Time to Presentation With Acute Myocardial Infarction in the Elderly
Associations With Race, Sex, and Socioeconomic Characteristics

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Background—Although prompt treatment is a cornerstone of the management of acute myocardial infarction (AMI), prior studies have shown that one fourth of AMI patients arrive at the hospital >6 hours after symptom onset. It would be valuable to identify individuals at highest risk for late arrival, but predisposing factors have yet to be fully characterized.

Methods and Results—Data from the Cooperative Cardiovascular Project, involving Medicare beneficiaries aged >65 years hospitalized between January 1994 and February 1996 with confirmed AMI, were used to identify patients who presented “late” (>6 hours after symptom onset). Patient characteristics were tested for associations with late presentation by use of backward stepwise logistic regression. Among 102,339 subjects, 29.4% arrived late. Significant predictors of late arrival (odds ratio, 95% CI) included diabetes (1.11, 1.07 to 1.14) and a history of angina (1.32, 1.28 to 1.35), whereas prior MI (0.82, 0.79 to 0.85), prior angioplasty (0.80, 0.75 to 0.85), prior bypass surgery (0.93, 0.89 to 0.98), and cardiac arrest (0.52, 0.46 to 0.58) predicted early presentation. Additionally, initial evaluation at an outpatient clinic (2.63, 2.51 to 2.75) and daytime presentation (1.67, 1.59 to 1.72) predicted late arrival. Finally, female sex, black race, and poverty, which were evaluated with an 8-level race–sex–socioeconomic status interaction term, were also risk factors for delay.

Conclusions—Delayed hospital presentation is a common problem among Medicare beneficiaries with AMI. Factors associated with delay include not only clinical and logistical issues but also race, sex, and socioeconomic characteristics. Education efforts designed to hasten AMI treatment should be directed at individuals with risk factors for late arrival.

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Key Words: myocardial infarction ■ sex ■ risk factors

Prompt initiation of therapy is a central goal in the management of patients with acute myocardial infarction (AMI). This paradigm is based largely on the results of trials of thrombolytic agents, which have demonstrated that the lifesaving benefits of these drugs are time dependent. However, for many patients, there are long gaps between the onset of symptoms and the delivery of care. Some of this delay occurs in the hospital, but about two thirds of the time to therapy is attributable to delays between symptom onset and hospital arrival. Of particular concern are data indicating that ≈25% of patients wait >6 hours before seeking care. The majority of them focused on patients treated in the early 1990s, and more recent trends are less well established. In addition, although these analyses indicated that older age, female sex, and diabetes were associated with delayed presentation, associations with other clinical issues and with race and socioeconomic characteristics have yet to be fully characterized.

The Cooperative Cardiovascular Project (CCP), initiated by the Health Care Financing Administration in 1992, is an ongoing national program designed to evaluate and improve the care provided to Medicare beneficiaries hospitalized with AMI. The program has gathered data regarding outcomes and processes of care, including time to presentation, for 234,769 hospitalizations. Therefore, we used the CCP database to
characterize patterns in time to presentation and to identify factors associated with delayed arrival.

**Methods**

**Study Sample**

Between January 1994 and February 1996, all nonfederal acute-care medical centers in the United States were sampled for >8 consecutive months for Medicare beneficiaries hospitalized with a principal discharge diagnosis of AMI (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 410). Charts were abstracted for patient demographics, medical history, arrival and discharge status, and treatments. The abstraction strategy has been discussed elsewhere. For subjects with repeat admissions, we excluded all subjects for whom time to presentation was not documented. We also removed from the eligible sample 3 individuals for whom survival status was undetermined or missing. Finally, we excluded individuals admitted directly from home or from an outpatient clinic.

For the present investigation, the baseline sample included all subjects aged ≥65 years who presented to the hospital with symptoms consistent with AMI and who had AMI confirmed by standardized criteria. Confirmed AMI was defined as an elevation of creatine kinase-MB level (>5% of total creatine kinase), an elevation of lactate dehydrogenase enzyme (LDH) level with isoenzyme reversal (LDH, >LDHH), or the presence of 2 of the following: chest pain during the 48 hours before admission, a 2-fold elevation in total creatine kinase, and diagnostic ECG changes (ST-segment elevation or new pathological Q waves).

Given the potential for confounding by delays at institutions other than the admitting hospital, we limited the study population to individuals admitted directly from home or from an outpatient clinic. We also removed from the eligible sample 3 individuals for whom survival status was undetermined or missing. Finally, we excluded subjects for whom time to presentation was not documented.

**Study Variables**

In CCP, time to presentation is coded as <6 hours, 6 to 12 hours, or >12 hours after the onset of symptoms. In addition, 140 other variables were abstracted, and we developed from these a list of candidate predictor variables. Candidate variables included patient race, sex, age, and “off-hour” presentation (arrival between 10:00 PM and 6:00 AM). Candidates’ clinical variables included prior myocardial infarction, angina, congestive heart failure, stroke, PTCA, or CABG, as well as other history and physical examination variables available on arrival.

To evaluate socioeconomic factors, we tested for associations between time to presentation and residence in an impoverished area (defined as a zip code with a median household income at or below the nation’s 15th percentile, based on 1990 US Census data). Finally, we examined associations with rural residency. To identify rural regions, we applied zip-code criteria established by the US Administration on Aging.

**Statistical Analyses**

First, we determined the number and percentage of individuals who presented in <6, 6 to 12, and >12 hours. To assess whether this distribution was consistent across important patient subsets, we repeated this evaluation for the group with and the group without ECG evidence of an evolving transmural infarction (ST-segment elevation or a new Q wave).

Second, we attempted to identify factors associated with time to presentation. Drawing from the list of candidate predictor variables, we compared the characteristics of those presenting in <6, 6 to 12, and >12 hours with χ² tests and ANOVA. Next, bivariate logistic regression analyses were performed to identify factors associated with arrival after >6 hours. In cases in which multiple study variables described the same characteristic, the most representative variables were analyzed. Otherwise, all patient characteristics with a population prevalence of >1% were tested, and significant factors (P<0.05) were then evaluated for independent associations via backward stepwise multiple logistic regression. The linearity of continuous predictors was tested by using the method of fractional polynomials. The goodness of fit of the regression model was assessed with a calibration plot of predicted versus actual probabilities.

The SAS 6.12 statistical analysis package (SAS Institute) was used for the statistical analyses. For all hypothesis testing, a value of P<0.05 was considered significant.

**Results**

**Study Population**

Among 234 769 subjects, 113 324 met eligibility criteria (Table 1). Of these, 102 339 patients had a documented time to presentation and constituted the study population. The mean age was 75.6 years. There were nearly equal proportions of men and women (53.6% men), and the vast majority of subjects (90.9%) were white. The prevalence of hypertension (61.7%) and diabetes (29.5%) was high, and more than half of the subjects had a prior history of coronary artery disease. Only 1 in 7 patients resided in an impoverished region. Study population characteristics, broken down by time category, are displayed in Table 2.

Background comparisons demonstrated differences between the study population and subjects who were excluded because of incomplete time to presentation data. Excluded subjects were, on average, older and were more likely to reside in impoverished regions. They also evidenced a higher prevalence of diabetes and hypertension and higher 1-year mortality (36.5% versus 26.3% for the study population, P<0.001). Thus, our study population represents a distinct subset of the CCP cohort, and our findings should be interpreted in this context.

**Factors Associated With Time to Presentation**

In our study population, 72 221 (70.6%) of patients presented within 6 hours of symptom onset, 11 905 (11.6%) presented in 6 to 12 hours, and 18 213 (17.8%) arrived after >12 hours. The distribution of time to presentation in those with evolving transmural infarction by ECG was similar.
Comparisons of <6-Hour, 6- to 12-Hour, and >12-Hour Groups

Individuals arriving after >6 hours, compared with subjects presenting within 6 hours, were, on average, older and were more likely to be women and nonwhite (Table 2). They had a greater prevalence of diabetes and prior angina, but they were less likely to have had a prior MI, PTCA, or CABG, and they were less likely to present with shock or arrest. Additionally, patients arriving late were more likely to reside in an impoverished area, to present to an outpatient clinic for initial evaluation, and to arrive during daytime hours.

Results of Logistic Regression Analyses

Bivariate logistic regression analyses identified 22 patient characteristics that were associated with presentation >6 hours after symptom onset, and in backward stepwise logistic regression modeling using a selection criterion of $P=0.05$, 16 associations were independent (Table 3). Older age and several clinical variables, including diabetes mellitus, a history of angina, chronic obstructive pulmonary disease, difficulty in walking, and active bleeding, were independently associated with arrival after >6 hours. Fractional polynomial modeling confirmed that the association with age was linear.
TABLE 3. Results of Multiple Logistic Regression Analysis: Independent Predictors of Time to Presentation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (5-y increments)</td>
<td>1.01 (1.00–1.01)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Race-sex-SES</td>
<td>...</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Cardiac history variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior MI</td>
<td>0.82 (0.79–0.85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior PTCA</td>
<td>0.80 (0.75–0.85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>0.93 (0.89–0.98)</td>
<td>0.003</td>
</tr>
<tr>
<td>History of angina</td>
<td>1.32 (1.28–1.35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Acute cardiac conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presenting with arrest</td>
<td>0.52 (0.46–0.58)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presenting with acute CHF</td>
<td>1.24 (1.20–1.29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Other clinical variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.11 (1.07–1.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COPD</td>
<td>1.12 (1.08–1.16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Difficulty walking</td>
<td>1.10 (1.06–1.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Actively bleeding</td>
<td>1.21 (1.10–1.33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recent surgery</td>
<td>0.90 (0.81–1.00)</td>
<td>0.039</td>
</tr>
<tr>
<td><strong>Process-of-care variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admitted from clinic</td>
<td>2.63 (2.51–2.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Off-hour presentation</td>
<td>0.60 (0.58–0.63)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Odds ratio (OR) >1.0 indicates that factor of interest is associated with arrival at hospital after >6 h. SES indicates socioeconomic status, based on residence in an impoverished area.

Meanwhile, cardiac arrest and prior MI, PTCA, and CABG were all associated with early arrival within 6 hours.

Race, sex, and socioeconomic characteristics were also significant. Nonwhite patients, women, and individuals residing in impoverished areas were significantly more likely to present after >6 hours. Because race, sex, and poverty qualify each other’s associations with several clinical issues, we tested for interactions between them. For each pairing of these variables, we created an interaction term, with a number of levels equal to the number of possible unique combinations of values for the original variables. One level of each term was selected as the referent value, and then we tested for independent differences in time to presentation between subjects with the referent value and those with other values for the interaction term. These analyses identified significant interactions between race and sex, race and socioeconomic status, and sex and socioeconomic status. We then combined these 3 variables to create an 8-level interaction term. Although this 3-way interaction did not achieve statistical significance, for ease of presentation and interpretation, we present odds ratios for these 8 groups in Table 4.

Finally, process-of-care issues were also associated with time to presentation. Initial presentation to an outpatient clinic, as well as hospital arrival between 6:00 AM and 10:00 PM, predicted arrival after >6 hours. A calibration plot indicated that the regression model was well calibrated across the range of predicted values. The $c$ index was 0.63.

### TABLE 4. Three-Way Interaction of Race, Sex, and Socioeconomic Status in Prediction of Time to Presentation With AMI

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, male, not poor</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>White, male, poor</td>
<td>1.12 (1.06–1.20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White, female, not poor</td>
<td>1.25 (1.11–1.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White, female, poor</td>
<td>1.31 (1.19–1.52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black, male, not poor</td>
<td>1.22 (1.06–1.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black, male, poor</td>
<td>1.33 (1.13–1.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black, female, not poor</td>
<td>1.17 (1.13–1.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black, female, poor</td>
<td>1.26 (1.18–1.34)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Odds ratio (OR) >1.0 indicates that factor of interest is associated with arrival at hospital after >6 h.

### Discussion

Over one fourth of elderly AMI patients present to the hospital >6 hours after symptom onset. In fact, the majority of this late-arriving group arrives >12 hours into the course of infarction. Factors predictive of delayed presentation include not only clinical characteristics but also sex, race, and socioeconomic status, as well as process-of-care factors.

### Distribution of Time to Presentation

Time to presentation with AMI continues to be an important public health problem. In prior analyses, 20% to 35% of AMI patients arrived at the hospital after >6 hours, and now we have shown that among Medicare beneficiaries, the frequency of late arrival remains in this range.

Perhaps even more disturbing is the large proportion of patients that presented after >12 hours, when the “window” of potential benefit from thrombolytic therapy is completely closed. Prior studies established that such delays are associated with increased mortality, and we also found univariate differences in 30-day mortality between patients arriving <6, 6 to 12, and >12 hours after symptom onset (13.8%, 16.8%, and 17.6%, respectively; $P=0.001$). These differences persisted at 1 year.

### Clinical Factors Associated With Time to Presentation

These findings emphasize a need for increased public awareness of the appropriate responses to AMI symptoms, and our multivariate model identified several groups that merit targeted education. These include persons with diabetes, who were shown to be at increased risk in the CCP study and in past investigations. This association may relate to diabetic neuropathy, which may alter perception of myocardial ischemia and lead to delayed arrival. Similarly, problems with symptom perception and interpretation may explain associations with prior angina and comorbid illnesses. Patients with frequent angina may initially interpret AMI as a typical anginal episode and thus delay presentation. Likewise, patients with significant comorbid conditions may have difficulty distinguishing the symptoms of AMI from other causes of discomfort.
In contrast, other clinical factors identified groups that arrived early. Whereas prior infarction had inconsistent associations in prior studies, in our analysis, it was an independent predictor of early arrival. Previous PTCA and CABG also predicted prompt presentation. This suggests that patients with prior coronary events tend to respond quickly to recurrent symptoms. Another clinical factor that predicted early arrival was cardiac arrest, which typically prompts rapid transport.

Demographic and Socioeconomic Factors Associated With Time to Presentation
This analysis demonstrated that demographic and socioeconomic characteristics are also associated with time to presentation. Relevant factors include older age, which had a small but significant influence in this study, and, as in prior studies, female sex. Explanations for the association with sex are probably multifactorial, but may relate to perceptions of the prevalence of coronary artery disease in women by both physicians and patients. Race and income were also significant. Although several prior studies have suggested that prehospital delays are disproportionately long in black patients and in poor patients, other investigations have yielded conflicting results. In this analysis of a larger cohort, however, we demonstrate independent associations of race and socioeconomic status with time to presentation. In addition, our evaluation of interactions suggests that individuals with multiple racial, socioeconomic, and sex-based predictors of delay are at particular risk of arriving late. Here, too, physician and patient perceptions may be contributing. Past studies indicate that black-white disparities in coronary care relate both to physician practice patterns, which may include differential patient counseling across races, and to patient trust and understanding of health care. These studies indicated that black patients face several other logistical barriers to treatment as well. It is likely that each of these factors also contributes to the associations of race and socioeconomic status with delayed arrival.

Consistent with prior studies, process-of-care factors, including initial presentation to an outpatient clinic and daytime arrival, were also associated with late presentation. Many patients who presented during the day had their first symptoms the previous night; thus, it appears that individuals with late-night symptom onset were reluctant to go to the hospital. These findings suggest that patients’ interpretations of their symptoms contribute significantly to time to presentation, and this hypothesis is supported by psychological studies. These investigations found that patients who delay arrival are less likely to know the typical symptoms of AMI or to interpret their symptoms as serious.

Study Limitations
The present investigation had several limitations. First, the coding of time to presentation may have been biased by patient recall and physician interpretation, and the use of 6-hour increments created the potential for unmeasured variation in the features of patients within any given time category. Analysis of shorter time intervals, particularly within the first 6 hours after symptom onset, could have provided valuable additional information. However, the CCP coding mechanism is clinically relevant, given the changes in thrombolytic efficacy that have been documented after 6 and 12 hours of delay. Second, we used zip-code data to evaluate poverty, but not all residents of impoverished regions are actually poor. However, zip-code variables have been identified as useful surrogates in the absence of patient-level information. Third, as in all clinical studies, there are complex issues that complicated the coding of race, and the codes used may not adequately reflect the races of all subjects. Finally, in the setting of a large study population and an expansive pool of candidate predictor variables, some associations may be statistically significant but not clinically meaningful. However, analysis of all available clinical variables proved valuable, because it facilitated the identification of novel predictors of time to presentation, and it prevented the subjective exclusion of potentially important variables.

Study Implications
Despite these limitations, the present analysis reinforces the need to reduce the time to presentation among elderly patients with AMI. Recognizing this need, the National, Heart, Lung, and Blood Institute in 1991 launched the National Heart Attack Alert Program, a nationwide campaign that encourages physicians to discuss this issue directly with patients. A recent point of emphasis has been the targeting of patients at highest risk. Our findings suggest that target groups should include women, minorities, and the poor, as well as patients with diabetes mellitus or chronic angina.

Educational efforts should also include broad public campaigns, but effective media strategies have yet to be delineated. In Goteborg, Sweden, after the initiation of a combined radio, print, and billboard campaign, the mean time to presentation with AMI decreased by almost an hour, and average cardiac enzyme levels decreased by $\approx 40\%$. However, the benefits of media programs have yet to be demonstrated in the United States, and this issue is currently being investigated in the Rapid Early Action for Coronary Treatment (REACT) trial. Such research is sorely needed, inasmuch as the development of effective education strategies holds the potential to hasten time to presentation and substantially improve patient outcomes.

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