

# Impact of Day Versus Night as Intervention Time on the Outcomes of Primary Angioplasty for Acute Myocardial Infarction

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**Background:** Conflicting datas exist regarding the outcomes of primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) when the intervention is performed during night hours. **Methods and Results:** 2,644 consecutive patients with STEMI (mean age  $56.7 \pm 11.9$ , years, 2,188 male) undergoing primary PCI between October 2003 and March 2008 were retrospectively enrolled into this study (single high-volume center: >3,000 PCIs/year). Day time was defined according to intervention between 08:00 am and 06:00 pm and night as intervention time between 06:00 pm and 08:00 am. 1,141 patients (43.2%) were treated during the day and 1,503 (56.8%) at night. The baseline characteristics of both groups were similar except for more frequent hypertension (42.6 vs. 36.5%;  $P = 0.002$ ), women (19.7 vs. 15.4%;  $P = 0.003$ ), and old ( $\geq 75$ y) patients (9.6 vs. 7.4;  $P = 0.046$ ) in the day time group. Compared with those treated during night time, day time patients had longer angina-reperfusion times (mean, 205 vs. 188 minutes,  $P = 0.016$ ). Door-to-balloon times were similar ( $P = 0.87$ ), and less than 90 minutes in both groups. There were no differences concerning clinical events and PCI success between the two groups. Hospital mortality was 6.1% during the day and 5.2% during the night (OR 0.98, 95% CI 0.7–1.36;  $P = 0.89$ ). The median follow-up time was 21 months. The Kaplan-Meier survival plot for long-term cardiovascular death was not different for both groups ( $P = 0.78$ ). In-hospital and long-term cardiovascular mortality was also similar in shock and nonshock subgroups. **Conclusions:** Primary PCI can be performed safely during the night at a high-volume PCI center with suitable and effective organization of cardiology department and catheterisation laboratory with 24 hours per day, 7 days per week onsite staffing. © 2009 Wiley-Liss, Inc.

**Key words:** primary angioplasty; acute myocardial infarction; diurnal variation

## INTRODUCTION

Primary percutaneous coronary intervention (PCI) has advantages over thrombolytic therapy such as rapid restoration of normal coronary blood flow in the infarct-related artery (IRA) independent of time from symptom onset, greater amount of salvaged myocardium, and assessment of coronary anatomy, hemodynamic status with risk stratification, and earlier hospital discharge in patients presenting with an ST-elevation myocardial infarction (STEMI) [1–5].

Primary PCI is similar to elective PCI. However, PCI in the early phase of STEMI can be more difficult and requires more experience because it is performed in conditions of increased risk due to hemodynamic and electrical instability, increased thrombogenicity and complete thrombotic occlusion of stenotic coronary arteries. So primary PCI should be done by a team of

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experienced interventional cardiologists in hospitals with well organization of cardiology department and catheterisation laboratory to keep the door-to-balloon time under 90 minutes [6].

There are conflicting data exist that primary PCI performed during the night is not successful compared with the day time intervention [7–9]. “Maximal Individual Therapy in Acute Myocardial Infarction (MITRA)” study [10] has shown comparable feasibility, safety, and results of primary PCI performed day or night in 491 patients. Ortolani et al. [11] in 985 patients, and Sadeghi et al. [12] in 2036 patients found similar results between day and night time intervention. The aim of this study was to evaluate results of primary PCI during day and night time without restrictions based on age, sex, clinical status, and shock in a high-volume tertiary center with a large population.

## METHODS

### Patient Population

We retrospectively evaluated 2,825 consecutive patients with STEMI who were admitted to the emergency department of our hospital and underwent urgent cardiac catheterization procedures between October 2003 and March 2008. Patients were enrolled in the study if they fulfilled the following criteria: (1) presenting within 12 hr (18 hr for cardiogenic shock) from the onset of symptoms (typical chest pain lasting for >30 min); (2) ST-segment elevation  $\geq 1$  mm in at least two contiguous electrocardiogram (ECG) leads or new onset of complete left bundle-branch block; (3) treatment with primary PCI (angioplasty and/or stent deployment). 181 patients were excluded; no indication for PCI ( $n = 96$ ), treated with coronary bypass surgery (i.e. not suitable for PCI) ( $n = 85$ ). Therefore, the final study population consisted of 2,644 patients. All primary PCI procedures during day and night time were performed in a single high-volume tertiary center (>3,000 PCIs/year) by expert operators performing >75 PCIs/year. The study protocol was approved by the hospital’s Ethics Committee.

### Data Sources

Demographic information and the clinical history of risk factors such as age, gender, diabetes mellitus (DM), hypertension, hypercholesterolemia, smoking, family history for coronary artery disease, myocardial infarction (MI) history, PCI, or bypass history were determined from medical records. Angina-to-reperfusion time and door-to-balloon time were calculated.

Blood values were determined at hospital admission (before catheterization procedures) and on a daily basis during the hospital stay. A 12-lead ECG was recorded in each patient just after hospital admission. Glomerular filtration rate (GFR) was estimated by the simplified MDRD (Modification of Diet in Renal Disease) equation [13,14].

Transthoracic echocardiography was performed by using a system V (Vingmed, GE) with a 2.5 MHz phased-array transducer. Recordings were taken on patients positioned in the left lateral decubitus position. The left ventricular ejection fraction (LVEF) was measured using modified Simpson’s rule [15].

### Hospital Characteristics

This study was done in Istanbul which is Turkey’s most populous city. Today its population is approximately 16 million (23% of Turkey), and increases at an estimated 700,000 immigrants per year from all areas of Turkey. So Istanbul is mosaic of Turkey.

Between 06.00 pm and 08.00 am (every day of week), and at weekend, there are 8 cardiology fellowships, 3 cardiologists (1 for emergency room, 1 for angioplasty, and 1 for intensive care units), 1 angiography nurse, and 1 radiology technician. These personnel and also surgeons stay at hospital. When a patient comes to emergency room, first these doctors examine the patient, record the times, and take ECG. When the fellowships call interventionalist doctor, the patient is transferred to angiography laboratory. Emergency room is next to door of hospital (10 meters). There are 50 meters between emergency room and laboratory. (Hospital door-to-laboratory time is 5–7 minutes).

### Coronary Angiography, Primary Angioplasty and Stenting

All patients received chewable aspirin (300 mg, unless contraindicated) and clopidogrel (300 mg loading dose) before coronary angiography. Angiographic data of the patients were obtained from the cardiac catheterization laboratory records. Emergency coronary angiography was performed by the percutaneous femoral approach. In all cases, nonionic low-osmolality contrast media was used. The contralateral artery was first injected. IRA was graded according to thrombolysis in MI (TIMI) classification [16]. Heparin (10,000 U) was administered after coronary anatomy was defined. Coronary artery stenosis >50% was considered clinically significant. Occlusion of the IRA was crossed by using a 0.014-inch guide wire. PCIs including balloon angioplasty and/or stent implantation were performed only for IRA according to lesion anatomy. For each

procedure, interventional success at the acute phase defined as an obstruction and stenosis of the IRA having been reduced to <50% stenosis with TIMI 2 or 3 flow after primary PCI. After angioplasty, all patients were admitted to the coronary care unit, where 500 U/hr of intravenous heparin or 1mg/kg/day of subcutaneous low molecular weight heparin were given; 100 mg aspirin and 75 mg clopidogrel were continued in all patients. The use of tirofiban was left to the discretion of the operator.

### Definitions

We compared the results of patients who underwent primary PCI during the day with those undergoing the procedure during the night. Day time was defined according to intervention as between 08:00 am and 6:00 pm, and night intervention time as between 06:00 pm and 8:00 am. Anemia was defined as a baseline hemoglobin concentration <13 mg/dl in men and <12 mg/dl in women. Cardiogenic shock was defined as marked and persistent (>30 min) hypotension with systolic arterial pressure less than 80 mmHg with signs of hypoperfusion due to the left ventricular dysfunction, right ventricular infarction, and mechanical complications. Patients were also evaluated according to Killip clinical examination classification [17]. Advanced heart failure was defined as New York Heart Association (NYHA) classification  $\geq 3$ . Multivessel disease was defined by a stenosis of >50% in three major epicardial coronary arteries. Hypertension was defined as a history of hypertension for >1 year that required the initiation of antihypertensive therapy by the primary physician. DM was defined by treatment with oral hypoglycemic agents or insulin regardless of glycemic status at admission. Admission hyperglycemia was defined as admission plasma glucose  $\geq 200$  mg/dl, regardless of diabetic status. Hypercholesterolemia was defined as total cholesterol  $\geq 200$  mg/dl. Positive family history for coronary artery disease (CAD) was defined as documented evidence of CAD in a parent or sibling before 60 years of age. Acute stent thrombosis is defined as an abrupt onset of cardiac symptoms (i.e., an acute coronary syndrome) along with an elevation in levels of biomarkers or electrocardiographic evidence of myocardial injury after stent deployment in the first 24 hr which is accompanied by angiographic evidence of a flow-limiting thrombus near a previously placed stent.

Cardiovascular mortality was defined as unexplained sudden death, death due to acute MI, heart failure, and arrhythmia. Reinfarction was described as elevation of serum CK-MB enzyme levels by two times of the upper limit of normal and ST-segment re-elevations.

### Follow-Up

Follow-up data were obtained from hospital records or by interviewing (directly or by telephone) patients, their families, or their personal physicians. Major adverse cardiac events (MACE) were defined as cardiovascular mortality, reinfarction, repeat target-vessel revascularization (TVR) (percutaneous or surgical). Only cardiovascular mortality was recorded. Serious ventricular arrhythmias (ventricular tachycardia and/or fibrillation), stroke, cardiopulmonary resuscitation, advanced heart failure, atrioventricular block, transient pace intervention, intra-aortic balloon pump, atrial fibrillation, major bleeding requiring  $\geq 2$ U of blood, dialysis, acute stent thrombosis, and MACE were also recorded during in-hospital period.

### Statistical Analysis

Quantitative variables were expressed as mean value  $\pm$  SD, and qualitative variables were expressed as percent (%). Comparison of parametric values between two groups were performed by means of two-tailed Student's *t* test. Categorical variables were compared by the likelihood-ratio  $\chi^2$  test or Fisher's exact test. Backward stepwise multivariable logistic regression analysis which included variables with  $P < 0.1$  by univariate analysis was performed to identify independent predictors of in-hospital cardiovascular mortality. The cumulative survival curves for cardiovascular mortality were constructed with the use of the Kaplan-Meier method with differences assessed with the log-rank test. A  $P$  value < 0.05 was considered statistically significant. All statistical studies were carried out with SPSS program (version 15.0, SPSS, Chicago, Illinois).

### RESULTS

The baseline characteristics in the two groups are summarized in Table I. Among the 2,644 study patients (mean age  $56.7 \pm 11.9$ , years, 2188 male), 1,141 patients (43.2%) were treated during the day and 1,503 (56.8%) at night. Patients in the day time group were more likely to be female, slightly older, and more commonly had hypertension, PCI history, and longer reperfusion time (Table I).

Table II lists the laboratory data of the patients. Admission baseline creatinine, cholesterol and glucose levels were not different between the two groups. Similar enzymatic peak, renal insufficiency, and admission anemia were observed in groups (Table II).

Angiographic and procedural characteristics are depicted in Table III. LVEF was similar in groups. Culprit lesions, preprocedural, postprocedural epicardial flow, and procedural success were also similar (Table III). Table IV presents the in-hospital adverse

TABLE I. Baseline Characteristics of Study Patients

	Day time (n = 1,141)	Night time (n = 1,503)	P value
Age, y	57.5 (11.9)	56 (11.9)	0.002
Age $\geq$ 75, y	109 (9.6)	111 (7.4)	0.046
Male	916 (80.3)	1272 (84.6)	0.003
Anterior MI	549 (48.1)	747 (49.7)	0.42
Hypertension	486 (42.6)	549 (36.5)	0.002
Hypercholesterolemia	394 (34.5)	492 (32.7)	0.16
DM	285 (25)	369 (24.6)	0.75
Current smoker	640 (56.1)	871 (58)	0.25
Family history for CAD	180 (15.8)	241 (16)	0.85
Bypass	39 (3.4)	39 (2.6)	0.21
PCI	108 (9.5)	102 (6.8)	0.01
MI history	132 (11.6)	154 (10.2)	0.27
Dialysis history	2 (0.2)	6 (0.4)	0.3
Admission cardiogenic shock	53 (4.6)	54 (3.6)	0.18
Killip >1	89 (7.8)	112 (7.5)	0.92
Reperfusion time, min	205 (157.4)	188 (133.3)	0.016
Door-to-balloon time, min	31 (20)	30 (22)	0.87
Admission systolic pressure, mmHg	123.4 (30.5)	125.3 (31.4)	0.28

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively.

MI: Myocardial infarction, CAD: coronary artery disease, DM: diabetes mellitus, PCI: percutaneous coronary intervention.

TABLE II. Laboratory Findings of Patients

	Day time (n = 1,141)	Night time (n = 1,503)	P value
Creatinine concentration at admission, mg/dl	0.98 (0.4)	0.99 (0.4)	0.47
GFR (MDRD) <60 ml/min/1.73 m <sup>2</sup>	140 (12.3)	178 (11.8)	0.72
Creatinine concentration at admission >1.5 mg/dl	41 (3.6)	58 (3.9)	0.73
Peak CK-MB, U/L	216.4 (179)	222.6 (187.2)	0.4
Total cholesterol, mg/dl	188.8 (42.7)	188.4 (42.3)	0.81
LDL-cholesterol, mg/dl	118.1 (33.4)	117.3 (36.4)	0.65
HDL-cholesterol, mg/dl	41.2 (9.1)	40.7 (9.3)	0.18
Triglycerides, mg/dl	150.7 (107.9)	150.5 (107.1)	0.98
Admission blood glucose concentration, mg/dl	155.4 (79.7)	158.5 (75.7)	0.31
Anemia at admission	282 (24.7)	368 (24.5)	0.85
Admission hyperglycemia	182 (16)	253 (16.8)	0.56

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively.

GFR: Glomerular filtration rate, MDRD: Modification of diet in renal disease.

outcomes after primary PCI. There were no differences between patients treated during the day and those treated at night concerning clinical events. The length of hospital stay was also similar. Hospital mortality was 6.1% during the day compared with 5.2% during the night (OR 0.98, 95% CI 0.7–1.36;  $P = 0.89$ ). In nonshock subgroup, in-hospital mortality was 2.9% for day and 3% for night group ( $P = 0.92$ ).

The median follow-up time was 21 months. Follow-up data after discharge were not obtained for 20 (1.8%) patients with day and 26 (1.7%) patients with night time intervention. Table V presents the long-term adverse outcomes. The Kaplan-Meier survival plot for cardiovascular death is presented in Figure 1a. The Kaplan-Meier survival plot for long-term cardiovascular death was not different for both groups ( $P = 0.78$ ). Long-term reinfarction, TVR, MACE, and advanced

heart failure showed the same significance as for cardiovascular mortality. Table VI reports results of univariate analysis to search for possible predictors of in-hospital cardiovascular mortality. Night time intervention showed no sign of association within-hospital mortality at univariate analysis (odds ratio [OR], 0.84; 95% confidence interval [CI], 0.60–1.17;  $P = 0.29$ ).

Multivariate logistic regression analysis demonstrated the following parameters to be independent predictors of cardiovascular mortality; DM (OR 4.1, 95% CI 1.59–10.6;  $P = 0.004$ ), cardiogenic shock (OR 13.2, 95% CI 4.7–37.1;  $P < 0.001$ ), GFR  $\leq$ 60 (OR 3.1, 95% CI 1.23–7.86;  $P = 0.017$ ), post-PCI LVEF <40% (OR 6.6, 95% CI 2.72–16;  $P < 0.001$ ), post-PCI TIMI-3 flow (OR 0.18, 95% CI 0.07–0.46;  $P < 0.001$ ), admission hyperglycemia (OR 4.46, 95% CI 1.72–11.6;  $P = 0.002$ ), and age 75 years or older (OR

**TABLE III. Angiographic and Procedural Characteristics of Patients**

	Day time ( <i>n</i> = 1,141)	Night time ( <i>n</i> = 1,503)	<i>P</i> value
Culprit lesion			
LMCA	4 (0.4)	2 (0.1)	0.74
LAD	550 (48.2)	751 (50)	0.68
CX	156 (13.7)	191 (12.7)	0.71
RCA	420 (36.8)	546 (36.3)	0.88
Others	11 (1)	13 (0.9)	0.83
No. of diseased vessels			
1	473 (41.4)	640 (42.6)	0.74
2	359 (31.5)	484 (32.2)	0.8
3	309 (27.1)	379 (25.2)	0.69
Pre TIMI grade			
0/1	995 (87.2)	1323 (88)	0.75
2	97 (8.5)	117 (7.8)	0.57
3	49 (4.3)	63 (4.2)	0.89
Post TIMI grade			
0/1	123 (10.8)	142 (9.5)	0.28
2	70 (6.1)	76 (5)	0.48
3	948 (83.1)	1285 (85.5)	0.61
Stent	906 (79.4)	1235 (82.2)	0.17
Stent length, mm	19.4 (6)	19.2 (6.8)	0.67
Stent diameter, mm	3.1 (0.34)	3.1 (0.35)	0.3
Stent type			
BMS	875 (96.6)	1200 (97.2)	0.51
PES	13 (1.4)	15 (1.2)	0.63
SES	18 (2)	20 (1.6)	0.44
Proximal location of the lesion	618 (54.2)	797 (53)	0.57
LVEF, (%)	47.4 (11.3)	47.2 (11.3)	0.8
Tirofiban	529 (46.4)	715 (47.6)	0.62
Success of the procedure	1015 (89)	1354 (90)	0.35

Mean values (SD) and % (*n*) are reported for continuous and categorical variables, respectively.

LMCA: Left main coronary artery, LAD: left anterior descending coronary artery, CX: circumflex coronary artery, RCA: right coronary artery, TIMI: thrombolysis in myocardial infarction, BMS: bare metal stent, PES: Paclitaxel eluting stent, SES: Sirolimus eluting stent, LVEF: left ventricular ejection fraction.

7.22, 95% CI 2.28–22.9; *P* = 0.001), (Table VII). Survival curves were similar within subgroup of patients with (*P* = 0.44) and without shock (*P* = 0.87).

## DISCUSSION

The major findings of this single-center study, the largest to date examining the impact of intervention time in patients undergoing primary PCI for STEMI, were that night time intervention was observed frequently, and it was not associated with an increase in-hospital and long-term mortality. The angiographic, clinical outcomes, procedural success, myocardial recovery, hospital stay, and door-to-balloon time were not different between the two groups. Also night time intervention was not an independent predictor of in-hospital mortality.

In this study, primary PCI procedure was frequent at night similarly to other reports [18]. Because a peak in

**TABLE IV. In-Hospital Cardiac Events and Complications**

	Day time ( <i>n</i> = 1,141)	Night time ( <i>n</i> = 1,503)	<i>P</i> value
In-hospital mortality	70 (6.1)	78 (5.2)	0.29
Reinfarction	19 (1.7)	34 (2.3)	0.28
Target-vessel revascularization	45 (3.9)	71 (4.7)	0.33
MACE	106 (9.3)	143 (9.5)	0.85
Stroke	7 (0.6)	12 (0.8)	0.58
Serious ventricular arrhythmia	66 (5.8)	83 (5.5)	0.77
Cardiopulmonary resuscitation	80 (7)	87 (5.9)	0.2
Advanced heart failure	167 (14.6)	202 (13.4)	0.38
Intra-aortic balloon pump	74 (6.5)	86 (5.7)	0.42
Renal failure requiring dialysis	10 (0.9)	9 (0.6)	0.4
New atrial fibrillation	13 (1.1)	24 (1.6)	0.32
Complete atrioventricular block requiring transient pacemaker	42 (3.7)	60 (4)	0.68
Major bleeding requiring blood transfusion	51 (4.5)	52 (3.5)	0.18
Acute stent thrombosis	11 (1)	13 (0.9)	0.79
Time of hospital stay, days	7.2 (6)	7.2 (4.8)	0.92

Mean values (SD) and % (*n*) are reported for continuous and categorical variables, respectively.

MACE: Major adverse cardiac events (cardiovascular death, reinfarction, target-vessel revascularization).

**TABLE V. Long-Term Cardiac Events**

	Day time ( <i>n</i> = 1,051) <sup>a</sup>	Night time ( <i>n</i> = 1,399) <sup>b</sup>	<i>P</i> value
Cardiovascular mortality	58 (5.5)	75 (5.4)	0.87
Reinfarction	94 (8.9)	105 (7.5)	0.2
Target-vessel revascularization	168 (16)	223 (15.9)	0.93
MACE	240 (22.8)	299 (21.4)	0.35
Advanced heart failure	91 (8.7)	94 (6.7)	0.08

% (*n*) are reported for categorical variables, respectively.

MACE: Major adverse cardiac events (cardiovascular death, reinfarction, target-vessel revascularization).

<sup>a</sup>*n* = 1,051 for day time (There is no follow-up for 20 patients and 70 patients died in-hospital).

<sup>b</sup>*n* = 1,399 for night time (There is no follow-up for 26 patients and 78 patients died in-hospital).

platelet aggregation and blood viscosity, and also different plaque characteristics with variation in coronary blood flow are seen at night [9]. We do not know the exact mechanism of frequent PCI and hypertension history in day time group but older and women patients perhaps were waiting the day for hospital admission because of atypical symptoms.

There are lots of evidence that lower postprocedural success and higher in-hospital mortality occurs in patients treated at night [7–9,19]. Magid et al. showed that door-to-balloon times were substantially longer during off-hours (116.1 minutes) than regular hours (94.8 minutes, *P* < 0.001). In this study, patients presenting during off-hours had significantly higher in-hospital mortality (OR, 1.07; 95% CI, 1.01–1.14; *P* =

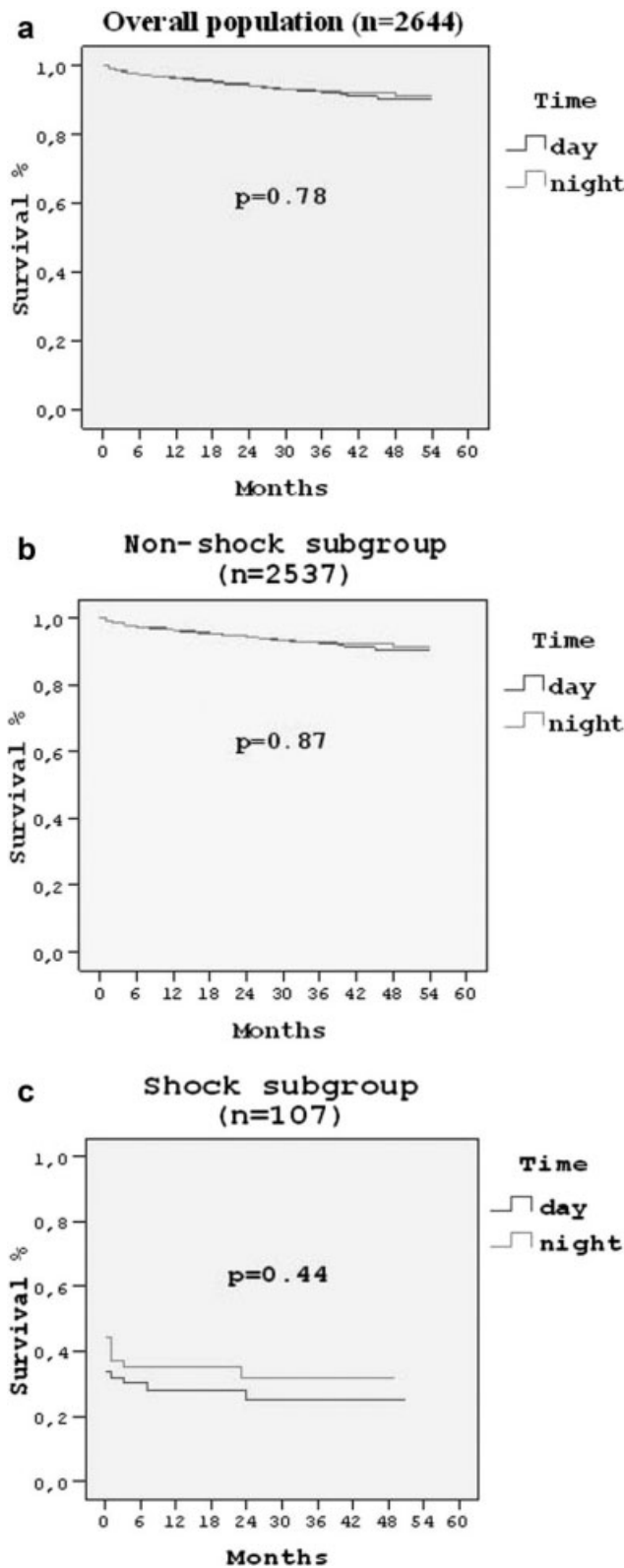


Fig. 1. Kaplan-Meier curve for long-term cardiovascular mortality according to day versus night time intervention. a: Data for overall population (n = 2,644), b: noncardiogenic shock (n = 2,537), c: cardiogenic shock (n = 107).

TABLE VI. Univariate Analysis for Possible predictors of In-Hospital Cardiovascular Mortality

Variables	OO	95% CI	P value
Female sex	2.06	1.43–2.99	<0.001
DM	5.31	3.6–7.82	<0.001
Hypertension	1.52	1.04–2.21	0.03
Anterior MI	1.39	0.99–1.94	0.05
Reperfusion time >6 h	2.44	1.24–4.8	0.01
3 vessels disease	3.14	2.08–4.75	<0.001
Success of the procedure	6.12	3.1–9.24	<0.001
Tirofiban administration	0.4	0.28–0.59	<0.001
Night intervention	0.84	0.6–1.17	0.29
Bypass history	2.11	0.99–4.49	0.051
PCI history	1.84	1.09–3.08	0.02
Admission cardiogenic shock	17.34	8.17–30.44	<0.001
Post-PCI LVEF <40%	10.48	5.56–19.77	<0.001
GFR (MDRD) ≤60 ml/min/1.73 m <sup>2</sup>	11.94	7.9–18.03	<0.001
Post-PCI TIMI 3 flow	0.11	0.04–0.37	<0.001
Age ≥75, y	4.03	2.69–6.05	<0.001
Admission hyperglycemia	6.81	4.57–10.17	<0.001

MI: Myocardial infarction, DM: diabetes mellitus, PCI: Percutaneous coronary intervention, LVEF: Left ventricular ejection fraction, TIMI: Thrombolysis In Myocardial Infarction, GFR: Glomerular filtration rate, MDRD: Modification of diet in renal disease.

TABLE VII. Multivariate Predictors of In-Hospital Cardiovascular Mortality

Variables	OO	95% CI	P value
DM	4.1	1.59–10.6	0.004
Cardiogenic shock	13.2	4.7–37.1	<0.001
Post-PCI TIMI 3 flow	0.18	0.07–0.46	<0.001
GFR (MDRD) ≤60 ml/min/1.73 m <sup>2</sup>	3.1	1.23–7.86	0.017
Post-PCI LVEF <40%	6.6	2.72–16	<0.001
Age ≥75, y	7.22	2.28–22.9	0.001
Admission hyperglycemia	4.46	1.72–11.6	0.002

DM: Diabetes mellitus, PCI: Percutaneous coronary intervention, LVEF: Left ventricular ejection fraction, TIMI: Thrombolysis In Myocardial Infarction, GFR: Glomerular filtration rate, MDRD: Modification of diet in renal disease.

0.02). [18] Glaser et al. compared clinical, angiographic, and procedural characteristics in consecutive patients (n = 685) undergoing primary PCI in the National Heart, Lung, and Blood Institute Dynamic Registry between 1997 and 2006 that were classified as occurring during routine-hours (07:00–18:59) or off-hours (19:00–06:59). In-hospital death, MI, and TVR were significantly higher in off-hours patients (OR 2.66, 95% CI 1.39–4.56; P = 0.002) [20].

In the “CADILLAC” trial [12], reperfusion and door-to-balloon times were significantly prolonged in patients presenting after hours compared with those presenting during peak hours (248 vs. 225 minutes, P < 0.0001) and (129 vs. 108 minutes, P < 0.0001). In “MITRA” trial [10], in-hospital time to treatment was 9 minutes longer (85 minutes day, 94 minutes night, P = 0.037). In this study, the procedural success

is not known, and there is no long-term follow-up. And only 23% of patients were treated at night because some centers had no 24-hour service. Ortolani et al. [11] found similar results that patients treated during off-hours tended to have longer reperfusion time (199 vs. 179 minutes,  $P = 0.052$ ) and showed longer median ECG-to-laboratory time (52 vs. 40 minutes  $P = 0.001$ ). Despite these delays in those trials, angiographic and clinical outcomes were similar in patients treated during day and night time. In contrast to these reports, reperfusion time was 17 minutes shorter at night in our study. Heavy traffic in day might be the reason. Also door-to-balloon time of our center was  $\sim 30$  minutes. But door-to-balloon time difference between our and above studies effect in-hospital mortality. In study by Ortolani et al. [11] and "MITRA" trial [10], in-hospital mortality was 7.9% but it was 5.6% in our study. In the "CADILLAC" trial [12], 30-day mortality was only 2% but patients with shock were excluded in this trial, and the ratio of smoker, DM, anterior MI, and multivessel disease were less according to our study. According to these results, very shorter door-to-balloon times effect mortality. Then it is meaningful to make all attempts to shorten the door-to-balloon time.

In previous studies, it was shown that patients with acute STEMI who were treated at high-volume angioplasty centers have a lower mortality rate than patients treated at low-volume centers and that high-volume centers perform primary angioplasty faster [21,22]. Using the New York State PCI registry, Srinivas et al. [23] examined yearly hospital volume, physician volume, and risk-adjusted mortality in 7,321 patients undergoing primary PCI. Primary PCI by high-volume hospitals ( $>50$  cases/year) and high-volume physicians ( $>10$  cases/year) were associated with lower mortality. The American College of Cardiology and the American Heart Association suggest that primary PCI should be used only if performed in a timely fashion (door-to-balloon time  $<90$  minutes) by individuals skilled in the procedure and supported by experienced personnel in high-volume centers. Primary PCI for STEMI should be done by experienced operators performing  $>75$  elective PCIs/year and, ideally, at least 11 primary PCIs/year. Ideally these should be performed in institutions performing  $>400$  elective PCIs and  $>36$  primary PCIs/year [24]. So primary PCI centers should provide primary PCI as routine for all kind of STEMI patients 24 hours per day, 7 days per week with adequate physician, nursing, and technical staff. And also regular meetings and educational programs should be done for high quality. In our center,  $>3000$  PCIs/year and  $>500$  primary PCIs/year are performed with suitable and

effective organization of cardiology department and catheterisation laboratory.

### Study Limitations

This study carries the well-known limitations of the retrospective design. These results represent a single-center experience. We do not have enough information about patient admission way (self-transportation, transfer from other peripheral hospitals without PCI facilities). So datas about preprocedural medications except for thrombolytics are limited.

In study by Ortolani et al. [11], GpIIb/IIIa agents were extensively administered (in about 80% of patients), most often just before primary PCI. These drugs might have neutralized the effect of higher thrombogenicity at night. In our study, the ratio of GpIIb/IIIa medication is not as much as above study and were used peri-or post-procedure. In multivariate analysis, tirofiban administration did not effect in-hospital cardiovascular mortality.

Circadian secretion of melatonin hormone or diurnal variations of inflammatory markers such as interleukin-6 and C-reactive protein, the activity of the tissue plasminogen activator, and catecholamines, all of which could stimulate the formation of blood clots in patients with STEMI [25–28]. None of these factors were analyzed in our study.

### Clinical Implications

This study shows that patients treated at night by primary PCI have similar clinical outcomes, complication rates, hospital stays, and equivalent mortality, both in-hospital and postdischarge with patients treated during day time if it is done at a high-volume PCI center by experienced operators with shorter door-to-balloon times. So useful strategies, organization, and educations should be planned for faster and effective primary PCI.

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### REFERENCES

1. Grines CL, Browne KF, Marco J, Pothbaum D, Stone GW, et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. Primary Angioplasty in Myocardial Infarction Study Group. *N Engl J Med* 1993;328: 673–679.
2. Gibbons RJ, Holmes DR, Reeder GS, Bailey KR, Hopfenspirger MR, Gersh BJ. The Mayo Coronary Care Unit and

- Catheterization Laboratory Group. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. The Mayo Coronary Care Unit and Catheterization Laboratory Group. *N Engl J Med* 1993;328:685–691.
3. Zijlstra F, de Boer MJ, Hoorntje JCA, Reiffers S, Reiber JHC, Suryapranata H. A comparison of immediate coronary angioplasty with intravenous streptokinase in acute myocardial infarction. *N Engl J Med* 1993;328:680–684.
  4. O'Neill W, Timmis GC, Bourdillon PD, Lai P, Ganghadarhan V, Walton Jr J, Ramos R, Laufer N, Gordon S, Schork MA, et al. A prospective randomized trial of intracoronary streptokinase versus coronary angioplasty for acute myocardial infarction. *N Engl J Med* 1986;314:812–818.
  5. Keeley EC, Grines CL. Primary coronary intervention for acute myocardial infarction. *JAMA* 2004;291:736–739.
  6. Caputo RP, Ho KKL, Stoler RC, Sukin CA, Lopez JJ, Cohen DJ, Kuntz RE, Berman A, Carrozza JP, Baim DS. Effect of continuous quality improvement analysis on the delivery of primary percutaneous transluminal angioplasty for acute myocardial infarction. *Am J Cardiol* 1997;79:1159–1164.
  7. Dominguez-Rodriguez A, Garcia-Gonzalez M, Abreu-Gonzalez P. Outcome of primary angioplasty for ST-segment elevation myocardial infarction during routine duty hours versus during off-hours. Results of a single-center in Spain. *Int J Cardiol* 2007;119:227–229.
  8. Henriques JPS, Haasdijk AP, Zijlstra F, Zwolle Myocardial Infarction Study Group. Outcome of primary angioplasty for acute myocardial infarction during routine duty hours versus during off-hours. *J Am Coll Cardiol* 2003;41:2138–2142.
  9. Assali AR, Brosh D, Vaknin-Assa H, Fuchs S, Teplitsky I, Sela O, Kornowski R. The impact of circadian variation on outcomes in emergency acute anterior myocardial infarction percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2006;67:221–226.
  10. Zahn R, Schiele R, Seidl K, Schuster S, Hauptmann KE, Voigtländer T, Gottwik M, Berg G, Kunz T, Glunz HG, Limbourg P, Senges J. Daytime and nighttime differences in patterns of performance of primary angioplasty in the treatment of patients with acute myocardial infarction. Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) Study Group. *Am Heart J* 1999;138:1111–1117.
  11. Ortolani P, Marzocchi A, Marzozzini C, Palmerini T, Saia F, Aquilina M, Baldazzi F, Silenzi S, Taglieri N, Grosseto D, Bacchi-Reggiani ML, Guastaroba P, Grilli R, Branzi A. Clinical comparison of “normal-hours” vs. “off-hours” percutaneous coronary interventions for ST-elevation myocardial infarction. *Am Heart J* 2007;154:366–372.
  12. Sadeghi HM, Grines CL, Chandra HR, Mehran R, Fahy M, Cox DA, Garcia E, Tchong JE, Griffin JJ, Stuckey TD, Lansky AJ, O'Neill WW, Stone GW. Magnitude and IMPACT OF TREATMENT DELAYS ON WEEKNIGHTS AND WEEKENDS IN PATIENTS UNDERGOING PRIMARY ANGIOPLASTY FOR ACUTE MYOCARDIAL INFARCTION (the CADILLAC Trial). *Am J Cardiol* 2004;94:637–640.
  13. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999;130:461–470.
  14. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function—measured and estimated glomerular filtration rate. *N Engl J Med* 2006;354:2473–2483.
  15. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, Gutgesell H, Reichek N, Sahn D, Schnittger I. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr* 1989;2:358–367.
  16. Chesebro JH, Knatterud G, Roberts R, Borer J, Cohen LS, Dalen J, Dodge HT, Francis CK, Hillis D, Ludbrook P. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: A comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. *Circulation* 1987;76:142–154.
  17. Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. *Am J Cardiol* 1967;20:457–464.
  18. Magid DJ, Wang Y, Herrin J, McNamara RL, Bradley EH, Curtis JP, Pollack CV Jr, French WJ, Blaney ME, Krumholz HM. Relationship between time of day, day of week, timeliness of reperfusion, and in-hospital mortality for patients with acute ST-segment elevation myocardial infarction. *JAMA* 2005;294:803–812.
  19. Saleem MA, Kannam H, Aronow WS, Weiss MB, Kalapatapu K, Pucillo AL, Monsen CE. The effects of off-normal hours, age, and gender for coronary angioplasty on hospital mortality in patients undergoing coronary angioplasty for acute myocardial infarction. *Am J Cardiol* 2004;93:763–764.
  20. Glaser R, Naidu SS, Selzer F, Jacobs AK, Laskey WK, Srinivas VS, Slater JN, Wilensky RL. Factors associated with poorer prognosis for patients undergoing primary percutaneous coronary intervention during off-hours: Biology or systems failure. *JACC Cardiovasc Interv* 2008;1:681–688.
  21. Canto JG, Every NR, Magid DJ, Rogers WJ, Malmgren JA, Frederick PD, French WJ, Tiefenbrunn AJ, Misra VK, Kiefe CI, Barron HV. The volume of primary angioplasty procedures and survival after acute myocardial infarction. National Registry of Myocardial Infarction 2 Investigators. *N Engl J Med* 2000;342:1573–1580.
  22. Moscucci M, Share D, Smith D, O'Donnell MJ, Riba A, McNamara R, Lalonde T, Defranco AC, Patel K, Kline Rogers E, D'Haem C, Karve M, Eagle KA. Relationship between operator volume and adverse outcome in contemporary percutaneous coronary intervention practice: An analysis of a quality-controlled multicenter percutaneous coronary intervention clinical database. *J Am Coll Cardiol* 2005;46:625–632.
  23. Srinivas VS, Hailpern SM, Koss E, Monrad ES, Alderman MH. Effect of physician volume on the relationship between hospital volume and mortality during primary angioplasty. *J Am Coll Cardiol* 2009;53:574–579.
  24. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB III, Morrison DA, O'Neill WW, Schaff HV, Whitlow PL, Williams DO, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). *J Am Coll Cardiol* 2006;3;47:e1–121.



25. Singh RB, Cornelissen G, Weydahl A, Schwartzkopff O, Katinas G, Otsuka K, Watanabe Y, Yano S, Mori H, Ichimaru Y, Mitsutake G, Pella D, Fanghong L, Zhao Z, Rao RS, Gvozdjakova A, Halberg F. Circadian heart rate and blood pressure variability considered for research and patient care. *Int J Cardiol* 2003;87:9–28.
26. Dominguez-Rodriguez A, Abreu-Gonzalez P, Garcia-Gonzalez M, Ferrer J, de la Rosa A, Vargas M, Reiter RJ. Light/dark patterns of interleukin-6 in relation to the pineal hormone melatonin in patients with acute myocardial infarction. *Cytokine* 2004;26:89–93.
27. Dominguez-Rodriguez A, Garcia-Gonzalez M, Abreu-Gonzalez P, Ferrer J, Kaski JC. Relation of nocturnal melatonin levels to C-reactive protein concentration in patients with ST-segment elevation myocardial infarction. *Am J Cardiol* 2006;97:10–12.
28. Dominguez-Rodriguez A, Garcia-Gonzalez M, Abreu-Gonzalez P. Link between arterial inflammation and circadian rhythm: The oversight aspect in the year 2004. *J Am Coll Cardiol* 2006;47:688–689.