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CLINICAL RESEARCH

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

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Objectives This study aims to evaluate whether results of "off-hours" and "regular-hours" primary angioplasty (primary percutaneous coronary intervention [pPCI]) are comparable in an unselected population of patients with ST-segment elevation acute myocardial infarction treated within a regional network organization.

Background Conflicting results exist on the outcome of off-hours pPCI.

Methods We analyzed in-hospital and 1-year cardiac mortality among 3,072 consecutive ST-segment elevation myocardial infarction (STEMI) patients treated with pPCI between January 1, 2004, and June 30, 2006, during regular-hours (weekdays 8:00 AM to 8:00 PM) and off-hours (weekdays 8:01 PM to 7:59 AM, weekends, and holidays) within the STEMI Network of the Italian Region Emilia-Romagna (28 hospitals: 19 spoke and 9 hub interventional centers).

Results Fifty-three percent of patients were treated off-hours. Baseline findings were comparable, although regular-hours patients were older and had more incidences of multivessel disease. Median pain-to-balloon (195 min, interquartile range [IQR]: 140 to 285 vs. 186 min, IQR: 130 to 280 min; $p = 0.03$) and door-to-balloon time (88 min, IQR: 60 to 122 vs. 77 min, IQR: 48 to 116 min; $p < 0.0001$) were longer for off-hours pPCI. However, unadjusted in-hospital (5.8% off-hours vs. 7.2% regular-hours, $p = 0.11$) and 1-year cardiac mortality (8.4% off-hours vs. 10.3% regular-hours, $p = 0.08$) were comparable. At multivariate analysis, off-hours pPCI did not predict an adverse outcome either for the overall population (odds ratio [OR]: 0.70, 95% confidence interval [CI]: 0.49 to 1.01) or for patients directly admitted to the interventional center (OR: 0.79, 95% CI: 0.52 to 1.20).

Conclusions When pPCI is performed within an efficient STEMI network focused on reperfusion, the clinical effectiveness of either off-hours or regular-hours pPCI is comparable. (J Am Coll Cardiol Intv 2011;4:270–8) © 2011 by the American College of Cardiology Foundation

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Primary percutaneous coronary intervention (pPCI) is the preferred reperfusion strategy for ST-segment elevation acute myocardial infarction when performed by an experienced team within 90 to 120 min from the first medical contact (1). However, conflicting results exist on the outcome of ST-segment elevation myocardial infarction (STEMI) patients undergoing "off-hours" (weekday nights, weekends, and holidays) pPCI (2–9). Some investigators have reported higher mortality rates for such patients (2–6), while others reported no differences (7–9). Although the causes of such worse outcomes in a real-world setting are largely unknown, health care delivery variations between night and day, fatigue and operator experience could play an important role (10,11). Nonetheless, this information is crucial because of the proliferation of "round-the-clock" programs of pPCI for STEMI patients.

See page 279

After the publication of the American College of Cardiology/American Heart Association guidelines (12), the Health Care Agency of the Italian Region of Emilia-Romagna promoted the development of a regional network for the treatment of STEMI patients (PRIMA-RER project [PRogetto sull'IMA nella Regione Emilia-Romagna]). According to this project, since January 1, 2004, all patients directly admitted to hospitals with interventional facilities are treated with pPCI as the preferred reperfusion strategy, whereas patients initially admitted to peripheral noninterventional hospitals are rapidly and systematically transferred for pPCI according to their risk profile and a reasonable extra delay owing to transfer organization.

Therefore, the aim of the present study is to evaluate whether "off-hours" pPCI is as effective as "regular-hours" mechanical reperfusion in an unselected population of consecutive patients with STEMI treated within a regional network.

Methods

Study design, setting population, and eligibility criteria. This is a retrospective cohort study based on a prospective assembled Internet-based database, the REAL (Registro Regionale Angioplastiche dell'Emilia-Romagna) registry (13), as previously described (14). In brief, this registry represents an on-going, prospective, observational quality program study and contains comprehensive clinical and procedural data of all consecutive patients undergoing percutaneous coronary intervention (PCI) in Emilia-Romagna. All interventional centers of the region collect data, using a common pre-specified dataset. These data are open for evaluation, and the Regional Health Care Administration performs periodic audits. Since the REAL registry is based on current clinical practice, only ordinary written informed consent for PCI and data collection was obtained for all patients. The study protocol is in accordance with the Declaration of Helsinki.

On January 1, 2004, according with the PRIMA-RER project (15), all STEMI patients directly admitted to centers with interventional facilities are treated with pPCI, whereas patients initially admitted to peripheral hospitals are rapidly transferred for pPCI according to their risk profile and an expected pPCI delay <120 min. Otherwise, thrombolytic therapy is administered. A pre-hospital electrocardiogram (ECG) is strongly encouraged in all patients rescued by emergency medical services. Further details of this organizational system have been described elsewhere (15). Briefly, the STEMI network covers the Italian Emilia-Romagna region and its 4.1 million inhabitants. It comprises 28 centers: 19 noninterventional (spoke) and 9 interventional intensive cardiac care units (hub centers). The latter are located in the main towns and provide round-the-clock service for pPCI. All hub hospitals are high-procedural volume centers (≥650 PCI/year), performing at least 80 pPCI per year (range 80 to 310 pPCI), and staffed by high-volume senior interventionalists (>180 PCI/year). The distance between the different spoke and hub centers ranges from 12 to 58 km.

From January 1, 2004 to June 30, 2006, 22,871 patients underwent elective or emergency PCI in the Emilia-Romagna region and were enrolled in the REAL registry. In the present study, we analyze data from 4,069 patients with STEMI (chest pain >30 min <12 h from symptom onset, associated with typical ECG changes as recorded at the first ECG), who were treated with pPCI either at the admitting hospital or after an interhospital transfer, and who were residents in the Emilia-Romagna region. The main outcome measures were in-hospital and 1-year cardiac mortality among patients treated with pPCI during regular-hours (defined as weekdays from 8:00 AM to 8:00 PM) and off-hours (weekdays from 8:01 PM to 7:59 AM, weekends, and holidays), when the interventional team is on call outside the hospital. Both pPCI cohorts were defined according to the pPCI start time. All-cause mortality was recorded as well. Additionally, the above-mentioned outcomes were analyzed among patients directly admitted to the interventional hospital.

Abbreviations and Acronyms

CI = confidence interval
DTB = door-to-balloon delay
ECG = electrocardiogram
IQR = interquartile range
OR = odds ratio
PCI = percutaneous coronary intervention
pPCI = primary PCI
STEMI = ST-segment elevation myocardial infarction
TIMI = Thrombolysis In Myocardial Infarction

Primary PCI protocol. Interventional strategy and device usage were left to the discretion of the attending physicians. Before pPCI, all patients received aspirin (250 mg intravenously) and intravenous heparin (weight-adjusted bolus dose, maximal 5,000 IU) according to standard protocols at the different hospitals. The use of glycoprotein IIb/IIIa inhibitors and beta-adrenergic blocking agents was strongly encouraged for all eligible patients as soon as possible after STEMI diagnosis. Heparin administration was continued for 24 h after pPCI in any patient who did not receive glycoprotein IIb/IIIa agents. Lifelong aspirin was then prescribed to all patients, unless contraindicated. If a stent was deployed, patients were given a loading dose of 300 mg clopidogrel as soon as possible followed by a maintenance dose of 75 mg for at least 1 month (6 to 12 months for drug-eluting stents).

STEMI diagnosis criteria and other study definitions. Diagnosis of STEMI was defined as an ST-segment elevation in at least 2 adjacent leads ≥0.1 mV in leads IIII, aVF, aVL, V_4 to V_6 and ≥0.2 mV in leads V_1 to V_3 or new onset left bundle-branch block as recorded in the first ECG (1). Thrombolysis In Myocardial Infarction (TIMI) flow grade rate of the infarct-related artery was assessed visually by the operator and classified accordingly (16). The TIMI risk index was calculated using the equation: (heart rate × $[age/10]^2$)/systolic blood pressure) (17). Cardiogenic shock was defined as a persistent systolic blood pressure <90 mm Hg (as recorded in the catheterization laboratory before pPCI or implantation of the intra-aortic balloon pump) unresponsive to intravenous fluid administration or that requires vasopressors (18). In all patients undergoing pPCI, the following time intervals were collected: time of symptom onset, time of arrival at the first hospital, time of ambulance departure from the peripheral hospital, time of arrival at the PCI center, and time of the first balloon inflation during pPCI. To calculate the door-to-balloon (DTB) delay, time of arrival at the first hospital was considered as the starting time either for patients initially observed at the emergency department of the PCI center or transferred from other peripheral hospitals. Among pre-hospital triage patients, DTB delay was the timing from the first ECG recording by the emergency medical service to the balloon implantation. Main comorbidities were recorded and a comprehensive risk profile was defined for each individual patient according to the Charlson index (19).

Data collection for in-hospital and long-term mortality. Follow-up data were obtained directly and independently by the Emilia-Romagna Regional Health Agency (updated every 3 months) through the analysis of hospital discharge records and mortality registries. This process ensures complete follow-up for 100% of the patients resident in the region, including all out-of-hospital deaths (this is the reason for a priori exclusion of patients who live outside the region). Specific queries were sent to the individual institutions to justify/correct discrepancies between the data recorded on the Internet-based registry (compiled by interventional cardiologists) and the administrative data (largely provided by independent cardiologists). Hospital records were reviewed for additional information whenever deemed necessary.

Statistical analysis. Continuous variables were expressed as mean ± SD and categorical data as percentages. For group comparisons, 2-tailed Student unpaired *t* test was used for continuous variables and chi-square test was used for categorical variables. According to the American College of Cardiology/American Heart Association Task Force on Performance Measures indications, median values for time delays (25th to 75th) were considered (20) and the nonparametric Wilcoxon rank-sum test was adopted for time-delay group comparisons (off-hours vs. regular-hours pPCI).

To avoid the potential bias introduced by transferred patients, we performed an additional analysis limited to patients directly admitted to hub hospitals. Differences in cardiac mortality rates between off-hours and regular-hours pPCI patients during the follow-up period were assessed by the Kaplan-Meier method and compared using the log-rank test. Multivariable logistic regression analysis was conducted to evaluate the adjusted effect estimates associated with off-hours pPCI. For this analysis, a multivariate logistic regression model was fitted, for which in-hospital cardiac mortality was the dependent variable of interest. The following 11 variables (potential confounders) were included in the multivariable model: age, male sex, Charlson index, diabetes, cardiogenic shock, off-hours pPCI, interhospital transfer for pPCI, left ventricular ejection fraction ≤35%, multivessel pPCI, glycoprotein IIb/IIIa inhibitor use and treatment center. To assess linearity, we categorized continuous variables as intervals and performed the score test for trend of odds on the proportions of death at each interval. The predictive accuracy of the model correlated well with the observed events (C-statistics = 0.90, Hosmer-Lemeshow goodness-of-fit, p = 0.15 for the total population). The 1-year risk of cardiac mortality was evaluated using Cox's proportional hazards models adjusting for all variables considered in the logistic regression analysis. All analyses were performed with the SAS 9.1 system (SAS Institute, Cary, North Carolina). All statistical tests were 2-sided ($p < 0.05$ was considered significant).

Results

From January 1, 2004 to June 30, 2006, 4,069 patients with STEMI (<12 h from symptom onset) underwent pPCI. From this population, 170 (4.2%) patients were excluded because they underwent a rescue or a planned PCI immediately after thrombolysis and 827 (20%) subjects because of missing or incomplete data. Therefore, our study population consisted of 3,072 patients: 1,628 (53%) who underwent off-hours pPCI and 1,444 patients who underwent pPCI during regular-hours (Fig. 1). Mean follow-up duration was 537 days (median 509 days, range 125 to 1,034 days).

Table 1 summarizes baseline clinical characteristics and risk factors for each of the 2 groups. Baseline findings were comparable, although in the regular-hours group, patients were older (67.2 vs. 66.2 years, $p = 0.03$), and there was a lower prevalence of smokers (30.6% vs. 35.3%, $p = 0.006$). Interestingly, triage modalities to pPCI were similar between the groups.

Primary PCI time delays. Overall, median pain-to-balloon delay (195 min, interquartile range [IQR]: 140 to 285 vs. 186 min, IQR: 130 to 280 min; $p = 0.030$) and DTB time (88 min, IQR: 60 to 122 vs. 77 min, IQR: 48 to 116 min; $p < 0.0001$) were longer for off-hours pPCI, although the absolute differences were rather small (9 and 11 min, respectively). Of note, DTB time was within 2 h in a large proportion of patients in both groups. Again, when the analysis was restricted to patients directly admitted to the hub, the median DTB delay of patients treated off-hours was only 6 min longer than that of subjects treated during regular-hours (51 min, IQR: 76 to 109 vs. 45 min, IQR: 65 to 99 min; $p < 0.0001$) and most of them had a DTB <120 min (Table 1).

Angiographic and procedural data. The angiographic and procedural data are reported in Table 2. Overall, there were some differences between off-hours and regular-hours pPCI. In particular, a higher prevalence of multivessel disease in patients treated during routine hours was observed. As a result, multivessel pPCI was more frequently performed during regular-hours. However, such differences were no longer observed when the analysis was restricted to patients directly admitted to hub centers. In addition, significantly more patients underwent left main pPCI during routine hours, especially if directly admitted to interventional centers. As opposed, an intra-aortic balloon pump was more often implanted during off-hours pPCI both in the global population and in patients directly admitted to hub centers.

Survival. Among the overall population, unadjusted in-hospital (5.8% off-hours vs. 7.2% regular-hours, $p = 0.11$) and 1-year cardiac mortality (8.4% off-hours vs. 10.3% regular-hours, $p = 0.08$) were similar in both groups (Table 3). Moreover, when the analysis was restricted to patients directly admitted to the hub, the in-hospital and long-term mortality rate did not differ either. Similar trends between the 2 groups were observed for all-cause in-hospital and 1-year mortality as well.

Kaplan-Meier adjusted curves demonstrated similar long-term cardiac mortality for patients treated off-hours both in the total population (Fig. 2A) and in the subgroup of patients directly admitted to the interventional center (Fig. 2B).

Analysis of predictors of in-hospital cardiac mortality. At logistic regression analysis, off-hours pPCI had no effect on in-hospital cardiac mortality either for the overall population (odds ratio [OR]: 0.70, 95% confidence interval [CI]: 0.49 to 1.01) or for patients directly admitted to interventional centers (OR: 0.79, 95% CI: 0.52 to 1.20). As expected, age (OR: 1.06, 95% CI: 1.04 to 1.07 per year),

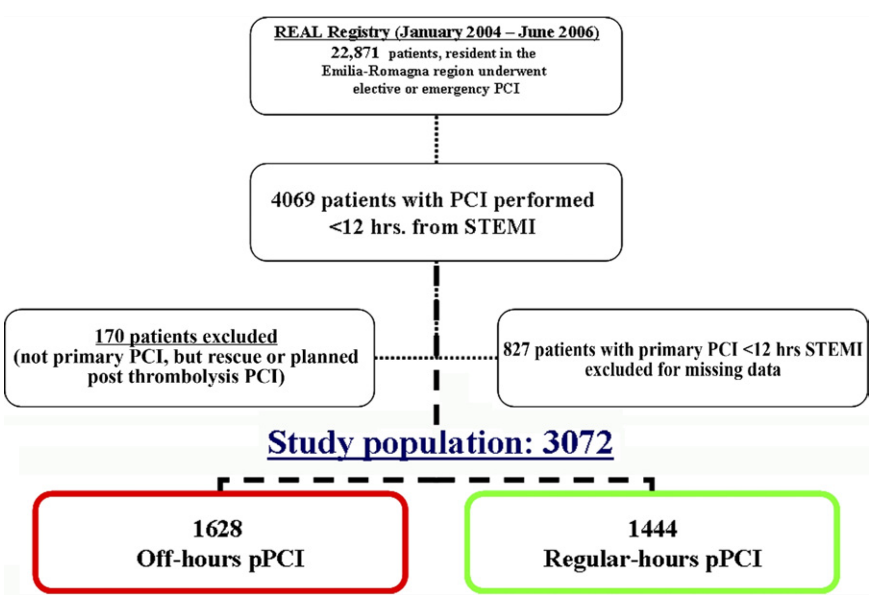

Figure 1. Flow Diagram of the Study

Study population comprises 3,072 consecutive patients (75.5% of the global primary percutaneous coronary intervention [pPCI] caseload) with pPCI performed <12 h from ST-segment elevation myocardial infarction (STEMI). Patients with rescue, planned post-fibrinolysis PCI or missing data were excluded. REAL = Registro Regionale Angioplastiche dell'Emilia-Romagna.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 4, NO. 3, 2011
MARCH 2011:270–8

Table 1. Baseline Demographic and Clinical Characteristics of the Study Patients According to Time of Interventions (Off-Hours vs. Regular-Hours pPCI) for the Global Population and for Patients Directly Admitted to Interventional Centers

	Overall Population			Direct Admission to Hub		
	Off-Hours pPCI (n = 1,628)	Regular-Hours pPCI (n = 1,444)	p Value	Off-Hours pPCI (n = 1,185)	Regular-Hours pPCI (n = 1,075)	p Value
Age, yrs	66.2 ± 13.0	67.2 ± 13.4	0.031	66.4 ± 13.0	67.5 ± 13.4	0.039
Male, %	71.0	71.5	0.778	70.5	70.3	0.907
Diabetes mellitus, %	20.5	19.4	0.469	20.1	19.2	0.616
Hypertension, %	60.4	61.2	0.647	59.7	60.3	0.761
Smokers, %	35.3	30.6	0.006	34.8	31.1	0.065
Hypercholesterolemia, %	51.0	49.6	0.356	49.4	49.2	0.929
Previous myocardial infarction, %	12.5	13.1	0.606	13.0	13.5	0.744
Previous revascularization, %	10.0	10.8	0.456	10.1	11.4	0.311
Anterior infarction, %	50.6	48.7	0.317	48.9	47.5	0.524
Charlson index	1.4 ± 1.0	1.5 ± 1.1	0.089	1.4 ± 1.0	1.5 ± 1.1	0.078
Systolic blood pressure, mm Hg	125 ± 28	126 ± 28	0.573	124 ± 28	126 ± 29	0.229
Heart rate, beats/min	76 ± 17	77 ± 19	0.157	76 ± 17	77 ± 19	0.257
Shock on admission, %	9.3	8.4	0.389	9.7	8.8	0.478
Post-PCI poor LVEF (EF <0.35), %	14.9	14.2	0.601	13	11.2	0.393
TIMI risk index, mean	30 ± 18.7	30.5 ± 17.3	0.524	30.3 ± 18	31.1 ± 18.4	0.398
Time delays, min						
Pain-to-admission	95 (60–170)	100 (60–163)	0.366	57 (95–170)	60 (98–163)	0.711
Door-to-balloon*	88 (60–122)	77 (48–116)	<0.0001	51 (76–109)	45 (65–99)	<0.0001
Pain-to-balloon	195 (140–285)	186 (130–280)	0.030	130 (182–272)	120 (170–270)	0.079
Triage modalities, %						
Fast-track (118 EMS bypass ER)	15.9	17.8	0.448	17.8	19.8	0.257
ER hub center	73.5	72.3		82.2	80.2	
ER spoke center	10.6	9.9		—	—	

Data are presented as mean ± SD, %, or median (25th to 75th percentile). *As described in text, to calculate DTB, time of arrival at the first hospital was considered as the starting time for patients transferred from other peripheral hospitals. As opposed, in pre-hospital triage patients, DTB delay was the timing of the ECG recording (by EMS) at the scene of STEMI to the balloon inflation.

DTB = door-to-balloon delay; ECG = electrocardiogram; EMS = emergency medical services; ER = emergency room; LVEF = left ventricular ejection fraction; pPCI = primary percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; TIMI = Thrombolysis In Myocardial Infarction.

Charlson index (OR: 1.28, 95% CI: 1.13 to 1.45), cardiogenic shock (OR: 10.67, 95% CI: 7.24 to 15.79), multivessel pPCI (OR: 1.99, 95% CI: 1.20 to 3.29), and reduced ejection fraction (OR: 6.10, 95% CI: 3.96 to 9.40) were independent predictors of in-hospital cardiac mortality in the overall population as well as in patients directly admitted to the hub. The predictive accuracy of the model correlated well with the observed events.

Discussion

The present study demonstrates that when primary PCI is performed within a highly specialized STEMI network organization focused on reperfusion, the clinical effectiveness of either off-hours or regular-hours pPCI is similar even at a regional level.

Previous studies have shown worse results of pPCI when performed off-hours (2–4). Possible explanations for such discrepancies include circadian variation in myocardial perfusion influencing STEMI mortality, pre-selection biases, differences in patient characteristics, or variations in health care delivery (6,21). In our study, baseline clinical and angiographic features of patients treated during regular-hours or off-hours were largely similar. However, these similarities are not surprising as in our network pPCI is the preferred reperfusion strategy, and this practice limits possible selection biases. As opposed, in the National Heart, Lung, and Blood Institute Dynamic Registry analysis, where pPCI was reserved to a highly selected population, patients treated off-hours were fewer and sicker than subjects treated during office-hours were (6). Thus, such selection bias could partially explain the differences with our study or other series of unselected STEMI patients (7,10). Furthermore, variations in the process of care could explain differences in outcomes of patients treated with pPCI off-hours. In fact, it has been observed that fewer uses of pPCI during weekends are associated with poorer outcomes of patients treated during those days (4,5). In addition, even in those who receive pPCI, longer DTB time during off-hours accounts for a reduced benefit. This finding has led to several efforts to reduce pPCI delays during off-hours

Table 2. Angiographic and Procedural Characteristics of the Study Patients According to Time of Interventions (Off-Hours vs. Regular-Hours pPCI)

	Overall Population			Direct Admission to Hub		
	Off-Hours pPCI (n = 1,628)	Regular-Hours pPCI (n = 1,444)	p Value	Off-Hours pPCI (n = 1,185)	Regular-Hours pPCI (n = 1,075)	p Value
Severity of disease						
Multivessel disease, %	51.8	56.0	0.031	51.9	54.6	0.230
Lesion treated						
Left main, %	1.5	2.4	0.075	1.2	2.5	0.018
Left anterior descending, %	49.8	47.4	0.199	47.6	46.4	0.576
Right coronary artery, %	34.3	37.5	0.060	35.9	37.9	0.347
Left circumflex, %	14.2	12.7	0.241	14.5	13.5	0.483
Graft (SVG or IMA), %	1.0	1.4	0.387	1.2	1.2	0.951
Lesion length, mm	19.5 ± 9	19.7 ± 9.1	0.408	19.3 ± 9.4	19.6 ± 9.1	0.484
Reference diameter, mm*	3.0 ± 0.5	3.0 ± 0.5	0.079	3 ± 0.5	3 ± 0.5	0.690
Multivessel PCI, %	6.9	9.1	0.024	7.2	9.1	0.090
Basal TIMI flow grade 0/1, %*	71.0	71.1	0.978	72.8	73.8	0.614
Final TIMI flow grade 3, %*	92.1	90.7	0.160	92.5	90.2	0.055
Angiographic success, %	96.2	96.5	0.674	96.7	96.3	0.580
Procedural issues, %						
POBA	11.9	10.6	0.270	11.5	11.5	0.965
BMS only, stent	72.2	72.6	0.803	71.6	71.5	0.989
DES only, stent	12.9	12.9	0.987	13.2	12.9	0.822
Mixed DES and BMS	3.1	3.9	0.186	3.7	4.0	0.723
Direct stenting	21.0	22.9	0.216	20.1	21.3	0.471
IABP	7.2	4.9	0.007	7.4	4.9	0.014
GP IIb/IIIa inhibitors	91.3	90.2	0.288	91.2	89.7	0.210

Data are presented as % or mean ± SD. *Visual estimation.
BMS = bare-metal stent(s); DES = drug-eluting stent(s); GP = glycoprotein; IABP = intra-aortic balloon pump; IMA = internal mammary artery graft; POBA = plain old balloon angioplasty; SVG = saphenous vein graft; other abbreviations as in Table 1.

(22). However, in our study, although off-hours patients had a median 11-min longer DTB delay, in-hospital or long-term outcomes were comparable. Interestingly, our findings are not in accordance with data from Rathore et al. (23), who observed, in 43,801 patients with STEMI treated with pPCI, that any delay after a patient arrives at the hospital is associated with higher mortality, even in centers providing pPCI within 90 min. In particular, a reduction in DTB time from 90 to 60 min was associated with a further 0.8% lower mortality (23). However, a large proportion of our patients had a DTB within 90 min and an ischemic time within 3 h whether they were observed during regular-hours, off-hours, or needed a transfer for pPCI. Unfortunately, ischemic time of patients enrolled in the National Cardiovascular Data Registry was not known (23), and from a patient perspective, this is not a trivial issue. Moreover, in our study, the DTB differential between off-hours and regular-hours was modest (median differences: 11 min for the overall population, but only 6 min for patients directly admitted to the hub). In the NRMI (National Registry of Myocardial Infarction) 3/4 registry, a substantial proportion of patients treated off-hours had a DTB longer than 120 min (41.5% off-hours vs. 27.7% regular-hours, $p < 0.001$), and this unfavorable finding was associated with a 21-min longer DTB delay (116-min off-hours vs. 95-min regular-hours; $p < 0.001$) (4). Glaser et al. (6), who analyzed the NHBLI Dynamic registry, reported similar results. Fur-

Table 3. Unadjusted Cumulative Frequencies of Cardiac and All-Cause Mortality According to Off-Hours or Regular-Hours pPCI Treatment

	Off-Hours pPCI (n = 1,628)	Regular-Hours pPCI (n = 1,444)	p Value
In-hospital cardiac mortality, %			
Global population	5.8	7.2	0.11
Nontransferred pPCI	6.2	7.4	0.26
Transferred pPCI	4.5	6.5	0.21
1-yr cardiac mortality			
Global population, %	8.4	10.3	0.08
In-hospital all-cause mortality, %			
Global population	6.1	7.8	0.06
Nontransferred pPCI	6.4	8.0	0.14
Transferred pPCI	5.2	7.0	0.26
1-yr all-cause mortality			
Global population, %	10.8	12.2	0.22

Values are presented as %.
Abbreviations as in Table 1.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 4, NO. 3, 2011
MARCH 2011:270–8

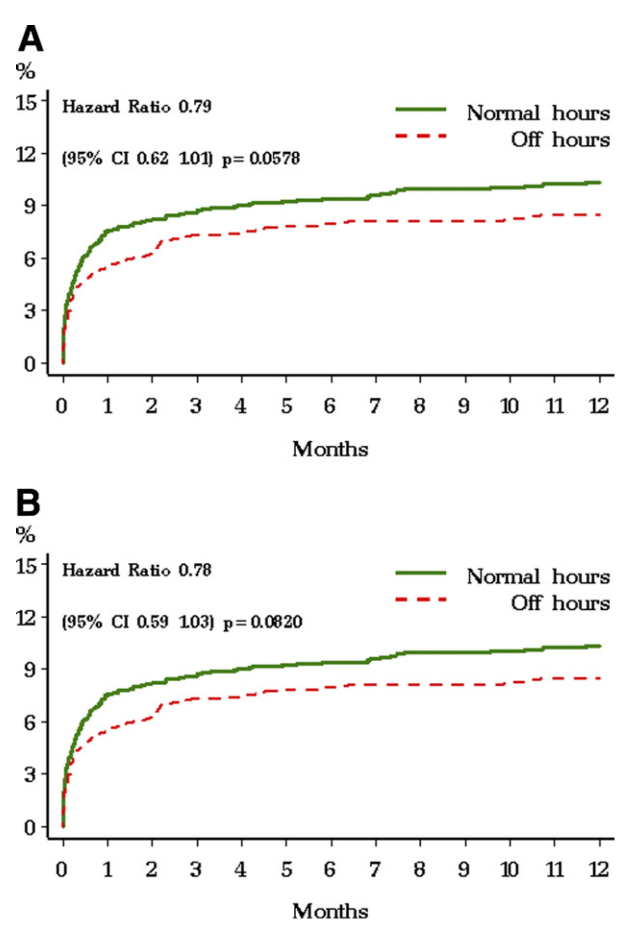

Figure 2. 1-year Adjusted Cardiac Mortality Among Patients Treated With pPCI During Regular-Hours or Off-Hours

(A) Overall population. **(B)** Patients directly admitted to the hub centers. **Green lines** represent patients treated during regular-hours. **Red dotted lines** represent patients treated during off-hours. CI = confidence interval; other abbreviations as in Figure 1.

thermore, when Rathore et al. (23) excluded patients who presented in cardiogenic shock, longer DTB continued to be associated with higher crude mortality, although the differences were substantially reduced. In particular, a reduction in DTB time from 90 to 60 min was associated with a 0.1% lower mortality (23). Therefore, this suggests that the negative effects of modestly longer DTB could be substantial in very high-risk patients such as those with cardiogenic shock (24), whereas these delays could have less effect on an overall population treated within the first 3 "golden hours."

Thus, we may argue that other differences in pPCI management, procedural complications, and success rates may be more relevant than the observed differences in DTB time (6,25). Most of our patients received an up-to-date pPCI as stents and glycoprotein IIb/IIIa inhibitors were extensively used in both groups, and in our network, only very experienced operators of high-volume centers perform pPCI. All these features have been demonstrated to improve the results of the procedure itself (26). In addition, since 2004, all the system recommendations to improve pre-hospital diagnosis and several other important patterns of care of STEMI patients have been progressively implemented in our network (Table 4).

Study limitations. Our analysis has several important limitations and should be interpreted accordingly. First, as an observational, matched cohort analysis, unaccounted differences may have remained after adjusting with multivariable analysis for confounders. Second, because we used the catheterization laboratory registry as a starting point, our study selected only patients eligible for pPCI who were transferred or admitted to the catheterization laboratory alive. Therefore, it does not represent all STEMI cases that occurred in our region during the study period. However, pPCI was strongly recommended in our network for all eligible patients and the proportion of subjects initially admitted to peripheral hospitals and not transferred decreased substantially during the study period (Table 4). Moreover, the aim of the study was to assess differences between routine or off-hours pPCI and such a pre-selection bias could have scarcely influenced our results. Furthermore, we cannot exclude that the trend toward a lower in-hospital mortality of off-hours treated patients could be explained by a residual selection bias. In fact, we may assume that even the most severe STEMI patient rescued within the network during the day is submitted to pPCI, whereas off-hours it could occasionally happen that the sickest or most challenging STEMI patients are not triaged or transferred correctly. In fact, when the analysis was restricted to patients directly admitted to the interventional center, the difference in in-hospital cardiac mortality between routine and off-hours pPCI was less evident. Finally, 827 patients (20% of cases) were excluded from the analysis owing to missing data. However, short- and long-term cardiac mortality of such excluded patients were similar to that observed in the overall study population (in-hospital cardiac mortality: 6.9% included vs. 7.1% excluded patients, p = 0.87; 1-year cardiac mortality: 12.6% included vs. 13.8% excluded patients, p = 0.60). Therefore, we believe that this bias would not alter the study results.

Conclusions

When pPCI is performed within a highly specialized STEMI network organization system focused on reperfusion, the clinical effectiveness of either off-hours or regular-hours pPCI is equivalent even at a regional level.

Table 4. Progressive Emilia-Romagna Region STEMI Network Implementation During the Study Period

Variables	1st Semester (2004)	2nd Semester (2004)	1st Semester (2005)	2nd Semester (2005)	1st Semester (2006)
Emilia-Romagna region pPCI caseload					
Age, yrs	65.5 ± 13.7	66.5 ± 13.3	67.6 ± 12.5	66.9 ± 13.1	66.9 ± 13.4
Charlson index	1.5 ± 1.2	1.5 ± 1.0	1.5 ± 1.0	1.4 ± 0.9	1.4 ± 0.9
Off-hours pPCI, n	307	256	325	344	396
Regular-hours pPCI, n	275	284	227	322	336
Fast track from EMS, %	14.1	15.4	15.1	17.3	21.6
GP IIb/IIIa inhibitor use, %	90.5	89.6	90.4	90.7	90.0
Network door-to-balloon time	85 (55–116)	80 (56–122)	82 (51–119)	83 (50–115)	84 (53–125)
In-hospital unadjusted total mortality, %	8.0	6.8	7.2	7.5	5.0
Nontransferred STEMI treated at non-PCI centers					
Nontransferred STEMI caseload, %	26.7	25.1	21.4	17.5	15.5
Age, yrs	76.8 ± 12.9	77.3 ± 12.9	78.2 ± 13	78.9 ± 12.4	81 ± 12
Charlson index	1.4 ± 1.6	1.7 ± 1.5	1.5 ± 1.7	1.7 ± 1.7	1.7 ± 1.8
In-hospital unadjusted total mortality, %	25.4	25.6	30.3	34.6	31.2

Data are presented as mean ± SD, n, %, or median (25th to 75th percentile).
Abbreviations as in Tables 1 and 2.

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Key Words: hospital network ■ myocardial infarction ■ off-hours ■ outcomes ■ primary coronary angioplasty.