Association Between Off-Hour Presentations And In-Hospital Mortality For Patients With Acute ST-Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention

Association Between Off-hour Presentations and In-hospital Mortality for Patients with Acute ST-Elevation Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention

Elnaz Javanshir [a], Elham Darzi Ramandi [a], Samad Ghaffari [a], Babak Nasiri [b], Haleh Bodagh [a], Ghiti Davarmoin [a], Naser Aslanabadi [a], Ahmad Separham [a],*

[a] Cardiovascular Research Center, Tabriz University of Medical Science, Madani Heart Center, Cardiology Department, Daneshgah Ave, Tabriz, Iran
[b] Cardiovascular Research Center, Tabriz University of Medical Science, Madani Heart Center, Cardiac Surgery Department, Daneshgah Ave, Tabriz, Iran

Abstract

Objectives: This study aimed to assess the effect of the admission time (on-hours versus off-hours) on in-hospital mortality in patients with ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PPCI) in a region without STEMI network.

Methods: We analysed in-hospital the mortality among 300 consecutive ST-segment elevation myocardial infarction (STEMI) patients treated with PPCI between March 2012 and February 2017. Patients were divided according to admission time into on-hours admission (08:00 AM until 08:00 PM on weekdays) versus off-hours admission (08:00 PM until 08:00 AM on weekdays and 24 h on weekends and holidays). Demographic and clinical data as well as in-hospital mortality were compared between the two groups.

Results: One hundred and seventy eight (59.3%) patients were admitted during on-hours, and 122 (40.7%) patients were presented in off-hours. The mean door-to-balloon time was 42.3 min in the off-hours group and 34.2 min in the on-hours group with no statistically significant difference (p = 0.39). The mortality rate was 3.9% at on-hours presentation versus 4.09% in off-hours admission (p = 0.58). Multivariate logistic regression analysis showed that off-hours presentation was not associated with in-hospital mortality. [odds ratio (OR) 0.74; 95% CI, 0.21−2.61, p = 0.64].

Conclusion: Despite no efficient STEMI network in present study, off-hour presentation had no significant impact on in-hospital prognosis in patients with STEMI treated with PPCI. Larger studies are warranted in order to determine the prognostic role of off-hour presentation in patients with STEMI undergoing PPCI.

Keywords: Acute myocardial infarction, In-hospital mortality, Off-hours, Primary percutaneous coronary intervention, STEMI network

1. Introduction

T reatment of ST-elevation myocardial infarction (STEMI) has been revolutionized drastically since the introduction of primary percutaneous coronary intervention (pPCI) [1]. However, only timely pPCI is the preferred therapy for this purpose indicating that "time is muscle". Although challenging, "timely" is generally defined as the shortest time from the onset of symptoms to the balloon inflation, which is associated with

higher myocardial salvage and lower mortality rates [2].

Another factor that may influence the outcome of STEMI patients is on-hours versus off-hours (i.e., non-working hours, weekends, and holidays) presentation. There is controversy about effect of off-hour admission time on short and long-term outcomes of patients treated with primary coronary angioplasty. Some studies have shown a higher mortality rate when it occurs over off-hours mainly due to logistic reasons [3,4] while others have shown contrary result as pPCI during off-hours was not associated with increased mortality rates [4,5].

The dilemma is further complicated because some evidence suggests that total ischemic time, may be longer in subjects who arrive at the pPCI-capable hospitals over on-hours than those presented during off-hours. This could be due to low traffic load in off-hours during transfer of patients from other non-pPCI-capable facilities [6].

On the other hand, most of these studies comes from countries with well-developed STEMI network with established transfer facilities and prehospital well-trained staffs. Little is known about the impact of off-hour admission in regions like Middle East with poor financial resources and major health problems including lack of efficient STEMI network. So, this study aimed to assess the effect of the admission time (on-hours versus off-hours) on in-hospital prognosis in patients with ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PPCI) in a region without STEMI network.

2. Methods and Materials

This was a retrospective single study that enrolled 300 patients with acute STEMI treated with pPCI in Madani hospital as main tertiary teaching heart center in Tabriz city in northwest of Iran between March 2012 and February 2017 (Fig. 1). Tabriz, the city in which the study was conducted, is an industrial city located in the northwest of Iran and has a population of about one million and seven hundred thousand according to 2016 census (https://www.amar.org.ir/).

Also, population density in this city is about 7559 per Km^2 (http://www.demographia.com/db-worldua.pdf). There are six hospitals in this city which perform coronary intervention, two of them including Madani heart center are public and the rest are private. The Madani heart center has four catheterization laboratory and eight interventional cardiologist work in this hospital.

Abbreviations

AM	before midday
BMS	Bare metal stent
DES	Drug eluting stent
ECG	Electrocardiogram
LAD	Left Anterior Descending artery
LCX	Left Circumflex artery
LM	Left Main artery
MI	Myocardial infarction
PPCI	primary percutaneous coronary intervention
PM	after midday
PCI	percutaneous coronary intervention
RCA	Right coronary artery
STEMI	ST-Elevation Myocardial Infarction
TIMI	Thrombolysis in myocardial infarction
24/7	twenty-four hours a day and seven days a week

Like most of other regions of country, there was no established STEMI network in this region at the time of study. Although, there has been some efforts for implementation of such network in recent years. The STEMI protocol applied in the hospital was based on diagnosis by the emergency physicians: if patient was eligible for reperfusion therapy, the decision on the type of reperfusion was made by the emergency physician considering availability of interventional devices like coronary guidewires, guiding catheters, balloons and stents in the hospital as shortage of these devices were not uncommon in the hospital during study period. If so, main reperfusion strategy was thrombolysis, otherwise patients were transferred to catheterization laboratory for primary angioplasty. All fibrinolysis were done in emergency room in this center and not in pre-hospital setting.

We excluded patients with incomplete data, unsuitable coronary anatomy, paced rhythm and non-diagnostic electrocardiogram (ECG) as well as patients receiving thrombolysis in this center or other centers. We also exclude rescue PCI cases. Patients were eligible if they were age 18 years or older and admitted with acute STEMI within 12 h of the onset of the symptoms. STEMI was diagnosed based on following criteria: typical chest pain lasting more than 30 min, ST segment elevation 0.1 mV in at least two contiguous leads and elevated troponin levels. A 12-lead ECG was recorded on admission and 60 min after PCI. ST-segment elevation was recorded 20 msec after the J point. ST-segment resolution ≥50% 1 h after primary angioplasty in the lead with maximal ST-segment elevation in baseline electrocardiogram were measured and recorded. All patients were given oral aspirin (325 mg) and Clopidogrel (600 mg) on admission in the
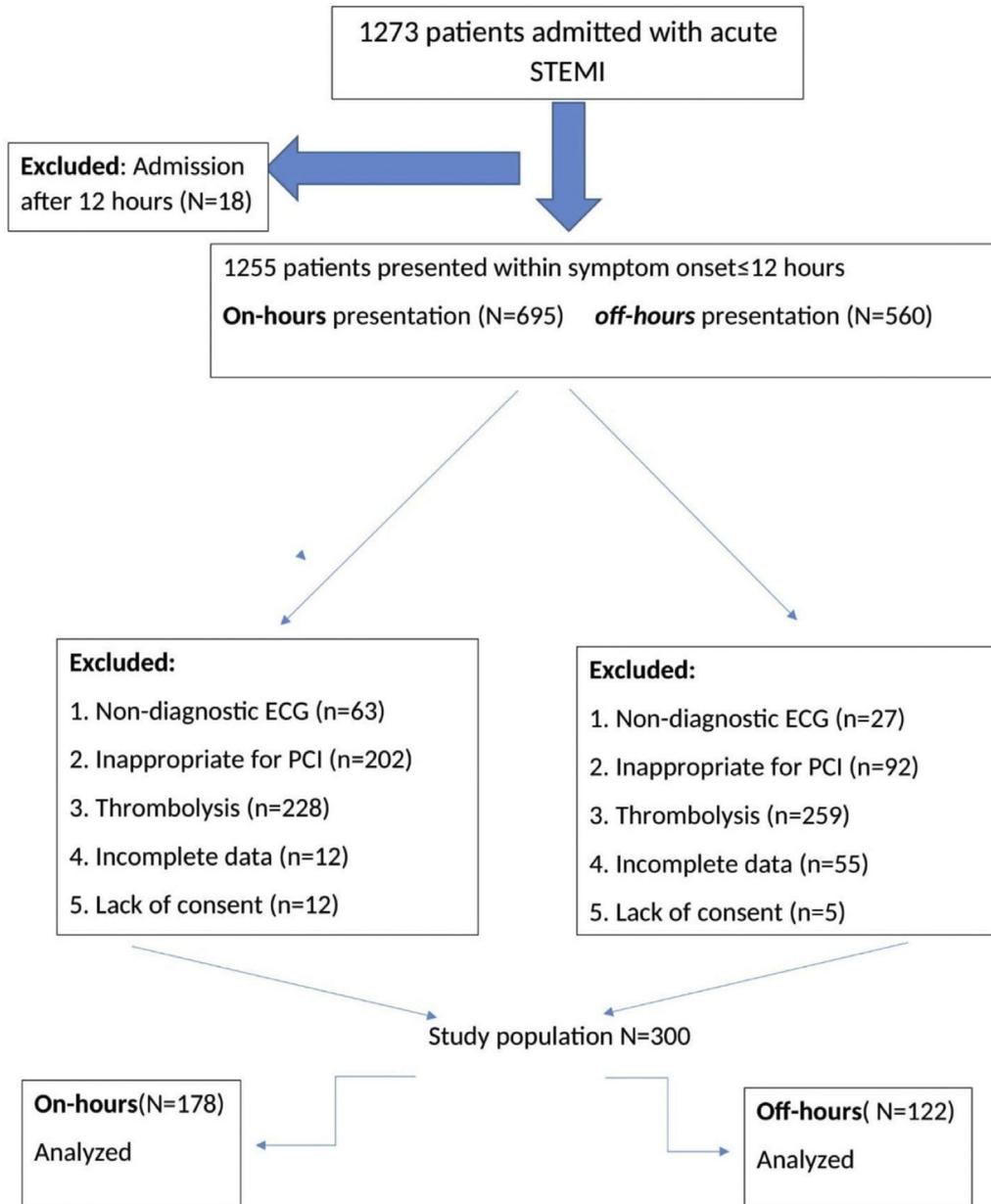
Fig. 1. Flow chart of the study.

emergency room. A bolus of 100 IU/kg of IV heparin was administrated before angioplasty. Thrombectomy device and Eptifibatide use was dependent on operator's decision. Baseline and post-PCI coronary flow were assessed by Thrombolysis in Myocardial Infarction (TIMI) flow grading system in the infarct-related artery. Patients were divided according to admission time into on-hours admission (08:00 AM until 08:00 PM on weekdays) versus off-hours admission (08:00 PM until 08:00 AM on weekdays and 24 h on weekends and holidays). Demographic and clinical data as well as in-hospital mortality as main outcome measure were compared between two groups. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki and was reviewed and approved by the Ethics Committee of the Tabriz University of Medicine. Informed written consent was obtained from all patients or appropriate legally authorized representatives.

3. Statistics Analysis

For continuous variables, data were expressed as means ± SD or median (quartile range) if the data were not normally distributed and categorical data as prevalence and percentages. Quantitative variables were compared using student t-test or

Wilcoxon signed-rank test for non-normally distributed data and categorical variables using chi-square test or Fisher's exact test. Univariate and multivariate logistic regression analyses were performed to identify the determinants of in-hospital mortality. For this analysis, the following variables (potential confounders) were included in the model: age, sex, diabetes mellitus, hypertension, total ischemic time, door to balloon time, ST-segment resolution >50%, initial TIMI flow, anterior wall myocardial infarction, and off-hours presentation.

All tests of significance were two-tailed, and p values of <0.05 were considered significant. The statistical analyses were performed by SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

4. Results

Among 300 patients, (59.3%) patients were admitted during on-hours, and 122 (40.7%) patients were presented in off-hours. The majority of patients (86%) presented to hospital by themselves and not ambulance services or other medical facilities. Table 1 summarizes baseline clinical and angiographic data for each of the 2 groups. Baseline findings were comparable although in the off-hours group there was a higher prevalence of hypertensive patients (43.4% vs 30.9%, p = 0.02).

Overall in-hospital mortality was 4% (n = 12). The mortality rate was 3.9% at on-hours presentation versus 4.09% in off-hours admission (p = 0.58). In multivariate logistic regression analysis, off-hour presentation was not associated with the inhospital mortality. [odds ratio (OR) 0.74; 95% CI, 0.21—2.61, p = 0.64]. On the other hand, diabetes mellitus and anterior wall myocardial infarction were independent predictors of in-hospital mortality (Table 2).

Also, angiographic data were similar in both groups. With respect to delay times, total ischemic time as well as door to balloon time were not significantly different between two groups. Longer total ischemic time in both groups could be due to lack of an integrated STEMI network in our region as mentioned previously. Complete ST-segment resolution as the main determinant of reperfusion success was comparable in both groups (71.4% vs. 64.8%; p = 0.22).

5. Discussion

The main findings of this study can be summarized as follows. First, Off-hour presentation didn't increase in-hospital mortality of patients with STEMI treated with pPCI in a region without efficient STEMI network. Second, time delay between symptom onset and mechanical reperfusion was relatively similar in on-hours and off-hours presenters. Third, off-hour presentation was not independent predictor of in-hospital mortality.

In present study, despite no established network for diagnosis and rapid transfer of patients with

Table 1. Baseline patient characteristics.

Variables		On-hours n = 178	Off-hours n = 122	p value
Age (mean ± SD, years)		58.53 ± 11.9	57.53 ± 12.2	0.48
Male n (%)		151 (84.8)	104 (85.2)	0.92
Previous PCI n (%)		0 (0)	1 (0.8)	0.4
Previous MI n (%)		1 (0.5)	1 (0.8)	0.6
Hypertension n (%)		55 (30.9)	53 (43.4)	0.02
Hyperlipidemia n (%)		1 (0.5)	2 (1.6)	0.36
Diabetes mellitus n (%)		32 (17.9)	29 (23.7)	0.22
Smoking n (%)		59 (33.1)	48 (39.3)	0.27
Total ischemic time (minutes) (Median (IQR))		480 (390—570)	487 (390—600)	0.34
Door to balloon time (minutes) (Median (IQR))		120 (90—150)	120 (90—165)	0.71
ST-segment resolution>50% n (%)		127 (71.4)	79 (64.8)	0.22
Anterior MI n (%)		97 (54.5)	67 (55)	0.94
Killip class n (%)	1	147 (82.6)	104 (85.5)	
	2	26 (14.6)	16 (13.3)	
	3	5 (2.8)	2 (1.1)	0.76
	4	0 (0)	0 (0)	
Angiographic data				
Initial coronary TIMI flow n (%)	0	128 (71.9)	88 (72.2)	
	1	12 (6.8)	9 (7.3)	0.8
	2	15 (8.4)	13 (10.6)	
	3	23 (12.9)	12 (9.9)	
Final coronary TIMI flow n (%)	0	1 (0.5)	0 (0)	
	1	2 (1.1)	0 (0)	0.23
	2	0 (0)	2 (1.6)	
	3	175 (98.4)	120 (98.4)	
BMS n (%)		51 (29.6)	23 (18.9)	0.45
DES n (%)		127 (71.4)	99 (81.1)	0.99
Culprit Vessel				
LM n (%)		16 (8.9)	14 (11.5)	0.44
LAD n (%)		130 (73.2)	79 (64.7)	
LCX n (%)		9 (5)	10 (8.2)	
RCA n (%)		23 (12.9)	19 (15.6)	

BMS: Bare metal stent; DES: Drug eluting stent; LAD: Left Anterior Descending artery; LCX: Left Circumflex artery; LM: Left Main artery; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; RCA: Right coronary artery; TIMI: Thrombolysis in myocardial infarction; Total ischemic time: The time from the onset of chest pain to the first balloon inflation.

Table 2. *Univariate and multivariate logistic regression analysis for in-hospital mortality.*

Variables	Univariate		Multivariate	
	OR (95%CI)	P-value	OR (95%CI)	P-value
Age	0.97 (0.93−1.02)	0.372		
Sex	1.95 (0.51−7.51)	0.330		
HTN	0.26 (0.07−0.91)	**0.034**	1.87 (0.47−7.36)	0.366
DM	0.165 (0.5−0.54)	**0.003**	5.94 (1.57−22.47)	**0.009**
Initial coronary TIMI flow	0.77 (0.48−1.24)	0.293		
Total ischemic time	1 (0.99−1)	0.580		
Door to balloon time	1 (0.99−1)	0.3		
ST-segment resolution'50%	1.1 (0.32−3.74)	0.879		
Anterior MI	3.8 (1−14.33)	**0.049**	0.21 (0.05−0.87)	**0.032**
Off-hour presentation	1.04 (0.32−3.36)	0.943	0.748 (0.21−2.61)	0.649

DM: Diabetes mellitus, HTN: Hypertension, TIMI: Thrombolysis in myocardial infarction. p values of <0.05 were considered significant.

acute STEMI for timely mechanical reperfusion, presentation during weekends or holidays and out of regular times (namely off-hours) wasn't associated with poor in-hospital outcomes. This was evident in angiographic finding and complete ST-segment resolution rate between study groups. ST-segment resolution $\geq 50\%$ as one of the most determinant factor for reperfusion success was similar between on-hours patients and off-hours patients. Also, TIMI flow III after procedure as one of the main predictor of myocardial salvage was identical in both groups. Longer ischemic time in present study may be due to lack of efficient STEMI network, as most patients in present study didn't use ambulance transportation (only 14%). Though, this long time could potentially affect patient's prognosis in present study, this was not the case. It seems that well-trained personnel staffs and physicians as well as high volume coronary angioplasty procedures in our hospital has attenuated the unfavorable effects of long ischemic time.

Timing of hospital admission (i.e., on-hours vs. off-hours) may partially affect the outcomes of STEMI patients undergoing pPCI. However, findings were not universal, and not all studies support the mentioned hypothesis. The results of present study are similar to recent studies that mostly conducted in countries with well-known and established STEMI network and "24/7 PPCI facilities" [7−9]. On the other hand, our results contradicts with the finding by Cubeddu et al. published in 2009 [4]. Better interventional device and improvement in pharmacotherapy during primary angioplasty in recent years may explain this difference.

Opposed to the findings of the present study and previous literature a comprehensive systematic review and meta-analysis of 48 studies [10−15] conducted on 1 896 859 patients assessed the impacts of off-hours presentation on the outcomes in patients with STEMI undergoing pPCI. The findings of this meta-analysis showed that off-hour presentation in subjects with STEMI was associated with higher short term mortality (OR 1.06, 95% confidence interval 1.04 to 1.09). This study also revealed that patients presented during off-hours tended to have lower rates of pPCI within 90 min (OR 0.40, 0.35 to 0.45) and longer door to balloon time as much as 14.8 min (95% confidence interval 10.7 to 19.0) [16].

The discrepancy found between the finding of this large meta-analysis and presented study could arise from several facts. These studies were mostly observational and non-randomized. As mentioned earlier, the country in which the study is performed seems to exert an important effect of the results. Publication bias is also a contributing factor to the observed differences between studies. Some confounding factors such as differences in sample sizes, race, culture, etc. could account for the observed effects and a high rate of heterogeneity between the existing data which could affect the outcomes. Differences between cares providing in off-times in different countries may also change the outcomes. This was visible in Becker et al., a study which showed that hospitalization during off times namely weekends provoked delayed provision of intensive procedures such pPCI and increased one-year mortality rate for patients presenting with STEMI [17].

Our study has several limitations: 1) limited number of patients, 2) retrospective, non- randomized and single center nature of the study and 3) lack of long-term follow-up. These shortcomings should be meticulously addressed in future studies.

In conclusion, despite no efficient STEMI network in present study, off-hour presentation had no significant impact on in-hospital prognosis in patients

with STEMI treated with primary PCI. Larger studies are warranted in order to determine prognostic role of off-hour presentation in patients with STEMI undergoing primary angioplasty.

Funding

Author Contribution

Elnaz Javanshir: Conception, Analysis And/Or Interpretation, Writer, Critical Review. **Ahmad Separham**: Conception, Analysis And/Or Interpretation, Writer, Critical Review. **Naser Aslanabadi**: Design, Critical Review. **Samad Ghaffar**: Supervision, Fundings, Critical Review. **Babak Nasiri**: Supervision. **Elham Darzi Ramandi**: Materials, Data Collection And/Or Processing, Critical Review. **Ghiti Davarmoin**: Literature Review. **Haleh Bodag**: Literature Review.

Declaration of Competing Interest

The authors declare no potential conflict of interest.

Acknowledgement

References

[1] van der Meer MG, Nathoe HM, van der Graaf Y, Doevendans PA, Appelman Y. Worse outcome in women with STEMI: a systematic review of prognostic studies. European J Clin Invest 2015;45:226—35.

[2] Bhatt DL. Timely PCI for STEMI–still the treatment of choice. N Engl J Med 2013;368:1446—7.

[3] Cubeddu RJ, Cruz-Gonzalez I, Kiernan TJ, Truong QA, Rosenfield K, Leinbach RC, et al. ST-elevation myocardial infarction mortality in a major academic center" on-" versus" off-" hours. J Invasive Cardiol 2009;21:518—23.

[4] Ortolani P, Marzocchi A, Marrozzini C, Palmerini T, Saia F, Aquilina M, et al. Clinical comparison of "normal-hours" vs "off-hours" percutaneous coronary interventions for ST-elevation myocardial infarction. Am Heart J 2007;154: 366—72.

[5] de Boer SP, Oemrawsingh RM, Lenzen MJ, van Mieghem NM, Schultz C, Akkerhuis KM, et al. Primary PCI during off-hours is not related to increased mortality. European heart J Acute cardiovascular care 2012;1:33—9.

[6] Mizuguchi Y, Shibutani H, Hashimoto S, Yamada T, Taniguchi N, Nakajima S, et al. Onset-to-device time of patients who arrive at off-hours: importance of prehospital management and public awareness for patients with ST-segment elevation myocardial infarction. Cardiovascular Ther 2016;34:475—81.

[7] Ogita M, Suwa S, Ebina H, Nakao K, Ozaki Y, Kimura K, et al. Off-hours presentation does not affect in-hospital mortality of Japanese patients with acute myocardial infarction: J-MINUET substudy. J Cardio. 2017;70:553—8.

[8] Casella G, Ottani F, Ortolani P, Guastaroba P, Santarelli A, Balducelli M, et al. Off-hour primary percutaneous coronary angioplasty does not affect outcome of patients with ST-Segment elevation acute myocardial infarction treated within a regional network for reperfusion: the REAL (Registro Regionale Angioplastiche dell'Emilia-Romagna) registry. JACC Cardiovasc Interv 2011;4:270—8.

[9] Tscharre M, Jäger B, Farhan S, et al. Impact of time of admission on short- and long-term mortality in the Vienna STEMI registry. Int J Cardiol 2017;244:1—6.

[10] Sadeghi HM, Grines CL, Chandra HR, Mehran R, Fahy M, Cox DA, et al. Magnitude and impact of treatment delays on weeknights and weekends in patients undergoing primary angioplasty for acute myocardial infarction (the CADILLAC trial). Am J Cardiol 2004;94:637—40.

[11] Kostis WJ, Demissie K, Marcella SW, Shao Y-H, Wilson AC, Moreyra AE. Weekend versus weekday admission and mortality from myocardial infarction. N Engl J Med 2007;356: 1099—109.

[12] Krüth P, Zeymer U, Gitt A, Jünger C, Wienbergen H, Niedermeier F, et al. Influence of presentation at the weekend on treatment and outcome in ST-elevation myocardial infarction in hospitals with catheterization laboratories. Clin Res Cardiol 2008;97:742.

[13] Magid DJ, Wang Y, Herrin J, McNamara RL, Bradley EH, Curtis JP, et al. Relationship between time of day, day of week, timeliness of reperfusion, and in-hospital mortality for patients with acute ST-segment elevation myocardial infarction. J Am Med Assoc 2005;294:803—12.

[14] Ryan JW, Peterson ED, Chen AY, Roe MT, Ohman EM, Cannon CP, et al. Optimal timing of intervention in non—ST-segment elevation acute coronary syndromes: insights from the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) Registry. Circulation 2005;112:3049—57.

[15] Jneid H, Fonarow GC, Cannon CP, Palacios IF, Kilic T, Moukarbel GV, et al. Impact of time of presentation on the care and outcomes of acute myocardial infarction. Circulation 2008;117:2502—9.

[16] Sorita A, Ahmed A, Starr SR, Thompson KM, Reed DA, Prokop L, et al. Off-hour presentation and outcomes in patients with acute myocardial infarction: systematic review and meta-analysis. BMJ 2014;348:f7393.

[17] Becker DJ. Do hospitals provide lower quality care on weekends? Health Serv Res 2007;42:1589—612.