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Use of Angiotensin-Converting Enzyme Inhibitors at Discharge in Patients With Acute Myocardial Infarction in the United States: Data From the National Registry of Myocardial Infarction 2

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Objectives: **This study was undertaken to examine recent trends in the use of angiotensin-converting enzyme (ACE) inhibitor therapy in patients discharged after acute myocardial infarction (AMI) and to identify clinical factors associated with ACE inhibitor prescribing patterns.**

Background: **Clinical trials have demonstrated a significant mortality benefit in patients treated with ACE inhibitors after AMI. Numerous studies have demonstrated underuse of other beneficial treatments for patients with AMI, such as beta-adrenergic blocking agents, aspirin and immediate reperfusion therapy.**

Methods: **Demographic, procedural and discharge medication data from 190,015 patients with AMI were collected at 1,470 U.S. hospitals participating in the National Registry of Myocardial Infarction 2.**

Results: **Prescriptions for ACE inhibitor therapy at hospital discharge increased from 25.0% in 1994 to 30.7% in 1996. Patients with a left ventricular ejection fraction ≤40% or evidence of congestive heart failure while in the hospital were discharged with ACE inhibitor treatment 42.6% of the time. Of patients experiencing an anterior wall myocardial infarction and no evidence of heart failure, 26.1% of patients were discharged with this treatment. Of the remaining patients, 15.6% received ACE inhibitors at discharge. ACE inhibitors were prescribed more often to elderly and diabetic patients as well as those requiring intraaortic balloon pump placement. This therapy was given less often to patients who underwent revascularization with coronary angioplasty or coronary artery bypass graft surgery or were treated with calcium channel blocking agents.**

Conclusions: **Physicians are prescribing ACE inhibitors in patients with myocardial infarction with increasing frequency. Those patients with the greatest expected benefit receive ACE inhibitor treatment most often. However, the majority of even these high risk patients were not discharged with this life-saving therapy.**

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Since the early 1980s when treatment with angiotensin-converting enzyme (ACE) inhibitors was shown to reduce myocardial infarction size and improve ventricular remodeling (1–6), >100,000 patients have been enrolled in randomized studies investigating the role of ACE inhibitors after myocardial infarction. Initially, ACE inhibitors were shown (7) to have a beneficial effect on symptoms and mortality in patients with severe congestive heart failure. This observation led to other studies demonstrating similar findings in postinfarction patients with less severe congestive heart failure (VHEFT II [8], SOLVD [9], AIRE [10], TRACE [11]) and asymptomatic left ventricular systolic dysfunction (SAVE [12]). More recent randomized trials have shown an additional mortality benefit when ACE inhibitor therapy is begun within 24 h of myocardial infarction (GISSI-3 [13], ISIS-4 [14], CCS-1 [15], SMILE [16]). Current American College of Cardiology (ACC) and American Heart Association (AHA) practice guidelines (17) state that oral ACE inhibitors should be started within the first 24 h of suspected acute myocardial infarction (AMI) and continued for 4 to 6 weeks in those patients without contraindications. In patients with left ventricular dysfunction, this therapy should be continued for at least 3 years (18).

To evaluate the impact of these clinical trials on physician practice patterns, we examined data from the National Registry of Myocardial Infarction 2, a large registry of patients with an AMI who were treated at selected U.S. hospitals. Specifically, we sought to determine whether there was a temporal increase in the use of ACE inhibitors at hospital discharge. In addition, we investigated which clinical characteristics were predictive of patients receiving ACE inhibitor treatment and whether particular

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Abbreviations and Acronyms

ACC = American College of Cardiology
ACE = angiotensin-converting enzyme
AHA = American Heart Association
AMI = acute myocardial infarction
CABG = coronary artery bypass graft surgery
CCP = Cooperative Cardiovascular Project
ECG = electrocardiographic
LVEF = left ventricular ejection fraction
NRMI 2 = National Registry of Myocardial Infarction 2
PTCA = percutaneous transluminal coronary angioplasty

patient groups with a greater absolute expected benefit from ACE inhibitors were more likely to receive this life-saving therapy.

Methods

Data sources. The National Registry of Myocardial Infarction 2 (NRMI 2) is a prospective, observational study sponsored by Genentech, Inc. (South San Francisco, California). NRMI 2, which was initiated in June 1994, contains data abstracted from the charts of patients with AMI admitted to registry hospitals. The completed case report form is forwarded from the registry hospital to an independent central data collection center (ClinTrials Research, Inc., Lexington, Kentucky) for processing and analysis.

The study coordinator from each participating hospital attended a half-day training course and was provided with a reference manual that included case report form definitions and examples of how to correctly complete the form. The data collection center used double-key entry to add data from each case report form to the database. Eight-seven electronic data checks were performed to detect internal inconsistencies, omissions, errors and out-of-range variables. National and periodic regional meetings of study coordinators and physician investigators were held to discuss data management issues. A quarterly study newsletter was also used to address these issues.

Additional data was collected in a subset of patients who were included in both the NRMI 2 and the national Cooperative Cardiovascular Project (CCP), a study sponsored by the Health Care Financing Administration (HCFA) to improve care for Medicare beneficiaries admitted to the hospital with AMI. The CCP file contains two creatinine variables—a baseline value and a highest recorded value—that were not included in NRMI 2. Acute care hospitals registered in the CCP from across the United States submitted 24,377 medical records for patients with AMI admitted to the hospital within specified 8-month periods between March 1, 1994 and June 30, 1995. The standardization and matching process to integrate the two databases has been described in detail (19). The final matched NRMI 2/CCP population included 1,076 providers and 25,664 patient-episodes.

Table 1. Baseline Demographic and Clinical Characteristics by Angiotensin-Converting Enzyme Inhibitor Treatment at Discharge

Characteristic	Therapy at Discharge (n = 52,668)	No Therapy at Discharge (n = 137,347)
Demographic		
Age (yr)	68.5 ± 13.2	65.5 ± 13.7
Women	41.3%	35.8%
African-American	7.7%	6.4%
Past medical history		
Diabetes mellitus	32.3%	22.2%
History of hypertension	58.1%	46.6%
Current tobacco use	24.6%	31.1%
History of stroke	9.2%	6.6%
Prior coronary angioplasty	7.5%	7.8%
Prior coronary artery bypass graft surgery	13.2%	10.2%
History of congestive heart failure	20.1%	8.8%
History of angina	19.8%	17.6%
Previous myocardial infarction	30.4%	22.4%

Data presented are mean value ± SD or percent of patients.

Study definitions. The method of diagnosis of AMI was defined by the study protocol as 1) a patient history and presentation suggestive of AMI accompanied by either a) total creatinine kinase greater than or equal to twice the upper limit of hospital laboratory normal or creatinine kinase-MB fraction greater than or equal to the upper limit of hospital laboratory normal, or b) electrocardiographic (ECG) evidence of AMI, or c) in the absence of definitive/available cardiac enzyme or ECG data, alternative enzymatic, scintigraphic, echocardiographic, angiographic or autopsy evidence indicative of AMI; or 2) an International Classification of Diseases, 9th revision, clinical modification, discharge diagnosis code for AMI, 410.01 through 410.91.

Killip class was assigned to patients on the basis of their most severe symptoms of heart failure at first assessment. *Killip Class I* was defined as the absence of rales in the lung fields and the absence of an S3 heart sound; *Killip class II* was defined as rales <50% of the lung fields, the presence of an S3 heart sound or jugular venous distention; *Killip class III* was defined as rales >50% of the lung fields; and *Killip class IV* was defined as the presence of pulmonary edema with hypotension.

All registry patients were classified into three mutually exclusive groups according to the degree of expected absolute benefit for treatment with ACE inhibitors. The first group of patients was categorized as having the greatest expected absolute benefit for ACE inhibitor therapy. These patients were defined as having a measured left ventricular ejection fraction (LVEF) ≤40% or evidence of congestive heart failure during the hospital period. The second group of patients included those with an intermediate expected absolute benefit from ACE inhibitor therapy: patients with anterior myocardial infarction and no evidence of congestive heart failure. The third group included all remaining patients in the registry.

In addition, detailed demographic data were collected and included age, gender, race, weight and additional medical

Table 2. In-Hospital Characteristics by Angiotensin-Converting Enzyme Inhibitor Treatment at Discharge

Characteristic	Therapy at Discharge (n = 52,668)	No Therapy at Discharge (n = 137,347)
Time from symptom onset to hospital arrival (h)	5.9 ± 9.9	5.5 ± 9.2
Systolic blood pressure		
<90 mm Hg	2.9%	3.0%
90–180 mm Hg	82.8%	85.6%
>180 mm Hg	14.3%	11.4%
Admission heart rate		
<50 beats/min	2.5%	3.2%
50–100 beats/min	69.3%	79.4%
>100 beats/min	28.2%	17.4%
Anterior myocardial infarction	37.2%	23.5%
Q wave myocardial infarction	53.2%	51.3%
Left ventricular ejection fraction <45%	59.0%	28.7%
Killip class		
I (no CHF)	64.4%	82.2%
II (rales, JVD)	22.9%	12.4%
III (pulmonary edema)	11.8%	4.9%
IV (cardiogenic shock)	0.9%	0.5%
In-hospital clinical events		
Hypotension	12.3%	11.1%
Recurrent ischemia	13.1%	12.6%
Recurrent infarction	2.4%	2.1%
Pulmonary edema	26.7%	11.3%
Cardiogenic shock	3.2%	1.6%
VT/VF	6.7%	5.1%

Data presented are mean value ± SD or percent of patients. CHF = congestive heart failure; JVD = jugular venous distention; VT/VF = ventricular tachycardia/ventricular fibrillation.

Table 3. In-Hospital Therapy by Angiotensin-Converting Enzyme Inhibitor Treatment at Discharge

Characteristic	Therapy at Discharge (n = 52,668)	No Therapy at Discharge (n = 137,347)
Admission medications		
Thrombolytic use	24.9%	29.3%
Aspirin	75.1%	77.9%
Beta-blocker	37.7%	41.4%
ACE inhibitor	38.5%	5.6%
Heparin	74.6%	77.6%
Calcium blocker	19.9%	21.5%
Procedures		
Coronary angiography	56.3%	65.2%
Coronary angioplasty	23.3%	29.4%
Intraaortic balloon pump	7.1%	4.6%
Coronary artery bypass	10.3%	15.2%
Echocardiography	59.0%	45.3%
Discharge medications		
Aspirin	70.6%	76.7%
Beta-blocker	38.7%	47.9%
Calcium blocker	19.2%	30.5%
Digoxin	34.1%	17.7%

Data presented are percent of patients. ACE = angiotensin-converting enzyme.

history variables as listed in Table 1. Presenting characteristics of patients included the time from symptom onset to hospital arrival, blood pressure and heart rate on admission as well as Killip class (Table 2). The location and type of AMI were designated, as was the occurrence of clinical events, such as hypotension, recurrent ischemia or infarction, pulmonary edema, cardiogenic shock, ventricular fibrillation and death. LVEF and its method of determination were recorded for those patients with known values. For patients with multiple measurements, the value measured closest to discharge was listed. The use of medications within 24 h of diagnosis was noted, as was the use of selected procedures during the hospital period (Table 3). Finally, medications prescribed at hospital discharge were indicated.

Registry hospitals were classified according to registration data on enrollment into NRMI 2. Hospitals were asked to indicate on enrollment whether they had the capability to perform cardiac catheterization, angioplasty or open heart surgery, alone or in combination. Hospitals were defined as "urban" if they were located in a county that had at least one city with >50,000 persons or twin cities with a combined population of 50,000 persons. The primary payer of hospital charges was identified as commercial, paid provider organization, health maintenance organization, Medicare, Medicaid, Department of Veterans Affairs, self, other or unknown.

Analysis. Baseline demographics, clinical events, use of medications and utilization of cardiac procedures were compared. Statistical differences were calculated between NRMI 2 and CCP. These analyses were performed in the matched NRMI 2/CCP population and among the NRMI 2 and CCP comparison populations. A regression analysis was then performed on each comparison population to determine whether associations existed between the health indexes and mortality.

Statistical methods. Chi-square and Student t tests were performed to determine whether differences existed within baseline characteristics, therapy and procedures of the comparison databases and matched database. A stepwise logistic regression model was developed to identify predictors of receiving ACE inhibitor therapy at discharge. The model included all variables shown in Tables 1 to 3, except time and was run for each of the three levels of expected benefit from ACE inhibitor use. After all variables entered the model, the time variable was included in the analysis to assess its association with ACE inhibitor use. Odds ratios and 95% confidence intervals are reported for each model (Tables 4 to 6). Logistic regression was utilized to determine correlation of in-hospital mortality and health indexes. All statistical calculations were performed with the SAS 6.12 statistical procedure (SAS Institute).

Time, the major independent variable, was defined in two ways: 1) For univariate analysis, the 25-month study period was divided into quartiles. 2) In the multivariate analysis, time was defined as the number of days from June 1, 1994 to hospital discharge. The major dependent variable used in this study was

Table 4. Predictors of Discharge Angiotensin-Converting Enzyme Inhibitor Use in Group 1: Treatment "Definitely" Indicated

Variable	Odds Ratio (lower–upper 95% CI)
Diabetes mellitus	1.16 (1.13–1.20)
History of hypertension	1.21 (1.17–1.25)
History of CHF	1.28 (1.23–1.33)
Previous myocardial infarction	1.19 (1.15–1.23)
Systolic BP (per 20-mm Hg increase)	1.02 (1.01–1.03)
Heart rate (per 10-beats/min increase)	1.03 (1.02–1.04)
Anterior myocardial infarction	1.56 (1.51–1.61)
LVEF*	
≤40%	1.93 (1.85–2.03)
Unknown	1.24 (1.18–1.31)
Killip class >I	1.10 (1.08–1.11)
Hypotension	0.90 (0.86–0.94)
CHF/pulmonary edema	1.47 (1.43–1.52)
Admission calcium blocker	0.78 (0.75–0.81)
No. of discharge medications	1.10 (1.08–1.11)
Coronary angiography	1.17 (1.12–1.22)
Coronary angioplasty	0.82 (0.78–0.86)
Intraaortic balloon pump	1.54 (1.44–1.65)
In-hospital coronary artery bypass	0.46 (0.43–0.48)
Echocardiography	1.22 (1.18–1.27)
Time from 6/1/94 to admission (per 180-day increase)	1.07 (1.06–1.09)

*>40% is reference category. BP = blood pressure; CI = confidence interval; LVEF = left ventricular ejection fraction; other abbreviations as in Table 2.

whether ACE inhibitors were prescribed at hospital discharge. Because the number of patients in this study was so large, assessing whether differences were statistically significant was not informative. Hence, p values were not reported for the univariate comparisons.

Results

Patient characteristics. From June 1, 1994 to June 30, 1996, we identified 275,560 patients with AMI from 1,470 hospitals in NRMI 2. Of these patients, 55,010 (20.0%) were transferred out of registry hospitals, and thus the discharge medications were unknown. These patients were excluded from the analysis. In addition, 27,941 patients (10.1%) died during the hospital period and were also excluded from the study. The resultant 192,609 patients made up the main study cohort. The mean age of patients included in the study was 66.6 years, and 62.5% were male. Information on the use of ACE inhibitors was available for 190,015 patients (98.6%). Other baseline demographic and clinical characteristics are shown in Table 1. The final matching process integrating the CCP database resulted in 25,664 cases (mean age 77 ± 7 years; 49% women).

Univariate analysis. In the first group of patients categorized with the greatest absolute benefit for ACE inhibitor therapy (i.e., LVEF ≤40% or evidence of congestive heart failure [n = 75,173]), 42.6% were prescribed ACE inhibitors

Table 5. Predictors of Discharge Angiotensin-Converting Enzyme Inhibitor Use in Group 2: Treatment "Probably" Indicated

Variable	Odds Ratio (lower–upper 95% CI)
Diabetes mellitus	1.29 (1.20–1.39)
History of hypertension	1.56 (1.47–1.66)
History of CHF	1.69 (1.46–1.96)
Heart Rate (per 10-beats/min increase)	1.05 (1.03–1.06)
Non-Q wave myocardial infarction	0.67 (0.63–0.71)
Intraaortic balloon pump	1.81 (1.59–2.05)
In-hospital coronary artery bypass	0.49 (0.44–0.54)
Echocardiography	1.43 (1.35–1.52)
Admission calcium blocker	0.80 (0.74–0.87)
Time from 6/1/94 to admission (per 180-day increase)	1.11 (1.08–1.15)

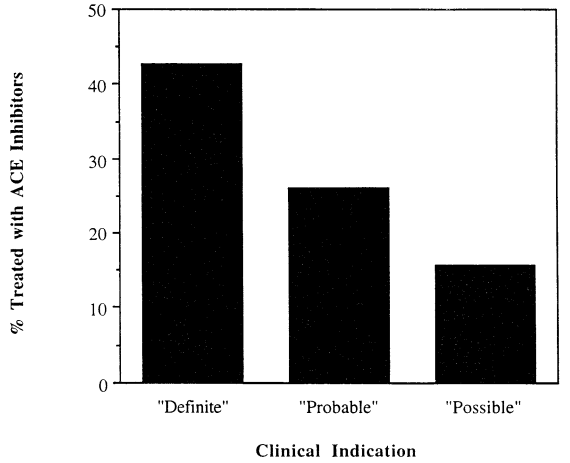
Abbreviations as in Tables 2 and 4.

Table 6. Predictors of Discharge Angiotensin-Converting Enzyme Inhibitor Use in Group 3: Treatment "Possibly" Indicated

Variable	Odds Ratio (lower–upper 95% CI)
Age (per 10-yr increase)	1.07 (1.05–1.09)
Diabetes mellitus	1.47 (1.41–1.54)
History of hypertension	2.00 (1.92–2.08)
History of tobacco use	0.90 (0.86–0.95)
History of stroke	1.19 (1.11–1.28)
Prior coronary artery bypass	1.40 (1.32–1.49)
History of CHF	2.58 (2.39–2.78)
Previous myocardial infarction	1.31 (1.25–1.37)
Systolic BP (per 20-mm Hg increase)	1.09 (1.07–1.10)
Heart Rate (per 10-beats/min increase)	1.03 (1.02–1.04)
Intraaortic balloon pump	1.65 (1.48–1.85)
In-hospital coronary artery bypass	0.70 (0.66–0.75)
Echocardiography	1.21 (1.16–1.26)
Admission calcium blocker	0.86 (0.82–0.91)
Number of discharge medications	0.95 (0.94–0.97)
Time from 6/1/94 to admission (per 180-day increase)	1.11 (1.09–1.14)

Abbreviations as in Tables 2 and 4.

Figure 1. Discharge ACE inhibitor use by clinical indication group.



(Fig. 1). Of those patients in the second group with an intermediate expected benefit (i.e., anterior infarction with no evidence of congestive heart failure [n = 26,209]), 26.1% received treatment, whereas 15.6% of the patients in the third group (n = 88,633) of remaining patients were prescribed ACE inhibitors. Patients prescribed ACE inhibitors at discharge were significantly older, with an average age of 68.5 years compared with 65.5 years for patients not treated with ACE inhibitors (Table 1). Women were more likely to be treated with ACE inhibitors, as were patients with diabetes mellitus, hypertension and a history of previous myocardial infarction or congestive heart failure. Patients with tachycardia on admission as well as those discharged with a diagnosis of anterior myocardial infarction were more likely to receive ACE inhibitor therapy. Of the 114,149 patients undergoing left ventricular function assessment, 59% of patients discharged with ACE inhibitors had an LVEF <45% compared with only 29% not treated with ACE inhibitors at hospital discharge. Similarly, patients with evidence of jugular venous distention, pulmonary edema and cardiogenic shock on admission were roughly twice as likely to be discharged with ACE inhibitors. Patients undergoing coronary angiography, percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG) surgery were all less likely to receive ACE inhibitor treatment.

Multivariate analysis. To evaluate which clinical, demographic and hospital-related factors independently influenced the use of ACE inhibitor therapy at the time of discharge, we constructed a series of multivariate logistic regression models. Independent predictors of ACE inhibitor therapy in the patients with the greatest expected absolute benefit for ACE inhibitor use included anterior myocardial infarction, LVEF ≤40%, congestive heart failure during hospitalization, Killip class >I and previous history of diabetes mellitus, congestive heart failure, myocardial infarction and hypertension (Table 4). Patients discharged with a diagnosis of anterior myocardial infarction had a 54% increased odds of receiving ACE inhibitors at hospital discharge compared with patients who had a myocardial infarction in any other location. The use of calcium channel blockers at hospital discharge was associated with a decreased odds of receiving ACE inhibitor treatment. Furthermore, there was a direct relation between the number of discharge medications and the odds of being discharged with an ACE inhibitor. Revascularization with PTCA or CABG was also associated with decreased use of ACE inhibitor therapy. When a time variable was introduced into the model, there was evidence that ACE inhibitors were being used more commonly in 1996 than in 1994. There was a 7% increase in the likelihood of use of ACE inhibitors for each 180-day increment.

For those patients with an intermediate expected absolute benefit for ACE inhibitor therapy, the significant independent predictors of receiving therapy included a history of diabetes mellitus, congestive heart failure and hypertension (Table 5). Patients who underwent CABG were less likely to receive ACE inhibitors, as were patients treated with calcium channel blockers. There was also a temporal relation with an 11% increased odds of ACE inhibitor treatment with each 180-day increment.

Table 7. Baseline and Highest Creatinine and Angiotensin-Converting Enzyme Inhibitor Use at Discharge

	Baseline mg/dl		Peak mg/dl	
Indication	≤2.0	>2.0	≤2.0	>2.0
Definite	43.9%	30.5%*	44.7%	35.0%*
Probable	25.8%	20.8%	25.7%	24.0%
Possible	17.6%	20.4%	17.5%	21.8%†

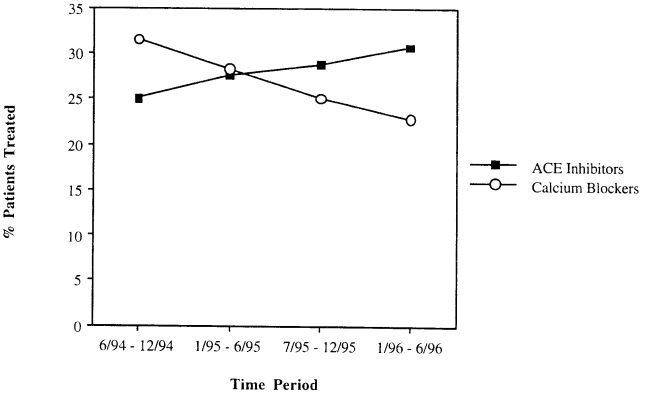
*$p < 0.0001$. †$p = 0.008$.

For patients in group three comprising all remaining patients with a possible indication for ACE inhibitor treatment, the independent predictors identified by the logistic regression analysis included a history of diabetes mellitus, congestive heart failure, hypertension, myocardial infarction and prior CABG (Table 6). Patients who underwent revascularization with PTCA or CABG during the present hospital period were less likely to receive ACE inhibitors, as were patients treated with either calcium channel or beta-blockers. Intraaortic balloon pump placement was also predictive of increased ACE inhibitor use. Similar to the second group in the model, there was an 11% increased odds of ACE inhibitor use during each 180-day period.

Table 7 shows ACE inhibitor use at discharge by levels of baseline and peak serum creatinine for the three groups. There was a significant association between less ACE inhibitor use when serum creatinine exceeded 2.0 either at baseline or at any time during the hospital period.

Temporal trends in use of ACE inhibitors. The use of ACE inhibitors in patients discharged after hospital admission for AMI increased by 22.8% in the 25-month period studied. From June 1, 1994 to December 31, 1994, 25.0% of patients received ACE inhibitors compared with 30.7% from January 1, 1996 to June 30, 1996 (Fig. 2). There was no clinically significant change in the use of digoxin over the study period (range 21.8% to 22.6%). Calcium channel blocker use decreased by 27.6%. For each 180-day period, there was a 7%, 11% and

Figure 2. Discharge ACE inhibitor (**squares**) and calcium channel blocker (**circles**) use by time period.



11% increased odds of receiving an ACE inhibitor in the clinical indication groups one, two and three, respectively, derived from the multivariate analysis.

Discussion

In our analysis of ACE inhibitor use in patients discharged from NRMI 2 hospitals after myocardial infarction, we made several observations.

1. We observed that clinicians prescribe ACE inhibitors more aggressively in patient groups where such therapy is likely to result in a greater absolute benefit, a pattern not seen with beta-blocker use after AMI (20). In the present study, patients with congestive heart failure or LVEF ≤40% during the hospital period were categorized as a group with the greatest expected benefit from ACE inhibitor treatment. Randomized trials (1–16) have shown that these patients have a significantly greater absolute mortality benefit when given ACE inhibitors after myocardial infarction. Our data reveal that although overall only 27.6% received ACE inhibitors at hospital discharge, 42.6% of patients in the first group with the greatest expected benefit for ACE inhibitors received such treatment (Fig. 1). Although patients most likely to benefit from ACE inhibitors are treated more often, it should be emphasized that most of these patients still did not receive this life-saving therapy.

2. Clinicians prescribed ACE inhibitors with increasing frequency over the 25-month period studied (from 25.0% in 1994 to 30.7% in 1996). This absolute increase of 2.7%/year represents an 11% relative annual increase. The increase in ACE inhibitor use over time was observed in all three clinical indication groups in the multivariate logistic regression model as well. In contrast, the use of calcium channel blockers fell by 4.2%/year, a 13% relative annual decrease. Interestingly, the use of a calcium channel blocker was significantly inversely associated with ACE inhibitor use at discharge in all three patient groups (Fig. 2). This observation suggests that clinicians are becoming increasingly accepting of the data supporting the use of ACE inhibitors in patients after AMI.

3. ACE inhibitors were prescribed more often to the elderly. Patients who received ACE inhibitors were 3 years older than those who received no therapy at discharge. Multivariate logistic regression analysis showed that increasing age was independently associated with ACE inhibitor use in patients with a possible indication for ACE inhibitor treatment. This is in contrast to many other studies that have observed that therapeutic measures that improve mortality in patients with myocardial infarction are given less frequently to the elderly (20–26). For example, treatment of patients with AMI with thrombolytics, aspirin and beta-blockers significantly decreases with advancing patient age (20–26). One possible explanation why ACE inhibitors are one of the few pharmacologic agents used more aggressively in elderly postinfarction patients is that because these agents have a relatively low incidence of reported side effects, clinicians feel more comfortable prescribing them to elderly patients.

4. We observed that in-hospital PTCA and CABG were independent predictors of not receiving ACE inhibitor therapy at discharge. Multivariate logistic regression analysis demonstrated that CABG was associated with a roughly 50% reduction in the odds of receiving an ACE inhibitor. This is surprising because there are insufficient clinical data to suggest that revascularization attenuates the mortality benefit of ACE inhibitors. One possible explanation for this finding is that ACE inhibitors may be less often prescribed by surgeons. Targeting educational efforts toward surgical or cardiology consult services may improve utilization of ACE inhibitors in this group of patients.

5. We also observed that diabetic patients were significantly more likely to receive ACE inhibitors. One possible explanation for this observation is that ACE inhibitors have been shown (27,28) to slow the progression of nephropathy in both insulin-dependent and non–insulin-dependent diabetic patients.

6. We also observed that simply undergoing echocardiography was independently associated with an increased use of ACE inhibitors in all three groups. We emphasize that this effect is noted while controlling for LVEF, anterior myocardial infarction, hypertension, congestive heart failure and the other variables included in our models. It is possible that obtaining an echocardiogram reveals other indications for vasodilator therapy not measured in this study, such as significant mitral or aortic insufficiency, left ventricular hypertrophy, regional wall motion abnormalities or aneurysm formation. It is also possible that clinicians who order echocardiograms are more likely to translate the information learned from randomized trials to clinical practice.

Study limitations. The limitations of the National Registry of Myocardial Infarction 1 registry have been previously described (22,29). Significantly more clinical data are now available for each patient in NRMI 2, such as cardiovascular risk factors and indicators of infarction size. The major limitation of the present study is that we did not have information regarding severity of the major contraindications to therapy, including renal dysfunction, hyperkalemia, history of bilateral renal artery stenosis and history of angioedema. We were able to obtain information regarding renal function for a subset of patients who were also registered in the CCP database. Using this data it did not appear that elevated serum creatinine was a major predictor of not receiving an ACE inhibitor. Another major contraindication to ACE inhibitor therapy is cardiogenic shock and persistent hypotension. Although 1% of patients in our study group had cardiogenic shock on presentation, and 11% had at least one episode of hypotension during their hospital stay, it is likely that the majority of patients were not hypotensive at hospital discharge, and therefore these patients were probably still candidates for long-term ACE inhibitor therapy.

In addition, we did not collect data regarding whether patients were not discharged with an ACE inhibitor due to a previous adverse reaction. Poor patient tolerance of ACE inhibitor treatment was unlikely to account for the dramatic

underuse observed in the present study because several randomized clinical trials have shown that ACE inhibitors are well tolerated by most patients. Rates of withdrawal due to adverse effects or patient choice are reported to be 10% to 20% (30,32). For example in ISIS-4, 83% of patients who began therapy with captopril were discharged with this ACE inhibitor, compared with 87% of patients continuing placebo drug to discharge (14). A small excess of renal dysfunction was noted in patients receiving ACE inhibitors in GISSI-3 (2.4% in the lisinopril group vs. 1.1% in the placebo group) and in ISIS-4 (1.1% in captopril-treated patients vs. 0.6% in placebo patients) (13,14).

Previous reports of Medicare patients admitted to the hospital for AMI suggest that of patients >65 years old, 4.9% had serum creatinine levels ≥3.0 mg/dl, 0.3% had an allergy to ACE inhibitors, and overall 8.7% of patients discontinued ACE inhibitor therapy during their hospital stay (32). Again, because we found that more than two-thirds of patients in the present study did not receive this therapy, we conclude that most patients who did not receive ACE inhibitors probably did not have a specific contraindication or develop a side effect.

Clinical implications. Current ACC/AHA practice guidelines (17) for the management of patients with AMI recommend initiating oral ACE inhibitor therapy within 24 hours of hospital admission in patients without hypotension or a contraindication. The ACE inhibitor should then be continued for 6 weeks for those patients without complications or left ventricular systolic dysfunction. In patients with impaired systolic function, ACE inhibitors should be continued indefinitely. Clinical trials have documented (13–15) that initiation of ACE inhibitor therapy early after myocardial infarction typically saves five lives per 1,000 patients treated in the first month. This finding complements the results of other trials (9,10,12) that have shown that starting long-term ACE inhibitor therapy in the weeks after infarction in patients with impaired ventricular function saves about two lives/1,000 patients per month of treatment for the first year, or 24 lives/year. Applying this additive mortality reduction of 29 lives/1,000 patients treated in the first year, if ACC/AHA guidelines had been used to treat all 75,173 patients in the present study categorized with the greatest absolute benefit for ACE inhibitor use, >1,800 additional lives would have been saved in the first year alone due to the effect of ACE inhibitors (assuming 15% of patients have a specific contraindication or are intolerant of ACE inhibitors) (36).

Conclusions. Although basic and clinical science has had a profound impact on identifying treatment for patients with AMI, translating these results into clinical practice is an equally important goal. NRMI 2 is a unique source of information and can be used to assess recent health care trends in the management of AMI in the United States. Recent data derived from this registry show trends toward the expanded use of ACE inhibitors in patients discharged after myocardial infarction. Although it appears that physicians are increasing their use of ACE inhibitors in patients discharged after AMI, far more patients could potentially benefit from this therapy. Through the analysis of large databases such as NRMI 2 and with novel educational programs, improvements in the quality of care of these patients may be attained.

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