

ORIGINAL RESEARCH & CONTRIBUTIONS

Factors Contributing to Door-to-Balloon Times of ≤ 90 Minutes in 97% of Patients with ST-Elevation Myocardial Infarction: Our One-Year Experience with a Heart Alert Protocol

Joel T Levis, MD, PhD, FACEP, FAAEM
Mary P Mercer, MD
Mark Thanassi, MD
James Lin, MD

Abstract

Context: Prompt percutaneous coronary intervention (PCI) for patients with ST-segment elevation myocardial infarction (STEMI) can significantly reduce mortality and morbidity, although its effectiveness may be limited by delays in delivery. In March 2008, our hospital implemented a Heart Alert protocol to rapidly identify and treat patients with STEMI presenting to our Emergency Department (ED) with PCI, using strategies previously described to reduce door-to-balloon times. Before the Heart Alert protocol start date, patients with STEMI presenting to our ED were treated with thrombolysis.

Objective: We evaluated data from patients with STEMI after one year of use of our Heart Alert protocol to determine protocol success on the basis of the percentage of patients for whom the recommended door-to-balloon times of ≤ 90 minutes were met. We examined factors involved in implementation of the protocol that contributed to these results.

Design: We conducted a retrospective data and chart review for patients in the ED with STEMI who underwent PCI after a Heart Alert protocol activation between March 17, 2008, and March 17, 2009.

Results: During the study period, our staff met the recommended door-to-balloon time of ≤ 90 minutes (mean door-to-balloon time, 57.3 ± 17.6 minutes) for 70 of 72 patients (97%) presenting to our ED with STEMI. Sixty-five of the 72 patients (90.3%) survived to hospital discharge.

Conclusion: Initiation of a Heart Alert protocol at our hospital resulted in achievement of door-to-balloon times of ≤ 90 minutes for 97% of patients with STEMI. This achievement was obtained through careful preparation, training, and interdepartmental collaboration and occurred despite immediate conversion from a previous thrombolytic protocol.

Introduction

Prompt percutaneous coronary intervention (PCI) for patients with ST-segment elevation myocardial infarction (STEMI) can significantly reduce mortality and morbidity; however, its effectiveness may be limited by delays in delivery.¹⁻³ Door-to-balloon time refers to the interval from arrival of the patient with STEMI at the Emergency Department (ED) to balloon angioplasty of the occluded coronary artery in the cardiac catheterization laboratory (CCL). Guidelines from the American College of Cardiology/American Heart Association and the European Society of Cardiology recommend a goal of ≤ 90 minutes for door-to-balloon time; this measure is incorporated into national, publicly reported quality indicators for hospital performance.⁴⁻⁶ The Centers for Medicare and Medicaid Services and the Joint Commission consider the ≤ 90 minute door-to-balloon time a benchmark goal, and facilities must track this as a core measure.^{7,8}

Strategies associated with shorter door-to-balloon times have been identified and include Emergency Medicine (EM) physician activation of the CCL through a single call to a central page operator while the patient is en route to the hospital, arrival of staff in the CCL within 20 minutes of activation, constant presence of an attending cardiologist on-site, real-time case feedback, and interdisciplinary collaboration throughout the process.⁹⁻¹¹ The D2B Alliance was developed by the American College of Cardiology to improve door-to-balloon times for patients with STEMI undergoing PCI, and it has enrolled approximately 1000 hospitals.¹² The D2B Alliance strategies include 1) EM physician activation of the CCL with a single call, 2) preparation

Joel T Levis, MD, PhD, FACEP, FAAEM, is a Senior Emergency Physician at the Santa Clara Medical Center. He is a Clinical Instructor of Emergency Medicine (Surgery) at Stanford University, and the Medical Director for the Foothill College Paramedic Program in CA. E-mail: joel.levis@kp.org.

Mary P Mercer, MD, is an Emergency Medical Services & Disaster Management Fellow, University of California San Francisco-San Francisco General Hospital Department of Emergency Medicine, San Francisco, CA, and graduate of the Stanford/Kaiser Emergency Medicine Residency Program. E-mail: mary.mercer@ucsf.edu.

Mark Thanassi, MD, is a Senior Emergency Physician and Emergency Department Quality Chair at the Santa Clara Medical Center in CA. E-mail: mark.thanassi@kp.org.

James Lin, MD, is a Senior Emergency Physician, Chief of Emergency Medicine, and an Assistant Physician in Chief at the Santa Clara Medical Center in CA. E-mail: james.lin@kp.org.

of the CCL team within 20 to 30 minutes of the call, 3) real-time case feedback, 4) a team-based approach, and 5) administrative support. The use of prehospital electrocardiograms (ECG) by emergency medical services (EMS) personnel to activate the CCL is an optional strategy. Hospitals have implemented several of these strategies in attempts to improve door-to-balloon times, with varying levels of success.¹³⁻¹⁶

In March 2008, our hospital initiated a Heart Alert protocol involving close collaboration between the Departments of EM, Cardiology, and Interventional Cardiology to efficiently identify and treat patients with STEMI presenting to our ED. Our protocol includes several of the key strategies to reduce door-to-balloon times and was preceded by careful training of both EM physicians, cardiology physicians, and staff before implementation. A unique feature of our protocol was the implementation of PCI for STEMI at the start of the Heart Alert protocol; before initiation of the Heart Alert protocol, all patients presenting with STEMI were treated using a thrombolytic protocol. Despite this, review of our first-year data indicates that we achieved door-to-balloon times of ≤ 90 minutes in 97% of patients with STEMI (70 of 72). This report describes the development, implementation, and key strategies of our system, as well as specific data resulting in the achievement of door-to-balloon times of ≤ 90 minutes. This report should benefit hospitals preparing to implement primary PCI for patients with STEMI, as well as those struggling to achieve target door-to-balloon times.

Methods

Development and Implementation of the Heart Alert System

The Santa Clara Medical Center is a suburban teaching hospital located in Santa Clara, CA, sponsoring a joint residency program in EM with Stanford University (Stanford/Kaiser EM Residency Program) and its own residencies in internal medicine, obstetrics-gynecology, and podiatry. Our hospital also hosts Stanford surgery and pediatrics residents, as well as Stanford University and visiting medical students. The hospital has 327 inpatient beds, a 46-bed ED with approximately 60,000 annual patient visits, and three cardiac catheterization laboratories and on-site cardiothoracic surgery. An average of 2260 diagnostic coronary angiograms and 1243 PCIs are performed each year. Our facility has six interventional cardiologists, each performing an average of 220 coronary catheterizations each year. Door-to-balloon times are reported to the American

College of Cardiology National Cardiovascular Data Registry, to the Joint Commission, and to the Santa Clara County EMS Agency.

In developing the Heart Alert protocol, an interdisciplinary group of cardiologists, EM physicians, nurses, and administrators convened to outline the actions and procedures necessary for achieving door-to-balloon times of ≤ 90 minutes. Strategies previously demonstrated to reduce door-to-balloon time were incorporated into our protocol, including EM physicians activating the CCL through a single call, arrival of staff in the CCL within 20 minutes after activation, real-time case feedback, and substantial interdisciplinary collaboration throughout the process. Attending cardiologists were available on-site during daytime hours and were available by page to arrive in the ED within 20 minutes of a Heart Alert activation during all other hours. Heart Alert activation by the EM physician

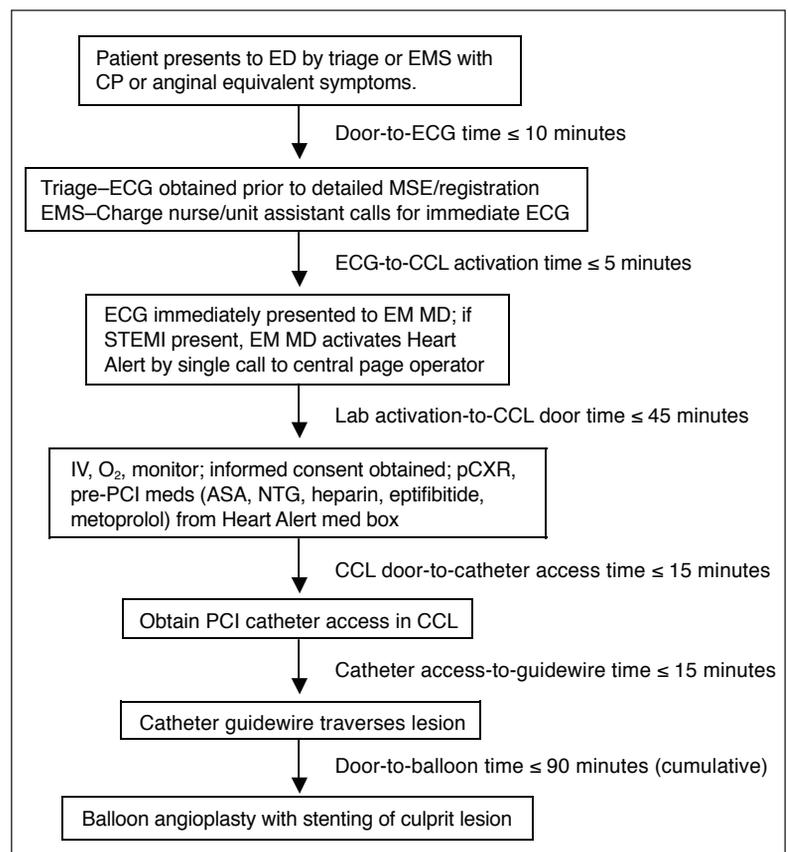


Figure 1. Steps involved in the Heart Alert protocol for achieving door-to-balloon times of ≤ 90 minutes in 97% of patients during the first year of protocol institution.

ASA = aspirin; CCL = cardiac catheterization laboratory; CP = chest pain; ECG = electrocardiogram; ED = emergency department; EM = emergency medicine; EMS = emergency medical services; MD = physician; MSE = medical screening examination; NTG = nitroglycerin; PCI = percutaneous coronary intervention; pCXR = portable chest radiograph; STEMI = ST-segment elevation myocardial infarction.

while a STEMI patient was en route to the hospital (on the basis of a prehospital ECG report) was encouraged but not mandated. Emergency medical services did not have the ability to transmit prehospital ECGs to our facility during this period.

The door-to-balloon time was broken down into the following clinically relevant intervals: door-to-ECG time (goal, ≤ 10 minutes), ECG-to-CCL activation time (goal, ≤ 5 minutes), CCL activation-to-CCL door time (goal, ≤ 45 minutes), CCL door-to-catheter access time (goal, ≤ 15 minutes), catheter access-to-guidewire time (goal, ≤ 15 minutes), for a door-to-balloon time goal of ≤ 90 minutes. Criteria for identification of STEMI on 12-lead ECGs included ST-segment elevation ≥ 1 mm (0.1 mV) in at least two anatomically oriented (contiguous) precordial or limb leads and new or presumably new left bundle branch

block with a strong clinical suspicion of acute myocardial infarction. Order sets were created to streamline ordering of tests, procedures, and medication administration in the ED after CCL activation. For rapid procurement and administration of medications (eg, aspirin, nitroglycerin, heparin, eptifibatide, metoprolol), a Heart Alert medication box was developed that would be immediately available in the event of a Heart

Alert activation. Figure 1 outlines the steps involved at each time interval of the Heart Alert protocol.

Our hospital began a number of educational initiatives in advance of initiation of the Heart Alert protocol. The interventional cardiologists presented a STEMI lecture series to the EM physicians and staff. Interdisciplinary Critical Event Team Training sessions were conducted with mock activation of the Heart Alert protocol, allowing staff in both the ED and the CCL to familiarize themselves with the protocol procedures and identify any improvement opportunities. Finally, results of each Heart Alert case (including STEMI ECG image, interval times, catheterization results, and patient outcomes void of patient identifiers) were provided to all EM physicians, residents, and staff via e-mail within one week of each case.

Data Collection and Analysis

The Kaiser Permanente Northern California Institutional Review Board approved our retrospective chart review and data analysis. We performed a chart review of all Heart Alert cases presenting to our ED that received emergency PCI (angioplasty and stent placement) during the first 12 months of the Heart Alert protocol (March 17, 2008, to March 17, 2009). A total of 72 cases met these criteria during the study

period. The following data were collected for each patient from electronic medical records: patient age, sex, race, presence and number of cardiac risk factors; history of coronary artery disease, previous PCI, or coronary artery bypass graft; mode of presentation (triage vs EMS); time from symptom onset to ED arrival; initial troponin I level; PCI results; and survival to hospital discharge. Data were then analyzed using the software program EpiInfo (Centers for Disease Control and Prevention, Atlanta, GA, USA) for statistical analysis.

Twelve percent of patients had no known cardiac risk factors ...

Table 1. Patient characteristics for STEMI Heart Alert cases (total 72 cases)

Characteristic	Value
Sex (number and % male)	56 (77.8)
Age (mean \pm SD)	61.3 \pm 13.5 years
Race	Number (%)
African American	2 (2.8)
Asian	14 (19.4)
Caucasian	50 (69.4)
Hispanic	3 (4.2)
Other	3 (4.2)
Cardiac risk factors	
Hypertension	42 (58.3)
Hyperlipidemia	32 (44.4)
Diabetes	15 (20.8)
Tobacco	14 (19.4)
Family history of CAD	13 (18.1)
No known risk factors	9 (12.5)
Personal history of CAD	23 (31.9)
Previous history of PCI	17 (23.6)
Previous history of CABG	3 (4.2)

CABG = coronary artery bypass graft; CAD = coronary artery disease; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Results

Patient characteristics for the 72 Heart Alert cases are shown in Table 1. Approximately 75% of the patients were men, with an average age of 61 years. The majority of patients (70%) were Caucasian, with a smaller percentage of Asian, Hispanic, and African-American patients. The most prevalent cardiac risk factor was hypertension (58%), followed by hyperlipidemia (44%), diabetes (21%), tobacco use (19%), and family history of CAD (18%). Twelve percent of patients had no known cardiac risk factors, 25% had undergone previous PCI, and 4% had a history of CABG. Sixty-five of the 72 patients (90.3%) in the cohort survived to hospital discharge. Six men and 1 woman comprised the 7 patients not surviving

to discharge, with a mean age of 70.9 ± 17.5 years (range, 40–88 years). The causes of death in these 7 patients were cardiogenic shock ($n = 5$), anoxic brain injury after cardiac arrest ($n = 1$), and severe sepsis ($n = 1$).

Table 2 shows the mean, standard deviation, median, and range for each interval period comprising the door-to-balloon times for the 72 patients with STEMI. The mean door-to-ECG time was 3.3 ± 10.8 minutes (range, –50 to 28 minutes). The mean ECG-to-CCL activation time was 7.5 ± 8.8 minutes, whereas the mean CCL activation-to-CCL door time was 27.2 ± 11.4 minutes. The mean door-to-balloon time for the 72 patients was 57.3 ± 17.6 minutes. The times for 2 patients fell outside of the 90-minute door-to-balloon goal of ≤ 90 minutes: 94 and 106 minutes.

Table 3 lists ED arrival mode (EMS vs triage), time from symptom onset to ED arrival, and initial troponin I level. Nearly three-quarters of the patients arrived by personal transportation. Analysis of time from symptom onset to ED arrival indicated that 35% of patients arrived to the ED within one hour of symptom onset; 28% arrived between two and six hours, and 7% arrived >12 hours after symptom onset. The mean for the initial troponin I level was 1.02 ± 2.86 ng/mL, with a median of 0.05 ng/mL and a range of <0.02 to 14.92 ng/mL, with 58% of the measurements within the range of 0.00 to 0.09 ng/mL.

Table 4 demonstrates the distribution of coronary arteries (culprit lesions) involved in the 72 STEMI. The most common lesion involved the left anterior descending coronary artery (42%), followed by the right coronary artery (39%); one patient was found to have a left main coronary artery occlusion.

Discussion

Primary PCI has become the preferred treatment option for patients presenting with STEMI because it has helped achieve higher rates of TIMI (thrombolysis in myocardial infarction) grade 3 flow than thrombolysis has.^{17,18} Primary PCI has also been shown to be superior to thrombolysis in reducing rates of mortality, reinfarction, and stroke.^{19,20} This benefit appears to be related to a much higher early mechanical reperfusion rate compared with thrombolysis, to the ability of simultaneously treating the underlying stenosis, and to the lower risk of severe bleeding.²¹ In March 2008, our hospital converted from a thrombolysis protocol to a PCI protocol for treating patients presenting to our ED with STEMI.

After development of a Heart Alert protocol, we

were able to achieve door-to-balloon times of ≤ 90 minutes in 97% of our patients with STEMI during the first year of implementation. The success of the Heart Alert protocol is predicated on its development on the basis of previous proven strategies,^{9–11} including published, continuous quality-improvement

Table 2. Mean time intervals (minutes) for STEMI Heart Alert cases (total of 72 cases)

Interval	Mean \pm SD	Median	Range
Door-to-ECG time	3.3 ± 10.8	2.0	–50.0 to 28
ECG-to-CCL activation time	7.5 ± 8.8	5.0	–12.0 to 42.0
CCL activation-to-CCL door time	27.2 ± 11.4	23.5	6.0 to 61.0
CCL door-to-access time	9.0 ± 3.7	8.5	3.0 to 24.0
Access-to-guidewire time	10.6 ± 6.2	9.0	1.0 to 34.0
Door-to-balloon time	57.3 ± 17.6	56.5	30.0 to 106.0

CCL = cardiac catheterization laboratory; ECG = electrocardiogram; SD = standard deviation; STEMI = ST-segment elevation myocardial infarction.

Table 3. Mode of ED arrival, time from symptom onset to ED arrival, and initial troponin I levels for STEMI Heart Alert cases (total of 72)

Aspect	Value
Mode of ED arrival	
Ambulance (EMS)	20 (27.8%)
Personal transportation	52 (72.2%)
Time from symptom onset to ED arrival	
≤ 1 hour	25 (35.2%)
1–2 hours	14 (19.7%)
2–6 hours	20 (28.2%)
6–12 hours	7 (9.9%)
>12 hours	5 (7.0%)
Unknown	1 (1.4%)
Initial troponin I level	
Mean \pm SD	1.02 ± 2.86 ng/mL
Median	0.05 ng/mL
Range	<0.02–14.92 ng/mL

ED = emergency department; EMS = emergency medical services; SD = standard deviation; STEMI = ST-segment elevation myocardial infarction.

Table 4. Coronary artery (culprit lesion) involved in STEMI for Heart Alert cases (total of 72 cases)

Coronary artery involved	Number (%)
Left main	1 (1.4)
LAD	30 (41.7)
RCA	28 (38.9)
LCx	6 (8.3)
Diagonal branch of LAD	2 (2.8)
Obtuse marginal branch of LCx	1 (1.4)
Posterior descending artery	4 (5.6)

LAD = left anterior descending; LCx = left circumflex artery; RCA = right coronary artery; STEMI = ST-segment elevation myocardial infarction.

analyses resulting in expedited PCI for patients with STEMI.²²⁻²⁴ Several factors contributed to the success of our protocol, including

- Organization of an interdisciplinary working group of cardiologists, EM physicians, nurses, and administrators whose chief role was to develop and outline the training and protocol implementation.
- Educational and training activities for staff and physicians before protocol implementation, including STEMI lectures and critical-event team training involving mock Heart Alert simulations.
- Breakdown of the door-to-balloon time into clinically relevant intervals, with continued quality analysis of these intervals to look for areas of improvement.
- Continuous feedback on all Heart Alert cases to all EM physicians and residents, using a Heart Alert case series provided by e-mail within one week of each case. A survey of EM physicians 20 months after implementation of this series indicated that most EM physicians reviewed the Heart Alert cases and found them useful as an educational tool.

Several strategies implemented at each door-to-balloon interval in our protocol have contributed to the ability to obtain door-to-balloon times of ≤ 90 minutes in such a large proportion of patients with STEMI (Figure 1). When patients present to our ED triage with chest discomfort or angina-equivalent symptoms, a 12-lead ECG is obtained immediately before a detailed medical screening examination and patient registration, enabling rapid ECG acquisition. For similar patients presenting to the ED by EMS, an ECG is immediately requested by the charge nurse or unit assistant as the patient is being roomed (before physician assignment), again reducing any potential delays in ECG acquisition. Once obtained, the ECG must be presented to an EM physician as soon as possible for early detection and recognition of STEMI. When STEMI is diagnosed, the EM physician activates a Heart Alert through a single call to a central page operator, requiring the CCL team to be prepared for emergency PCI within 20 minutes of the page. Use of a Heart Alert medication box during the laboratory activation-to-CCL door interval contributes significantly to reducing this time interval, allowing nurses to quickly obtain a single medication box containing all of the necessary pre-PCI medications rather than needing to remove each medication piecemeal from the automated medication-dispensing system.

The number of STEMI cases in our first year of the protocol (72) is similar to those reported for other large hospitals with high-volume PCI capabilities.^{14,15}

The majority of patients with STEMI in our study were men (78%; Table 1) with an average age of 61.3 years, similar to the sex and age distribution for patients with STEMI found in a large retrospective review of the National Registry of Myocardial Infarction (NRMI) for 2006.²⁵ The racial and ethnic breakdown as well as the presence and distribution of documented cardiac risk factors for our patients with STEMI were similar to results found for patients with STEMI in the NRMI data review. The percentage of our patients who had previously undergone PCI was slightly higher than that noted in the 2006 NRMI registry (23.6% vs 15.5%), whereas the percentage of patients with previous CABG in both studies was low (4.2% vs 7.9%).

Evaluation of the interval times for our protocol indicated that the mean door-to-ECG time for all patients with STEMI was 3.3 ± 10.8 minutes, with a median of 2.0 minutes and a range of -50.0 to +28.0 minutes (Table 2). Door-to-ECG times for 85% of patients were ≤ 10 minutes. In one patient, STEMI was diagnosed by ECG in a clinic (door-to-ECG time, -50 minutes) before ED transport. After omitting this time from the data analysis, the mean door-to-ECG time for the remaining 71 patients was 4.1 ± 8.7 minutes. Phelan et al identified two main causes of door-to-ECG times >10 minutes in a study to assess and find ways to decrease door-to-ECG times in their ED: 1) priority delay (eg, completing triage and registration data entry before obtaining ECGs) and 2) failure to recognize patients with non-chest-pain STEMI.²⁶ Before our protocol implementation, all ED staff were educated about the importance of obtaining ECGs for all patients presenting with chest pain or symptoms suggestive of ischemia without further delay, as well as about how to recognize potential non-chest-pain acute coronary syndrome symptoms. Once obtained, ECGs are immediately presented to an EM physician for rapid review.

Use of prehospital ECGs for STEMI activation before patient arrival can improve door-to-balloon times.²⁷⁻³⁰ This practice is noted as an optional strategy by the D2B Alliance. In the first year of our protocol, approximately 28% of patients with STEMI arrived to the ED by ambulance (Table 3), and half of those patients had Heart Alert activations that were based on prehospital ECG reports. All door-to-balloon times for the 10 STEMI cases in which an alert was activated before arrival fell below 50 minutes (36.5 ± 5.7 minutes; median, 35 minutes; range, 30-49 minutes). Transmission of prehospital ECGs for rapid triage of patients with STEMI has also been shown to reduce door-to-balloon times and can improve early survival of these patients.^{27,31}

Our county is currently developing a prehospital ECG transmission system to better improve the sensitivity and specificity of this application.

EM physician activation of the CCL team decreases door-to-balloon times.³²⁻³⁴ Mean ECG-to-CCL activation time during our study period (7.5 ± 8.8 minutes) exceeded the recommended goal of ≤ 5 minutes, with a total of 31 of 72 cases exceeding this goal. One case demonstrated an ECG-to-CCL activation time of 42 minutes. Review of that case indicated that the chief complaint was epigastric pain, and the door-to-ECG time for the same case was 0 minutes. It is likely that the symptoms were not recognized as potentially cardiac, possibly leading to delays in ECG presentation to and review by the EM physician. Evaluation of ambiguous ECGs may also result in delay of CCL activation (eg, ECGs obtained early in the evolution of a STEMI). Continued case feedback using the Heart Alert case series, as well as ability of EM physicians to fax ambiguous ECGs to the on-call cardiologist 24 hours/day should aid in further reduction of this time interval in our protocol.

The largest component of door-to-balloon time is typically the time spent within the ED before transfer to the CCL.¹⁴ Our mean CCL activation-to-CCL door time fell well within our recommended interval (27.2 ± 11.4 minutes; median, 23.5 minutes; recommended goal, ≤ 45 minutes; Table 2). Only 5 cases (7%) fell outside of the recommended interval. Careful preparation and training of the ED staff, well-designed and preprinted STEMI order sets, use of a Heart Alert medication box for pre-PCI medications, and careful coordination among EM physicians, interventional cardiologists, and ancillary staff contributed to the efficiency of patient preparation prior to CCL transfer. Use of an electronic STEMI order set implemented after the first year of the Heart Alert protocol should further improve the efficiency of this process.

Time from symptom onset to ED arrival is listed in Table 3. The percentage of patients presenting within the first hour of symptom onset in our study (35.2%) is nearly identical to that found in a similar study involving an identical number of patients (36%, Code STEMI study).¹⁴ In our study period, a smaller percentage of patients presented between 1 and 2 hours of symptom onset (19.7%), whereas more presented in the range of 2 to 6 hours (28.2%). The lowest proportion of patients with STEMI in our study period presented in the range of 6 to 12 hours (9.9%) and after >12 hours (7%) range, findings similar to the Code STEMI study.¹⁴ In the US, median delay time from symptom onset to hospital ar-

rival ranges from 1.5 to 6.0 hours.³⁵ Numerous factors, including old age, female sex, low education level, low socioeconomic status, race and ethnic differences, and presence of chronic health conditions and high-risk behaviors, have been associated with additional delays in patients seeking treatment for ACS.³⁵

Approximately 58% of the initial troponin I results for patients with STEMI fell within the normal range of 0.00 to 0.09 ng/mL. Because troponin I levels rise within 4 to 6 hours of myocardial injury, these results indicate that the majority of our patients with STEMI presented to the ED relatively early in the disease process. Although initial troponin I levels are less useful in diagnosing STEMI (compared with non-STEMI and unstable angina), baseline troponin levels have been shown to be independent predictors of 30-day cardiovascular death in patients with STEMI.³⁶ The most common coronary artery involved in STEMI in our patients was the left anterior descending (41.7%), followed closely by the right coronary artery (38.9%) and the left circumflex coronary artery (8.3%) (Table 4). This distribution of coronary artery involvement is similar to that found in the Code STEMI study cited earlier, in which the right coronary artery (31%), left anterior descending (27%), and left circumflex (14%) were most commonly involved.¹⁴

Sixty-five of the 72 patients (90.3%) in our study cohort survived to hospital discharge. The all-cause in-hospital mortality rate for our cohort (9.7%) was higher than rates reported after implementation of two similar STEMI protocols (4.2% and 4.7%, respectively).^{14,37} This discrepancy may be due, in part, to the severity of illness in the nonsurvivors in our cohort. Five of 7 patients not surviving to discharge died from cardiogenic shock, 1 after out-of-hospital cardiac arrest and 1 after development of severe sepsis, all conditions associated with significantly higher in-hospital mortality rates.³⁸⁻⁴⁰ Further data acquisition and analysis over a longer time period will be required to determine a true survival benefit from our Heart Alert protocol.

Initiation of a Heart Alert protocol at our hospital has resulted in excellent door-to-balloon times during our first year of implementation, with the achievement of door-to-balloon times ≤ 90 minutes in 97% of patients with STEMI. This achievement was made possible by careful preparation, training, and interdepartmental collaboration and occurred despite immediate conversion from a previous thrombolytic protocol. A similar disciplined system can be readily implemented in hospitals

The largest component of door-to-balloon time is typically the time spent within the ED before transfer to the CCL.

that are considering developing PCI capability or by those in need of improvement of door-to-balloon times, using techniques described in this report. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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The Chief

Of all the ailments which may blow out life's little candle,
heart disease is the chief.

—William Boyd, 1885-1979, Scottish-Canadian pathologist and academic