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Delays in thrombolytic therapy for acute myocardial infarction: Association with mode of transportation to the hospital, age, sex, and race

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Abstract:

BACKGROUND: Although increased myocardial salvage and reduced mortality are associated with timely thrombolytic therapy for acute myocardial infarction, some patients still experience delays in treatment. OBJECTIVES: To examine treatment times in patients with acute myocardial infarction treated with thrombolytic therapy and to determine whether delays in treatment are associated with mode of transportation to the hospital, age, sex, or race. METHODS: Medical records of 176 patients with acute myocardial infarction treated with thrombolytic therapy at a community hospital were reviewed and analyzed retrospectively. RESULTS: Median times for the interval between arrival at the hospital and acquisition of a diagnostic electrocardiogram (door-to-electrocardiography time) and the interval between arrival and start of thrombolytic therapy (door-to-drug time) were 6 minutes and 34 minutes, respectively. However, 76.1% of the patients met the recommendation of the American College of Cardiology/American Heart Association of door-to-electrocardiography time of 10 minutes, and 47.2% met the recommendation of door-to-drug time of 30 minutes or less. Door-to-drug times did not differ significantly according to race or mode of transportation to the hospital. Door-to-electrocardiography and electrocardiography-to-drug times were significantly longer for older patients than for younger patients ($P = .005$ and $P < .001$, respectively), and electrocardiography-to-drug times were significantly longer for females than for males ($P = .01$). CONCLUSIONS: With increased emphasis on recognition and rapid treatment of patients with acute myocardial infarction at highest risk for delays in treatment, that is, women and the elderly, benefits of thrombolytic therapy might be maximized.

Keywords: acute myocardial infarction | treatment delay | thrombolytic therapy

Article:

Patients with acute myocardial infarction should receive reperfusion therapy as soon as possible after the onset of signs and symptoms of the infarction. The Global Utilization of Streptokinase

and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) study[1] recommended that for maximum benefits, thrombolytic therapy should be started within 90 minutes of the onset of signs and symptoms. The Food and Drug Administration recommends that treatment with tissue plasminogen activator be started within 3 hours of the onset of signs and symptoms.[2] The American College of Cardiology/American Heart Association (ACC)/AHA) guidelines[3] recommend that thrombolytic therapy be started within 12 hours of the onset of signs and symptoms but emphasize that starting treatment within 6 hours is most beneficial. Shorter times between the onset of signs and symptoms and reperfusion are associated with benefits such as increased myocardial salvage and reduced mortality.[4-7] However, some patients with acute myocardial infarction still experience delays in treatment with thrombolytic agents.

In order to further study potential delays in treatment, treatment times are divided into intervals. A patient's response time, the symptom-to-door time, is the interval between the onset of signs and symptoms and arrival at the hospital. The door-to-drug time is the interval between arrival at the emergency department and the start of thrombolytic therapy. Because hospital personnel have no control over patients' symptom-to-door times, the goals of hospital staff have been to reduce the time between arrival and diagnostic electrocardiography (ECG), or door-to-ECG time, and the time between diagnostic ECG and the start of thrombolytic therapy, or ECG-to-drug time, in an effort to meet the ACC/AHA recommendations[8] of obtaining an ECG indicative of myocardial infarction within 10 minutes after a patient's arrival and of starting reperfusion therapy within 30 minutes after the arrival.

Newby et al[9] examined symptom-to-door and door-to-drug times in AMI patients receiving thrombolytic therapy in the GUSTO-1 trial. Symptom-to-door times were longer in females and the elderly than in other patients. Door-to-drug times were longer in the elderly, females, and nonwhite minorities than in other patients. Not surprising, more adverse outcomes were associated with delays in start of treatment. Reasons for the delays included the finding that the elderly and females were more likely than other patients to have atypical initial signs and symptoms.[9] Additionally, physicians' uncertainty about risks versus benefits when making the decision to treat elderly patients with thrombolytic therapy may have been greater.[9]

A similar study[10] done in Quebec found that although no delays occurred in obtaining ECGs for the elderly or for women, the delay between diagnostic ECG and the decision to administer thrombolytic treatment was significantly longer for women and the elderly. Median times from obtaining ECGs to making a decision were 17 minutes for women and 11 minutes for men; median door-to-drug times were 65 minutes and 57 minutes, respectively. Median door-to-drug times were 55 minutes for patients aged 65 years or less and 65 minutes for patients more than 65 years old.[10] Additional studies found similar delays in time between onset of signs and symptoms and start of treatment for women[11-14] and the elderly.[14,15]

Research is inconclusive as to whether symptom-to-door times and door-to-drug times are longer for African Americans than for whites. In a review of the literature, Lee[16] concluded that blacks generally had longer symptom-to-door times than did whites. Newby et al[9] found no significant differences between symptom-to-door times according to race; however, door-to-drug times were significantly longer for blacks and for other nonwhite minorities. Richards et al[17] reported that symptom-to-door times tended to be longer for African Americans than for whites, although

the difference was not statistically significant. Further research is needed to better understand if delays exist according to race and to determine the mechanisms of delays if delays exist.

The North Carolina Coronary Acute Response ECG Study (NC CARES) was organized in 1994 by Duke University Cooperative Cardiovascular Society to aid North Carolina hospitals in decreasing door-to-drug times. Sixteen medical centers located in eastern and central North Carolina participated in the study. The primary efforts were implementation of programs to reduce door-to-drug times, such as programs for patients with chest pain that involve obtaining ECGs before the patients arrive at the hospital or rapid recording of ECGs after the patients arrive.

In one NC CARES study, Griffin et al[11] found that start of thrombolytic therapy was delayed in the elderly, with a trend toward longer delays for women. These findings were preliminary, and replication with a larger sample size was needed to determine whether the start of thrombolytic therapy in AMI patients differs according to sex and age. The study reported here was designed to determine treatment times of AMI patients who received thrombolytic therapy at a community hospital and to determine if delays in treatment exist according to mode of transportation to the hospital, age, sex, or race. On the basis of the study by Griffin et al at the same community hospital, the following assumptions were made:

* The door-to-ECG times would meet ACC/AHA and GUSTO recommendations because of the rapid ECG protocol used at this community hospital.
* The door-to-ECG times would be longer for self-transported patients than for patients who arrived by ambulance.
* Delays in treatment would be longer for older patients and female patients than for other patients.

Methods

Setting

Alamance Regional Medical Center, a 238-bed regional medical center located in central North Carolina, was a participant in the NC CARES program. The primary focus of the emergency department staff at this community hospital is obtaining a standard 12-lead diagnostic ECG as rapidly as possible. Standing orders allow the nurses to obtain a standard 12-lead ECG as soon as patients are brought to the treatment area. Prehospital ECGs are not used at this facility. Prehospital communication by radio transmission alerts the emergency department staff of the pending arrival by ambulance of patients with suspected AMI. The rapid ECG protocol for this regional medical center is discussed in an earlier article.[11] The cardiology staff at this community hospital do not perform primary percutaneous transluminal coronary angioplasty.

Study Sample

Participants in this study were selected during a 40-month period: November 1994 to February 1998. All patients selected met all of the following study criteria: the patient's first ECG was diagnostic of AMI, the patient did not have prehospital ECG, and thrombolytic therapy was the

initial form of treatment. A total of 224 patients with a diagnosis of AMI were treated with thrombolytic therapy during the study period. Of these, 41 were excluded from the study because their first ECG was not diagnostic, and 7 were excluded because of missing or incomplete data. Thus, the final study sample had a total of 176 patients.

Data Collection

Retrospective chart analysis was done as part of a continuous quality improvement project for the emergency department of the hospital. Therefore, informed consent from individual patients was not needed. Data collection was made possible through the implementation of the second phase of the National Registry of Myocardial Infarction (NRMI-2), which began in June 1994. NRMI is an ongoing observational phase 4 study supported by Genentech, Inc, South San Francisco, Calif. The NRMI examines practice patterns and outcomes in patients who have AMI. NRMI has been previously described.[18] Dates and times of (1) the onset of signs and symptoms of AMI, (2) arrival at the hospital, (3) acquisition of first ECG, (4) acquisition of a diagnostic ECG, and (5) the start of drug therapy were obtained in accordance with the NRMI-2 guidelines.

Symptom-to-door times were calculated by subtracting the time of onset of signs and symptoms of AMI reported by the patient from the time of arrival at the hospital. Door-to-ECG times were calculated by subtracting the time of arrival at the hospital from the time of acquisition of a diagnostic ECG. ECG-to-drug times were calculated by subtracting the time of acquisition of a diagnostic ECG from the time of initiation of thrombolytic therapy. Door-to-drug times were calculated by adding door-to-ECG and ECG-to-drug times.

Statistical Analysis

Mean and median symptom-to-door, door-to-ECG, ECG-to-drug, and overall door-to-drug times were calculated according to the method of transportation to the emergency department, age, sex, and race. Medians with 25th and 75th percentiles were calculated for continuous baseline variables. Categoric variables are expressed as percentages. The nonparametric Wilcoxon rank sum test was used to examine differences in continuous variables. All statistical results are unadjusted for other covariates.

Results

Characteristics of the Sample

Baseline characteristics of the sample are given in Table 1. The sample was mostly male and mostly white, with a mean age of 61 years.

Symptom-to-Door Time

Figure 1 shows the distribution of symptom-to-door times for all 176 patients. The mean time was 228 minutes (3.8 hours); the median time was 97 minutes (1.6 hours). Times ranged from 15 minutes to 5033 minutes (83.9 hours). Approximately three quarters (76.1%) of the patients had a symptom-to-door time of 3 hours or less.

Table 1. Baseline characteristics

Characteristic	No. of patients	%
Mode of transportation*		
Ambulance	90	51.7
Private vehicle	84	48.3
Age, years†		
<70	126	72
≥70	49	28
Sex†		
Male	119	68
Female	56	32
Race†		
White	153	87.4
African American	22	12.6

*Based on N = 174; data could not be determined for 2 patients.
†Based on N = 175; data could not be determined for 1 patient.

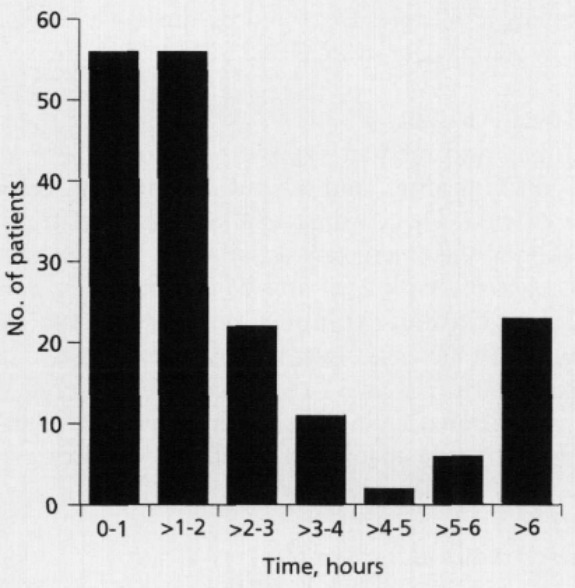

Figure 1. Time between onset of sign and symptoms of acute myocardial infarction and arrival at the hospital (symptom-to-door time; total number of patients = 176).

Door-to-ECG Time

Figure 2 shows the distribution of the door-to-ECG times, by 5-minute intervals, for all 176 patients. The mean door-to-ECG time was 7.53 minutes; the median time was 6 minutes. In 134 patients (76.1 %), a diagnostic ECG was obtained within 10 minutes of arrival at the hospital.

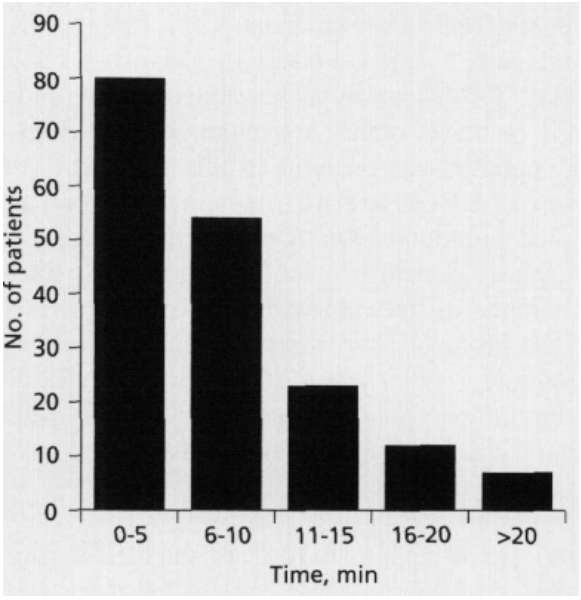

Figure 2. Time between arrival at the hospital and acquisition of a diagnostic electrocardiogram for patients with acute myocardial infarction (door-to-ECG time; total number of patients = 176).

ECG-to-Drug Time

Figure 3 shows the distribution of ECG-to-drug times, by 10-minute intervals, of all patients. The mean ECG-to-drug time was 33.2 minutes; the median time was 26 minutes.

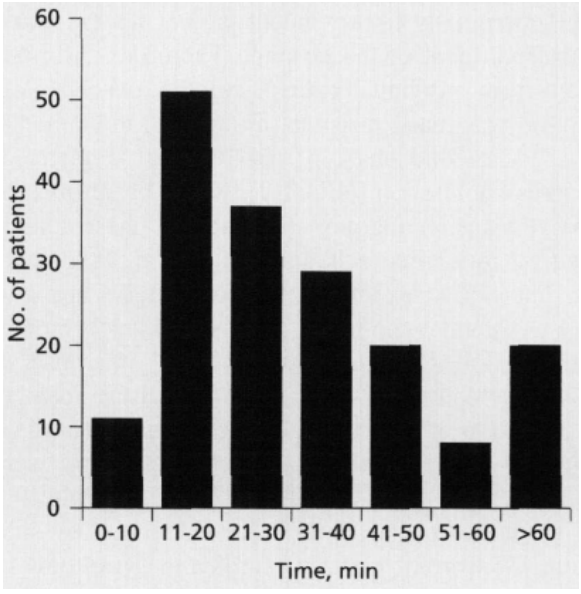

Figure 3. Time between acquisition of diagnostic electrocardiogram and start of thrombolytic therapy for patients with acute myocardial infarction (ECG-to-drug time; total number of patients = 176).

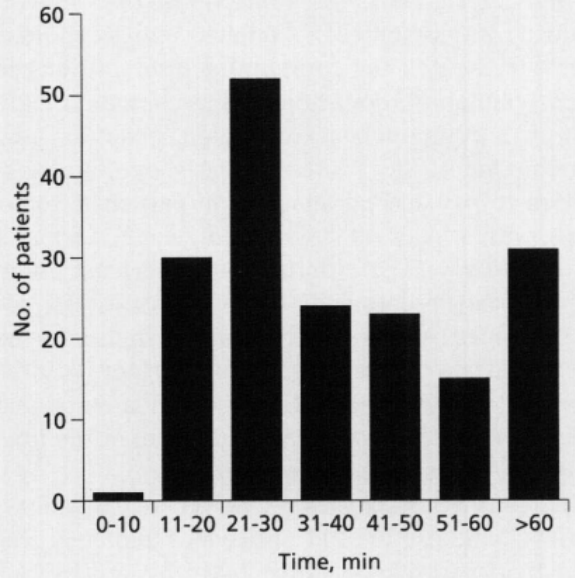

Figure 4. Time between arrival at the hospital and start of thrombolytic therapy for patients with acute myocardial infarction (door-to-drug time; total number of patients = 176).

Table 2. Time between arrival at the hospital and acquisition of a diagnostic electrocardiogram

Variable	No. of patients	Time, min: Median (25th, 75th quartiles)	Time, min: Mean	*P*
Mode of transportation*				
Ambulance	90	5 (2, 9)	7	.004
Private vehicle	84	8 (4, 11)	8	
Age, years†				
<70	126	5 (2, 10)	7	.005
≥70	49	8 (5, 12)	10	
Sex†				
Male	119	6 (2, 10)	7	.32
Female	56	7 (4, 10)	8	
Race†				
African American	22	5.5 (2, 10)	7	.48
White	153	7 (3, 10)	8	

*Based on N = 174; data could not be determined for 2 patients.
†Based on N = 175; data could not be determined for 1 patient.

Door-to-Drug Time

Figure 4 shows the distribution of the overall door-to-drug times for all patients. The times ranged from 10 minutes to 155 minutes (2.58 hours). The mean time was 40.74 minutes; the

median time was 34 minutes. Nearly half of the patients (47.2%) received thrombolytic therapy within 30 minutes or less after arrival at the hospital.

Comparison of Times According to Baseline Characteristics

Symptom-to-door times did not differ significantly according to mode of transportation to the emergency department, age, sex, or race.

The door to-ECG times according to baseline characteristics are given in Table 2. Door-to-ECG times did not differ significantly according to race or sex. However, differences between patients who arrived at the hospital by ambulance and patients who arrived via private vehicle were significant; median times were 5 minutes and 8 minutes, respectively. Also, patients less than 70 years old had significantly shorter door-to-ECG times than did patients 70 years or older; median times were 5 minutes and 8 minutes, respectively. Outliers were included in all calculations.

The ECG-to-drug times according to baseline characteristics are given in Table 3. ECG-to-drug times did not differ significantly according to mode of transportation to the hospital or race. However, ECG-to-drug times were significantly lower for patients less than 70 years old than for patients 70 years or older; median times were 24 minutes and 34 minutes, respectively. In addition, ECG-to-drug times differed significantly according to sex; females had longer times than did males.

Table 3. Time between acquisition of a diagnostic electrocardiogram and start of thrombolytic theory

Variable	No. of patients	Time, min: Median (25th, 75th quartiles)	Time, min: Mean	*P*
Mode of transportation*				
Ambulance	90	26 (18, 42)	34	.80
Private vehicle	84	28 (17, 42)	33	
Age, years†				
<70 years	126	24 (16, 36)	29	<.001
≥70 years	49	34 (22, 53)	43	
Sex†				
Male	119	23 (17, 37)	31	.01
Female	56	33 (22, 46)	38	
Race†				
African American	22	20 (26, 32)	29	.69
White	153	26 (18, 43)	34	

*Based on N = 174; data could not be determined for 2 patients.
†Based on N = 175; data could not be determined for 1 patient.

Overall door-to-drug times according to baseline characteristics are given in Table 4. Overall door-to-drug times did not differ significantly according to mode of transportation or race. Door-to-drug times did differ significantly according to sex; median times were 30 minutes for males and 42 minutes for females. Additionally, door-to-drug times differed significantly according to age; median times were 30 minutes for patients less than 70 years old and 45 minutes for patients 70 years or older.

Table 4. Time between arrival at the hospital and start of thrombolytic therapy

Variable	No. of patients	Time, min: Median (25th, 75th quartiles)	Time, min: Mean	*P*
Mode of transportation*				
Ambulance	90	30 (23, 49)	41	.62
Private vehicle	84	36 (25, 52)	41	
Age, years†				
<70	126	30 (23, 43)	36	<.001
≥70	49	45 (30, 67)	53	
Sex†				
Male	119	30 (23, 45)	38	.01
Female	56	42 (30, 57)	46	
Race†				
African American	22	30 (25, 42)	36	.46
White	153	35 (24, 55)	41	

*Based on N = 174; data could not be determined for 2 patients.
†Based on N = 175; data could not be determined for 1 patient.

Discussion

With a mean symptom-to-door time of 3.8 hours, some patients in the sample had already lost maximal benefit from thrombolytic therapy, exceeding both the GUSTO and the Food and Drug Administration recommendations that patients receive thrombolytic therapy within 90 minutes and 3 hours, respectively, of the onset of signs and symptoms of AMI. This area is one in which patients need to take more initiative. Several studies[9,10,14,15,19-21] found that the elderly and women are more likely to have longer symptom-to-door times, a situation that may compound delays in the start of thrombolytic therapy. Meischke et al[22] found that patients who were less educated or who felt more embarrassed about going to the emergency department were more likely than other patients to delay action for treatment of signs and symptoms. Interestingly, patients prompted by health professionals to go to the emergency department because of signs or symptoms of AMI were less likely than other patients to report an intention to delay seeking treatment if similar signs or symptoms occurred in the future.[22]

Perhaps awareness programs designed to teach the signs and symptoms of AMI and stress the importance of going to the hospital as soon as possible after the onset of signs or symptoms suggestive of AMI should be implemented.[23-25] Alonzo and Reynolds" suggest strategies for community interventions to reduce symptom-to-door time that are based on regulation of 3 components: knowledge, behavior, and emotion. One of the 7 interventions they describe is the need to pay special attention to particular social groups, with a focus on the different needs of females and the elderly. The elderly know the least about coronary heart disease and are at the greatest risk for poor outcomes. Alonzo and Reynolds also discuss the need to educate the public to recognize not only the signs and symptoms of AMI, but also the emotional sequelae that often distort clear judgment at the time of onset of such signs and symptoms.

In addition, as per ACC/AHA recommendations, patients should use the 911 ambulance and emergency medical services system. As indicated by our study, use of emergency medical services for transport to the hospital helps lower door-to-ECG times. Although not demonstrated in our study, with the shorter door-to-ECG times, overall door-to-drug times might decrease if patients with signs and symptoms of AMI were transported by ambulance.

Overall, Alamance Regional Medical Center is efficient in rapidly obtaining ECGs for patients with suspected AMI. For 76.1% of all patients, ECGs were obtained within 10 minutes of arrival at the hospital, thus meeting ACC/AHA recommendations. However, patients transported by private vehicle had longer door-to-ECG times than did patients transported by ambulance. One reason for this time difference may be the fact that the emergency department receives information from paramedics to prepare for incoming patients with suspected AMI. This practice may be the reason differences in ECG-to-drug times and overall door-to-drug times did not differ significantly according to mode of transportation.

Overall door-to-drug times did not differ significantly according to race. The relatively small number of African Americans in the study sample may account for the lack of racial differences. Our results differ from those of Newby et al.[9] Further research is needed to determine whether race influences treatment times for AMI patients.

Our results indicate that compared with males, females have delays in treatment, in particular, longer ECG-to-drug times. This finding is consistent with the results of previous studies.[9-13] Compared with men, women may have different initial signs and symptoms, have different precipitating causes of chest pain, and are more likely to be older when signs and symptoms of coronary artery disease occur.[19] In addition, men may "appear" more ill when they arrive at the emergency department, or a perception may exist that men have more risk factors for AMI or an increased prevalence of coronary artery disease.[12] Arslanian-Engoren[27] reported that when making triage decisions, emergency department nurses had different perceptions based on sex and age about the significance and likelihood of AMI. The nurses associated older male patients with cardiac causes requiring more medical attention. These reasons may be why providers may treat women less aggressively.[27] More research is needed to investigate why women have delays in the start of thrombolytic therapy, even after a diagnostic ECG has been obtained.

Older patients had significantly longer door-to-- ECG and ECG-to-drug times than younger patients did. Not surprising, the elderly also had longer overall door-to-drug times. These

findings are consistent with those of previous studies.[9,10] In the study by Griffin et al,[11] also done at Alamance Regional Medical Center, median door-to-ECG times were 8 minutes for patients 70 years or older and 2.5 minutes for patients less than 70 years old, and median door-to-drug times were 49 minutes and 30 minutes, respectively.

Perhaps older patients, without the help of friends or family members, cannot articulate their signs and symptoms to the emergency department staff as well as younger patients can. Older patients more often have atypical signs and symptoms that may mask the correct diagnosis.[28] The signs or symptoms may be vague or poorly localized. Patients may have dyspnea, diaphoresis, syncope, confusion, altered mental status, weakness, fatigue, or restlessness.[28] The additional time required to obtain a history, move the patient to the treatment area, and prepare the patient for ECG might account for longer door-to-ECG times for older patients. Because older patients have more relative contraindications to treatment with thrombolytics and more comorbid conditions than younger patients do, additional delay may occur in determining the suitability of thrombolytic therapy. However, outcomes in older patients can be markedly improved by decreasing time to treatment.[9]

Study Limitations

Nonsignificant results in subgroup analyses may not indicate lack of differences, but instead may indicate lack of power. Point estimates are less stable with smaller sample sizes. A larger sample size would provide more confidence in the reliability of our results. Without a sufficiently powered, controlled, randomized study, factors such as mode of transportation to the emergency department, age, sex, and race cannot be cited as factors influencing treatment times. Although the differences in door-to-ECG and ECG-to-drug times may be associated with the variables examined, other variables associated with particular subgroups may have influenced these times.

The low door-to-ECG times in our study may not be attainable in all hospitals. Alamance Regional Medical Center uses a single thrombolytic agent as the standard care for reperfusion in patients with AMI. Differences in door-to-drug times may vary for hospitals that use more than one thrombolytic agent or have primary percutaneous transluminal coronary angioplasty available as a choice for reperfusion.

We did not determine the accuracy of the medical center in the diagnosis of AMI. A future study would be required to determine whether sacrifices in accuracy occurred as a result of efforts to treat patients rapidly. Examining the ECGs of patients who did not have a diagnosis of AMI made in the emergency department would reveal whether such inaccuracies in diagnosis occurred.

Conclusion

Our results provide insights into factors associated with delays in treatment of patients with suspected AMI at one community hospital. Interventions must be aimed at ensuring that all patients, especially those at high risk for long delays, such as the elderly and women, receive timely evaluation and treatment. Healthcare providers should be more aware of the association between delays in treatment and the age and sex of a patient. In addition, community

intervention may help facilitate shorter symptom-to-door times for all patients and thus maximize the benefits of thrombolytic therapy.

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