry Evaluating Outcomes After Myocardial Infarction: Events and Recovery (PREMIER) registry. Full details of participant recruitment and data collection have been previously described. Briefly, consecutive patients with an AMI presenting to a national sample of academic, rural, and inner-city institutions were screened for participation. Inclusion criteria included age older than 18 years, elevated cardiac biomarkers within 24 hours of admission, and other documented evidence for AMI. Evidence for AMI included at least 1 of the following: prolonged (>20 minutes) ischemic signs or symptoms, at least 1 electrocardiogram with ST elevation or ST depression in 2 or more consecutive leads, and/or other clinical evidence of AMI. Biomarkers were considered elevated if the creatine kinase–MB fraction was more than twice the upper limit of the reference range or if the troponin I or T level was greater than the institutional myocardial infarction (MI) threshold.

Patients surviving to hospital discharge who completed a 1-month follow-up evaluation were included. Because the 1-month interview was timed from admission date, patients with a length of stay exceeding 7 days were excluded because those with longer stays would have less out-of-hospital exposure time to complete follow-up. Furthermore, patients with extended stays may have had more unmeasured complicating factors, which could bias the results. In addition, those transferred from another facility within 24 hours after initial presentation were excluded. At the time of discharge, comprehensive lists of discharge medications were recorded.

Follow-up interviews were conducted by a specialized center at 1 month and 6 months after enrollment and included information on current medications and interval events. During interviews, patients were asked whether they had seen a provider outside of the hospital for their heart condition and what type of provider they had seen.

### EXPOSURE VARIABLES

For the primary analyses, the exposure variable was self-reported outpatient follow-up with any provider within 1 month of study enrollment. In secondary analyses, the exposure variables included the specialty of the outpatient providers. The 2 provider specialties considered were cardiology or primary care (family practice, internal medicine, or any other PCP). Patients were categorized as having cardiologist follow-up alone, PCP follow-up alone, or collaborative follow-up.

### OUTCOME VARIABLES

For the primary analyses of medication use based on 1-month follow-up status, the study population included only those patients completing both 1-month and 6-month interviews (N=1516). The outcome variables for these analyses were the 6-month use of aspirin, β-blockers, statins, and angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) among ideal candidates. All patients were considered to be ideal candidates for β-blockers and aspirin unless they had a documented allergy or contraindication to therapy at enrollment. Because current guidelines recommend low-density lipoprotein cholesterol (LDL-C) targets of at least 100 mg/dL for patients with established coronary artery disease (CAD) but also support more aggressive therapy,17 2 groups of patients without treatment contraindications were considered: (1) patients with LDL-C level 100 mg/dL or higher and (2) patients regardless of LDL levels. (To convert LDL-C to millimoles per liter, multiply by 0.0259.) candidacy for an ACE inhibitor or an ARB required documented left ventricular systolic dysfunction (ejection fraction, <0.40, or at least moderate left ventricular systolic dysfunction) and no documented contraindications to ACE inhibitor therapy at study enrollment. In secondary analyses, diabetes mellitus was added as an indication for ACE inhibitor or ARB therapy; these results were not notably different from the primary analysis and are not reported.

Additional analyses assessing all-cause mortality between the 1-month and 6-month assessments were also performed. In these analyses, the association between early follow-up and 6-month mortality included all patients who initially completed 1-month interviews (n=1677). Because this analysis was designed to determine outcomes related to early outpatient follow-up, mortality was restricted to 6 months. Mortality was determined by follow-up contacts with family members and was verified with data from the Social Security Administration Death Master File.28 Deaths were ascertained through September 15, 2005.

### STATISTICAL ANALYSIS

Baseline demographic and clinical characteristics were compared among those with follow-up vs those without any follow-up, using t tests for continuous variables and χ² or Fisher exact tests for categorical variables. Secondary bivariate analyses were conducted to examine the relationship between baseline characteristics and follow-up by provider specialty.

Multivariable regression models were used to assess the relationship between 1-month follow-up and 6-month medication use. Variables entered into these models included study site; baseline demographics (age, sex, race, marital status); socioeconomic factors (education, insurance status); patients’ avoidance of medications or care owing to cost; psychosocial factors (baseline depression score,29 patient-perceived social support30); medical history, including history of MI, percutaneous coronary intervention, prior coronary artery bypass grafting, congestive heart failure, diabetes mellitus, hypercholesterolemia, hypertension, tobacco use, peripheral arterial disease, prior cerebral vascular accident, lung disease, renal failure, and cancer; clinical status on admission (heart rate, systolic blood pressure, anxiety, glucose level, estimated glomerular filtration rate); participation in cardiac rehabilitation; and MI characteristics (number of diseased vessels, primary reperfusion, any revascularization.
tions during admission). The multivariable models also adjusted for discharge prescription of each of the medications. In addition, interactions between provider follow-up status and age, sex, race, insurance status, and cost barriers to obtaining medications were tested for each medication and not found to be significant (P > .05 for all interaction terms). Because medication usage rates were not rare events, relative risks (RRs) were estimated directly using a modified Poisson regression model22 rather than logistic regression, which overestimates RRs. In secondary analyses by provider specialty, P values and confidence intervals (CIs) were adjusted for multiple comparisons using simulation-based methods to account for correlations between the different tests.22

In additional analyses, a propensity score method was used to adjust for differences between the 2 groups.23 A nonparsimonious model was constructed to predict the probability that a patient would receive early follow-up, and the propensity to receive early follow-up was included as a covariate in the multivariable models. The propensity score was entered nonlin-
early using restricted cubic splines. Because these results were similar to those of the multivariable analyses, they are not reported separately.

Among those patients completing 1-month follow-up interviews, unadjusted mortality rates within 6 months were compared using Kaplan-Meier estimates, and adjusted hazard ratios (HRs) were calculated from Cox proportional hazards models. The relatively small number of deaths at 6 months did not allow for consideration of multivariable models with several predictor variables. Thus, a propensity score method was used to adjust for differences between the 2 groups, and the propensity score was included as a covariate in the multivariable models.23 All analyses were performed using SAS statistical software (version 9.1.3; SAS Institute Inc, Cary, North Carolina).

RESULTS

BASELINE CHARACTERISTICS

During the study period, 3953 patients met enrollment criteria, and 2498 (63%) enrolled in PREMIER. A total of 2481 survived to discharge, and 1943 had hospital stays of 7 days or less, of whom 1677 (86.3%) completed 1-month interviews. In the subsequent 5-month interval, 161 patients were lost to follow-up, were too ill to participate, refused to participate, or died, leaving 1516 who completed both 1-month and 6-month interviews (Figure 1).

Among the 1516 participants completing both follow-up interviews, 34% reported no follow-up visits within 1 month of enrollment, 52% had only PCP or cardiologist visits, and 14% had collaborative follow-up. At 1 month, compared with patients who reported no follow-up, patients who reported any follow-up were more likely to be white, have completed higher education, have private insurance, have fewer comorbidities, and have undergone primary reperfusion or revascularization (Table).

EVIDENCE-BASED THERAPIES

Of those completing both 1-month and 6-month follow-up interviews (n = 1516), the percentages who were candidates for aspirin, β-blockers, ACE inhibitor or ARB, and statins (LDL-C level ≥100 mg/dL) were 98%, 96%, 41%, and 44%, respectively. Of these, 96.2% were discharged while receiving aspirin, 93.5% were discharged while receiving a β-blocker, 86.7% were prescribed an ACE inhibitor or ARB, and 91.2% were prescribed a statin. Using expanded criteria for statins (regardless of LDL-C level), 97.4% of the cohort had no documented contra-indication to statins, and of these patients, 88.0% were discharged while receiving a statin.

For each medication, discharge prescription rates among appropriate candidates were similar irrespective of follow-up status or the follow-up provider specialty. Among patients completing both 1-month and 6-month interviews (n = 1516), those with any early follow-up were more likely to be prescribed β-blockers (80.9% vs 71.3%; RR, 1.13; 95% CI, 1.06-1.21), aspirin (82.9% vs 77.1%; RR, 1.08; 95% CI, 1.02-1.14), or statins (among eligible candidates with LDL-C levels ≥100 mg/dL: 79.4% vs 72.3%; RR, 1.09; 95% CI, 1.0-1.20; among eligible candidates regardless of LDL-C levels: 75.9% vs 68.6%; RR, 1.11; 95% CI, 1.03-1.18) at 6 months compared with those without any form of follow-up (Figure 2). No significant difference in ACE inhibitor or ARB use was seen in those with any early follow-up compared with those who did not have early follow-up (RR, 1.03; 95% CI, 0.93-1.14; P = .60).

In multivariable analyses, those with early follow-up had significantly higher rates of β-blocker use (RR, 1.08; 95% CI, 1.02-1.15) at 6 months, with a trend toward higher aspirin use (RR, 1.05; 95% CI, 1.00-1.11). Neither statin use (among eligible candidates with LDL-C levels ≥100 mg/dL, P = .20; among eligible candidates regardless of LDL-C levels, P = .28) nor ACE inhibitor or ARB use (P = .97) was significantly different according to early follow-up status in the multivariable analysis (Figure 3).

In secondary analyses according to provider specialty, patients with collaborative follow-up compared with those with either follow-up alone were more likely to be using a β-blocker at 6 months (87.7% vs 79.2%; RR, 1.11;
Table. Baseline Characteristics

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Abbreviations: BMI (body mass index, calculated as weight in kilograms divided by height in meters squared); CABG, coronary artery bypass grafting; Card, cardiologist; CHF, congestive heart failure; CVA, cerebral vascular accident; ETOH, alcohol; FU, follow-up; HI, health insurance; HMO, health maintenance organization; LDL-C, low-density lipoprotein cholesterol; LV, left ventricular; MI, myocardial infarction; PCI, percutaneous intervention; PPO, preferred provider organization; SBP, systolic blood pressure; STEMI, ST-elevation myocardial infarction.

SI conversion factors: To convert hemoglobin A1C to the proportion of total hemoglobin, multiply by 0.01; to convert LDL-C to millimoles per liter, multiply by 0.0259.

*All data are expressed as percentages unless otherwise stated.
95% CI, 1.03-1.19) and a statin (among eligible candidates with an LDL-C level $\geq 100$ mg/dL), 87.4% vs 77.4%; RR, 1.13; 95% CI, 1.00-1.27; among eligible candidates regardless of LDL-C level, 82.7% vs 74.2%; RR, 1.12; 95% CI, 0.99-1.15). The use of ACE inhibitors or ARBs did not vary significantly according to provider specialty ($P = 0.49$). In further analyses comparing follow-up with either a PCP or a cardiologist alone, no significant differences in 6-month medication use were found (aspirin use, $P = 0.51$; β-blocker use, $P > 0.99$; ACE inhibitor or ARB use, $P > 0.99$). Statin use among eligible candidates with an LDL-C level $\geq 100$ mg/dL, $P = 0.16$; among eligible candidates regardless of LDL-C level, $P = 0.20$.

In multivariable analyses, statin use (regardless of LDL-C level) remained significantly higher among eligible candidates who received collaborative follow-up (RR, 1.11; 95% CI, 1.01-1.22; $P = 0.02$) compared with those with either follow-up alone. Adjusted rates of β-blocker use (RR, 1.08; 95% CI, 1.0-1.17; $P = 0.06$), aspirin (RR, 1.05; 95% CI, 0.97-1.13; $P = 0.32$), and statin use among eligible candidates with an LDL-C level higher than 100 mg/dL (RR, 1.12; 95% CI, 0.98-1.29; $P = 0.11$) were higher among patients receiving collaborative follow-up, the differences were not statistically significant.

MORTALITY

Patients who had any follow-up at 1 month compared with those who had none were more likely to be alive at 6 months (98.5% vs 96.9%, unadjusted HR, 0.46; 95% CI, 0.23-0.91). In the model adjusted for the probability of receiving early follow-up, survival among those without any follow-up remained lower but was no longer significant (HR, 0.62; 95% CI, 0.31-1.26). In a secondary analysis, 6-month survival was higher but did not differ significantly when comparing those with collaborative follow-up with those with either follow-up alone (99.1% vs 98.4%; unadjusted HR, 0.55; 95% CI, 0.13-2.44).

The objective of this study was to assess the relationship between early outpatient follow-up and the use of evidence-based medications after hospitalization for AMI. We found that, in general, evidence-based medication use at 6 months was greater in patients receiving any form of early follow-up after AMI. Early follow-up was associated with higher rates of β-blocker use after accounting for differences in patient characteristics, with a trend toward more aspirin use. When considering follow-up provider specialty, collaborative follow-up compared with either follow-up alone was independently associated with higher rates of statin use. These results suggest that outpatient follow-up, including collaborative follow-up within the first weeks after AMI, may result in higher-quality patient care.

Current American College of Cardiology/American Heart Association guidelines for ST-elevation myocardial infarction (STEMI) support outpatient medical follow-up to assess symptoms, to ensure appropriate medication use, and to provide counseling on secondary prevention and other lifestyle modifications. The guidelines state that “it is common practice to see the patient three to six weeks after discharge.” Similarly, for patients with non-STEMI, current guidelines recommend outpatient follow-up for low-risk patients and those patients who have undergone revascularization within 2 to 6 weeks, and earlier follow-up for higher-risk patients. The support for these recommendations, however, is limited to expert opinion.

We identified consistent trends toward higher use of several cardioprotective medications in those who saw a health provider of any kind during the month following AMI hospitalization. Despite consistent evidence and guidelines recommending the use of β-blockers, aspirin, and statins in patients with a history of CAD, gaps in the use of these medi-
The consistent use of guideline-recommended therapies for secondary prevention in patients with CAD reduces mortality. In our study, a high percentage of appropriate candidates was prescribed cardioprotective medications at discharge. However, use began to taper at both 1- and 6-month interviews, with medication use remaining highest among those patients who had any early follow-up. Greater use of evidence-based medications among patients receiving early outpatient evaluation following AMI supports current guideline recommendations for AMI care after hospitalization.

Although guidelines recommend early follow-up, the specialty of the provider is not specified. Several studies have suggested that inpatient care by a cardiologist affects both immediate- and long-term outcomes. In addition, others have proposed that multispecialty, or collaborative, follow-up is the best structure for optimizing guideline compliance and survival. Even after adjustment for patient, hospital, and therapy characteristics, our results imply that evidence-based medication use tended to be higher in those who received collaborative follow-up compared with either follow-up alone. This study provides evidence suggesting that concurrent, collaborative outpatient management between PCPs and cardiologists may improve medication use.

Certain issues should be considered in the interpretation of these results. Owing to the initial registry design, we were unable to investigate alternative early follow-up intervals or medication use in those with longer hospital stays. We were also unable to determine whether those who did not complete follow-up failed to adhere to a scheduled appointment, whether they were never referred for follow-up, or whether there was selection bias for cardiologist follow-up. In addition, medication use may be a surrogate for patient compliance with other guideline recommendations. Those who completed follow-up may also be more likely to adhere to medication use owing to their inherent characteristics to comply with all forms of therapy. However, we were able to adjust for a range of characteristics that may be associated with follow-up and medication use, such as insurance, including coverage for medications and comorbidities. Even after controlling for these differences, those who completed follow-up were more likely to use certain medications. Finally, we were unable to determine whether follow-up status was associated with differences in risk factors over time. Thus, further studies should explore the causal relationship between early outpatient follow-up, medication use, and risk factor modification after AMI.

Our study found an association between collaborative follow-up and medication use compared with single-provider follow-up with either a PCP or cardiologist. Because we did not adjudicate or adjust for the number of patient visits completed by 1 month, we were unable to conclusively distinguish whether the collaborative advantage was due to a higher frequency of overall visits or dual-specialty involvement. Patients may benefit from specialty collaboration owing to increased interprovider communication, greater opportunity for education, and higher rates of appropriate medication prescriptions, all of which could translate into improved survival. Future studies should further investigate the optimal outpatient care structure needed to maximize outcomes following AMI. Finally, we were unable to demonstrate an effect of early follow-up on outcomes, such as all-cause mortality. Prior studies in cardiovascular populations have suggested that early outpatient follow-up may have an impact on outcomes such as hospitalization and mortality. In the study described herein, patients who received early follow-up had lower mortality compared with those who did not receive follow-up, but the relationship was no longer significant after accounting for patient characteristics (P = .19). Given the short duration of our follow-up and low event rates, it is likely that our study was underpowered to detect a meaningful effect of early follow-up on mortality.

In conclusion, in this study of patients discharged after AMI, early outpatient follow-up was associated with higher rates of evidence-based medication use. In addition, collaborative follow-up between a PCP and a cardiologist revealed a trend toward improved medication use compared with either alone. Although further prospective studies should determine whether the relationship between follow-up and medication use is causal, and whether differences in medication use result in improved long-term outcomes, these results support current guideline recommendations for prompt outpatient care after AMI and suggest a structure for this follow-up.

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REFERENCE


