



# Effect of Chinese national holidays and weekends versus weekday admission on clinical outcomes in patients with STEMI undergoing primary PCI

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## Abstract

**Background** Data regarding the influence of weekends and Chinese national holiday's admission on the outcomes of patients with ST-elevated myocardial infarction (STEMI) is lacking. This study sought to investigate the effect of Chinese national holidays and weekend admission on outcomes in patients with STEMI undergoing primary percutaneous coronary intervention (PPCI). **Methods** Patients presenting with STEMI within 12 h of symptom onset who underwent PPCI were retrospectively enrolled. The primary outcome of in-hospital mortality and major adverse cardiovascular events in patients presenting Chinese national holidays and weekends versus weekdays was evaluated. **Results** A total of 441 STEMI patients were enrolled in this study. Of these, 129 (29.3%) patients were admitted during Chinese national holidays and weekends and 312 (70.7%) during weekdays. Patients admitted during holidays and weekends were more likely to present with Killip class III-IV. Patients admitted during holidays and weekends experienced a significantly longer door-to-balloon time, symptom onset-to-door time as well as symptom onset-to-balloon time. The in-hospital mortality between patients presenting holidays and weekends versus weekdays was comparable. However, patients admitted during holidays and weekends have a significantly higher rate of in-hospital major adverse cardiovascular events. Multivariate analysis demonstrated that holidays and weekends admission was independently associated with adverse outcomes. **Conclusions** In China, STEMI patients undergoing PPCI during national holidays and weekends have worse in-hospital outcomes compared to those admitted during weekdays. These findings suggest that continuous efforts should be undertaken to enhance the Chinese healthcare system and to ensure that comparable outcomes are achieved for all STEMI patients regardless of time of presentation.

*J Geriatr Cardiol* 2017; 14: 604–613. doi:10.11909/j.issn.1671-5411.2017.10.003

**Keywords:** Holidays; Myocardial infarction; Percutaneous coronary intervention; Weekends

## 1 Introduction

Acute myocardial infarction (AMI) remains a leading cause of death in both developed and developing countries.<sup>[1]</sup> Improvement in clinical outcomes after ST-segment elevation myocardial infarction (STEMI) depends greatly on the timely utilization of evidence-based therapies with emphasis on the time to reperfusion.<sup>[2,3]</sup> Primary percutaneous coronary intervention (PPCI) is the preferred reperfusion strategy for STEMI when the first medical contact-to-balloon

time is achieved within 90 min and performed by experienced operators at high-volume hospitals.<sup>[3]</sup> Successful completion of PPCI procedures requires a team of interventional cardiologists and a well-established “on-call” system to minimize the time between admission to mechanical reperfusion therapy.<sup>[4]</sup> Thus, concerns have been raised by some investigators that PPCI performed during off-hours may not achieve comparable outcomes as compared to counterpart procedures performed during on-hours. Several prior studies have demonstrated that patients with STEMI undergoing PPCI during off-hours (weekday nights, weekends, and holidays) have higher mortality as compared to those admitted within regular working hours.<sup>[5–10]</sup> However, the data published to date remains controversial, because recent studies have reported inconsistent results.<sup>[11–15]</sup> Moreover, the influence of off-hours admission on clinical outcomes in patients with STEMI treated with PPCI varied among countries and most of the available data were derived from the Western developed countries.

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**Received:** May 7, 2017 **Revised:** August 20, 2017

**Accepted:** September 1, 2017 **Published online:** October 28, 2017

In China, the number of national holidays including traditional festival and weekend days has dramatically increased in from 59 days per year in 1949 to 108 days per year with the improvement of living standards and social welfare level. In recent years, a majority of Chinese medical facilities have adopted a therapeutic strategy of “around the clock” emergency PCI for STEMI patients. In spite of the changes in STEMI emergency care systems, it is unclear whether patients with STEMI undergoing PPCI during off-hours experienced similar mortality and clinical outcomes as those presenting during on-hours in China. However, this issue is of interest, as the Chinese healthcare system remains imperfect and reducing staffing may contribute to gaps in the quality of care during off-hours.<sup>[16–18]</sup> To date, data regarding the influence of off-hours admission on the clinical outcomes in patients with STEMI treated with PPCI in China is still lacking. Therefore, the goal of the present study was to investigate the effect of Chinese national holidays and weekends admission on short-term clinical outcomes in patients with STEMI undergoing PPCI.

## 2 Methods

### 2.1 Study population

Patients presenting with STEMI within 12 h of symptom onset who underwent PPCI at the Second Xiangya Hospital of Central South University from January 2010 to December 2015 were retrospectively enrolled in this study. The diagnosis of STEMI was based on chest pain lasting for more than 30 min, persistent ST-segment elevation ( $\geq 0.2$  mV in precordial leads) in at least two contiguous leads on a 12-lead ECG or a newly developed left bundle-branch block, and later confirmed by cardiac markers increase [e.g., cardiac troponin I (cTnI) > the 99<sup>th</sup> percentile upper reference limit].<sup>[2]</sup> Patients were excluded from the analysis if they presented with severe chronic renal or hepatic impairment and neoplastic disease, did not receive PPCI and underwent a rescue or a planned PCI immediately after thrombolysis, discharged to other medical facilities within 48 h, or had records with missing or incomplete data. The study was conducted in accordance with the Declaration of Helsinki and approved by the local hospital ethics committee.

Hospital arrival time was the primary basis for classification of the study cohort. Patients were classified into two groups: holidays-group (presenting during national holidays and weekends) and weekdays-group (presenting during regular weekdays) according to the day when they were admitted. Chinese national holidays included New Year's Day (3 days), Spring Festival (7 days), Qing Ming Festival

(3 days), International Labor Day (3 days), Dragon Boat Festival (3 days), Mid-autumn Festival (3 days) and Chinese National Day (7 days). The weekend was defined as the period from midnight on Friday to midnight on Sunday. All other times were defined as regular weekdays.

### 2.2 PPCI

During holidays and weekends, an on-call team was contacted upon acceptance of an STEMI patient for PPCI. Following an alert, the entire on-call team would arrive at the hospital within 30 min. During weekdays, an on-call team is always in the hospital and can perform PPCI as soon as necessary. PPCI was performed according to contemporary standard international guidelines at our institution.<sup>[19]</sup> All patients received loading oral dose of aspirin (300 mg) and clopidogrel (300 mg) on admission in the emergency department. All PPCI procedures were performed through the radial approach with a 6 French guiding catheter. An intravenous bolus of weight-adjusted unfractionated heparin was administered to achieve an activated clotting time of 200 to 250 s. Additional heparin, guided by activated clotting time, was administered during PCI. Use of either intracoronary or systemic bolus of tirofiban followed by a 12–24 h continuous infusion was left at the operator's discretion. Thrombus aspiration was recommended depending on relevant thrombus. Direct stenting (without balloon pre-dilatation) implantation was performed whenever possible. In case of multivessel disease, only the culprit vessel was treated during the initial PPCI. The PCI procedure was considered successful if stent deployment carried out at the desired site yielded residual stenosis  $\leq 20\%$  and achievement of TIMI grade-3 flow.<sup>[20]</sup> Post-PCI medication consisted of double anti-platelet therapy with aspirin 100 mg/d for lifelong and clopidogrel 75 mg/day for at least 12 months,  $\beta$ -blockers, angiotensin converting enzyme inhibitors, and statins were also given according to current guidelines.

### 2.3 Data collection

The clinical data were collected by trained staff reviewing medical records of all patients. Baseline variables included demographics, cardiovascular risk factors, medical history, physical findings and Killip classification on admission, left ventricular ejection fraction, laboratory tests, and the occurrence of mechanical complications of STEMI. We also specifically examined the differences in in-hospital therapies, including early medical treatments (within 24 h after hospital arrival), angiographic, procedural characteristics and the timeliness of reperfusion (including symptom-to-door time, door-to-balloon (DTB) time, the symp-

tom onset to-balloon time) among STEMI patients admitted during Chinese holidays and weekends versus weekdays.

## 2.4 Clinical outcomes

All adverse clinical events were adjudicated through the use of original source documentation by an independent committee who was unaware of the treatment allocation. The primary end points were in-hospital all-cause mortality and major adverse cardiovascular events (MACEs), which was defined as a composite of death, nonfatal reinfarction, target vessel revascularization, new-onset congestive heart failure and stroke during hospitalization.<sup>[21,22]</sup> Nonfatal myocardial infarction was defined as recurrent chest pain lasting for > 30 min, associated with new Q waves or recurrent ST-segment elevation  $\geq 0.1$  mV in standard leads and a re-elevation of creatine kinase-MB isoform to at least twice the upper limit of normal and/or > 50% greater than the previous value after the index procedure. In-hospital new-onset congestive heart failure was defined as the presence of dyspnea, Killip class  $\geq$  II, a third heart sound or evidence of pulmonary congestion on chest X-rays. Stroke was defined as neurological deficiencies that developed within 24 h of the PPCI procedure and that lasted for at least 12 h.

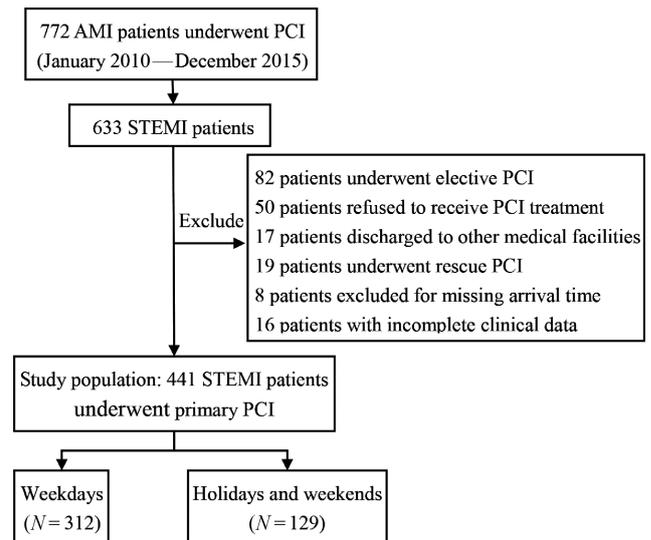
## 2.5 Statistical analysis

Continuous variables were tested for normal distribution by Kolmogorov-Smirnov test. Continuous data were reported as mean  $\pm$  SD or median with 25<sup>th</sup> and 75<sup>th</sup> percentiles (interquartile range, IQR) if not normally distributed and compared using Student's *t* test. Categorical data were expressed as percentages and compared by the chi-square test or Fisher's exact test. Multivariate logistic regression analysis was used to identify independent predictors of in-hospital MACEs. All variables with *P* values < 0.10 by univariate analysis were included in this multiple regression model. All statistical tests were performed using SPSS software, version 17.0 (SPSS Inc, Chicago, IL, USA). A *P* value of < 0.05 was regarded as statistically significant.

## 3 Results

### 3.1 Baseline characteristics

Of 633 consecutive patients who presented with STEMI within 12 h of symptom onset and scheduled for PPCI from January 2010 to December 2015, a total of 441 patients fit the inclusion criteria for this study. As shown in the Figure 1, there were 192 patients excluded from the study. The principal reasons for exclusion were: PCI was performed elec-



**Figure 1. Study population flow diagram.** AMI: acute myocardial infarction; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.

tively (82), refused to receive PCI treatment (50), discharged to other medical facilities within 48 h (17), rescue PCI after thrombolytic therapy performed (19), arrival time missing (8) and incomplete clinical data (16). Among this study population, 129 (29.3%) patients admitted during Chinese national holidays and weekends and 312 (70.7%) during weekdays.

Demographic, baseline clinical characteristics and laboratory variables of the enrolled patients are listed in Table 1. Baseline findings were comparable, although patients in the holidays-group had, on average, a significantly lower LVEF; moreover, those patients were more likely to present with Killip class III-IV. Otherwise, there were no significant differences between the two groups in terms of patient demographics, medical history, prevalence of coronary risk factors, physical findings on admission and concomitant medications. With respect to baseline laboratory findings, the plasma N-terminal pro-brain natriuretic peptide level on admission was significantly higher in the holidays-group.

The baseline angiographic features and procedural data are summarized in Table 2. No significant difference was observed between the two groups with regard to the location of culprit artery, initial TIMI flow grade, and prevalence of multivessel diseases. The intra-aortic balloon pump was used more often in holidays-group (*P* = 0.019). Other key procedural characteristics, such as the rate of direct stenting, and the frequency of thrombus aspiration use etc., indicate no significant difference between the two groups. Percent stent implantations were also similar between groups. The procedural success, as previously defined, was reached in

**Table 1. Baseline clinical characteristics.**

	Holidays-group (n = 129)	Weekdays-group (n = 312)	Statistic	P value
<b>Demographics</b>				
Age, yrs	61.18 ± 13.96	61.76 ± 12.18	-0.435*	0.660
Male sex	95 (73.6%)	250 (80.1%)	2.254 <sup>†</sup>	0.133
Body mass index, kg/m <sup>2</sup>	24.68 ± 2.37	24.96 ± 2.51	-2.375*	0.279
Admission at night	24 (18.6%)	61 (19.6%)	0.053 <sup>†</sup>	0.819
<b>Cardiovascular risk factors</b>				
Diabetes mellitus	32 (24.8%)	65 (20.8%)	0.840 <sup>†</sup>	0.360
Hypertension (> 140/90 mmHg)	76 (58.9%)	185 (59.3%)	0.005 <sup>†</sup>	0.941
Hyperlipidemia	39 (30.2%)	118 (37.8%)	2.292 <sup>†</sup>	0.130
Current smoker	75 (58.1%)	173 (55.4%)	0.268 <sup>†</sup>	0.604
<b>Number of cardiovascular risk factors</b>				
≥ 3	25 (19.4%)	65 (20.8%)	0.119 <sup>†</sup>	0.730
2	50 (38.8%)	117 (37.5%)	0.062 <sup>†</sup>	0.804
1	43 (33.3%)	103 (33.0%)	0.004 <sup>†</sup>	0.948
0	11 (8.5%)	27 (8.7%)	0.002 <sup>†</sup>	0.966
<b>Medical history</b>				
History of PCI	9 (7.0%)	20 (6.4%)	0.048 <sup>†</sup>	0.827
History of CABG	3 (2.3%)	6 (1.9%)	—	0.725
Previous MI	8 (6.2%)	21 (6.7%)	0.042 <sup>†</sup>	0.838
<b>Physical findings on admission</b>				
Systolic blood pressure, mmHg	114.7 ± 22.49	116.6 ± 23.73	-0.777*	0.441
Heart rate, beats/min	84 ± 19	82 ± 17	1.139*	0.256
<b>Killip classification on admission, n (%)</b>				
Class I	64 (49.6%)	167 (53.5%)	0.560 <sup>†</sup>	0.454
Class II	27 (20.9%)	85 (27.2%)	1.920 <sup>†</sup>	0.166
Class III- IV	38 (29.5%)	60 (19.2%)	5.522 <sup>†</sup>	0.019
Left ventricular ejection fraction	49.3% ± 12.1%	54.2% ± 10.9%	-4.156*	< 0.001
Ventricular septal rupture	8 (6.2%)	13 (4.2%)	0.833 <sup>†</sup>	0.361
<b>Medication within 24 h of hospital arrival</b>				
Aspirin	124 (96.1%)	291 (93.3%)	1.341 <sup>†</sup>	0.247
P2Y12 receptor inhibitor	125 (96.9%)	297 (95.2%)	0.645 <sup>†</sup>	0.422
GP IIb/IIIa receptor inhibitor	117 (90.7%)	279 (89.4%)	0.162 <sup>†</sup>	0.687
Beta-blockers	72 (55.8%)	195 (62.5%)	1.708 <sup>†</sup>	0.191
Statins	124 (96.1%)	298 (95.5%)	0.083 <sup>†</sup>	0.774
Angiotensin-converting enzyme inhibitors/ Angiotensin receptor blockers	87 (67.4%)	184(58.9%)	2.762 <sup>†</sup>	0.097
<b>Laboratory tests</b>				
Peak troponin I, pg/mL	12870 (2410–16000)	16000 (5889–16000)	-1.421 <sup>‡</sup>	0.174
Peak CK, U/L	2343.6 (1588.3–3930.5)	1612.9 (756.7–3122.1)	1.513 <sup>‡</sup>	0.116
Peak CK-MB, U/L	211.6 (59.7–359.8)	198.2 (89.9–382.4)	0.298 <sup>‡</sup>	0.783
NT-proBNP, pg/mL	2973.8 (1318.3–5167.7)	1506.1 (774.2–4045.3)	2.182 <sup>‡</sup>	0.037

Data are expressed as mean ± SD, n (%), or as median (Q<sub>1</sub>–Q<sub>3</sub>). \**t* value; <sup>†</sup> $\chi^2$  value; <sup>‡</sup>*U* value; —: data not available (Fisher exact test). CABG: coronary artery bypass graft; CK-MB: creatine kinase MB fractions; MI: myocardial infarction; PCI: percutaneous coronary intervention.

86.0% patients in the holidays-group and in 91.0% patients in the weekdays-group ( $P = 0.149$ ).

The intervals recorded during the study are summarized in Table 2. The total PPCI procedure time were similar between the two groups; However, patients admitted during

holidays and weekends had significantly longer symptom onset-to-door time (229 min, IQR: 157–315 min vs. 143 min, IQR: 72–232 min;  $P < 0.001$ ), DTB time (109 min, IQR: 75–152 min vs. 84 min, IQR: 59–121 min;  $P < 0.001$ ) as well as symptom onset to balloon (329 min, IQR: 210–478 min

**Table 2. Angiographic characteristics and procedural data.**

	Holidays-group ( <i>n</i> = 129)	Weekdays-group ( <i>n</i> = 312)	Statistic	<i>P</i> value
Time delays, min				
Symptom onset to balloon	329 (210–478)	211 (137–341)	11.273 <sup>‡</sup>	< 0.001
Door-to-balloon	109 (75–152)	84 (59–121)	10.856 <sup>‡</sup>	< 0.001
Symptom onset to door	229 (157–315)	143 (72–232)	12.363 <sup>‡</sup>	< 0.001
Total procedure time	52 (38–69)	48 (39–63)	1.162 <sup>‡</sup>	0.212
Infarct-related artery				
LM	4 (3.1%)	13 (4.2%)	—	0.787
LAD	76 (58.9%)	163 (52.2%)	1.636 <sup>†</sup>	0.201
LCX	11 (8.5%)	45 (14.4%)	2.862 <sup>†</sup>	0.091
RCA	38 (29.5%)	91 (29.2%)	0.004 <sup>†</sup>	0.951
Multivessel disease	79 (61.2%)	178 (56.1%)	0.659 <sup>†</sup>	0.417
Procedural issues				
Radial access	108 (83.7%)	272 (87.2%)	0.916 <sup>†</sup>	0.339
Stent use	119 (92.2%)	284 (91.0%)	0.173 <sup>†</sup>	0.677
Direct stenting	78 (60.5%)	206 (66%)	1.231 <sup>†</sup>	0.267
thrombus aspiration	50 (38.6%)	93 (29.8%)	3.338 <sup>†</sup>	0.068
IABP use	29 (22.5%)	42 (13.5%)	5.496 <sup>†</sup>	0.019
Procedural success	111 (86.0%)	283 (91.0%)	2.080 <sup>†</sup>	0.149
Complications	10 (7.8%)	23 (7.4%)	0.019 <sup>†</sup>	0.890
Initial TIMI flow grade (pre-PCI)				
TIMI flow grade 0–1	109 (84.5%)	269 (86.2%)	0.221 <sup>†</sup>	0.638
TIMI flow grade 2–3	20 (15.5%)	43 (13.8%)		
Final TIMI flow grade (post-PCI)				
TIMI flow grade 0–1	14 (10.9%)	19 (6.0%)	2.991 <sup>†</sup>	0.084
TIMI flow grade 2–3	115 (89.1%)	293 (94.0%)		

Data are expressed as *n* (%) or as median (Q<sub>1</sub>–Q<sub>3</sub>). <sup>†</sup> $\chi^2$  value; <sup>‡</sup>*U* value; —: data not available (Fisher exact test). IABP: intra-aortic balloon pump; LAD: left anterior descending artery; LCX: left circumflex artery; LM: left main coronary artery; PCI: percutaneous coronary intervention; RCA: right coronary artery; TIMI: thrombolysis in myocardial infarction.

vs. 211 min, IQR: 137–341 min; *P* < 0.001). No differences were observed in the total procedure time.

### 3.5 Clinical outcomes

There was no significant difference in the median hospital length of stay between the two groups. During a median hospital stay of 10 days, there were 11 deaths (8.5%) in the holidays-group and 24 deaths (7.7%) in the weekdays-group, therefore, no significant difference in in-hospital mortality was found between these two groups (*P* = 0.768). There was a strong trend toward a higher incidence of nonfatal reinfarction in holidays-group compared with those in weekdays-group [8 (6.2%) vs. 8 (2.6%), *P* = 0.089], although statistically non-significant. The need for target vessel revascularization was 3 (2.3%) patients in the holidays-group, vs. 5 (1.6%) in the weekdays-group (*P* = 0.697). There was also no difference in ischemic stroke between these two groups. However, the holidays-group had a significantly higher in-

cidence of CHF than the weekdays-group [16 (12.4%) vs. 12 (3.8%), *P* = 0.001]. Consequently, the cumulative composite MACEs were significantly higher in the holidays-group [38 (29.5%) vs. 51 (16.3%), *P* = 0.002; (Table 3)]. Furthermore, to assess whether night shifts in holidays and weekends were associated with poor outcomes compared to the counterpart in weekdays, we conducted a sub-analysis of the in-hospital mortality and MACEs in four subgroups that classified according to daytime and night-time admission. These analyses showed that both daytime and night-time admission during the holidays and weekends were significantly associated with higher in-hospital MACEs (Table 4). Interestingly, there was no significant difference in in-hospital MACEs between the night-time and day-time admission during holidays and weekends [9/24(37.5) vs. 29/105(27.6), *P* = 0.338]. Significant predictors of MACEs in the multivariable regression analysis are listed in Table 5. In a multivariable logistic regression model by using in-hospital

**Table 3. Clinical outcomes data.**

	Holidays-group (n =129)	Weekdays-group (n = 312)	Statistics	P Value
Length of stay, days	10 (7–15)	10 (7–15)	−0.217 <sup>‡</sup>	0.861
In-hospital death	11 (8.5%)	24 (7.7%)	0.087 <sup>†</sup>	0.768
Non-fatal MI	8 (6.2%)	8 (2.6%)	—	0.089
Non-fatal stroke	0	2 (0.6%)	—	1.000
Congestive heart failure	16 (12.4%)	12 (3.8%)	11.239 <sup>†</sup>	0.001
Target vessel revascularization	3 (2.3%)	5 (1.6%)	—	0.697
Cumulative MACEs	38 (29.5%)	51 (16.3%)	9.739 <sup>†</sup>	0.002

Data are expressed as *n* (%), or as median (Q<sub>1</sub>–Q<sub>3</sub>). <sup>†</sup> $\chi^2$  value; <sup>‡</sup>*U* value; —: data not available (Fisher exact test). MACEs: major adverse cardiovascular events; MI: myocardial infarction.

**Table 4. Stratified analyses for clinical outcome according to the admission time.**

	Holidays-group (n =129)	Weekdays-group (n =312)	Statistics	P Value
In-hospital death				
Night-time	2/24 (8.3%)	6/61 (9.8%)	—	1.000
Day-time	9/105 (8.6%)	18/251 (7.2%)	0.207 <sup>†</sup>	0.649
MACEs				
Night-time	9/24 (37.5%)	10/61 (16.4%)	4.411 <sup>†</sup>	0.036
Day-time	29/105 (27.6%)	41/251 (16.3%)	5.968 <sup>†</sup>	0.015

Data are expressed as *n* (%). <sup>†</sup> $\chi^2$  value; —: data not available (Fisher exact test). MACEs: major adverse cardiovascular events.

**Table 5. Effects of various variables on MACEs in univariate and multivariate logistic regression analysis.**

	Univariable		Multivariable	
	OR (95% CI)	P value	OR (95% CI)	P value
Holidays and weekends admission	2.05 (1.63–2.98)	< 0.001	1.67 (1.24–2.63)	0.002
Symptom onset to balloon time > 240 min	3.46 (2.12–7.62)	< 0.001	3.23 (1.93–5.94)	< 0.001
DTB time > 90 min	2.86 (1.32–6.34)	0.020	2.01 (1.28–5.22)	0.011
Killip class IV	1.68 (1.41–2.26)	0.023	1.52 (1.26–1.88)	0.031
Ventricular septal rupture	2.35 (1.39–3.56)	0.010	2.46 (1.06–3.87)	0.018
Post-PCI TIMI flow (0–1)	2.38 (1.09–4.25)	0.003	2.89 (1.92–4.53)	0.001

*N* = 441. DTB: door-to-balloon; MACEs: major adverse cardiovascular events; PCI: percutaneous coronary intervention; TIMI: thrombolysis in myocardial infarction.

MACEs as the dependent variable with adjustments for significant variables as identified from the univariable regression analysis, the only significant predictors of in-hospital MACEs were the holidays and weekends admission, Killip class IV, ventricular septal rupture, Post-PCI TIMI flow grade 0 to 1, DTB time > 90 min together with symptom onset to balloon time > 240 min. Overall, there were 89 (20.1%) observed in-hospital MACEs among the 441 patients studied (Table 3). Using the current multivariate regression model, 83 (18.8%) in-hospital MACEs were predicted and the area under the receiver operating characteristics curve (ROC) was 0.79, indicating an excellent ability to discriminate between patients who had MACEs during the index hospitalization and those who did not. Moreover, the

Hosmer-Lemeshow goodness-of-fit *P* value was 0.38, which indicates that there were no statistical differences between observed and predicted in-hospital MACEs using the current multivariate model among this study population. Therefore, this model is reliable for predicting in-hospital MACEs in Chinese patients with STEMI undergoing PPCI.

## 4 Discussion

In the present report, we conducted a retrospective analysis in 441 STEMI patients undergoing PPCI and compared the clinical outcomes of patients presenting during Chinese national holidays and weekends versus weekdays. Although no significant difference was found between the two groups

for in-hospital mortality, patients admitted during holidays and weekends have a significantly higher rate of in-hospital MACEs. In addition, patients admitted during Chinese holidays and weekends experienced a significantly longer DTB time and symptoms onset-to-balloon time. These findings indicated a considerable “holiday effect” in patients with STEMI undergoing PPCI in China.

Disparities in care and clinical outcomes among patients presenting with STEMI during off-hours versus on-hours remain an issue of considerable interest and this type of research has been continuously reported. However, the results of previous studies comparing the effect of off-hours and on-hours admission on clinical outcomes in STEMI patients were inconsistent. Using data from the National Registry of Myocardial Infarction database, Magid, *et al.*<sup>[5]</sup> evaluated this issue in 33,647 patients with STEMI and showed that adjusted in-hospital mortality was significantly higher for patients presenting during off-hours compared with those presenting during regular hours. In a recent analysis of the ACTION-GWTG database, Dasari, *et al.*<sup>[9]</sup> found that, among 43,242 patients with STEMI, those presenting during off-hours had a risk-adjusted in-hospital mortality of 13% higher than did those presenting on-hours. Moreover, a recent meta-analysis conducted by Sorita, *et al.*<sup>[23]</sup> also drew similar conclusions. Notably, the observed mortality differences in these studies could be largely attributable to lower rates of PPCI procedures performed on off-hours across the various studies.<sup>[5,6,23]</sup> As demonstrated in a recent study by Kumar *et al.*,<sup>[15]</sup> the mortality risk on off-hours declined and became similar to that on weekdays after adjusting for invasive procedures in the regression model.

With the increasing attention being paid to the holiday effect and implementation of organized systems of care to optimize timeliness of PPCI for STEMI patients, the prognostic differences between patients admitted during off-hours and those admitted on-hours has diminished significantly in developed Western countries.<sup>[11,24]</sup> For example, a study conducted by Noman, *et al.*<sup>[25]</sup> in United Kingdom showed that the in-hospital and long-term mortality of STEMI patients admitted during off-hours had no significant difference from their weekday counterparts. Similarly, Cubeddu, *et al.*<sup>[12]</sup> conducted a sub-study using the large database of the HORIZONS-AMI trial and indicated that STEMI patients presenting to PPCI-capable hospitals during off-hours have experienced similar short- and long-term survival and clinical outcomes as those arriving during on-hours. Moreover, findings reported by Casella, *et al.*<sup>[14]</sup> confirmed that, when PPCI is performed within an efficient STEMI network focused on reperfusion, the clinical effec-

tiveness of either off-hours or regular-hours PPCI were comparable. This further suggests that the excess mortality risk during off-hours may be alleviated with institutional systems improvement. However, the clinical care and outcomes of patients with STEMI undergoing PPCI during off-hours in developing countries such as in China, which have poorer healthcare systems than developed countries,<sup>[16]</sup> remains worrying.

In the present study, we found that patients who received PPCI during Chinese national holidays and weekends had a greater incidence of short-term MACEs and experienced significantly longer delays to revascularization than those treated during weekdays. However, the difference in in-hospital mortality was found to be not significant; this could be attributed to the relatively small sample size of this study. In addition, this study did not further analyze the differences between high-risk STEMI patients admitted at different times. Perhaps more significant differences in mortality and MACEs will be observed in high-risk STEMI patients. Our observations were remarkably similar to those reported by Casella, *et al.*,<sup>[14]</sup> as well as Jneid, *et al.*,<sup>[26]</sup> Cubeddu, *et al.*,<sup>[12]</sup> who also found that STEMI patients presenting during off-hours have a significantly longer DTB time, however, the in-hospital mortality were comparable.

Although the exact reasons for the excess MACEs rate observed on the Chinese holidays and weekends have not been ascertained, the possible explanations might include: (1) patients presenting during holidays and weekends experienced longer hospital delays for administration of reperfusion therapy—median DTB time was delayed by an average of 25 min, and these delays in mechanical reperfusion definitely correlated with adverse outcomes.<sup>[27,28]</sup> Moreover, this absolute difference in DTB time in our analysis was obviously longer than that reported by Cubeddu, *et al.*<sup>[12]</sup> (17 min), Dasari, *et al.*<sup>[9]</sup> (16 min), and Casella, *et al.*<sup>[14]</sup> (11 min). This difference was mainly attributable to a longer time interval from catheterization laboratory activation to catheterization laboratory arrival during off hours, suggesting the absence of an on-site PPCI response team and patients often waited for an on-call team during holidays, as reported in previous studies.<sup>[10]</sup> The delay in DTB time may also be partially explained by delays in diagnosis at the emergency department due to decreased expertise of staff level. (2) The median symptom-to-door time was 86 minutes delayed in patients presenting holidays and weekends, i.e., there was a remarkable pre-hospital delay. Chinese patients have insufficient understanding of the harmfulness of AMI and choose to endure the pain more often than patients in other countries, resulting in delays in treatment because

they wait till holidays or weekends to seek medical care. In addition, a substantial increase in travel time takes place during holidays, especially traditional Chinese holidays, because more vehicles are on the roads, causing traffic congestion and STEMI patients transfer from onset location to the PPCI-capable hospital therefore takes more time. (3) In this study, we found that patients admitted during holidays were more likely to present with Killip class III to IV compared with those admitted during weekdays, which was similar to those reported by Sorita *et al.*<sup>[13]</sup> Some STEMI patients with less severe symptoms may postpone seeing a doctor during holidays, whereas those with severe symptoms would be admitted. Therefore, patients admitted during holidays may be more severe. Recently, a retrospective study conducted by Isogai, *et al.*<sup>[10]</sup> also showed that patients admitted on weekends were tended to have higher Killip class, higher rates of shock, pulmonary edema, and cardiac arrhythmias. In addition, hospital staffing is reduced on holidays and weekends, both numerically and in terms of available expertise on site, as reported in previous studies.<sup>[17,18,29]</sup> In most Chinese medical facilities, the main providers of care for patients during holidays and weekends are residents, which have less seniority and experience than those who work on weekdays. Therefore, the quality of care for STEMI patients would be compromised at holidays and weekends than during the weekdays.

The present study might have important health policy implications. Although the in-hospital mortality between holidays versus weekdays was comparable, Chinese holidays and weekends admission was significantly associated with higher MACE rates, especially congestive heart failure. Therefore, continuous efforts should be undertaken to enhance the Chinese healthcare system and to ensure that comparable outcomes are achieved for all STEMI patients regardless of time of presentation. Currently, organized systems of care for patients with STEMI have been implemented in many developed countries to closing the outcomes gap between off-hours and regular hours. Maier, *et al.*<sup>[7]</sup> analyzed data from the Berlin Myocardial Infarction Registry that comprises 2131 patients with STEMI and treated with PPCI. They found that the differences in DTB and hospital mortality between patients admitted in-hours and off-hours were reduced to a non-significant when the physician-escorted emergency medical services were applied. Similarly, Holmes, *et al.*<sup>[30]</sup> reported that the disparity of care between off-hours and regular hours for patients with STEMI can be significantly improved by implementing a regional coordinated system of care. Gratifyingly, several Chinese medical facilities are actively establishing a

local healthcare delivery system—Chinese chest pain central, which aims to provide optimal treatment to STEMI patients with emphasis on timely reperfusion.<sup>[31]</sup> We believe that the clinical outcomes of patients with STEMI will gradually improved after implementation this organized system. Additionally, in China, it is very necessary to actively develop the community healthcare education to shorten the pre-hospital delay.

Some limitations of the present study should be acknowledged. First, this study enrolled a relatively small number of patients, so it was underpowered to detect a significant difference in the in-hospital mortality between the two study groups. Furthermore, this study did not further analyze the differences between high-risk STEMI patients admitted at different times. Perhaps more significant findings will be observed in high-risk STEMI patients. Second, the clinical data of this study were obtained retrospectively. Hence, further prospective studies on larger group of patients will be warranted to evaluate the “holiday’s effect” on clinical outcomes in Chinese patients with STEMI undergoing PPCI. Finally, the present study specifically investigated the clinical outcomes of patients that were homogeneously treated with PPCI. Patients initially arrived at non-PCI capacity hospitals that were treated with thrombolysis and subsequently transferred for rescue PCI were excluded from the present analysis to avoid a potential selection bias or any unaccountable difference in referral patterns that might exist during holidays and weekends. Thus, the study patients might not reflect the broad population of patients with STEMI.

In conclusion, the present study demonstrated that, in China, patients with STEMI undergoing PPCI during national holidays and weekends have worse in-hospital outcomes and experienced significant longer delays to revascularization as compared to those treated during weekdays. There are many opportunities to improve the delivery of care in what has been viewed as an imperfect healthcare system in China. Increasing staffing during national holidays and weekends may reduce the gaps in quality of care. Additionally, the Chinese healthcare system should strive to develop organized systems of care to optimize timeliness of PPCI and provide comparable outcomes to all patients with STEMI, regardless of the time of presentation. Further investigations in adequately powered large trials to validate the findings suggested by the current study are warranted.

## Acknowledgments

This work was supported in part by a grant from the Yu-

Ying Plan of the Central South University (No. 502034007). The authors would like to express their sincere appreciation to Dawn Witt, PhD, managing scientist of Minneapolis Heart Institute Foundation, Minneapolis, Minnesota, USA, for her help in revising the English language and grammar problems in our manuscript. The authors thank all the nurses and technicians at our catheterization laboratory for their invaluable help in this study. There is no conflict of interest to declare.

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