Total ischemic time and outcomes for patients with ST-elevation myocardial infarction: does time of admission make a difference?

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Abstract

Objective To investigate whether admission time was associated with the delay of reperfusion therapy and in-hospital death in patients with ST-elevation myocardial infarction (STEMI).

Methods All patients with STEMI who were admitted to the emergency department and underwent primary percutaneous coronary intervention at Peking University People’s Hospital between April 2012 and March 2015 were included. We examined differences in clinical characteristics, total ischemic time, and in-hospital death between patients admitted during off-hours and those admitted during regular hours. Multivariate logistic regression was used to estimate the relationship between off-hours admission and clinical outcome.

Results The sample comprised 184 and 105 patients with STEMI admitted to hospital during off-hours and regular hours, respectively. Total ischemic and onset-to-door times were significantly shorter in patients admitted during off-hours than among those admitted during regular hours (all \( P < 0.05 \)). Door-to-balloon (DTB) time, the rate of DTB time \( \leq 90 \) min, and in-hospital death were comparable between groups. Multivariate logistic regression showed that age and creatinine level, but not off-hours admission, were associated independently with increased in-hospital death.

Conclusions Off-hours admission did not result in delayed reperfusion therapy or increased in-hospital mortality in patients with STEMI. Further efforts should focus on identifying pivotal factors associated with the pre-hospital and in-hospital delay of reperfusion therapy, and implementing quality improvement initiatives for reperfusion programs.

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1 Introduction

Myocardial reperfusion with primary percutaneous coronary intervention (PCI), performed in a timely fashion, is the central therapy for ST-segment elevation myocardial infarction (STEMI). The maximum myocardial salvage gained from reperfusion therapy is generally accepted to occur within the first few hours of symptom onset, the amount of salvage then decreases sharply over subsequent hours. The total ischemic time, measured from symptom onset to the provision of reperfusion therapy, is thus of paramount importance for the outcomes of patients with STEMI, and it should be considered carefully in assessing the time to reperfusion.

With the implementation of various quality improvement strategies for patients with STEMI, the timeliness of reperfusion therapy has improved substantially. A plateau in clinical outcomes may have been achieved in developed countries. However, the majority of patients with STEMI are still not treated within the guideline-recommended door-to-balloon time of \( \leq 90 \) min. In China, pre-hospital and in-hospital delays in the initiation of reperfusion therapy with primary PCI remain significant. In addition, in-hospital mortality of patients with STEMI has not decreased in the past decade, according to the most recent nationally representative China PEACE study. Thus, the identification of patient- and doctor-related reasons for delays in reperfusion therapy and adverse clinical outcomes in China is urgently needed.
Due to the circadian variation in the onset of acute myocardial infarction (AMI), several studies have investigated the relationship between the time of patient admission and the performance of reperfusion therapy or clinical outcomes. These studies have consistently shown that patients with STEMI who arrive at hospitals during “off-hours” (weekday nights, weekends, and holidays) are less likely to receive timely reperfusion than are those who arrive at hospitals during regular hours. However, results on differences in clinical outcomes related to these admission times are conflicting due mainly to differences in patient characteristics and health care systems.

All of the studies mentioned above were performed in developed countries. Marked differences in patients’ knowledge about AMI, emergency medical services (EMS), and PCI team components of care exist between these developed countries and China. At present, little is known about whether off-hours admission is associated with delayed reperfusion therapy with primary PCI and/or worse clinical outcomes in China. Thus, this study aimed to compare the effect of admission time (off-hours vs. regular hours) on total ischemic time in patients with STEMI, and to evaluate whether this factor affects in-hospital death in clinical practice.

2 Methods

2.1 Study population and setting

All patients with STEMI who were admitted to the emergency department and underwent primary PCI within 12 h of symptom onset at Peking University People’s Hospital between April 2012 and March 2015 were included in this study. Our hospital, one of the academic teaching centers of Peking University, performs about 800 PCIs annually and provides 24/7 interventional cardiac care. The hospital’s primary PCI protocol for patients with STEMI was developed to provide rapid and optimal reperfusion therapy, and it represents the majority of practice at PCI-capable hospitals in China. The study was approved by our institutional review board.

2.2 STEMI and primary PCI

STEMI was diagnosed and treated in accordance with the most recent guidelines. Briefly, STEMI was defined as new ST-segment elevation > 0.1 mV on at least two contiguous electrocardiographic leads or left bundle-branch block in patients with AMI. Experienced interventional cardiologists performed primary PCI in all eligible patients with STEMI with symptom onset within the previous 12 h. Routine medical therapies administered during the perioperative period consisted of aspirin (300 mg orally followed by 100 mg once daily), clopidogrel (300 mg orally followed by 75 mg once daily), low-molecular-weight heparin, and/or platelet glycoprotein IIb/IIIa receptor antagonists. In addition, secondary preventive therapies, including statins, β-blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers, were indicated for all patients with STEMI in the absence of contraindication.

2.3 Time of admission

Patients with STEMI were divided into the regular hours and off-hours groups according to the day and time of admission. Based on the conventional working schedules of hospitals in China, regular hours were defined as weekdays from 8:00 AM to 6:00 PM, and off-hours were defined as weekdays from 6:01 PM to 7:59 AM and all weekends and holidays.

2.4 Total ischemic time

Total ischemic time was defined as the time from the onset of chest pain to the first balloon inflation during primary PCI. This period consisted of onset-to-door and door-to-balloon times. Onset-to-door time was defined as the time from symptom onset to emergency department arrival, and door-to-balloon time denoted the time from emergency department arrival to the first balloon inflation. Information on the timing of symptom onset was obtained by patient interviews. The times of emergency department arrival and the first balloon inflation were obtained from patients’ medical records.

2.5 Clinical data and outcome measures

Demographic and clinical characteristics of patients with STEMI (age, sex, medical history, Killip class, peak cardiac troponin I and creatine kinase-MB isoenzyme levels, lipid profiles, serum creatinine and hemoglobin concentrations) were recorded. The angiographic and procedural characteristics recorded were the number of diseased vessels, culprit lesion, and intra-aortic balloon pump or temporary pacemaker use. In addition, data on medical therapies administered during hospitalization were collected. The primary outcome for patients with STEMI was in-hospital death.

2.6 Statistical analysis

Statistical analysis was performed with SPSS software (ver. 20.0; IBM Corporation, Armonk, NY, USA). Continuous variables with normal and skewed distributions were presented as means ± SD and medians (25th, 75th per-

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centiles), respectively. Continuous variables were compared using the unpaired Student’s t test or the Mann–Whitney U test, according to the distribution of data. Categorical variables were described by absolute counts (percentages) and assessed using the chi-squared test. The primary analyses were performed at the admission-time level (off-hours vs. regular hours). Next, multiple logistic regression models were used to estimate whether admission time was associated independently with the primary outcome of in-hospital death. Statistical significance was defined as $P < 0.05$.

3 Results

3.1 Baseline characteristics

A total of 289 patients with STEMI who underwent primary PCI were included in this study. Among these patients, 105 and 184 were admitted during regular hours and off-hours, respectively. The frequency of stroke history was significantly higher (12.5% vs. 3.8%, $P = 0.015$) and that of statins prescription was slightly lower (89.7% vs. 96.2%, $P = 0.049$) in the off-hours group than in the regular hours group (Table 1). No significant difference in any other demographic, clinical, angiographic, or procedural characteristic or medical therapy was found between groups.

3.2 Total ischemic time

In the total sample, total ischemic time, onset-to-door time, door-to-balloon time and the rate of door-to-balloon time were performed at the admission-time level (off-hours ($n = 105$), or median (25th–75th percentile). Continuous variables were compared using the unpaired Student’s t test or the Mann–Whitney U test, according to the distribution of data. Categorical variables were described by absolute counts (percentages) and assessed using the chi-squared test. The primary analyses were performed at the admission-time level (off-hours vs. regular hours). Next, multiple logistic regression models were used to estimate whether admission time was associated independently with the primary outcome of in-hospital death. Statistical significance was defined as $P < 0.05$.

3.3 Clinical outcomes

The rate of in-hospital death did not differ significantly between the off-hours and regular hours groups (6.5% vs. 1.9%, $P = 0.146$). Primary univariate analyses showed significant differences in age, sex, diabetes, stroke history, heart rate, creatinine level, hemoglobin level, intra-aortic balloon pump use, and the lack of antiplatelet drug, statin, and β-blocker prescription between patients who did and did not die in hospital (all $P < 0.05$; Table 3). However, the

| Characteristic | Regular hours ($n = 105$) | Off-hours ($n = 184$) | $P$ |
|---------------|-----------------|-----------------|----|
| Males | 78 (74.3%) | 139 (75.5%) | 0.812 |
| Age, yrs | 63.2 ± 13.1 | 62.1 ± 13.4 | 0.502 |
| Medical history | | | |
| Hypertension | 55 (52.4%) | 115 (62.5%) | 0.093 |
| Diabetes | 23 (21.9%) | 55 (29.9%) | 0.142 |
| Hyperlipidemia | 27 (25.7%) | 52 (28.3%) | 0.641 |
| CHD | 15 (14.3%) | 32 (17.4%) | 0.492 |
| Prior MI | 3 (2.9%) | 15 (8.2%) | 0.074 |
| Stroke | 4 (3.8%) | 23 (12.5%) | 0.015 |
| Smoking | 57 (54.3%) | 112 (60.9%) | 0.275 |
| CHD family history | 15 (14.3%) | 28 (15.2%) | 0.829 |
| SBP, mmHg | 118.1 ± 17.6 | 117.9 ± 20.1 | 0.957 |
| DBP, mmHg | 70.6 ± 12.9 | 70.7 ± 12.8 | 0.959 |
| Killip class | 0.615 | | |
| I | 86 (81.9%) | 146 (79.3%) | |
| II | 15 (14.3%) | 24 (13.0%) | |
| III | 1 (1.0%) | 5 (2.7%) | |
| IV | 3 (2.9%) | 9 (4.9%) | |
| Peak Tnl, ng/dL | 39.4 (12.5, 97.0) | 51.0 (16.6, 97.0) | 0.417 |
| Peak CK-MB, U/L | 132.0 (49.8, 297.4) | 162.8 (54.7, 300.0) | 0.193 |
| CHO, mmol/L | 4.49 ± 0.94 | 4.63 ± 1.05 | 0.261 |
| TG, mmol/L | 1.42 (1.03, 2.04) | 1.53 (0.99, 2.33) | 0.225 |
| HDL-C, mmol/L | 0.93 (0.83, 1.11) | 0.95 (0.80, 1.12) | 0.568 |
| LDL-C, mmol/L | 2.94 (1.03, 2.04) | 2.96 (0.99, 2.33) | 0.225 |
| HGB, g/L | 136.8 ± 19.1 | 140.7 ± 19.4 | 0.098 |
| Number of coronary vessels | 0.422 | | |
| 1 | 23 (21.9%) | 43 (23.6%) | |
| 2 | 39 (37.1%) | 54 (29.7%) | |
| 3 | 43 (41.0%) | 85 (46.7%) | |
| LM | 10 (9.5%) | 17 (9.2%) | 0.733 |
| Culprit lesion | 0.859 | | |
| LAD | 56 (53.3%) | 106 (57.8%) | |
| LCX | 11 (10.5%) | 20 (10.9%) | |
| RCA | 37 (35.2%) | 57 (31.0%) | |
| LM | 1 (1.0%) | 1 (0.5%) | |
| IABP use | 3 (2.9%) | 6 (3.3%) | 0.849 |
| Temporary pacemaker | 2 (1.9%) | 2 (1.1%) | 0.567 |
| Aspirin | 104 (99.0%) | 182 (98.9%) | 0.914 |
| Clopidogrel | 104 (99.0%) | 182 (98.9%) | 0.914 |
| Statins | 101 (96.2%) | 165 (96.2%) | 0.049 |
| β-blockers | 96 (91.4%) | 158 (85.9%) | 0.164 |

Data are presented as mean ± SD, n (%), or median (25th–75th percentile). CHD: coronary heart disease; CHO: cholesterol; CK-MB: creatine kinase-MB isoenzymes; CRE: creatinine; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; HGB: hemoglobin; IABP: intra-aortic balloon pump; LAD: left anterior descending; LCX: left circumflex; LDL-C: low-density lipoprotein cholesterol; LM: left main; MI: myocardial infarction; RCA: right coronary artery; SBP: systolic blood pressure; TG: triglyceride; Tnl: troponin I.
percentages of admission during off-hours were comparable between these groups. Multivariate logistic regression analysis showed that only age [odds ratio (OR): 1.100, 95% confidence interval (CI): 1.005–1.203; \( P = 0.039 \)] and creatinine level (OR: 1.007, 95% CI: 1.001–1.012; \( P = 0.017 \)), and not admission time or other clinical characteristics, were associated independently with increased in-hospital death (Table 4).

### Table 2. Treatment times for patients with STEMI according to admission time.

| Variable       | Regular hours \((n = 105)\) | Off-hours \((n = 184)\) | \( P \) |
|----------------|-----------------------------|------------------------|------|
| OTD time, min  | 153.00 (61.00, 300.00)       | 111.50 (60.00, 197.80) | 0.018|
| DBT time, min  | 116.00 (94.50, 168.50)       | 128.50 (101.25, 170.50) | 0.336|
| DTB time \(\leq 90\) min | 19.0% | 15.8% | 0.474|
| TI time, min   | 314.50 (205.75, 512.50)      | 263.50 (191.25, 383.75) | 0.040|

Data are presented as median (25th–75th percentile) or percent. DTB: door-to-balloon; OTD: onset-to-door; TI: total ischemic.

### Table 3. Baseline characteristics of patients with STEMI according to in-hospital death.

| Characteristic | All \((n = 289)\) | In-hospital death \((n = 14)\) | No in-hospital death \((n = 275)\) | \( P \) |
|---------------|-----------------|-----------------|-----------------|------|
| Males         | 217 (75.1%)     | 5 (35.7%)       | 212 (77.1%)     | 0.000|
| Age, yrs      | 62.5 ± 13.3     | 78.1 ± 12.1     | 61.8 ± 12.9     | 0.000|
| Hypertension  | 170 (58.8%)     | 10 (71.4%)      | 160 (58.2%)     | 0.326|
| Diabetes      | 78 (27.0%)      | 7 (50.0%)       | 71 (25.8%)      | 0.047|
| Hyperlipidemia| 79 (27.3%)      | 3 (21.4%)       | 76 (27.6%)      | 0.611|
| CHD           | 47 (16.3%)      | 3 (21.4%)       | 44 (16.0%)      | 0.591|
| Stroke        | 27 (9.3%)       | 6 (42.9%)       | 21 (7.6%)       | 0.000|
| Smoking       | 169 (58.5%)     | 5 (35.7%)       | 164 (59.6%)     | 0.076|
| CHD family history | 43 (14.9%) | 1 (7.1%) | 42 (15.3%) | 0.599|
| SBP, mmHg     | 118.0 ± 19.2    | 113.6 ± 21.2    | 118.2 ± 19.1    | 0.387|
| DBP, mmHg     | 70.7 ± 12.8     | 66.4 ± 11.1     | 70.9 ± 12.9     | 0.206|
| Heart rate, beats/min | 79.3 ± 15.2 | 89.1 ± 16.4 | 78.8 ± 15.0 | 0.013|
| Peak TnI, ng/dL | 5.02 (4.0, 9.70) | 95.6 (39.1, 100.0) | 48.2 (13.9, 97.0) | 0.208|
| Peak CK-MB, U/L | 154.5 (49.6, 300.0) | 299.0 (44.4, 310.0) | 151.1 (49.8, 299.1) | 0.107|
| CHO, mmol/L   | 4.58 ± 1.01     | 4.27 ± 1.15     | 4.59 ± 1.01     | 0.264|
| TG, mmol/L    | 1.49 (1.01, 2.17) | 1.12 (0.74, 2.30) | 1.50 (1.03, 2.16) | 0.260|
| HDL-C, mmol/L | 0.94 (0.82, 1.11) | 0.84 (0.72, 1.06) | 0.94 (0.82, 1.12) | 0.257|
| LDL-C, mmol/L | 2.95 ± 0.95     | 2.59 ± 0.86     | 2.97 ± 0.95     | 0.159|
| CRE, μmol/L   | 74.5 (63.0, 89.0) | 103.0 (73.5, 210.3) | 74.0 (62.0, 88.0) | 0.001|
| HGB, g/L      | 139.3 ± 19.3    | 121.4 ± 16.0    | 140.1 ± 19.1    | 0.001|
| IABP use      | 9 (3.1%)        | 4 (28.6%)       | 5 (1.8%)        | 0.000|
| Temporary pacemaker | 4 (1.4%) | 1 (7.1%) | 3 (1.1%) | 0.059|
| Aspirin       | 286 (99.0%)     | 13 (92.9%)      | 273 (99.3%)     | 0.021|
| Clopidogrel   | 286 (99.0%)     | 13 (92.9%)      | 273 (99.3%)     | 0.021|
| Statins       | 254 (87.9%)     | 7 (50%)         | 247 (89.8%)     | 0.000|
| β-blockers    | 266 (92.0%)     | 8 (57.1%)       | 258 (93.8%)     | 0.000|
| TI time       | 273.0 (195.8, 421.8) | 305.5 (200.8, 462.8) | 273.0 (195.0, 421.3) | 0.676|
| DTB time      | 126.0 (100.3, 169.0) | 136.0 (99.5, 173.3) | 125.5 (100.8, 167.5) | 0.924|
| OTD time      | 122.0 (60.0, 218.5) | 158.0 (70.0, 343.0) | 122.0 (60.0, 217.0) | 0.409|
| Off-hours admission | 184 (63.6%) | 12 (85.7%) | 172 (62.5%) | 0.079|

Data are presented as mean ± SD, \( n \) (%), or median (25th–75th percentile). CHD: coronary heart disease; CHO: cholesterol; CK-MB: creatine kinase-MB isoenzymes; CRE: creatinine; DBP: diastolic blood pressure; DTB: door-to-balloon; HDL-C: high-density lipoprotein cholesterol; HGB: hemoglobin; IABP: intra-aortic balloon pump; LDL-C: low-density lipoprotein cholesterol; OTD: onset-to-door; SBP: systolic blood pressure; TG: triglyceride; TI: total ischemic; TnI: troponin I.

4 Discussion

In the context of modern STEMI treatment in China, this study investigated whether hospital admission time was associated with delayed reperfusion therapy and adverse in-hospital outcome. The major findings were as follows: (1) an important gap exists between the clinical performance of timely reperfusion therapy and the guideline-recommended timing for patients with STEMI; (2) total ischemic time and...
onset-to-door time were significantly shorter in patients with STEMI admitted during off-hours than in those admitted during regular hours, but the door-to-balloon time and the rate of door-to-balloon time ≤ 90 min were comparable; and (3) no significant difference in in-hospital death was found between patients admitted during off-hours and regular hours, and off-hours admission was not associated with increased in-hospital death for patients with STEMI undergoing primary PCI.

The principle of “time is muscle, time is life” is generally accepted to guide AMI management decisions. Timely myocardial reperfusion with primary PCI is the central therapy for STEMI. The Chinese medical care system has developed rapidly, and reperfusion strategies with primary PCI for patients with STEMI have improved gradually in the past decade. However, a series of studies has shown that an important gap still exists between the clinical performance of timely reperfusion therapy and the guideline-recommended timing for patients with STEMI. The CPACS-1 study, which included 2973 patients admitted to 51 hospitals in 18 provinces of China between September 2004 and May 2005, showed that only 6.6%–16.3% of patients with STEMI were not treated with PCI in a timely fashion, with significant delays in total ischemic time, onset-to-door time, and door-to-balloon time. According to previous studies and our clinical observations, the significantly longer total ischemic time can be accounted for mainly by patients’ lack of knowledge about heart attack symptoms and underuse of ambulances,[17–19] the delay in obtaining informed consent,[16] and the procedural complexity of hospital admission and PCI team activation.[16] Thus, further improvement of the quality of reperfusion therapy for patients with STEMI in China, through patient education and redesign of procedures involving EMS, emergency departments, and cardiac catheterization, is critically needed.

The term “off-hour effect” refers to the potential for increased reperfusion time and worse clinical outcomes in patients with AMI who present to the hospital during off-hours. Although numerous studies have investigated this effect in patients with STEMI, the results remain controversial.[6–12] In this study, we found no significant delay of reperfusion time in patients with STEMI who underwent primary PCI during off-hours. On the contrary, these patients had substantially shorter onset-to-door and total ischemic times than did those admitted during regular hours, with comparable door-to-balloon time and rate of door-to-balloon time ≤ 90 min.

Our onset-to-door time results are similar to those of a German chest pain unit registry study,[18] but differ from those of a retrospective study conducted in the UK,[19] a registry study conducted in Italy,[10] and a prospective study conducted in the USA.[6] In these studies, the median onset-to-door times during off-hours and regular hours ranged from 95 to 135 min and from 100 to 196 min, respectively. The significant variation in onset-to-door time among countries indicates that pre-hospital delay is a widespread issue for patients with STEMI, and that urgent measures should be taken to address it. Differences in onset-to-door time between off-hours and regular-hours admissions are associated closely with patient and EMS factors. Results of previous studies have suggested that patient awareness about cardiac arrest symptom, EMS usage, and traffic could account for the difference in onset-to-door time between off-hours and regular hours.[18] Therefore, further efforts must focus on patient knowledge about high-risk chest pain and use of EMS, and the optimization of EMS procedures for patients with STEMI.

Table 4. Multivariate analysis of in-hospital death among patients with STEMI.

| Variable         | OR    | 95% CI       | P   |
|------------------|-------|--------------|-----|
| Age              | 1.100 | 1.005–1.203  | 0.039 |
| Males            | 4.993 | 0.911–27.354 | 0.064 |
| Stroke           | 2.309 | 0.276–19.344 | 0.440 |
| Heart rate       | 1.033 | 0.994–1.073  | 0.096 |
| CRE              | 1.007 | 1.001–1.012  | 0.017 |
| HGB              | 0.994 | 0.952–1.037  | 0.764 |
| IABP use         | 6.176 | 0.886–43.069 | 0.066 |
| Statins          | 1.104 | 0.089–13.672 | 0.939 |
| β-blockers       | 0.207 | 0.019–1.325  | 0.109 |

CRE: creatinine; HGB: hemoglobin; IABP: intra-aortic balloon pump; STEMI: ST-segment elevation myocardial infarction.

According to previous studies and our clinical observations, the significantly longer total ischemic time can be accounted for mainly by patients’ lack of knowledge about heart attack symptoms and underuse of ambulances,[17–19] the delay in obtaining informed consent,[16] and the procedural complexity of hospital admission and PCI team activation.[16] Thus, further improvement of the quality of reperfusion therapy for patients with STEMI in China, through patient education and redesign of procedures involving EMS, emergency departments, and cardiac catheterization, is critically needed.

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Because door-to-balloon time is among the most important criteria for quality of PCI care in patients with STEMI, it has been investigated extensively in studies of the off-hours effect. The majority of registry and prospective studies and meta-analyses have shown that patients with STEMI presenting during off-hours were less likely to receive PCI within 90 min and had longer door-to-balloon times than did those presenting during regular hours.\cite{6-12} These differences were present, but not significant, in this study. The lengthening of door-to-balloon time is likely related to the availability of cardiologists and/or nurses for the cardiac catheterization laboratory; 24/7 interventional cardiac care with on-site PCI teams is not uniformly available. Hence, in-hospital programs in China and other countries should be improved to provide identical availability and quality of PCI care for patients with STEMI during off-hours and regular hours. Importantly, the delay represented by the door-to-balloon time was about two times longer in this study than in studies performed in the USA and Europe.\cite{6-12,18-20} This finding indicates that the quality of timely in-hospital reperfusion in China remains unsatisfactory, despite the implementation of quality improvement initiatives for several years. Further studies are needed to identify the determining factor associated with the in-hospital delay of reperfusion treatment, and effective measures should then be taken to reduce the delay in door-to-balloon time.

The difference in total ischemic time between off-hours and regular-hours admission in this study was driven by the compensatory effects of onset-to-door and door-to-balloon times. The shorter onset-to-door time and slightly longer door-to-balloon time during off-hours led to the reduced total ischemic time in the off-hours group. In studies performed in other countries, total ischemic time during off-hours has been significantly longer than\cite{6,10} or similar to\cite{18,19} that achieved during regular hours. This inconsistency of results is related mainly to variations in onset-to-door and door-to-balloon times among studies. In addition, total ischemic time during off-hours and regular hours was markedly longer in our study than in the studies mentioned above, driven largely by the significant delay in door-to-balloon time. Thus, hospital decision makers should pay more attention to these times and take urgent measures to shorten total ischemic time for patients with STEMI in China.

Although significant, the difference in total ischemic time did not have a meaningful effect on the short-term outcome of in-hospital death in this study. Similarly, most\cite{6,7,10-12,18-20} but not all\cite{9} studies have failed to identify worse clinical outcomes among patients with STEMI who were admitted during off-hours. These studies have documented slightly worse or similar outcomes during off-hours when differences in door-to-balloon and total ischemic times are \( < 30 \) min and \( < 60 \) min, respectively, although every minute of delay in reperfusion treatment can affect mortality in patients with STEMI. In the present study, the differences in door-to-balloon and total ischemic times were only \( 12.5 \) min and \( 51 \) min, respectively, which may explain the comparability of outcomes. The negligible effects of off-hours admission on short-term outcomes can also be explained by the overall improvement in STEMI reperfusion programs and evidence-based treatment through national or local quality improvement initiatives around the world. Similar clinical outcomes have been reported for STEMI patients admitted during off-hours and regular hours at hospitals with 24/7 on-site PCI teams in Turkey,\cite{21} Hungary,\cite{22} Poland\cite{23} and the Netherlands\cite{24}.

Our hospital has provided 24/7 interventional cardiac care with cardiologists and catheterization laboratory nurses since 2000. In addition, clinical outcomes did not differ according to admission time at hospitals participating in an established regional STEMI network in Italy,\cite{19} and the Get With The Guidelines program in the USA.\cite{7}

This study has several limitations. First, it was performed in a single academic hospital with a relatively small sample, which made it difficult to avoid selection bias. Thus, generalization of the results to other hospitals in China should be undertaken with caution. Second, because the in-hospital mortality rates were low, this study may not have adjusted for type II error. Third, our study may have been subject to recall bias, as patient interviews were used to determine the time of symptom onset. Fourth, information about the pathway of arrival at our hospital and inter-hospital transfer was not collected in this study, which may have affected the differences in total ischemic and onset-to-door times between regular hours and off-hours arrivals.

In summary, this study showed that pre-hospital and in-hospital delays were common and significant for patients with STEMI entering the modern health care system in China. These findings indicate the need to improve public education about heart attacks and redesign the health care system for patients with STEMI. We also found that total ischemic and onset-to-door times were shorter for these patients during off-hours than during regular hours, whereas the door-to-balloon time and the rate of door-to-balloon time \( \leq 90 \) min were similar. These findings indicate the need to improve pre-hospital care seeking (through patient education) and in-hospital programs (by optimizing interventional cardiac care for patients with STEMI). Finally, arrival time did not affect in-hospital mortality in patients with STEMI. These results underline the importance of short-
ening total ischemic time and implementing quality improvement initiatives for reperfusion programs to improve the prognoses of patients with STEMI.

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