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Complete List of Authors:	Park , Yoo Seok ; Yonsei University College of Medicine Chung, Sung Phil; Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, Korea YOU, JE SUNG; Emergency Medicine Kim, Min Joung; Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, Korea, Chung, Hyun Soo; Yonsei University College of Medicine, Emergency Medicine Hong, Jung Hwa; Yonsei University College of Medicine, Department of Research Affairs, Biostatistics Collaboration Unit Lee, Hye Sun; Yonsei University College of Medicine, Biostatistics Wang, Jinwon ; Yonsei University College of Medicine, Department of Emergency Medicine park, Incheol; Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, Korea, Emergency medicine

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A multidisciplinary critical pathway based on a computerized physician order entry system for ST-elevation myocardial infarction management attenuates off-hour and weekend effects in the emergency department

Yoo Seok Park MD, PhD [1], Sung Phil Chung, MD, PhD [1], Je Sung You, MD [1*], Min Joung Kim, MD, PhD [1], Hyun Soo Chung MD, PhD [1], Jung Hwa Hong, MS [2], Hye Sun Lee, MS [2], Jinwon Wang, MD [1], Incheol Park MD, PhD [1]

1. Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

2. Department of Research Affairs, Biostatistics Collaboration Unit, Yonsei University College of Medicine, Seoul, Republic of Korea

Corresponding author

Je Sung You, MD

Department of Emergency Medicine, Yonsei University College of Medicine

211 Eonju-Ro, Gangnam-Gu, Seoul 135-720, Republic of Korea

Tel: 82-2-2019-3030, Fax: 82-2-2019-4820

E-mail: 751117@daum.net (JSY)

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A multidisciplinary critical pathway based on a computerized physician order entry system for ST-elevation myocardial infarction management attenuates off-hour and weekend effects in the emergency department

ABSTRACT

Objectives: The purpose of this study was to investigate whether a multidisciplinary organized critical pathway (CP) for ST-elevation myocardial infarction (STEMI) management can significantly attenuate differences in the duration from emergency department (ED) arrival to evaluation and treatment, regardless of arrival time, by eliminating off-hour and weekend effects.

Design: Retrospective observational cohort study

Setting: Two tertiary academic hospitals

Participants: Consecutive patients in the Fast Interrogation Rule for ST-elevation myocardial infarction (FIRST) program

Interventions: A study was conducted on patients in the FIRST program, which uses a computerized physician order entry (CPOE) system. Demographics, time intervals, and clinical outcomes were analysed based on arrival time in the ED: group 1, normal working hours on weekdays; group 2, off-hours on weekdays; group 3, normal working hours on weekends; and group 4, off-hours on weekends.

Primary and Secondary Outcome Measures: Clinical outcomes were categorized according to 30-day mortality, in-hospital mortality, and the length of stay.

Results: The duration from door to data or FIRST activation did not differ significantly among the four groups. The median duration between arrival and balloon placement in percutaneous coronary intervention (PCI) did not significantly exceed 90 minutes. The proportions (89.6–95.1% in the four groups) of patients with door-to-balloon times within 90 minutes did not reveal significant differences, regardless of ED arrival time ($p = 0.147$).

Differences in 30-day (p = 0.8173) and in-hospital mortality (p = 0.9107) were not observed in patients with STEMI.

Conclusions: A multidisciplinary CP for STEMI based on a CPOE system can effectively decrease disparities in the door-to-data duration and proportions of patients with door-to-balloon times within 90 minutes, regardless of ED arrival time. The application of a multidisciplinary CP may also help to attenuate off-hour and weekend effects in STEMI clinical outcomes.

Strengths and limitations of this study

The Fast Interrogation Rule for ST-elevation MI (FIRST) program, which is based on a computerized physician order entry (CPOE) and an automated short-messaging system (SMS), has been used to operate an effective pre-existing FIRST team for rapid ST-elevation MI management in our two affiliated hospitals.

To date, many studies have focused on weekends or off-hours and have not considered outcomes during off-hours and weekends simultaneously. The purpose of this study was to investigate whether an organized critical pathway for the management of STEMI can effectively attenuate differences in the duration from ED arrival to evaluation and treatment, regardless of the time of arrival in the ED, by eliminating off-hour and weekend effects.

A multidisciplinary CP based on a CPOE and SMS system for STEMI can effectively decrease disparities in the door-to-data interval and the proportions of patients with door-to-balloon times within 90 minutes, regardless of ED arrival time. The application of a multidisciplinary CP may also help to attenuate off-hour and weekend effects in clinical outcomes after STEMI.

As retrospective study, it was impossible to perform a direct internal comparison with clinical data before implementation, because it was difficult to select a cohort with similar inclusion criteria as that of our study

INTRODUCTION

Acute myocardial infarction (AMI) is one of the important leading causes of disability and mortality worldwide [1 2]. Mozaffarian et al. estimated that approximately 15% of those who experience a heart attack will die of myocardial infarction (MI) [3]. The percentage of ST-segment elevation myocardial infarction (STEMI) in acute coronary syndrome (ACS) or MI cases varies in different reports [3]. Several studies reported that approximately 29–47% of patients with ACS have STEMI [3]. Acute STEMI usually means complete occlusion of an epicardial coronary artery [4]. The primary goal in life salvage is early reperfusion therapy through intravenous administration of fibrinolytics (tissue plasminogen activator [IV-tPA]) or emergency cardiac procedures such as a primary percutaneous coronary intervention (PCI) [4-6]. Ideally, primary PCI should be conducted with a door-to-balloon time within 90 minutes in patients with STEMI [7]. An earlier door-to-balloon time was significantly associated with survival rate improvement and good outcomes [8]. A delay of approximately 30 minutes in the door-to-balloon time could increase in-hospital morality by 20–30% in patients with STEMI, regardless of door-to-balloon times of up to 180 minutes [2]. However, there is often limited staff availability during off-hours admissions versus admissions during regular working hours [9]. Previous studies have shown increased mortality in different conditions such as cancer, aortic aneurysm, stroke, duodenal ulcer, epiglottitis, and pulmonary embolism, among others, when patients are admitted during off-hours or on weekends [10 11]. This phenomenon has usually been defined as the "weekend effect" or the "off-hour effect" [10 12]. Although off-hour and weekend effects on mortality in AMI have been controversial, recent studies suggested that patients with AMI admitted during off-hours and on weekends had delayed door-to-balloon times and higher short-term mortality [2 9]. However, it is difficult to continuously maintain specialized and standardized care, which could prevent disparities in critical factors in STEMI management, such as delays in the acquisition of an electrocardiogram (ECG), blood tests, and the use of thrombolytic treatment, based on emergency department (ED) arrival time during regular working hours versus off-hours. It may be the most important factor in consistent management, and could improve the system of care 24 hours/day and 7 days/week [2]. Considering the low level of awareness of the public and emergency medical services (EMS) in Korea of the importance of the rapid diagnosis and treatment of ACS, the Fast Interrogation Rule for ST-elevation MI (FIRST) program, which is based on a computerized physician order entry (CPOE) system, has been used to operate an effective pre-existing FIRST team for rapid STEMI management in our two affiliated hospitals since 2007. To date, many studies have focused on weekends or off-hours and have not considered outcomes during off-hours and weekends simultaneously. The purpose of this study was to investigate whether an organized critical pathway for the management of STEMI can effectively attenuate differences in the duration from ED arrival to evaluation and treatment, regardless of the time of arrival in the ED, by eliminating off-hour and weekend effects.

MATERIALS AND METHODS

A retrospective, observational cohort study for all consecutive patients included in the FIRST program was conducted at two tertiary academic hospitals with annual ED censuses of 65,000 and 85,000, respectively, during the study period. The institutional review board of Yonsei University Health System (No.3-2015-056) reviewed and approved the study. In 2007, we implemented a multidisciplinary CP based on a CPOE system, known as FIRST, at the Yonsei University College of Medicine-affiliated Severance and Gangnam Severance Hospitals. The study included all patients admitted between 1 January 2010 and 30 December 2012 with STEMI who presented to the ED within 12 hours of the onset of chest pain. The CPOE system was used for program activation and deactivation, communication and consultation, entering pre-determined standing order sets, providing specific protocols and current guidelines, and to assess program efficacy [3 11]. Upon arrival of a patient in the ED, physicians, nurses, and emergency medical technicians in the triage area identified candidates for the FIRST program as soon as possible according to pre-determined protocols. Preferentially, patients with typical or non-specific suspected symptoms of AMI (chest pain, epigastric pain, syncope, dizziness, vertigo, shock, dyspnoea, nausea, or vomiting) should be examined simultaneously and a 12-lead ECG performed in the triage area. The guidelines included criteria for critical pathway (CP) activation based on the ECG criteria in the standard STEMI guidelines and the duration after the onset of chest pain (Fig. 1). These ST-segment elevations in the ECG criteria were prepared from standard guidelines. ST-segment elevations in the ECG criteria were defined as (1) J-point elevation on two or more contiguous leads, with a threshold of more than 2 mm in the precordial leads or more than 1 mm in other leads, and (2) a new or presumed new left bundle branch block (LBBB). When a patient had at least one

ECG warning criterion and arrived within 12 hours of the onset of symptoms, an ED physician in the triage area activated the FIRST program by selecting the activation icon on the order entry window. Once the program is activated, the name of the patient is highlighted in bright yellow in the patient list; thus, each team member could easily and immediately recognize the patients in the FIRST program [3 11]. The mobile phone number of each member of the FIRST team was previously registered in a computerized order-entry database for physicians. A program that linked consultation orders to an automated short-messaging system (SMS) was developed. The SMS text was immediately transmitted to members of the team after consultation. At the same time, an ED physician immediately consulted with an on-call cardiologist, or coronary catheterization staff and a senior ED physician. Medical orders for blood tests were automatically displayed, and an alarm with a beeping sound and pop-up window was added to the technician's monitor [3 11]. Thus, at the same time that medical orders were submitted, laboratory technicians were alerted and could prepare for the arrival of blood samples. The on-call cardiologist and coronary catheterization staff were also alerted and could prepare for the arrival of the patient. These preparations enable immediate and rapid examinations. The FIRST program was deactivated either after the intravenous administration of IV-tPA, PCI, after determining that thrombolytic treatment was not indicated, or when PCI was considered as a delayed procedure by the on-call cardiologist [3 11]. To compare time-related factors among the four groups, patients were excluded from the study if out-of-hospital cardiac arrest or ST-segment elevation on follow-up ECG was revealed in patients who were included in the CP. The patient's demographics, Killip class, PCI lesions, and laboratory tests for cardiac enzymes were examined. The time intervals that were assessed were door to ECG, ECG to FIRST activation, FIRST to PCI or t-PA, and door to PCI. The patients were classified based on arrival time in the ED. Patients who arrived between 9:00 and 18:00 hours were arbitrarily designated as having arrived during working hours; patients who arrived between 18:00 and 9:00 hours were arbitrarily designated as having arrived during off-hours. The weekend was defined as the period from Saturday to Sunday. National holidays were also included in the weekend. Patients were divided into four groups: group 1 (patients who arrived during working hours on a weekday), group 2 (those who arrived during off-hours on a weekday), group 3 (those who arrived during working hours on a weekend), and group 4 (those who arrived during off-hours on a weekend) [10] . Clinical outcomes were categorized according to 30-day mortality, overall in-hospital mortality, and single length of stay (LOS).

Statistics

Demographic and clinical data are presented as the median (minimum, maximum), frequency, or mean ± standard deviation (SD) as appropriate. Differences in demographic characteristics, time intervals, mortality, and LOS among the four groups were compared with the Kruskal-Wallis test for continuous variables or the chi-squared or Fisher's exact test for categorical variables. The post hoc analysis was performed with the Dunn procedure for continuous variables and the chi-squared or Fisher's exact test for two pairs of categorical variables. A univariate Cox regression was performed to identify the effects on mortality of the door-to-PCI and FIRST activation-to-PCI intervals. Survival curves were obtained with a Kaplan-Meier analysis, and the log-rank test was performed for comparisons among the four groups. Values of $p < 0.05$ were considered significant. Statistical analyses were conducted with SAS version 9.2 (SAS Institute Inc., Cary, NC, USA).

RESULTS

At the two affiliated hospitals, there were 1043 consecutive patients admitted to our EDs who were included in the FIRST CP. A total of 560 (53.7%) patients were diagnosed with STEMI among 729 (69.9%) patients who underwent emergency coronary angiography. However, 82 patients were excluded from the analysis because of time delay factors such as out-of-hospital cardiac arrest (n = 23), ST-segment elevation on follow-up ECG (n = 24), delayed PCI because of a Q wave without symptoms (n = 22), and do not attempt resuscitation (DNAR) status (n = 3). A total of 488 STEMI patients were enrolled in this study. There were no significant differences, except in family history for coronary artery disease (CAD) and weight among the demographic characteristics of the four groups (Table 1). The time interval between arrival in the ED and ECG or the activation of FIRST did not differ significantly among the four groups (Table 2). However, the time intervals from FIRST activation to PCI and door to PCI showed significant differences among the four groups. The door-to-balloon duration in patients with STEMI should be within 90 minutes. Among patients who underwent PCI in the four groups, the median duration between arrival in the ED and PCI balloon placement did not significantly exceed 90 minutes (Table 3). The proportions of patients with door-to-balloon times within 90 minutes ranged from 89.6–95.1% in the four groups (Fig. 1). The proportions of patients with door-to-balloon times within 90 minutes did not reveal significant differences between patients who were admitted to the ED during off-hours, regular hours, the weekend, or on weekdays (p = 0.147). A univariate Cox regression was performed to identify the effects on mortality of the durations of door to PCI balloon placement and the activation of FIRST to PCI balloon placement. The duration from door to PCI balloon placement and the activation of FIRST to PCI balloon placement did not affect in-hospital or 30-day mortality, regardless of ED arrival time (Table 3). The survival curves for in-hospital mortality (p = 0.8668) and 30-day mortality (p = 0.8963) did not differ significantly among all patients, regardless of ED arrival time. In-hospital and 30-day mortality rates during a single LOS were 7.99% and 8.4%, respectively, among patients with STEMI. Although the median LOS was 5 days, LOSs were not significantly different among the four groups (p = 0.3127) (Table 2). Moreover, differences in 30-day (p = 0.8173) and in-hospital mortality (p = 0.9107) were not observed in patients with STEMI who underwent PCI.

DISCUSSION

Previously, many studies have suggested that patients with AMI who were admitted during off-hours including weekends and/or nights may have higher mortality due to a lower likelihood of evidence-based treatment, timely reperfusion therapies, and the availability and experience of the staff [13]. To date, no systematic review or meta-analysis has been performed of off-hour presentations and outcomes in AMI. Recently, a systematic review by Sorita et al. demonstrated that mortality in patients with STEMI who presented during off-hours was higher than those who presented during working hours [2]. Additionally, longer door-to-balloon times during off-hours for patients with STEMI may contribute to higher mortality than in those admitted during regular hours [2]. In patients with STEMI who underwent PCI, recent guidelines recommend a door-to-balloon time goal within 90 minutes [7]. A multidisciplinary CP requires a functional, well-organized team approach that includes human resources and available equipment at the appropriate times [14 15]. At our institutions, the application of CPOE-based multidisciplinary CPs for ischemic stroke and postpartum haemorrhage have demonstrated attenuations in the durations of presentation to therapy [16 17]. Our CP for AMI management was also designed to reduce unnecessary in-hospital time delays through a CPOE-based alert system, SMS, and simple standing orders through the activation stage. Despite the small disparities in door-to-balloon times among the four groups, all groups had a median door-to-balloon time within 90 minutes. Moreover, the proportions of patients with door-to-balloon times within 90 minutes did not reveal significant differences among patients who were admitted to the ED during off-hours, regular hours, weekends, and weekdays. Firstly, mortality and LOS for patients with STEMI who underwent PCI were not significantly different among the four groups. During off-hours, the rate of PCI and differences in door-to-balloon times were likely associated with limited staff availability [2]. Many institutions have made efforts to constantly maintain cardiologist and support staff availability for cardiac catheterization in recent years. Parikh et al. reported that "Code STEMI" could decrease the median door-to-balloon duration (112 min before and 74 min after Code STEMI; $p < 0.001$) and LOS (4 days before and 3 days after Code STEMI; $p < 0.01$) [15]. Holmes et al. also suggested that the application of a "STEMI protocol" could significantly reduce median door-to-balloon times (98 min [interquartile range (IQR), 70–125 min] before and 74 min [IQR, 60–93 min] after implementation of a STEMI protocol; $p = 0.005$) in patients with STEMI during off-hours. There was no significant difference in all-cause mortality [18]. However, a systematic review and meta-analysis revealed higher in-hospital and 30-day mortality in patients with AMI during off-hours versus those admitted during regular hours [2]. Disparities in mortality may be increased in patients with STEMI and in studies that were conducted outside of North America, and more importantly, may have worsened in recent years [2]. Until now, increased in-hospital mortality in AMI was associated with off-hour admission in developing countries. In Iraq, Al-Asadi et al. reported that off-hour admission (25.5%) was significantly associated with higher mortality versus admission during working hours (3%) ($p < 0.001$) [19]. Magid et al. suggested that door-to-balloon times during off-hours were longer than during regular hours primarily because of a longer interval from completion of the ECG to arrival in the catheterization laboratory (off-hours, 69.8 minutes vs. regular hours, 49.1 minutes; $p < 0.001$). This pattern was consistent across all hospitals [2 20]. If we consider the lower levels of public awareness and education about AMI among EMS and staff in many countries, implementation of an organized CP for AMI management could attenuate differences in the critical process during off-hours and weekends versus during working hours and weekdays. First of all, the FIRST CP focused on patients with suspected or distracting symptoms for AMI who were admitted to the ED and had a shorter door-to-data (completion of an ECG) interval in the ED. Although there were no significant differences in the median duration (1–3 minutes among the four groups; p = 0.0749) of the door-to-data interval in the ED during off-hours and weekends, atypical symptoms are often present in patients with STEMI. Na et al. showed that STEMI patients presenting without chest pain had longer door-to-data and door-to-PCI times than patients presenting with chest pain. Presentation without chest pain was an independent predictor of hospital mortality in patients with STEMI after a primary PCI [21]. Unfortunately, the acquisition of an ECG may be omitted in the initial assessments of these patients in the ED. The delayed door-to-data interval may be the most critical factor causing longer door-to-balloon times in patients with STEMI. This standardization of the door-to-data protocol can help to improve early recognition in emergency situations [15]. Several studies reported that the proportion of AMI patients with door-to-balloon times less than 90 min was variable, and ranged from 6.3–98.5% [11 15 20]. Despite a setting of an academic suburban ED in North America, only 52% of patients with STEMI underwent PCI within 90 minutes after arrival after the implementation of a central paging system for the interventional cardiology team [22]. Pan et al. showed that implementing specific strategies improved the proportion of patients who underwent PCI within 90 minutes from 59.4% to 98.5% (p < 0.001) [11]. Our study did not show significant differences in the proportions of patients who underwent PCI within 90 minutes, regardless of arrival time in the ED, which ranged from 89.6–95.1%. Several studies reported that patients with AMI showed no significant difference in mortality between regular hours and off-hours [2 21 23 24]. However, patients with AMI admitted during off-hours were less likely to undergo primary PCI and more likely to undergo fibrinolytic therapy. Consequently, there was no difference in the overall usage of reperfusion therapy, irrespective of arrival time [24]. The clinical effectiveness of PCI when performed in a highly specialized STEMI network system was equivalent between regular and off-hours admissions at a regional level [23]. A dedicated cardiac care network usually consists of a prehospital pathway, EMS training, priority for laboratory studies and emergency care, and 24 hours/day and 7 days/week availability of specialized cardiologists [10]. The coordination of many elements can overcome the deleterious effects of admission during off-hours and weekends [10]. However, many reports were conducted in areas with well-organized cardiac care centres in developed countries. Practice guidelines for decision support and disease-specific order sets can be embedded in the CPOE system [10 11 25]. In clinical practice, a CPOE system based on predetermined order sets is not simply a computer network, but can provide many communication advantages including clarification and tracking the completion of orders and errors [11]. Our FIRST protocols based on a CPOE system facilitates the simultaneous utilization of a multidisciplinary team approach, which has benefits for reducing medical errors and improving the quality of the critical process [10]. However, the successful operation of a CP requires standardization and simple protocols, regular educational opportunities, and feedback from clinical results [10]. Multidisciplinary and expedient approaches are certainly necessary to achieve favourable outcomes [16]. All members of the cardiac team have to be alerted to the scene in time for effective thrombolysis because of the limited time period. As in the story of "crying wolf" in Aesop's fables, repeated false and true alarms may cause an alarm fatigue effect and desensitization to alarms [26]. In ischemic stroke, it is well known that the behaviour of the physician may result in a 3-hour effect [17]. The 3-hour effect means that patients who are admitted very soon after the onset of symptoms experience longer door-to-needle waiting times than patients admitted just before the end of the 3-hour timeline [27]. Nevertheless, several studies suggested that approaches to reduce alarm fatigue can be performed appropriately with a multidisciplinary team approach and education on issues, the optimization of alarms, and a systematic perspective for reducing alarm fatigue [26 28].

The study should be considered in the context of several limitations. Firstly, because it was difficult to select a cohort with similar inclusion criteria as that of our study, it was impossible to perform a direct internal comparison with clinical data before implementation. Second, we only assessed mortality during a 30-day period and a single LOS because we could not evaluate long-term mortality. Third, despite increased mortality caused by delayed diagnosis and severe disease, patients who experienced out-of-hospital cardiac arrest or ST-segment elevation on follow-up on ECG were not included in the study because it was impossible to purely compare time factors among the four groups.

CONCLUSION

A multidisciplinary CP based on a CPOE system for STEMI can effectively decrease disparities in the door-to-data interval and the proportions of patients with door-to-balloon times within 90 minutes, regardless of ED arrival time. The application of a multidisciplinary CP may also help to attenuate off-hour and weekend effects in clinical outcomes after STEMI.

a. contributorship statement

Conceived and designed the study: YSP, SPC, HSL, JHH, and JSY

Performed the study: YSP, MJK, HSC, SPC, JWW, IP and JSY,

Analyzed the data: YSP, SPC, HSL, JHH, IP and JSY

Contributed to the writing of the manuscript: YSP, JSY, and SPC

Other (Manuscript editing) : all authors

b. competing interests

The authors declare no conflict of interest.

c. funding

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d. data sharing statement

No additional data are available.

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Figure Legends

Table 1. The demographic characteristics of all patients

Table 2. The time intervals and clinical outcomes of all patients

Table 3. The effect of the door-to-balloon duration in PCI and the activation of FIRST to balloon duration in PCI on in-hospital and 30-day mortality with respect to ED arrival time

Figure 1. The proportions of patients with door-to-balloon times within 90 minutes with respect to ED arrival time.

Figure 2. Survival curves were obtained by a Kaplan-Meier analysis, and the log-rank test was performed for comparisons of in-hospital (A) and 30-day mortality (B) with respect to emergency department arrival time.

FIRST: the Fast Interrogation Rule for ST-elevation myocardial infarction program

Demography	Median(Min-Max)				Overall	Post hoc analysis p-value					
	(1) (n = 206)	(2) (n = 154)	(3) (n = 61)	(4) (n = 67)		(1) vs. (2)	(1) vs. (3)	(1) vs. (4)	(2) vs. (3)	(2) vs. (4)	(3) vs. (4)
Age	64(32-98)	62(29-91)	63(41-91)	63(28-92)	0.8381						
Sex					0.2205						
Male	162(78.64)	131(85.06)	45(73.77)	52(77.61)							
Female	44(21.36)	23(14.94)	16(26.23)	15(22.39)							
Systolic blood pressure (BP)	125(43-223)	131(59-268)	130(68-220)	133(65-202)	0.4672						
Diastolic BP	79.5(9-133)	82.5(43-184)	82(40-122)	80(43-125)	0.1289						
Pulse rate	79.5(34-150)	80(35-145)	82(43-134)	81(34-156)	0.7674						
Diabetic mellitus	67(32.52)	48(31.17)	21(34.43)	25(37.31)	0.8251						
Hypertension	115(55.83)	75(48.7)	26(42.62)	41(61.19)	0.1028						
Chronic kidney disease	11(5.34)	8(5.19)	1(1.64)	4(5.97)	0.666						
Stroke	12(5.83)	11(7.14)	2(3.28)	3(4.48)	0.7574						
Variant angina	3(1.46)	1(0.65)	1(1.64)	1(1.49)	0.8251						
Stable angina	5(2.43)	4(2.6)	2(3.28)	2(2.99)	0.9306						
Myocardial infarction	12(5.83)	12(7.79)	1(1.64)	4(5.97)	0.4066						
Heart failure	3(1.46)	3(1.95)	1(1.64)	1(1.49)	0.9534						
S/P PTCA	17(8.25)	19(12.34)	4(6.56)	10(14.93)	0.2487						
S/P CABG	1(0.49)	1(0.65)	1(1.64)	1(1.49)	0.4873						
Current smoker	81(39.32)	74(48.05)	20(32.79)	35(52.24)	0.0535						

Hypercholesterolemia	17(8.25)	11(7.14)	3(4.92)	6(8.96)	0.8339						
Family history of CAD					0.0122*	0.0096	0.5918	0.6816	0.0217	0.2422	0.4972
0	201(97.57)	141(91.56)	61(100)	65(97.01)							
1	5(2.43)	13(8.44)	0(0)	2(2.99)							
Height (cm)	167(140-186)	168(140-183)	167(146-178)	168(140-190)	0.4864						
Weight (kg)	65(43-96)	69.3(37.5-120)	65.3(17.2-86)	68.3(36.1-133)	0.0417*	0.0334	0.3858	0.1586	0.0189	0.8591	0.0657
Creatine kinase (CK)	143.5(20-5514)	127(14-10560)	122(53-8400)	110(25-2132)	0.222						
CK-MB	4.43(0.56-619.4)	3.32(0.7-638)	5.29(0.92-600)	3.5(0.76-172.8)	0.2161						
Troponin-T	0.06(0-10)	0.03(0-9.86)	0.06(0-10)	0.04(0-18.22)	0.0959						
Mode of transport					0.3446						
1	105(50.97)	88(57.14)	38(63.33)	37(55.22)							
2	101(49.03)	66(42.86)	22(36.67)	30(44.78)							
Killip class					0.3609						
1	125(60.68)	104(67.53)	34(56.67)	42(62.69)							
2	28(13.59)	13(8.44)	8(13.33)	13(19.4)							
3	23(11.17)	20(12.99)	7(11.67)	7(10.45)							
4	30(14.56)	17(11.04)	11(18.33)	5(7.46)							
CPR in ED					0.1134						
0	201(97.57)	154(100)	59(96.72)	66(98.51)							
1	5(2.43)	0(0)	2(3.28)	1(1.49)							
Chest pain					0.8045						
0	23(11.17)	13(8.44)	5(8.2)	6(8.96)							

1	183(88.83)	141(91.56)	56(91.8)	61(91.04)	
PCI lesion					0.191
1	94(46.08)	65(42.76)	39(65)	31(46.27)	
2	77(37.75)	52(34.21)	15(25)	24(35.82)	
3	9(4.41)	12(7.89)	1(1.67)	4(5.97)	
4	24(11.76)	23(15.13)	5(8.33)	8(11.94)	

Table 1. The demographic characteristics of all patients

Patients were divided into four groups: group 1 (patients who arrived during working hours on a weekday), group 2 (those who arrived during off-hours on a weekday), group 3 (those who arrived during working hours on a weekend), and group 4 (those who arrived during off-hours on a weekend).

PTCA: percutaneous transluminal coronary angioplasty; CABG: coronary artery bypass graft; CPR: cardiopulmonary resuscitation; PCI: percutaneous coronary intervention; CAD: coronary artery disease;*: $p < 0.05$

	Median(Min-Max)				Overall	Post hoc analysis p-value					
	(1) (n = 206)	(2) (n = 154)	(3) (n = 61)	(4) (n = 67)	p-value	(1) vs. (2)	(1) vs. (3)	(1) vs. (4)	(2) vs. (3)	(2) vs. (4)	(3) vs. (4)
Time outcomes											
door to ECG (min)	3(0-64)	2(0-26)	1(0-38)	3(0-49)	0.0749	0.1503	0.0648	0.437	0.4433	0.0728	0.0324*
ECG to FIRST (min)	4(0-64)	4(0-29)	4(0-26)	4(0-27)	0.7129	0.6651	0.3966	0.7804	0.262	0.9623	0.3577
FIRST to balloon (min)	41.5(16-210)	52(22-147)	53(13-96)	59(25-98)	<.0001*	<.0001*	<.0001*	<.0001*	0.9656	0.0102*	0.0368*
Door to balloon (min)	51.5(22-226)	62(31-152)	61(26-130)	71(27-124)	<.0001*	<.0001*	0.0024*	<.0001*	0.5535	0.0078*	0.0068*
Length of stay	5(1-61)	5(1-54)	5(3-55)	5(1-43)	0.3127	0.2591	0.5076	0.0781	0.8758	0.3835	0.393
Clinical outcomes											
In-hospital mortality (1-5)					0.9107	0.5822	0.7922	0.9565	0.5764	0.6421	0.8644
1	188(91.26)	143(92.86)	55(90.16)	61(91.04)							
2	18(8.74)	11(7.14)	6(9.84)	6(8.96)							
30-day mortality					0.8173	0.4315	0.7922	0.7441	0.3981	0.7767	0.6323
1	188(91.26)	144(93.51)	55(90.16)	62(92.54)							
2	18(8.74)	10(6.49)	6(9.84)	5(7.46)							

Table 2. The time intervals and clinical outcomes of all patients

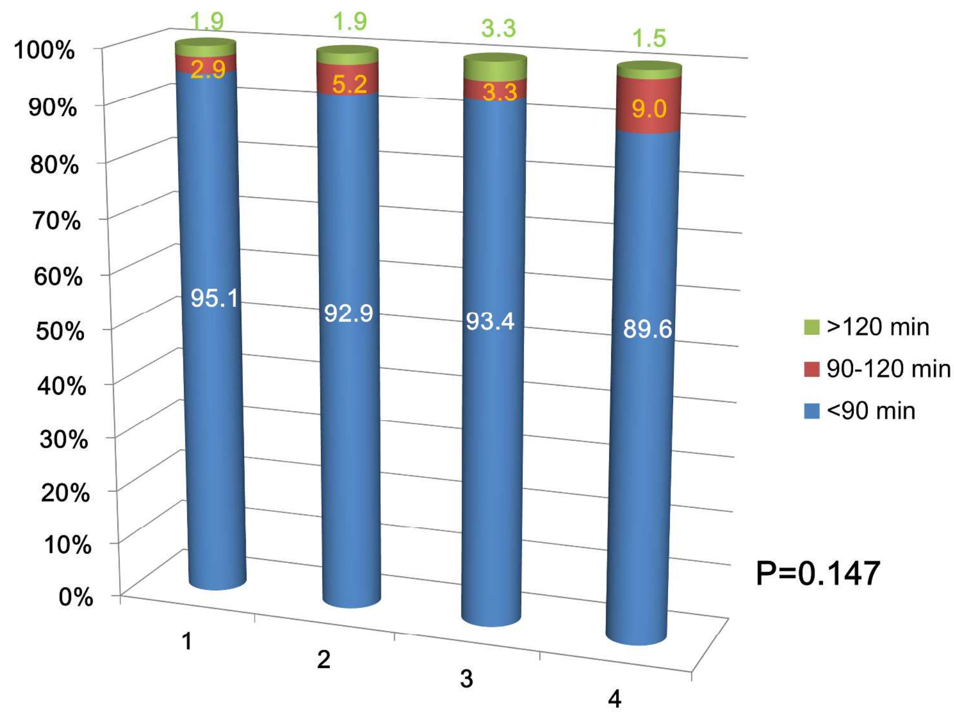
Patients were divided into four groups: group 1 (patients who arrived during working hours on a weekday), group 2 (those who arrived during off-hours on a weekday), group 3 (those who arrived during working hours on a weekend), and group 4 (those who arrived during off-hours on a weekend).

ECG: electrocardiography; FIRST: the **F**ast **I**nterrogation **R**ule for **ST-**elevation myocardial infarction program;*: $p < 0.05$

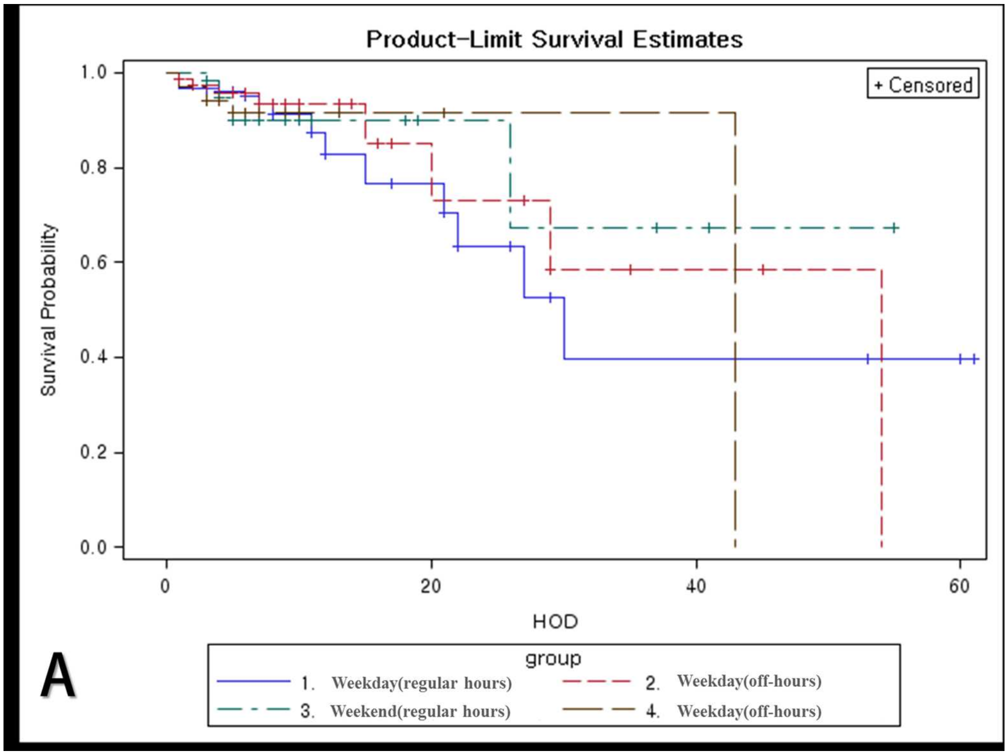
In-hospital mortality	HR(95% CI)	p-value
FIRST to PCI (min)	1.005(0.992-1.019)	0.4522
Door to PCI (min)	1.000(0.987-1.014)	0.9851
30-day mortality	**HR(95% CI)**	**p-value**
FIRST to PCI (min)	1.000(0.987-1.014)	0.9851
Door to PCI (min)	1.006(0.992-1.019)	0.4122

Table 3. The effect of the door-to-balloon duration in PCI and the activation of FIRST to balloon duration in PCI on in-hospital and 30-day mortality with respect to ED arrival time

FIRST: the **F**ast **I**nterrogation **R**ule for **ST**-elevation myocardial infarction (FIRST) program; PCI: percutaneous coronary intervention

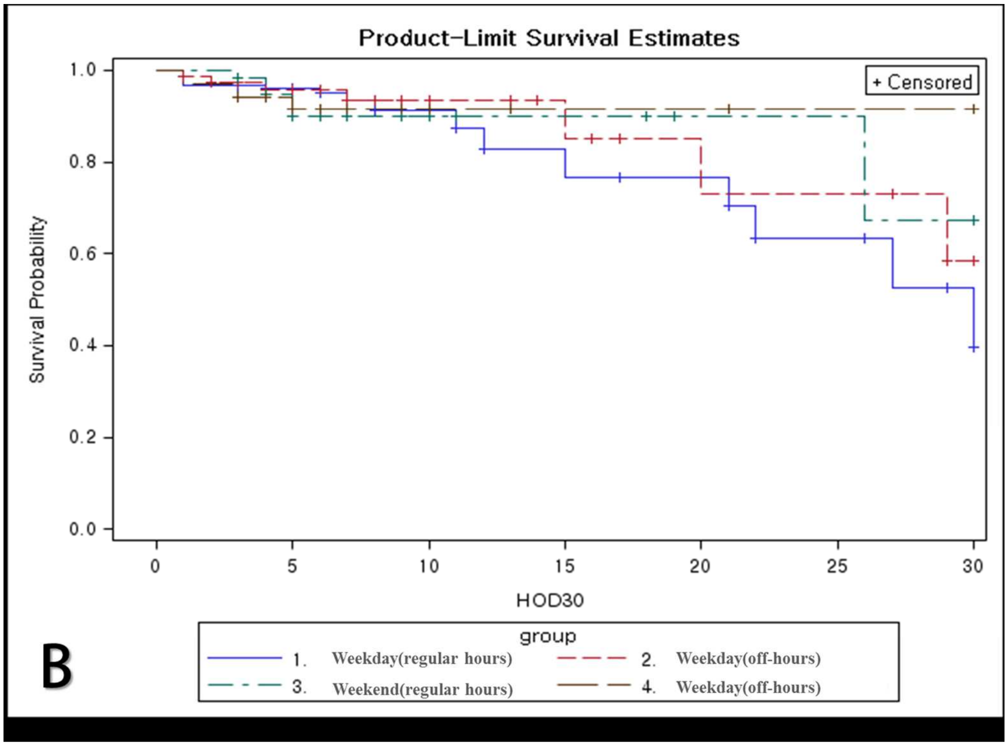


The proportions of patients with door-to-balloon times within 90 minutes with respect to ED arrival time.
254x190mm (300 x 300 DPI)



Survival curves were obtained by a Kaplan-Meier analysis, and the log-rank test was performed for comparisons of in-hospital (A) and 30-day mortality (B) with respect to emergency department arrival time. FIRST: the Fast Interrogation Rule for ST-elevation myocardial infarction program

246x183mm (300 x 300 DPI)



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246x181mm (300 x 300 DPI)

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Effectiveness of a multidisciplinary critical pathway based on a computerized physician order entry system for ST-elevation myocardial infarction management in the emergency department: a retrospective observational study

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Complete List of Authors:	Park , Yoo Seok ; Yonsei University College of Medicine Chung, Sung Phil; Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, Korea YOU, JE SUNG; Emergency Medicine Kim, Min Joung; Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, Korea, Chung, Hyun Soo; Yonsei University College of Medicine, Emergency Medicine Hong, Jung Hwa; Yonsei University College of Medicine, Department of Research Affairs, Biostatistics Collaboration Unit Lee, Hye Sun; Yonsei University College of Medicine, Biostatistics Wang, Jinwon ; Yonsei University College of Medicine, Department of Emergency Medicine park, Incheol; Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, Korea, Emergency medicine

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Effectiveness of a multidisciplinary critical pathway based on a computerized physician order entry system for ST-elevation myocardial infarction management in the emergency department: a retrospective observational study

Yoo Seok Park MD, PhD [1], Sung Phil Chung, MD, PhD [1], Je Sung You, MD [1*], Min Joung Kim, MD, PhD [1], Hyun Soo Chung MD, PhD [1], Jung Hwa Hong, MS [2], Hye Sun Lee, MS [2], Jinwon Wang, MD [1], Incheol Park MD, PhD [1]

1. Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

2. Department of Research Affairs, Biostatistics Collaboration Unit, Yonsei University College of Medicine, Seoul, Republic of Korea

Corresponding author

Je Sung You, MD

Department of Emergency Medicine, Yonsei University College of Medicine

211 Eonju-Ro, Gangnam-Gu, Seoul 135-720, Republic of Korea

Tel: +82-2-2019-3030, Fax: +82-2-2019-4820

E-mail: youjsmd@yuhs.ac

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ABSTRACT

Objectives: The purpose of this study was to investigate whether a multidisciplinary organized critical pathway (CP) for ST-elevation myocardial infarction (STEMI) management can significantly attenuate differences in the duration from emergency department (ED) arrival to evaluation and treatment, regardless of the arrival time, by eliminating off-hour and weekend effects.

Design: Retrospective observational cohort study.

Setting: Two tertiary academic hospitals.

Participants: Consecutive patients in the Fast Interrogation Rule for ST-elevation myocardial infarction (FIRST) program.

Interventions: A study was conducted on patients in the FIRST program, which uses a computerized physician order entry (CPOE) system. The patient demographics, time intervals, and clinical outcomes were analyzed based on the arrival time to the ED: group 1, normal working hours on weekdays; group 2, off-hours on weekdays; group 3, normal working hours on weekends; and group 4, off-hours on weekends.

Primary and Secondary Outcome Measures: Clinical outcomes categorized according to 30-day mortality, in-hospital mortality, and the length of stay.

Results: The duration from door-to-data or FIRST activation did not differ significantly among the four groups. The median duration between arrival and balloon placement during percutaneous coronary intervention (PCI) did not significantly exceed 90 minutes, and the proportions (89.6–95.1%) of patients with door-to-balloon times within 90 minutes did not significantly differ among the four groups, regardless of the ED arrival time ($p = 0.147$). Moreover, no differences in the 30-day ($p = 0.8173$) and in-hospital mortality ($p = 0.9107$) were observed in STEMI patients.

Conclusions: A multidisciplinary CP for STEMI based on a CPOE system can effectively decrease disparities in the door-to-data duration and proportions of patients with door-to-balloon times within 90 minutes, regardless of the ED arrival time. The application of a multidisciplinary CP may also help attenuate off-hour and weekend effects in STEMI clinical

outcomes.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- In the present study, the Fast Interrogation Rule for ST-elevation myocardial infarction (FIRST) program, based on a computerized physician order entry (CPOE) and an automated short message service (SMS), was used to operate an effective pre-existing FIRST team for rapid ST-elevation myocardial infarction (STEMI) management in our two affiliated hospitals.
- A multidisciplinary critical pathway (CP) for STEMI was found to effectively decrease disparities in the door-to-data interval and the proportions of patients with door-to-balloon times within 90 minutes, regardless of the emergency department (ED) arrival time.
- The application of a multidisciplinary CP could also help attenuate off-hour and weekend effects in terms of the clinical outcomes after STEMI.
- However, due to the retrospective observational nature of the study, it was impossible to perform a direct internal comparison with clinical data obtained before the implementation, because it was difficult to select a cohort with similar inclusion criteria as that of the cohort in the present study.

INTRODUCTION

Acute myocardial infarction (AMI), defined as complete occlusion of the epicardial coronary artery, is a leading cause of disability and mortality worldwide.[1-3] Approximately 15% of those who experience myocardial infarction (MI) reportedly die.[4] The primary goal in the treatment of AMI is therefore early reperfusion therapy through intravenous administration of tissue plasminogen activator (IV-tPA) or through emergency cardiac procedures such as a primary percutaneous coronary intervention (PCI).[3 5 6] Ideally, primary PCI should be conducted with a door-to-balloon time within 90 minutes in patients with STEMI.[7] A delay of approximately 30 minutes in the door-to-balloon time has been reported to increase in-hospital morality by 20–30% in patients with STEMI, regardless of door-to-balloon times of up to 180 minutes.[2] However, there is often limited staff availability during off-hours admissions as compared to for admissions during regular working hours.[8] Previous studies have shown increased mortality in different conditions such as cancer, aortic aneurysm, stroke, duodenal ulcer, epiglottitis, and pulmonary embolism, among others, when patients are admitted during off-hours or on weekends.[9 10] This phenomenon is commonly referred to as the "weekend effect" or "off-hour effect".[10 11] Although off-hour and weekend effects on mortality in AMI patients are controversial, recent studies have suggested that patients with AMI admitted during off-hours and on weekends show delayed door-to-balloon times and higher short-term mortality.[2 8] However, it may be difficult to continuously maintain specialized and standardized care, which in turn may result in disparities in critical factors in STEMI management, such as delays in the acquisitions of electrocardiograms (ECG) and blood tests, and the use of thrombolytic treatment, according to the emergency department (ED) arrival time. At our institutions, the applications of CPOE-based multidisciplinary CPs for ischemic stroke and postpartum haemorrhage have demonstrated attenuations in the durations of presentation to therapy.[12 13] In our hospitals, considering the low level of awareness of the public and emergency medical services (EMS) in Korea regarding the importance of rapid diagnosis and treatment of acute coronary syndrome, the Fast Interrogation Rule for ST-elevation MI (FIRST) program, which is based on a computerized physician order entry (CPOE) system, has been used to operate an effective pre-existing FIRST team for rapid STEMI management since 2007. The purpose of the present study was to investigate whether an organized critical pathway (CP) for the management of STEMI can effectively attenuate the differences in the duration from ED arrival to evaluation and treatment, regardless of the time of arrival to the ED, by eliminating the off-hour and weekend effects.

MATERIALS AND METHODS

A retrospective, observational cohort study for all consecutive patients included in the FIRST program was conducted at two tertiary academic hospitals, Yonsei University College of Medicine-affiliated Severance and Gangnam Severance Hospitals, with annual ED censuses of 65,000 and 85,000, respectively, during the study period. The institutional review board of Yonsei University Health System (No.3-2015-056) reviewed and approved the study. In 2007, we implemented a multidisciplinary CP based on a CPOE system, known as FIRST, at the two hospitals. Our CP for AMI management was designed to reduce unnecessary in-hospital time delays through a CPOE-based alert system, SMS, and simple standing orders through the activation stage. The study included all patients admitted between 1 January 2010 and 30 December 2012 with STEMI who presented to the ED within 12 hours of the onset of chest pain. The CPOE system was used for program activation and deactivation, communication and consultation, entering pre-determined standing order sets, providing specific protocols and current guidelines, and to assess program efficacy.[4 9] Upon arrival of a patient to the ED, the physicians, nurses, and emergency medical technicians in the triage area identified candidates for the FIRST program as soon as possible according to pre-determined protocols. Preferentially, patients with typical or non-specific suspected symptoms of AMI (chest pain, epigastric pain, syncope, dizziness, vertigo, shock, dyspnea, nausea, and/or vomiting) were examined simultaneously as a 12-lead ECG is performed in the triage area. The guidelines included criteria for CP activation based on the ECG criteria in the standard STEMI guidelines and the duration after the onset of chest pain. The ST-segment elevations in the ECG criteria were defined as (1) a J-point elevation on two or more contiguous leads, with a threshold of more than 2 mm in the precordial leads or more than 1 mm in other leads, and (2) a new or presumed new left bundle branch block. When a patient had at least one ECG warning criterion by predetermined ST-segment elevations on ED arrival within 12 hours of the onset of symptoms, an ED physician in the triage area activated the FIRST program by selecting the activation icon on the order entry window. Once the program is activated, the name of the patient is highlighted in bright yellow in the patient list; thereby, each team member can easily and immediately recognize the patients in the FIRST program.[4 9] The mobile phone number of each member of the FIRST team has been previously registered in a computerized order-entry database for physicians, and a program that links consultation orders to an automated short message service (SMS) has been developed. The SMS text is immediately transmitted to the team members after consultation. At the same time, an ED physician immediately consults with an on-call cardiologist, or with coronary catheterization staff and a senior ED physician. Medical orders for blood tests are automatically displayed, and an alarm with a beeping sound and pop-up window is added to the technician's monitor.[4 9] Thus, at the same time that medical orders are submitted, laboratory technicians are alerted and can prepare for the arrival of blood samples. The on-call cardiologist and coronary catheterization staff are also alerted and can prepare for the arrival of the patient. These preparations enable immediate and rapid examinations. All members can indirectly identify SMS reception using the CPOE system and directly by using their mobile phone. After activation of the FIRST CP, predetermined orders are also activated using CPOE. All members who receive an SMS should change the status of the charging order using CPOE from “order” to “registration”. In addition, all members of the CP can share ECG data and information of patients in real time using the CPOE system, including electronic medical records. The on-call cardiologists first assess the ECG for STEMI, symptoms characteristics, medical history of the patient, and risk stratification in the emergency department. Subsequently, they determine whether emergent thrombolytic treatment is indicated or whether PCI is considered as a delayed procedure. Furthermore, they decide whether intravenous t-PA or primary PCI is suitable for the treatment. Finally, they decide to deactivate the FIRST program using CPOE. In the present study, to compare time-related factors among the groups, patients were excluded from the study if return of spontaneous circulation occurred after out-of-hospital cardiac arrest or if ST-segment elevation was revealed only on follow-up ECG in patients who were included in the CP, because these factors increase the door-to-balloon time. Patients with ST-segment elevation revealed only on follow-up ECG were defined as those who were admitted to the ED within 12 hours of the onset of chest pain but did not reveal the ST-segment elevations of the ECG criteria on the initial ECG in the ED. Because of ongoing chest pain, these patients were followed-up by ECG during their ED stay and often revealed ST-segment elevations on the follow-up ECG. The patients’ demographics, Killip class, PCI lesions, and laboratory tests for cardiac enzymes were examined. The time intervals assessed included the door-to-ECG, ECG-to-FIRST activation, FIRST-to-PCI or t-PA, and door-to-PCI times. The patients were classified based on the arrival time to the ED. Patients who arrived between 9:00 and 18:00 and between 18:00 and 9:00 were arbitrarily designated as having arrived during working hours and off-hours, respectively. The weekend was defined as the period from Saturday to Sunday. National holidays were also included in the weekend classification. The patients were divided into four groups according to their arrival time: group 1 (patients who arrived during working hours on a weekday), group 2 (patients who arrived during off-hours on a weekday), group 3 (patients who arrived during working hours on a weekend), and group 4 (patients who arrived during off-hours on a weekend).[10] The clinical outcomes were categorized and examined according to the 30-day mortality, overall in-hospital mortality, and single length of stay (LOS), and compared between the four groups.

Statistics

Demographic and clinical data are presented as the median (minimum, maximum), frequency, or mean ± standard deviation as appropriate. Differences in the demographic characteristics, time intervals, mortality, and LOS among the four groups were compared with the Kruskal-Wallis test for continuous variables and the chi-squared or Fisher's exact test for categorical variables. Post hoc analysis was performed with the Dunn procedure for continuous variables and the chi-squared or Fisher's exact test for two pairs of categorical variables. Univariate Cox regression was performed to identify the effects on mortality of the door-to-PCI and FIRST activation-to-PCI intervals. Survival curves were obtained using Kaplan-Meier analysis, and the log-rank test was performed for survival comparisons among the four groups. All statistical analyses were conducted with SAS version 9.2 (SAS Institute Inc., Cary, NC, USA), and p values < 0.05 were considered significant.

RESULTS

At the two affiliated hospitals, there were 1043 consecutive patients admitted to the EDs included in the FIRST CP. Among 729 (69.9%) patients who underwent emergency coronary angiography, 560 (53.7%) patients were diagnosed with STEMI. However, 82 patients were excluded from the analysis because of time delay factors such as out-of-hospital cardiac arrest (n = 23), ST-segment elevation on follow-up ECG only (n = 24), delayed PCI because of a Q wave without symptoms (n = 22), and "do not attempt resuscitation" status (n = 3). Thus, a total of 488 STEMI patients were finally enrolled in this study. There were no significant differences, except in the family history for coronary artery disease and weight, among the demographic characteristics of the four groups (Table 1). The time interval between arrival to the ED and ECG or the activation of FIRST did not differ significantly among the four groups (Table 2). However, the time intervals from FIRST activation-to-PCI and door-to-PCI showed significant differences among the four groups. The door-to-balloon duration in patients with STEMI should be within 90 minutes. Among patients who underwent PCI in the four groups, the median duration between the arrival to the ED and PCI balloon placement did not significantly exceed 90 minutes (Table 3). The proportions of patients with door-to-balloon times within 90 minutes ranged between 89.6–95.1% in the four groups (Figure. 1) and did not reveal any significant differences ($p = 0.147$). Univariate Cox regression was performed to identify the effects on mortality according to the durations of door-to-PCI balloon placement and the activation of FIRST-to-PCI balloon placement; these did not affect in-hospital or 30-day mortality, regardless of the ED arrival time (Table 3).

The survival curves for in-hospital mortality ($p = 0.8668$) and 30-day mortality ($p = 0.8963$) did not differ significantly among all patients, regardless of the ED arrival time (Figure. 2A and B). The in-hospital and 30-day mortality rates during a single hospital stay were 7.99%

and 8.4%, respectively, among patients with STEMI. The median LOS was 5 days, and the LOS did not significantly differ among the four groups (p = 0.3127) (Table 2). Moreover, differences in the 30-day (p = 0.8173) and in-hospital mortality (p = 0.9107) were not observed in STEMI patients undergoing PCI.

DISCUSSION

Recently, a systematic review by Sorita et al. demonstrated that mortality in patients with STEMI who presented during off-hours was higher than in those who presented during working hours. The authors speculated that the longer door-to-balloon times during off-hours for patients with STEMI may have contributed to the higher mortality compared to in patients admitted during regular hours.[2] In the present study, despite minor disparities in the door-to-balloon times among the four groups, all groups had a median door-to-balloon time within 90 minutes. Moreover, the proportions of patients with door-to-balloon times within 90 minutes did not reveal significant differences among patients who were admitted to the ED during off-hours, regular hours, weekends, and weekdays. During off-hours, the rate of PCI and differences in door-to-balloon times have been reported to likely be associated with limited staff availability.[2] However, Parikh et al. reported that "Code STEMI" could decrease the median door-to-balloon duration (112 min before vs. 74 min after Code STEMI; p < 0.001) and LOS (4 days before vs. 3 days after; p < 0.01).[14] In one previous study, there was no significant difference in all-cause mortality;[15] however, a systematic review and meta-analysis revealed higher in-hospital and 30-day mortality in patients with AMI during off-hours versus those admitted during regular hours.[2] The observed disparities in mortality between studies may be due to differences in the demographics of the patients with STEMI, with the mortality rates being especially high in studies conducted outside of North America, and, importantly, these rates appear to have worsened in recent years.[2] Increased in-hospital mortality in AMI has been reported to be associated with off-hour admission in developing countries of EMS. For example, in Iraq, Al-Asadi et al. reported that off-hour admission was significantly associated with higher mortality as compared to admission during working hours (25.5% vs. 3%; $p < 0.001$).[16] The delay of the time from onset of symptoms to successful PCI was closely associated with poor short-term outcomes.[17] The current guidelines suggest a first medical contact-to-device time system within 90 minutes as the optimal time for treatment.[5 17 18] Besides decreasing the door-to-balloon time, additional efforts are needed to reduce the prehospital time after symptom onset, such as increased education efforts and campaigns for the general population and EMS, coordination between the EMS and ED, performance of 12-lead ECG by the EMS at the site of first medical contact, and prehospital transmission of ECG.[18] If we consider the lower levels of public awareness and education about AMI among the EMS and staff in many developing countries of EMS, implementation of an organized CP for AMI management could theoretically attenuate differences in the CP during off-hours and weekends compared to during working hours and weekdays. Herein, the FIRST CP focused on patients with suspected or distracting symptoms for AMI admitted to the ED and who had a relatively short door-to-data (completion of an ECG) interval in the ED. Atypical symptoms are often present in patients with STEMI. Na et al. showed that STEMI patients presenting without chest pain had longer door-to-data and door-to-PCI times than patients presenting with chest pain. In fact, presentation without chest pain was an independent predictor of hospital mortality in patients with STEMI after primary PCI.[19] Unfortunately, the acquisition of an ECG may be omitted in the initial assessments of these patients to the ED, and a delayed door-to-data interval may be the most critical factor for longer door-to-balloon times in patients with STEMI. Thus, standardization of the door-to-data protocol can help improve early recognition in emergency situations.[14]

The low level of awareness of the public and EMS in Korea may lead to the importance of rapid recognition, diagnosis, and treatment of ACS and cardiac arrest being neglected. Frequently, patients with STEMI do not exactly describe symptoms characteristic of STEMI. Despite risk stratification in the ED, it is thus possible that cardiologists might aggressively conduct primary PCI. Several studies have reported that the proportion of AMI patients with door-to-balloon times less than 90 min varies, ranging from 6.3–98.5%.[14 20] Pan et al. showed that implementing specific strategies improved the proportion of patients who underwent PCI within 90 minutes from 59.4% to 98.5% ($p < 0.001$).[9] On the other hand, our study did not show significant differences in the proportions of patients who underwent PCI within 90 minutes, regardless of the arrival time to the ED, ranging from 89.6–95.1%. Several studies have moreover reported that there was no significant difference in mortality in patients with AMI admitted during regular vs. off-hours.[21 19 22] However, in one study, patients with AMI admitted during off-hours were less likely to undergo primary PCI and more likely to undergo fibrinolytic therapy. Consequently, there was no difference in the overall usage of reperfusion therapy, irrespective of the arrival time.[21] In another study, the clinical effectiveness of PCI performed in a highly specialized STEMI network system was equivalent between regular and off-hours admissions at the regional level.[22.] A dedicated cardiac care network usually consists of a prehospital pathway, EMS training, priority for laboratory studies and emergency care, and 24 hours/day and 7 days/week availability of specialized cardiologists.[10] The coordination of the above elements can overcome the deleterious effects of admission during off-hours and weekends.[10] However, it should be noted that many of the previous studies on the topic were conducted in areas with well-organized cardiac care centers in developed countries.

Practice guidelines for decision support and disease-specific order sets can be embedded in the CPOE system.[9 10 23] In clinical practice, a CPOE system based on predetermined order sets is not simply a computer network, but can provide many communication advantages, including clarification and tracking of the completion of orders and errors.[9] Our FIRST protocol, based on a CPOE system, facilitates the simultaneous utilization of a multidisciplinary team approach, which has benefits for reducing medical errors and improving the quality of the critical process.[10] However, the successful operation of a CP requires standardization and simple protocols, regular educational opportunities, and feedback from clinical results.[10] As in the story of "crying wolf" in Aesop's fables, repeated false and true alarms may cause an alarm fatigue effect and desensitization to alarms.[24] In ischemic stroke patients, it has been reported that the behavior of the physician may result in a so-called 3-hour effect and a longer door-to-needle waiting time.[12] Nevertheless, alarm fatigue can be reduced and that the behavior of physicians can be changed by using a multidisciplinary team approach and education on the relevant issues, the optimization of alarms, and a systematic perspective for reducing alarm fatigue.[24 25]

The present study should be considered in the context of several limitations. First, it was impossible to perform a direct internal comparison with clinical data obtained before the implementation of a CP based on the CPOE system, because it was difficult to select a cohort with similar inclusion criteria as that of our current study population. Further studies are needed to assess the outcomes before and after the implementation of a CP based on CPOE for patients with AMI. Second, we only assessed short-term mortality and time factors in a relatively small population during a 30-day period and a single LOS. In the future, prospective multicenter studies with a larger number of patients will be needed to confirm the usefulness of implementation of this CP in terms of the time factors and mortality, including long-term outcomes, in patients with STEMI. Lastly, delayed diagnosis of STEMI and the presence of severe disease can increase the door-to-balloon time and mortality; however, patients who experienced return of spontaneous circulation after out-of-hospital cardiac arrest or ST-segment elevation on follow-up ECG only were not included in the present study, because it would have been impossible to compare the time factors based on the arrival time to the ED for these patients.

CONCLUSION

A multidisciplinary CP based on a CPOE system for STEMI can effectively decrease disparities in the door-to-data interval and the proportions of patients with door-to-balloon times within 90 minutes, regardless of the ED arrival time. The application of a multidisciplinary CP may also help attenuate off-hour and weekend effects in the clinical outcomes of STEMI patients.

Contributors

Conceived and designed the study: YSP, SPC, HSL, JHH, and JSY

Performed the study: YSP, MJK, HSC, SPC, JWW, IP and JSY,

Analyzed the data: YSP, SPC, HSL, JHH, IP and JSY

Contributed to the writing of the manuscript: YSP, JSY, and SPC

Other (Manuscript editing): all authors

Competing interests

The authors declare no conflict of interest.

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Data Sharing Statement

No additional data are available.

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Figure and Table Legends

Table 1. Clinicodemographic characteristics of all patients

Table 2. Time intervals and clinical outcomes of all patients

Table 3. Effects of the door-to-balloon duration during PCI and the activation of FIRST-to-balloon duration during PCI on in-hospital and 30-day mortality with respect to the ED arrival time

Figure 1. Proportions of patients with door-to-balloon times within 90 minutes with respect to the emergency department arrival time.

Figure 2. Kaplan-Meier survival curves with log-rank test analysis for comparisons of in-hospital (A) and 30-day (B) mortality with respect to the emergency department arrival time.

FIRST: the Fast Interrogation Rule for ST-elevation myocardial infarction program.

Characteristics	Median(Min-Max)				Overall	Post hoc analysis p-value					
	(Group 1) (n = 206)	(Group 2) (n = 154)	(Group 3) (n = 61)	(Group 4) (n = 67)		(1) vs. (2)	(1) vs. (3)	(1) vs. (4)	(2) vs. (3)	(2) vs. (4)	(3) vs. (4)
Age (years)	64 (32-98)	62 (29-91)	63 (41-91)	63 (28-92)	0.8381						
Sex					0.2205						
Male	162 (78.64)	131 (85.06)	45 (73.77)	52 (77.61)							
Female	44 (21.36)	23 (14.94)	16 (26.23)	15 (22.39)							
Systolic BP (mmHg)	125 (43-223)	131 (59-268)	130 (68-220)	133 (65-202)	0.4672						
Diastolic BP (mmHg)	79.5 (9-133)	82.5 (43-184)	82 (40-122)	80 (43-125)	0.1289						
Pulse rate (bpm)	79.5 (34-150)	80 (35-145)	82 (43-134)	81 (34-156)	0.7674						
Diabetic mellitus	67 (32.52)	48 (31.17)	21 (34.43)	25 (37.31)	0.8251						
Hypertension	115 (55.83)	75 (48.7)	26 (42.62)	41 (61.19)	0.1028						
Chronic kidney disease	11 (5.34)	8 (5.19)	1 (1.64)	4 (5.97)	0.666						
Stroke	12 (5.83)	11 (7.14)	2 (3.28)	3 (4.48)	0.7574						
Variant angina	3 (1.46)	1 (0.65)	1 (1.64)	1 (1.49)	0.8251						
Stable angina	5 (2.43)	4 (2.6)	2 (3.28)	2 (2.99)	0.9306						
Myocardial infarction	12 (5.83)	12 (7.79)	1 (1.64)	4 (5.97)	0.4066						
Heart failure	3 (1.46)	3 (1.95)	1 (1.64)	1 (1.49)	0.9534						
S/P PTCA	17 (8.25)	19 (12.34)	4 (6.56)	10 (14.93)	0.2487						
S/P CABG	1 (0.49)	1 (0.65)	1 (1.64)	1 (1.49)	0.4873						
Current smoker	81 (39.32)	74 (48.05)	20 (32.79)	35 (52.24)	0.0535						
Hypercholesterolemia	17 (8.25)	11 (7.14)	3 (4.92)	6 (8.96)	0.8339						
Family history of					0.0122*	0.0096	0.5918	0.6816	0.0217	0.2422	0.4972

CAD											
No	201 (97.57)	141 (91.56)	61 (100)	65 (97.01)							
Yes	5 (2.43)	13 (8.44)	0 (0)	2 (2.99)							
Height (cm)	167 (140-186)	168 (140-183)	167 (146-178)	168 (140-190)	0.4864						
Weight (kg)	65 (43-96)	69.3 (37.5-120)	65.3 (17.2-86)	68.3 (36.1-133)	0.0417*	0.0334	0.3858	0.1586	0.0189	0.8591	0.0657
Creatine kinase	143.5 (20-5514)	127 (14-10560)	122 (53-8400)	110 (25-2132)	0.222						
Creatine kinase -MB	4.43 (0.56-619.4)	3.32 (0.7-638)	5.29 (0.92-600)	3.5 (0.76-172.8)	0.2161						
Troponin-T	0.06 (0-10)	0.03 (0-9.86)	0.06 (0-10)	0.04 (0-18.22)	0.0959						
Mode of transport					0.3446						
1	105 (50.97)	88 (57.14)	38 (63.33)	37 (55.22)							
2	101 (49.03)	66 (42.86)	22 (36.67)	30 (44.78)							
Killip class					0.3609						
1	125 (60.68)	104 (67.53)	34 (56.67)	42 (62.69)							
2	28 (13.59)	13 (8.44)	8 (13.33)	13 (19.4)							
3	23 (11.17)	20 (12.99)	7 (11.67)	7 (10.45)							
4	30 (14.56)	17 (11.04)	11 (18.33)	5 (7.46)							
CPR in ED					0.1134						
No	201 (97.57)	154 (100)	59 (96.72)	66 (98.51)							
Yes	5 (2.43)	0(0)	2 (3.28)	1 (1.49)							
Chest pain					0.8045						
No	23 (11.17)	13 (8.44)	5 (8.2)	6 (8.96)							
Yes	183 (88.83)	141 (91.56)	56 (91.8)	61 (91.04)							
PCI lesion					0.191						
1	94 (46.08)	65 (42.76)	39 (65)	31 (46.27)							
2	77 (37.75)	52 (34.21)	15 (25)	24 (35.82)							

3	9 (4.41)	12 (7.89)	1 (1.67)	4 (5.97)
4	24 (11.76)	23 (15.13)	5 (8.33)	8 (11.94)

Table 1. Clinicodemographic characteristics of all patients

The patients were divided into four groups: group 1 (patients who arrived during working hours on a weekday), group 2 (patients who arrived during off-hours on a weekday), group 3 (patients who arrived during working hours on a weekend), and group 4 (patients who arrived during off-hours on a weekend).

BP: blood pressure; PTCA: percutaneous transluminal coronary angioplasty; CABG: coronary artery bypass graft; CPR: cardiopulmonary resuscitation; ED: emergency department; PCI: percutaneous coronary intervention; CAD: coronary artery disease; *: $p < 0.05$.

	Median(Min-Max)				Overall	Post hoc analysis p-value					
	(Group 1) (n = 206)	(Group 2) (n = 154)	(Group 3) (n = 61)	(Group 4) (n = 67)	p-value	(1) vs. (2)	(1) vs. (3)	(1) vs. (4)	(2) vs. (3)	(2) vs. (4)	(3) vs. (4)
Time outcomes											
Door to ECG (min)	3 (0-64)	2 (0-26)	1 (0-38)	3 (0-49)	0.0749	0.1503	0.0648	0.437	0.4433	0.0728	0.0324*
ECG to FIRST (min)	4 (0-64)	4 (0-29)	4 (0-26)	4 (0-27)	0.7129	0.6651	0.3966	0.7804	0.262	0.9623	0.3577
FIRST to balloon (min)	41.5 (16-210)	52 (22-147)	53 (13-96)	59 (25-98)	<.0001*	<.0001*	<.0001*	<.0001*	0.9656	0.0102*	0.0368*
Door to balloon (min)	51.5 (22-226)	62 (31-152)	61 (26-130)	71 (27-124)	<.0001*	<.0001*	0.0024*	<.0001*	0.5535	0.0078*	0.0068*
Length of stay	5 (1-61)	5 (1-54)	5 (3-55)	5 (1-43)	0.3127	0.2591	0.5076	0.0781	0.8758	0.3835	0.393
Clinical outcomes											
In-hospital mortality (1-5)					0.9107	0.5822	0.7922	0.9565	0.5764	0.6421	0.8644
1	188 (91.26)	143 (92.86)	55 (90.16)	61 (91.04)							
2	18 (8.74)	11 (7.14)	6 (9.84)	6 (8.96)							
30-day mortality					0.8173	0.4315	0.7922	0.7441	0.3981	0.7767	0.6323
1	188 (91.26)	144 (93.51)	55 (90.16)	62 (92.54)							
2	18 (8.74)	10(6.49)	6 (9.84)	5 (7.46)							

Table 2. Time intervals and clinical outcomes of all patients

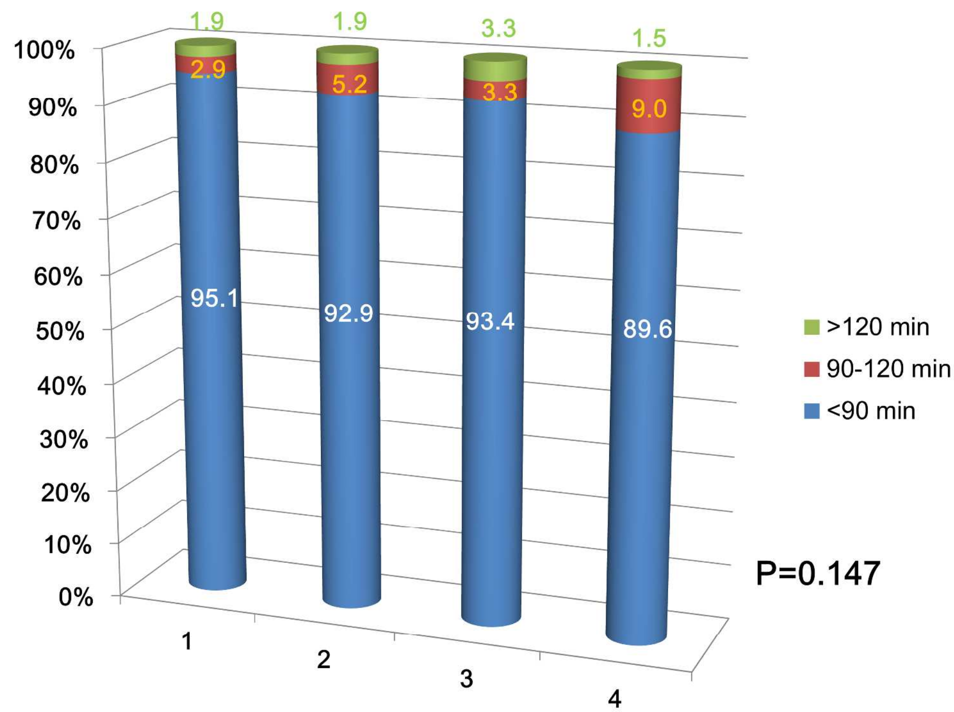
The patients were divided into four groups: group 1 (patients who arrived during working hours on a weekday), group 2 (patients who arrived during off-hours on a weekday), group 3 (patients who arrived during working hours on a weekend), and group 4 (patients who arrived during off-hours on a weekend).

ECG: electrocardiography; FIRST: the **F**ast **I**nterrogation **R**ule for **ST-**elevation myocardial infarction program; *: $p < 0.05$.

In-hospital mortality	HR(95% CI)	p-value
FIRST to PCI (min)	1.005 (0.992-1.019)	0.4522
Door to PCI (min)	1.000 (0.987-1.014)	0.9851
30-day mortality	**HR(95% CI)**	**p-value**
FIRST to PCI (min)	1.000 (0.987-1.014)	0.9851
Door to PCI (min)	1.006 (0.992-1.019)	0.4122

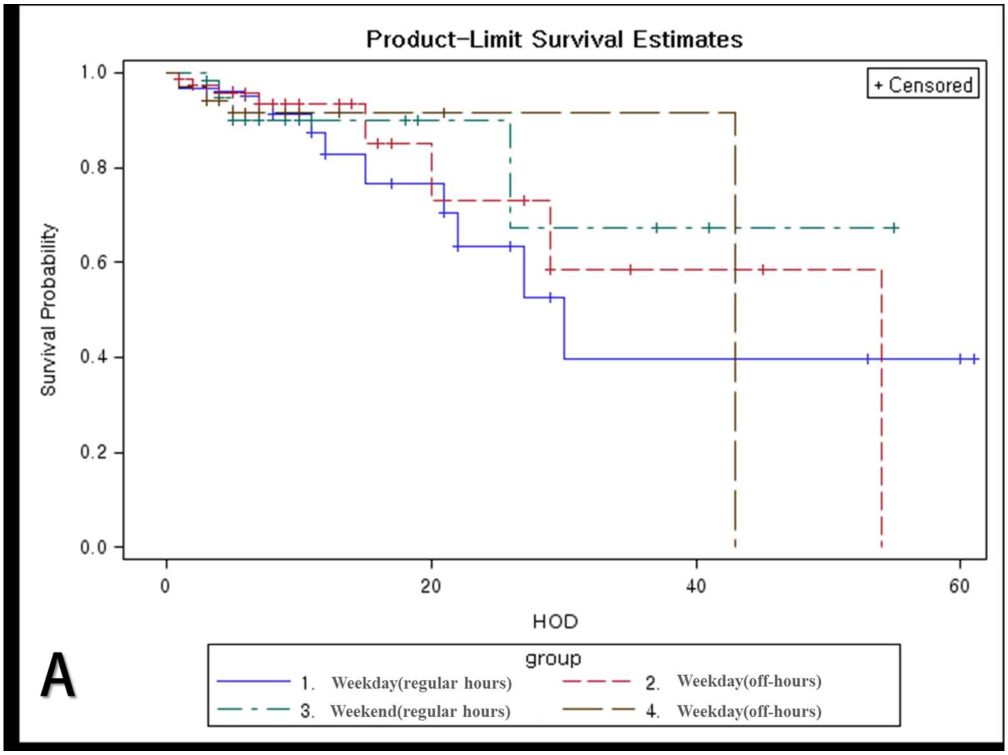
Table 3. Effects of the door-to-balloon duration for PCI and the activation of FIRST-to-balloon duration for PCI on in-hospital and 30-day mortality with respect to the ED arrival time

HR: hazard ratio; CI: confidence interval; FIRST: the **F**ast **I**nterrogation **R**ule for **ST**-elevation myocardial infarction (FIRST) program; PCI: percutaneous coronary intervention.



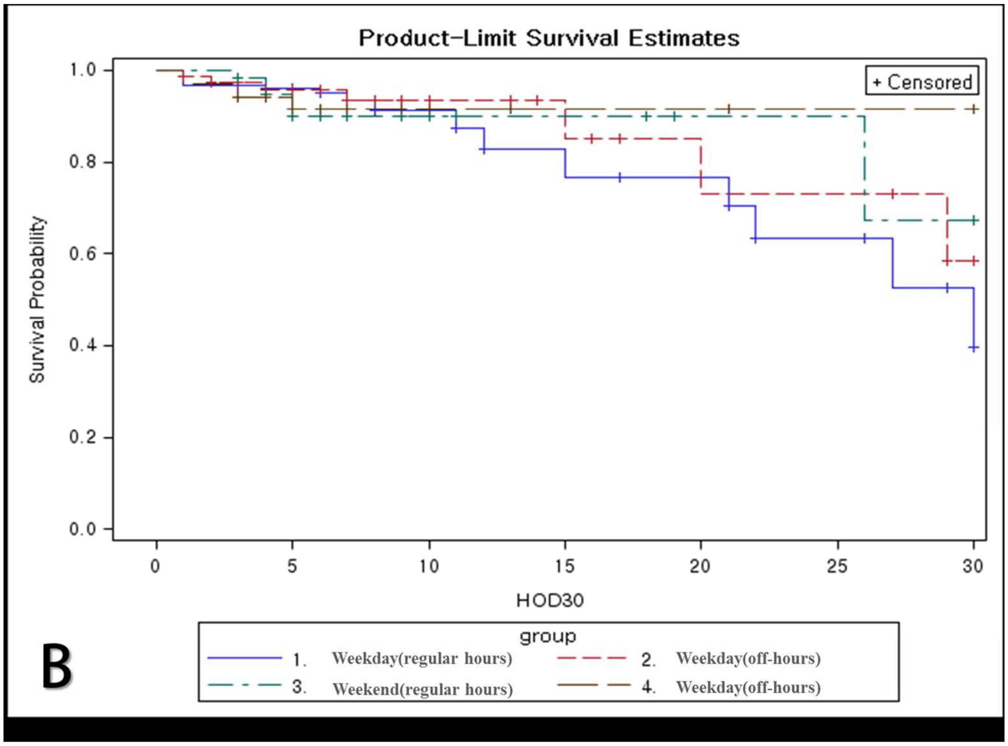
The proportions of patients with door-to-balloon times within 90 minutes with respect to ED arrival time.

254x190mm (300 x 300 DPI)



Survival curves were obtained by a Kaplan-Meier analysis, and the log-rank test was performed for comparisons of in-hospital (A) and 30-day mortality (B) with respect to emergency department arrival time. FIRST: the Fast Interrogation Rule for ST-elevation myocardial infarction program

246x183mm (300 x 300 DPI)



Survival curves were obtained by a Kaplan-Meier analysis, and the log-rank test was performed for comparisons of in-hospital (A) and 30-day mortality (B) with respect to emergency department arrival time.
FIRST: the Fast Interrogation Rule for ST-elevation myocardial infarction program

246x181mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6,7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6,7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7-9
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	7-9
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8,9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8,9
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	6,7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8,9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			NA

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	10-11
Outcome data	15*	Report numbers of outcome events or summary measures over time	10-11, Table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11, Table 2
		(*b*) Report category boundaries when continuous variables were categorized	10-11, Table2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Table 3
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14,15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.