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Persistence of Evidence-Based Medication Use After Discharge from Academic Versus Nonacademic Hospitals Among Patients With Non–ST-Segment Elevation Myocardial Infarction

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Abstract

There is increasing emphasis on optimizing evidence-based medication (EBM) persistence as a means to improve longitudinal patient outcomes after acute myocardial infarction (MI); yet it is unknown whether differences in medication persistence exist between patients discharged from academic versus nonacademic hospitals. We linked Medicare pharmacy claims data with 3,184 patients with none–ST-segment elevation MI >65 years of age who were treated in 2006 at 253 hospitals participating in the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology and American Heart Association guidelines registry. Using multivariate regression, we compared persistent filling of β blockers, angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers, clopidogrel, and statins at 90 days and 1 year postdischarge between patients discharged from academic and nonacademic hospitals. Patients treated at academic hospitals were more frequently nonwhite (19% vs 8%, p <0.001) and had a greater co-morbidity burden (Charlson score ≥4 in 36% vs 30%, p = 0.001) than patients treated at nonacademic hospitals. Composite persistence to all EBMs prescribed at discharge was low and not significantly different between academic and nonacademic hospitals at 90 days (46% vs 45%, adjusted incidence rate ratio = 0.99, 95% confidence interval 0.95 to 1.04) and at 1 year (39% vs 39%, adjusted incidence rate ratio = 1.02, 95% confidence interval 0.98 to 1.07). Rates of persistence to EBMs were similar between patients with MI >65 years old treated at academic versus nonacademic hospitals; however, persistence rates are low both early and late postdischarge, highlighting a continued need for quality improvement efforts to optimize post-MI management.

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Several previous studies have observed that patients with myocardial infarction (MI) treated at academic hospitals are more likely to receive evidence-based medications (EBMs) in-hospital and at discharge compared with those treated at nonacademic hospitals[1–3]; yet whether a similar relation is seen for postdischarge persistence of EBMs between patients with MI cared for at academic and nonacademic hospitals remains unknown. In this study, we propose to compare the rates of EBM persistence between patients with MI treated at academic and nonacademic hospitals. We hypothesize that there will be a significant difference in persistence early after MI discharge at 90 days, but this difference will no longer be significant 1 year after the initial hospitalization. In secondary analyses, we will examine differences in length of initial hospitalization, in-hospital and predischarge treatments, and time to first postdischarge follow-up visit that may potentially explain persistence differences between patients treated at academic versus nonacademic hospitals.

Methods

The Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology and American Heart Association guidelines (CRUSADE) registry was a voluntary quality improvement initiative designed to track guideline adherence, provide performance feedback, and develop tools to improve adherence to the American College of Cardiology and American Heart Association guidelines for patients with non–ST-segment elevation acute coronary syndrome.[4] Inclusion and exclusion criteria and data collection processes have been described previously.[5] Briefly, patients were included if they presented within 24 hours of anginal symptom onset lasting >10 minutes and had an electrocardiogram showing >1 mV of ST-segment depression or transient ST-segment elevation for <30 minutes, or elevated serum cardiac biomarkers. The institutional review board of each hospital approved participation in CRUSADE. All data were abstracted retrospectively and anonymously; therefore, informed consent was not required.

In 2006, Medicare implemented the Part D prescription drug benefit program. By linking the CRUSADE registry with Medicare Part D pharmacy data, we had the opportunity to study prescription medication filling patterns after hospital discharge for patients with non–ST-elevation MI (NSTEMI) >65 years of age. As data in CRUSADE were collected anonymously without direct patient identifiers, we performed a probabilistic linkage of patients included in CRUSADE with unique Medicare records using a combination of indirect identifiers (hospital, admission date, discharge date, age, and gender), as previously described.[6] This probabilistic linkage resulted in the availability of linked medication data on 5,312 patients with NSTEMI >65 years who were admitted to CRUSADE hospitals from January 1, 2006 to December 31, 2006, and were enrolled in Part D within 1 year of discharge. We excluded patients who died during the index hospitalization (n = 259), patients who were transferred to another acute care hospital for whom we do not have information on their discharge medications (n = 1,597), and patients who were discharged on none of the indicated evidence-based therapies (n = 272). After exclusions, our final study population consisted of 3,184 patients with NSTEMI treated at 253 hospitals in the United States.

We identified academic hospitals by their membership in the Council of Teaching Hospital of the Association of American Medical Colleges as listed in the American Hospital Association Annual Survey database.

We examined medication persistence, defined as the proportion of patients still taking a medication prescribed at discharge, as well as at 90 days and 1 year postdischarge from the index MI hospitalization. Using Medicare Part D data, we determined whether the preceding date and quantity of prescription filling covered the time point of interest for each of the following EBMs: β blockers, clopidogrel, statins, and angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers. We did not examine aspirin use, as this was often purchased over the counter and not captured in pharmacy data. We summarized composite persistence as the number of EBM classes that the patient remains on at either the 90-day or 1-year time point divided by the total number of EBM classes that the patient was discharged on during the index MI hospitalization. For instance, if a patient filled a prescription for 2 medication classes, but was initially discharged on 3, then the overall persistence rate would be 66%. Substitutions of medications within a class did not affect persistence.

Baseline, in-hospital, and discharge characteristics were compared between patients treated at academic versus nonacademic hospitals. Categorical variables are presented as percentages and differences were assessed using the chi-square test when the sample size was sufficient; otherwise an exact test was used. Continuous variables are presented as medians (twenty-fifth and seventy-fifth percentiles) and were compared using the Wilcoxon rank-sum test.

Poisson regression with generalized estimating equations to account for within-hospital correlation was used to assess the association between persistence rates and academic versus nonacademic hospital status. The results were expressed as incident rate ratios with 95% confidence intervals (CIs). Variables for adjustment were adapted from the validated CRUSADE long-term mortality risk score model and included age, initial serum creatinine, initial systolic blood pressure, signs of heart failure at presentation, initial heart rate, weight, previous heart failure, initial hematocrit, initial troponin value, previous stroke, diabetes, gender, previous peripheral artery disease, and Charlson co-morbidity index >3.[7] Categorical variables were imputed to the most frequent group. Systolic blood pressure, hematocrit, and heart rate were imputed to the median of the nonmissing values. Weight, creatinine, and troponin were imputed to the gender-specific median of the nonmissing values. Finally, we compared the risk of 1-year major adverse cardiovascular events (MACEs) between patients treated at academic versus nonacademic hospitals. MACE was defined as the composite risk of death or readmission for MI, stroke, heart failure, percutaneous coronary intervention, or coronary artery bypass graft surgery. For these outcomes, we performed Cox regression adjusting for the variables described previously.

To graphically display hospital variation in overall persistence rates, we estimated the distribution of hospital persistence rates separately for academic and nonacademic hospitals using a hierarchical model for persistence with hospital as a random effect. Including hospital as a random effect allowed us to remove the effect of random sampling variation

due to small sample sizes per hospital. Persistence to medications out of total discharge medications was modeled using an unadjusted grouped logistic regression model. The log-odds for a random hospital is typically assumed to be normally distributed with mean equal to the intercept and variance equal to the random effect variance. We estimated these parameters and transformed from the log-odds scale to the probability scale.

Statistical significance was defined as $p < 0.05$ with no correction for multiple comparisons. All statistical tests were 2-sided. SAS statistical software, version 9.2 (SAS Institute, Cary, North Carolina) was used for all calculations.

Results

The study population comprised of 253 CRUSADE hospitals in the United States; of these, 65 (26%) were academic hospitals and 185 (74%) were nonacademic hospitals. Compared with nonacademic hospitals, academic ones were larger (median number of beds 594 vs 325, $p < 0.001$), not-for-profit (89.8% vs 87.2%, $p = 0.03$), have cardiac surgery capability (97.6% vs 83.2%, $p < 0.001$), and have a cardiologist (as opposed to a noncardiologist like a hospitalist and intern) who primarily cares for patients with MI (71.2% vs 59.7%, $p < 0.001$).

Of the total 3,184 patients with NSTEMI in the CRUSADE registry from January to December 2006, 1,107 patients (34.8%) were admitted to academic hospitals and 2,077 patients (65.2%) were admitted to nonacademic ones. The baseline characteristics of patients treated at academic versus nonacademic hospitals are listed in Table 1.

Academic and nonacademic hospitals had similar rates of diagnostic catheterization, revascularization, and occurrence of in-hospital complications, including cardiogenic shock, heart failure, stroke, and recurrent MI. The median length of stay for both academic and nonacademic hospitals was 4 days (Table 2). There were no significant differences in weekend discharges between academic and nonacademic hospitals (19.7% vs 20.4%, $p = 0.63$). Rates of discharge EBM prescriptions were similar, with the exception of clopidogrel and statin prescription. Academic hospitals were significantly more likely to prescribe a statin on discharge, but less likely to prescribe clopidogrel. Nonacademic hospitals were more likely to offer cardiac rehabilitation referral and smoking cessation counseling before discharge (67.4% vs 55.6%, $p < 0.001$ and 88.6% vs 84.5%, $p < 0.001$, respectively).

Table 3 lists generally low rates of persistence to individual EBMs at 90 days and at 1 year postdischarge. There were no significant differences between academic and nonacademic hospitals in individual medication persistence rates at 90 days and 1 year postdischarge. Rates of overall persistence to all EBMs prescribed at discharge comparing patients treated at academic versus nonacademic hospitals were 46.0% versus 44.5% ($p = 0.44$) at 90 days and 39.0% versus 38.9% ($p = 0.93$) at 1 year postdischarge, respectively. Figure 1 displays hospital variation in overall persistence rates at 90 days and at 1 year. The distribution of hospital persistence rates was estimated separately for academic and nonacademic hospitals. Similar patterns were observed for patients discharged from academic and nonacademic hospitals. The variance in individual hospital persistence rates did not differ significantly between academic and nonacademic hospitals. After multivariate adjustment, there remained

no significant association between academic hospital status and medication persistence: incidence rate ratio 0.99, 95% CI 0.95 to 1.04 at 90 days and incidence rate ratio 1.02, 95% CI 0.98 to 1.07 at 1 year. Although observed MACE rates were numerically lower among patients treated at academic hospitals, there was no significant difference in either unadjusted or adjusted risk of MACEs at 1 year: 31.3% versus 34.0%, p = 0.19, adjusted hazard ratio 0.88, 95% CI 0.77 to 1.01.

Discussion

In the present study, we found no significant differences in medication persistence rates either early or long-term postdischarge between patients treated at academic versus nonacademic hospitals. In contrast to previous studies that showed academic hospitals to have greater adherence to in-hospital MI treatment metrics and lower in-hospital mortality, we observed no difference in transition of care characteristics between patients. Furthermore, there was no significant difference in 1-year risk of MACEs between patients treated at academic and nonacademic hospitals.

Our initial hypothesis was that academic hospitals would be associated with greater early EBM persistence, but not with late medication persistence. In a previous study of all-aged patients with MI, academic hospitals performed significantly better than nonacademic hospitals across several in-hospital quality indicators, including the prescription of EBMs at discharge.[1] An earlier study of Medicare patients found that those admitted to academic hospitals with acute MI had lower 2-year mortality compared with those admitted to nonacademic hospitals.[2] As academic hospitals are typically larger, situated in urban areas, and often draw access to greater resources,[1] we postulated that various processes, such as discharge counseling and inpatient services, might be significantly better and lead to greater early EBM persistence for patients discharged from academic hospitals. Previous studies have demonstrated an association of inpatient counseling on early medication filling rates after discharge.[8]

In contrast to our hypothesis, in this population of patients with NSTEMI >65 years of age enrolled in Medicare Part D, we observed no difference in medication persistence rates between academic and nonacademic hospitals either early (at 90 days) or later (1 year) postdischarge. This lack of difference may be explained by the similarity in various factors postulated to impact early EBM persistence rates. Although academic hospitals were more likely to care for sicker patients (higher Charlson index scores) and patients with previous MIs, the prevalence of other co-morbid conditions was high and did not substantially differ between academic and nonacademic hospitals. As the number of medications that patients are taking before hospitalization for MI is significantly associated with early discontinuation of post-MI EBMs, similarities in co-morbidities before the index hospitalization was important in the present study.[9] Presumably, a more complicated hospital course may influence early persistence; however, rates of invasive management and in-hospital complications, as well as length of stay, did not significantly differ between patients treated at academic versus nonacademic hospitals. Additionally, there were no significant differences in weekend discharges between academic and nonacademic hospitals.

Furthermore, we hypothesized that differences in the discharge process and transition of care would have a significant impact on early persistence rates. These factors included prescription of EBMs at discharge, smoking cessation counseling, referral for cardiac rehabilitation, time to first follow-up visit, and intensity of follow-up appointments. Nevertheless, in our study population, the prescription of EBMs on discharge did not differ appreciably between academic and nonacademic hospitals (with the exception of statin and clopidogrel prescriptions), and the rate of cardiac rehabilitation referral was lower among academic hospitals. Time to follow-up and number of follow-up appointments did not differ within 90 days after discharge, which could potentially be 1 reason why there was no difference in persistence rates detected between academic and nonacademic hospitals.

Even early after discharge, persistence rates of most EBM medications decrease to nearly 70%. These low rates are consistent with contemporary studies examining post-MI medication adherence.[9,10] Although we studied various aspects of the index hospitalization and discharge process with ultimately few significant differences detected, the discharge process is quite complex, and our data may not have captured certain transition of care measures that may be targeted to improve medication persistence rates. For instance, we were not able to discern what materials patients were getting at discharge, to what degree they were educated on how and when to take their medications, and if post-discharge telephone calls were made to ascertain persistence. Furthermore, other socioeconomic factors could play a role in patient persistence. Although all patients in the present study were Medicare patients enrolled in a prescription payment plan, their physical access to a pharmacy, mental health, and social support are all factors potentially impacting persistence, but not captured in our data.

Our study showed no significant difference in the long-term risks of MACEs between patients treated at academic versus nonacademic hospitals. Improving medication persistence in the post-MI population has the potential to prevent secondary events such as recurrent ischemia and death.[11,12] Focusing on improved EBM persistence also has the potential of impacting readmissions at a time where increased pressure is being exerted on health systems to reduce 30-day readmission rates.

Our study had several limitations. First, we only included Medicare Part D beneficiaries; therefore, we were unable to capture differences in persistence that may exist in a younger patient population or a population with variable insurance status. Second, although we were able to capture the prescription of statins, β blockers, clopidogrel, and angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers, we were not able to capture the persistence of aspirin, given that this medication is often obtained over the counter. Some Medicare beneficiaries may have alternate prescription coverage that offers lower out-of-pocket expenses (e.g., 3 patients in our study also had Veterans Administration health coverage); we could not ascertain medications filled through these alternative plans. Third, the only hospitals included in our study were those participating in CRUSADE; we recognize that there may be potential differences in the emphasis on quality improvement and guideline adherence between those hospitals that participate in a quality improvement registry and those that do not. Although this study examined hospital performance in 2006, contemporary studies of patients with acute MI continue to demonstrate very low rates of

EBM persistence. A 2013 study using data from the National Cardiovascular Data Registry ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry-GWTG Get With The Guidelines (January 2007 to March 2011) demonstrated that although 10% of patients had an indication for aldosterone antagonists, only 14.5% of these patients received this medication.[13] Finally, there is the potential for unmeasured confounding when examining outcomes in an observational study. When using registry data to discuss outcomes, such as MACE, there can be a high likelihood of unmeasured confounding.

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FURTHER POINTS

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- If the PDF files contain colour images, and if you do have a local colour printer available, then it will be likely that you will not be able to correctly reproduce the colours on it, as local variations can occur.
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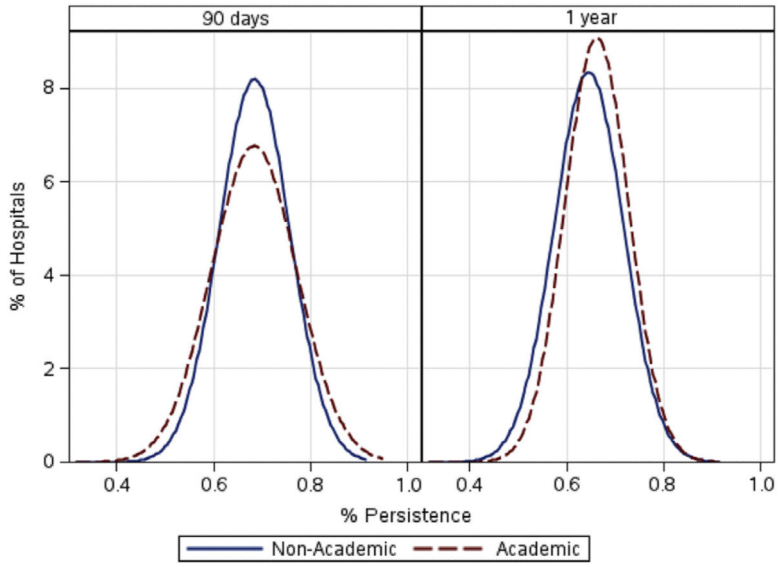

Figure 1.

Hospital variation in persistence. This figure displays hospital variation in persistence among academic and nonacademic hospitals at 90 days and 1 year.

Table 1

Characteristics of patients admitted to an academic versus nonacademic hospital for non–ST-segment elevation myocardial infarction

Variable	Overall (n = 3,184)	Academic (n = 1,107)	Nonacademic (n = 2,077)	p-Value
Age (years), median (IQR)	76 (70, 82)	76 (70, 82)	76 (70, 82)	0.90
Women	53.4 (%)	53.2 (%)	53.5 (%)	0.88
				<0.0001
European American	83.7 (%)	77.4%	87.0%	
African-American	9.2%	15.5%	5.8%	
Asian	1.1%	1.3%	1.0%	
Hispanic	3.3%	3.0%	3.5%	
Other	1.7%	2.2%	1.4%	
Prior myocardial infarction	29.8%	33.0%	28.2%	0.01
Prior percutaneous coronary intervention	25.0%	27.0%	24.0%	0.14
Prior coronary artery bypass graft surgery	23.4%	23.9%	23.1%	0.87
Prior heart failure	18.3%	19.0%	18.0%	0.64
Hypertension	78.7%	81.3%	77.4%	0.06
Diabetes mellitus	34.6%	35.7%	33.9%	0.49
Current/recent smoker	15.4%	15.5%	15.3%	0.96
Dyslipidemia	58.9%	59.2%	58.8%	0.70
Chronic obstructive pulmonary disease	27.5%	27.8%	27.3%	0.75
Cancer	4.2%	3.9%	4.3%	0.59
Dementia	2.6%	3.2%	2.4%	0.18
Charlson index ≥4	31.9%	35.7%	29.9%	0.008
Presenting signs				
Signs of congestive heart failure	24.4%	24.9%	24.2%	0.83
Systolic blood pressure (mm Hg), median (IQR)	147 (127, 168)	145 (127, 167)	148 (128, 168)	0.13
Weight (kg), median (IQR)	76.4 (65.0, 88.8)	75.8 (65.0, 88.7)	77.0 (64.9, 88.8)	0.50
Troponin (xULN), median (IQR)	2.0 (0.5, 8.0)	1.9 (0.4, 7.3)	2.0 (0.5, 8.3)	0.11
Hematocrit (%), median (IQR)	39.4 (35.5, 42.8)	39.0 (35.1, 42.4)	39.7 (35.9, 42.9)	0.004

Table 2

Discharge care in academic and nonacademic hospitals

Variable	Overall (n = 3,184)	Academic (n = 1,107)	Nonacademic (n = 2,077)	p-Value
Median LOS (days), median (IQR)	4 (3, 6)	4 (3, 6)	4 (3, 6)	0.51
Discharge prescriptions				
ACEI/ARBS	70.4%	70.4%	70.4%	0.74
B-blockers	94.9%	95.1%	94.8%	0.81
Statin	85.1%	87.2%	84.0%	0.02
Clopidogrel	75.9%	72.2%	77.9%	0.0002
All four agents	52.0%	51.9%	52.1%	0.92
Discharge services				
Cardiac rehabilitation referral	63.3%	55.6%	67.4%	<0.0001
Smoking cessation counseling	86.9%	84.2%	88.4%	0.06
Time to follow-up (days), median (IQR)				
Days to first follow-up visit with any specialty*	13 (7, 23)	12 (7, 22)	13 (7, 23)	0.18
Days to first follow-up visit with cardiologist	28 (16, 55)	28 (15, 53.5)	28 (16, 56)	0.25
Number of cardiac follow-up visits within 90 days post-discharge	1 (0, 2)	1 (0, 2)	1 (0, 1)	0.19
Number of any specialty follow-up visits within 90 days post-discharge	3 (2, 5)	3 (2, 5)	3 (2, 5)	0.20

*Continuous variables are presented as median (IQR).

Table 3

Individual medication persistence (%) at 90 days and 1 year

	Overall (n = 3,184)	Academic (n = 1,107)	Nonacademic (n = 2,077)	p-Value
Persistence at 90 days				
ACEI/ARB	67.4%	68.1%	67.0%	0.62
Statin	63.9%	62.9%	64.4%	0.47
B-blocker	71.1%	70.1%	71.7%	0.40
Clopidogrel	72.8%	72.4%	73.0%	0.76
Persistence at 1 year				
ACEI/ARB	63.4%	65.3%	62.5%	0.23
Statin	63.2%	62.0%	63.9%	0.37
B-blocker	69.1%	69.2%	69.1%	0.95
Clopidogrel	63.3%	65.8%	62.0%	0.10