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Dependence of clinical outcomes on time of hospital admission in patients with ST-segment elevation myocardial infarction

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Citation: Ozbek M, Ildirimli K, Arik B, Aktan A, Coskun, MS, et al. Dependence of clinical outcomes on time of hospital admission in patients with ST-segment elevation myocardial infarction. Ann Saudi Med 2023; 43(1): 25-34. DOI: 10.5144/0256-4947.2023.25

Received: October 12, 2022

Accepted: November 7, 2022

Published: February 2, 2023

Funding: None.

BACKGROUND: There are conflicting results in studies investigating the effects of percutaneous coronary intervention (PCI) on the prognosis of patients with ST-segment elevation myocardial infarction (STEMI) during or outside of usual hospital working hours. While some researchers have reported higher mortality rates in STEMI patients admitted outside of working hours, others did not find a statistically significant difference.

OBJECTIVES: Investigate the short-term endpoints and long-term outcomes of STEMI patients by time of admission.

DESIGN: Retrospective

SETTING: Tertiary percutaneous coronary intervention center.

PATIENTS AND METHODS: Patients were grouped by admission, which consisted of four intervals: 06:00 to <12:00, 12:00 to <18:00, 18:00 to <24:00, and 24:00 to <06:00. We analyzed demographic, clinical and mortality by admission time interval and mortality by multivariate analyses, including the time intervals.

MAIN OUTCOME MEASURES: Clinical data and mortality

SAMPLE SIZE: 735 patients; median (IQR) age 62 (22) years; 215 (29.3%) women.

RESULTS: Patients admitted at night were 1.37 times more likely to experience pulmonary edema than patients whose symptoms started in the daytime (*P*=.012); 32.9% of the patients whose symptoms started at night presented with Killip class II-IV, while during the daytime, 21.4% presented with Killip class II-IV (*P*=.001). Among the patients, the most common was inferior STEMI (38.6%). However, no-reflow was significantly higher during the daytime compared to the nighttime (*P*=.12). The risk of the cardiac arrest on admission was 1.2 times higher in patients admitted at night (*P*=.034). Neither time interval of admission nor several other variables had an effect on clinical outcome or mortality.

CONCLUSIONS: While patients admitted at night presented with pulmonary edema and cardiogenic shock more frequently, no reflow was observed during the day after the procedure. Although patients admitted at night with STEMI presented with worse clinical conditions, similar results were observed between the groups in clinical outcomes.

LIMITATIONS: More "real world" results might have been obtained if the study had replicated more typical referral conditions for PCI.

CONFLICT OF INTEREST: None.

ST-segment elevation myocardial infarction (STEMI) occurs as a result of complete occlusion of any of the coronary arteries that perfuse myocardial tissue and is one of the most common causes of death in the world.[1] Percutaneous coronary intervention (PCI) has positive effects on all-cause mortality and cardiovascular endpoints and has been shown to be the most effective method in achieving target vessel revascularization.[2]

There are conflicting results in studies investigating the effects of PCI on the prognosis of patients with STEMI during or outside of working hours. While some researchers reported higher mortality rates in STEMI patients admitted outside of working hours, others did not find a significant difference.[3,4] Factors that may affect differences in the routine catheterization laboratory, day and night hospitalization, operator fatigue at night and operator experience with PCI.[5] Even small increases in the risk of death or complication rates that might be related to working hours could be important due to the high incidence and case fatality rate in the general population of STEMI. Therefore, we conducted a study investigating the short-term endpoints and long-term outcomes of STEMI patients according to admission time.

PATIENTS AND METHODS

Study design and inclusion criteria

In this retrospective study, 1200 patients who were admitted to Diyarbakır Dicle University between January 2012 and January 2015 with STEMI onset within the last 12 hours on electrocardiogram (ECG) and underwent PCI were sequentially investigated. STEMI was defined as the presence of symptoms of ischemic origin in more than one significant lead on the ECG and the presence of a new ST-segment elevation >1 mm measured from the J point. Patients with cancer, hematological disorder, inflammatory or infectious disease history, and bleeding diathesis were excluded from the study. According to the design of the study, patients who were not treated with primary PCI, patients who died before blood parameters could be determined were not included; patients who could not be evaluated by echocardiography or who could not obtain long-term follow-up information were also excluded from the study. Three investigators (BA, MSC, and KI, unaware of the patient groups) independently reviewed the reports. After the application of exclusion criteria, patients who met the inclusion criteria were investigated in detail. Disease histories and drug histories of our population were recorded by accessing their information through the health system.

In-hospital mortality, 1-year, and 5-year mortality, demographic data, coronary artery disease risk factors and physical examination records were recorded. Existing clinical symptoms and signs were also recorded in detail. Patients were evaluated by the Killip classification on heart failure prognosis according to clinical examination guidelines. According to the physical examination of the patients, those without signs of heart failure were grouped as Class I, those with mild heart failure findings as Class II, those with crepitant rales over the middle zone of the lung as Class III, and those with cardiogenic shock were grouped as Class IV.

Transthoracic echocardiography was performed at admission to determine left ventricular ejection fraction. Selective coronary angiography was performed on all patients using the Judkins technique. PCI was performed using the standard femoral approach with the necessary pharmacological support using a 7F guiding catheter. The names of the physicians who performed PCI were recorded to determine the operator effect on the results. Troponin and CK-MB levels were monitored during the hospitalization period of all patients. Peak troponin and peak CK-MB values were noted. The amount of ST segment resolution was calculated by comparing the amount of ST segments in the first ECG taken at the beginning and after the completion of PCI. According to these recordings, the decrease in the amount of ECG ST segment was calculated and recorded. Absolute cell counts were used to perform subsequent analyses.

Angiographic analysis and definitions

Both PCI strategy and device selection were determined by the attending physician. All pharmacological treatments supporting PCI or preventing STEMI complications were administered according to current guidelines.[6] Myocardial blush grade (MBG) was determined by the primary operator immediately after PCI and added to the operative notes. MBG 0 was defined as either no myocardial blush or persistent myocardial blush 'staining'. MBG 1 was defined as minimal myocardial blush or contrast density. MBG 2 was defined as moderate myocardial blush or contrast density, but less than that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery. MBG 3 was defined as normal myocardial blush or contrast density that is comparable with that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery. The patients with an MBG of 3 were defined as the reflow group, while the patients with an MBG below 3 were determined as the no-reflow group.

Main outcome measures

Patients were grouped into the four intervals: 06:00 to <12:00, 12:00 to <18:00, 18:00 to <24:00, and 24:00 to <06:00. The patient group with STEMI was also evaluated for localization. We used in-hospital, 1-year, and 5-year mortality as the main outcome. We analyzed each death outcome separately. Other endpoints were hospitalization for heart failure, ischemic, hemorrhagic stroke or transient ischemic stroke attacks, and recurrent myocardial infarction within 1 year.

Statistical analysis

We analyzed our data using IBM SPSS for Windows version 25.0. We analyzed the normality of the distribution using the Kolmogorov-Smirnov test. We expressed abnormally distributed continuous variables as the median and IQR (interquartile range). We calculated the categorical variables we created in large numbers as percentage (%) and compared them using the chi-square test or Fisher exact test. In the case of more than one group, we compared used one-way analysis of variance (ANOVA) or, as appropriate, the Kruskal-Wallis test. The Bonferroni correction was used for post hoc analyses.The mean infarct size over time intervals was evaluated with a nonlinear cubic spline to identify any potential nonlinear relationship between exposure time and infarct size. The effect of time intervals on cardiogenic shock and pulmonary edema was analyzed. In addition, a forest plot was drawn to determine the effect of admission time interval on clinical endpoints. Univariate and multivariate logistic regression models were used to determine predictors of in-hospital mortality and 1-year mortality. According to the results of the univariate analysis, we selected the independent variables for the multivariate logistic analysis of in-hospital mortality and 1-year mortality. In addition, we used a multivariate Cox regression model to determine whether admission time interval was an independent predictor of 5-year mortality. The independent variables determined from the first univariate analysis were included in this multivariate Cox regression model. The survival analyses for 1-year mortality and 5-year mortality were performed using Kaplan-Meier analysis. A *P* value of <.05 was considered significant.

RESULTS

Of the 12:00 patients, 735 patients with a median (IQR) age of 62 (22) years, including 215 (29.3%) women, were eligible for the study (**Table 1**). More patients admitted from 24:00 to <06:00 had diabetes (41.8%) compared with other time periods (*P*=.010). Six percent of patients with symptom onset from 24:00 to <06:00 had previous coronary artery bypass graft operation compared to no patients with 18:00 to <24:00 symptom onset (*P*=.032). Of patients admitted from 24:00 to <06:00, 14.9% received clopidogrel, while 32% of patients with symptoms starting at 06:00 to <1200 received clopidogrel (*P*=.022). We did not observe any statistically significant differences in the use of aspirin, statins, ACE inhibitors, calcium channel blockers or beta blockers prior to the procedure between the four admission time intervals.

There were significant differences in terms of cardiogenic shock, pulmonary edema, Killip classification, MI classification, and peak CK-MB (**Table 2**). Presentation with cardiogenic shock was encountered in 17.9% of patients in the 24:00 to <06:00 group and cardiogenic shock was more common in patients with pulmonary edema than in patients admitted at other times of the day (**Figure 1**). Patients admitted at night (n=207) were 1.37 times more likely to experience pulmonary edema than patients whose symptoms started in the morning (*P*=.012) (**Figure 2**). No reflow was significantly higher in the daytime group compared to the nighttime group (*P*=.012). The risk of cardiac arrest on admission was 1.2 times higher in nighttime patients (*P*=.034). Although nighttime admission increased the risk of 5-year mortality by 10%, there were no significant differences between the day-night time intervals (*P*=.07, **Figure 2**).

As shown in **Figure 3**, 32.9% of the patients admitted at night presented with Killip class II-IV, while admission during the day, 21.4% presented with Killip class II-IV (*P*=.001). The most common type of MI was inferior STEMI (38.6%) . When the duration from the onset of symptoms to hospital admission was compared, time was significantly shorter in the 24:00 to <06:00 group (*P*=.001) (**Table 2**).

The highest peak CK-MB values were observed in patients in the 18:00 to <24:00 group and the lowest values were observed in patients in the 12:00 to <18:00 group (*P*=.024, **Table 2**). The highest peak of CK-MB was observed between 18:00 to <24:00 patients and the lowest peak of CK-MB was observed between 06:00 to <12:00 patients. However, nonlinearity testing using confined cubic curves was not significant (*P*=.108).

There were no significant differences in in-hospital, 1-year, and 5-year mortality between the time period groups (**Table 3**). However, no-reflow was significantly higher in the daytime group compared to the nighttime group (*P*=.012, **Figure 2**). The risk of cardiac arrest on admission was 1.2 times higher in nighttime patients (*P*=.034, **Figure 2**). Although nighttime admission increased the risk of 5-year mortality by 10%, there was no significant differences between the day-night time

intervals (*P*=.07, **Figure 2**).

A multivariate logistic regression model adjusted for age, heart rate per minute, thrombosis in myocardial infarction (TIMI) score, ejection fraction, diabetes mellitus, gender, history of cerebrovascular accident, and no reflow phenomenon with time of admission as an independent predictor of in-hospital and 1-year mortality and a Cox multivariate showed no significant differences by time of admission. (**Table 4**). The Kaplan-Meier 1-year and 5-year survival estimates for each of the four time periods, 06:00 to <12:00 had lower survival than the other three time periods, but the difference was not statistically significant (**Figure 4**).

DISCUSSION

In our study, we show the effect of intervals of hospital admission time clinical findings, complications encountered in those undergoing PCI, and short- and long-term follow-up endpoints in patients admitted for STEMI who underwent PCI. In our population of patients undergoing PCI, cardiac arrest, pulmonary edema, and cardiogenic shock were significantly more likely to occur in the night-onset period group; no-reflow development occurred unexpectedly more in the day-onset period group; peak CK-MB value after PCI was higher in patients admitted at night compared to daytime admission. Our findings show that the time interval of admission had little effect on outcomes.

In one study, it was determined that patient groups who underwent PCI during and outside working hours had similar angiographic and clinical findings.[7] It is known that the experience of the catheterization laboratory, operator experience and the use of additional treatments affect patient mortality.[7] To minimize inter-

Table 1. Baseline characteristics of the patients by time period.

	24:00 to <06:00 (n=67)	06:00 to <12:00 (n=200)	12:00 to <18:00 (n=328)	18:00 to <24:00 (n=140)	*P* value
Age (years)	61 (22.5)	61 (22)	62 (22)	66 (21.2)	.767
Female (% of total population)	22 (2.9)	60 (8.2)	93 (12.6)	40 (5.4)	.861
Ejection fraction (%)	45 (20)	45 (15)	45 (20)	45 (15)	.258
Current smoker	37 (55.2)	96 (48)	158 (48.2)	75 (54)	.502
Hypertension	26 (38.8)	72 (36)	119 (36.4)	43 (30.9)	.632
Diabetes mellitus	28 (41.8)	46 (23)	93 (28.4)	49 (35.3)	**.010**
Dyslipidemia	4 (6)	6 (3)	22 (6.7)	6 (4.3)	.285
Past myocardial infarction	5 (7.5)	12 (6)	14 (4.3)	4 (2.9)	.395
Past cerebrovascular events	3 (4.5)	9 (4.5)	12 (3.7)	4 (2.9)	.875
Past percutaneous coronary intervention	4 (6.1)	14 (7)	23 (7)	8 (5.8)	.956
Past coronary artery bypass graft operation	4 (6)	6 (3)	7 (2.1)	0	**.032**[a]
Medications on admission					
Acetylsalicylic acid	24 (35.8)	96 (48)	129 (39.3)	51 (36.4)	.094
Clopidogrel	10 (14.9)	64 (32)	89 (27.1)	30 (21.4)	**.022**
Beta blockers	5 (7.5)	14 (7)	21 (6.4)	5 (3.6)	.550
Calcium channel blockers	0	5 (2.5)	4 (1.2)	1 (0.7)	.493[a]
Angiotensin converting enzyme inhibitors	3 (4.5)	10 (5)	24 (7.3)	3 (2.1)	.145
Statins	3 (4.5)	8 (4)	18 (5.5)	2 (1.4)	.257

Data are expressed as number (percentage) or median (interquartile range) for age and ejection fraction %. [a]Fisher exact test.

ference in terms of operator differences, we included cases of operators with more than 5 years of catheter laboratory experience in our study. We found that angiographic and clinical results were similar in STEMI patients who were divided into groups according to patient admission hours.

In another study, STEMI localization and duration of post-symptom procedure were reported to be important predictors of all-cause mortality at 1-month follow-up. In this study, the percentage of patients exhibiting a higher Killip class was greater with nighttime admission.[8] It was observed that the basic clinical and angiographic features did not differ between patients admitted during the daytime and nighttime hours, but some important differences were noted, such as the clinical status at hospitalization and the type of STEMI.[8] In our study, it was observed that the Killip class was worse in the patient group who were admitted at night, and admissions with pulmonary edema clinic and cardiogenic shock clinic were more common. Although patients admitted at night were more severely ill than those admitted during the day, the similar mortality rates show that other factors are also important in the management of these patients. These include greater ambulance accessibility, less dense and faster transport facilities, no elective procedures in the laboratory, and a reduction in the burden of catheterization laboratories. Observation of more no reflow in the morning hours can also be explained by laboratory working conditions.

In a recent well-designed study,[9] it was shown that being positive or negative for the COVID-19 virus in STEMI patients during the pandemic period did not affect the periprocedural mortality and complication rates. Although the duration of the first medical contact is longer in COVID-19 positive patients, it has been shown that this prolongation does not have a significant

Table 2. Clinical characteristics of the patients on admission.

	24:00 to <06:00 (n=67)	06:00 to <12:00 (n=200)	12:00 to <18:00 (n=328)	18:00 to <24:00 (n=140)	*P* value
Cardiac arrest on admission	9 (13.4)	17 (8.5)	21 (6.4)	16 (11.4)	.163
Acute heart failure	10 (14.9)	18 (9)	38 (11.6)	17 (12.2)	.555
Pulmonary edema	7 (10.4)	7 (3.5)	11 (3.4)	9 (6.4)	**.046**
Cardiogenic shock	12 (17.9)	14 (7)	24 (7.3)	13 (9.4)	**.031**
Atrioventricular complete block	5 (7.5)	11 (5.5)	12 (3.7)	2 (1.4)	.132
Ventricular tachycardia	10 (14.9)	14 (7)	29 (8.8)	15 (10.8)	.238
Ventricular fibrillation	9 (13.4)	14 (7)	22 (6.7)	11 (7.9)	.298
CPR	7 (10.4)	16 (8)	17 (5.2)	10 (7.1)	.356
Symptom onset to hospital admission (hours)	4 (3)	6 (4)	6 (5)	6 (5)	**.001**
Culprit vessel					
Left anterior descending artery	36 (53.7)	90 (45)	131 (40)	72 (51.4)	.199
Right coronary artery	22 (32.8)	73 (36.5)	139 (42.4)	42 (30)	
Circumflex coronary artery	8 (12)	33 (16.5)	55 (17)	22 (15.7)	
Others	1 (1.5)	4 (2)	3 (0.9)	4 (2.9)	
TIMI score	4 (3)	4 (3)	4 (4)	4 (4)	.519
Killip classification					
Killip I	39 (58.2)	153 (76.5)	262 (79.9)	100 (71.4)	
Killip II	11 (16.4)	26 (13)	41 (12.5)	18 (12.9)	
Killip III	7 (10.4)	6 (3)	8 (2.4)	7 (5)	**.005**
Killip IV	10 (14.9)	15 (7.5)	17 (5.2)	15 (10.7)	

Table 2 (cont.). Clinical characteristics of the patients on admission.

	24:00 to <06:00 (n=67)	06:00 to <12:00 (n=200)	12:00 to <18:00 (n=328)	18:00 to <24:00 (n=140)	*P* value
Myocardial infarction classification					
Anterior	33 (49.3)	64 (32)	102 (31)	57 (40.7)	
İnferior	24 (35.8)	74 (37)	141 (43)	45 (32)	
İnferolateral	4 (6)	18 (9)	40 (12.2)	10 (7.1)	**.006**
Anteroseptal	3 (4.5)	26 (13)	25 (7.6)	10 (7.1)	
Other	2 (3.8)	18 (9)	20 (6.1)	18 (12.9)	
Peak highly sensitive troponin I (ng/L)	50.5 (77.3)	50.9 (79.5)	43.0 (78.5)	66.4 (72.7)	.289
Peak CK-MB (µg/L)	159 (223)	170 (237)	164 (233)	273 (190)	.053
ECG resolution after intervention					
<30%	7 (10.4)	32 (16)	43 (13.1)	9 (6.4)	
30-50%	0	9 (4.5)	9 (2.7)	5 (3.6)	
50-70%	21 (31.3)	39 (19.5)	65 (19.8)	29 (20.7)	**.077**
>70%	30 (44.8)	70 (35)	132 (40.2)	59 (42.1)	
100%	9 (13.4)	50 (25)	79 (24.1)	38 (27.1)	

Data are number (percentage) or median (interquartile range).

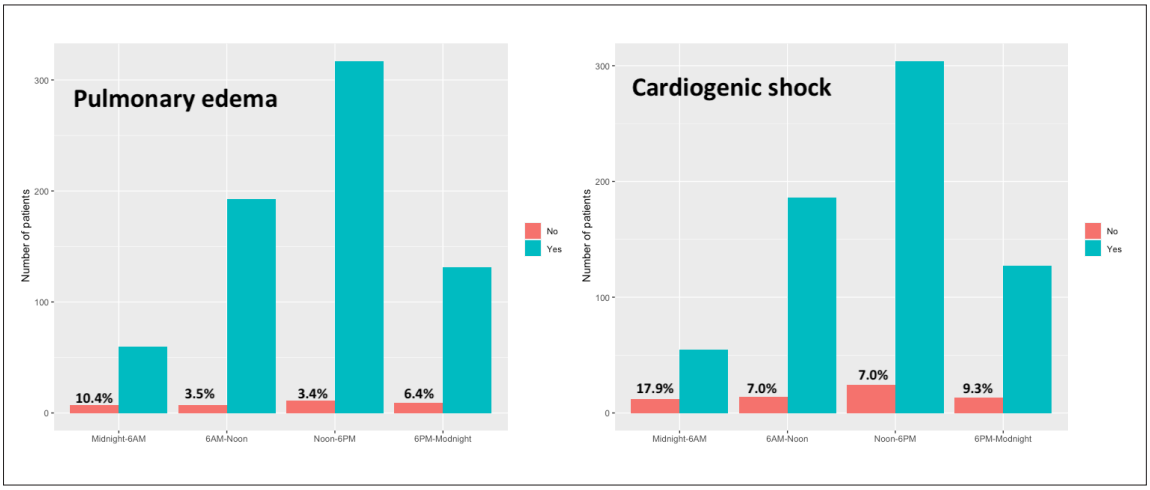

Figure 1. Admissions with cardiogenic shock (right) (*P*=.031) and pulmonary edema (left) (*P*=.046) by time of admission (percentages are of all patients in each time period).

effect on mortality and complication rates. No significant difference was observed in the endpoints of both on-hours and off-hours groups. When we look at our study in parallel with the results of this study, it can be expected that a well-designed medical care program will result in positive results and similar endpoints between groups, despite poor initial admission data. In addition, we think that the shorter admission time delay in the night admission group consisting of patients with poor clinical presentation is a factor that reduces the expectation of poor outcome. From this point of view, we think that the existence of a well-planned medical care organization creates positive results.

The lack of experienced physicians, the number of

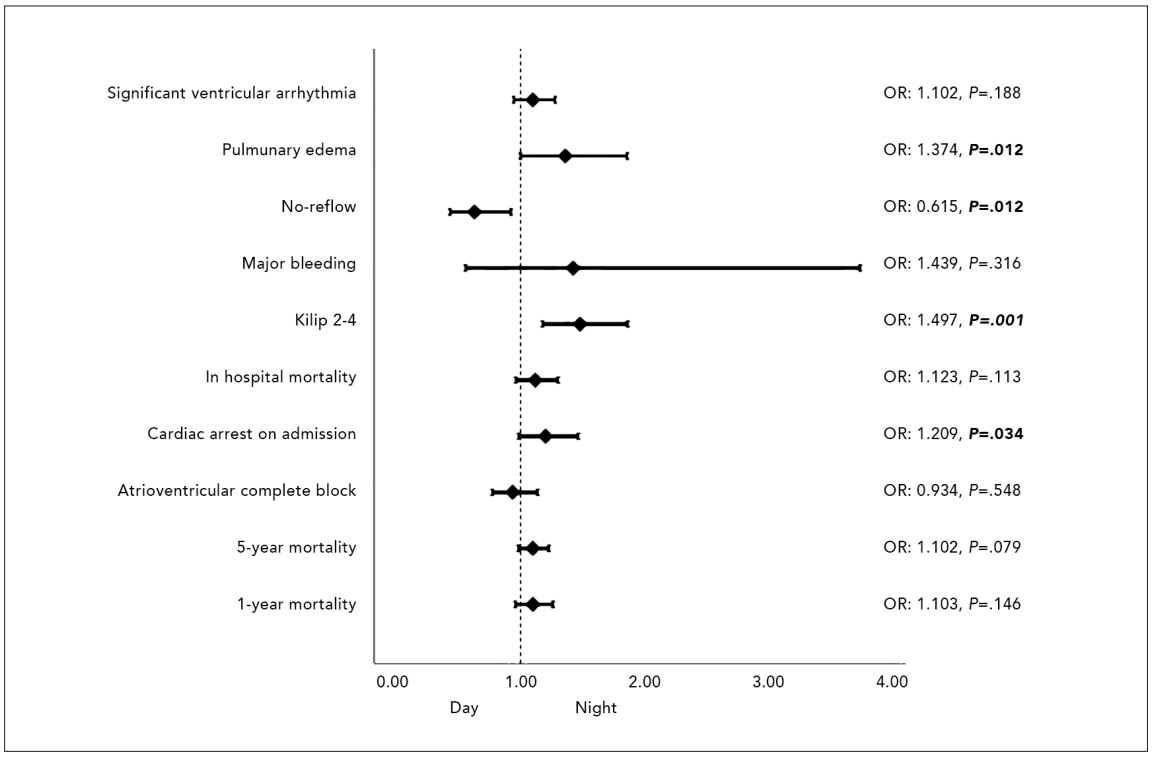

Figure 2. Risk of clinical effects and mortality by patients admitted during daytime (06:00 to <18:00) and nighttime (18:00 to <24:00).

nurses in the cardiac intensive care unit, and human factors such as sleep deprivation and fatigue have been accepted as risk factors that predispose a patient to an increased risk of death outside of working hours.[10] Despite the presence of the factor that can affect it so badly at night and the worse clinical condition at the time of admission, the similarity of mortality and complication outcomes shows how important it is to use well-structured out-of-hours work planning and a good and effective referral system in STEMI patients.

Medical periprocedural stress can profoundly affect both interventional cardiologists and patients. There is evidence that exposure to stress may promote the development of atherosclerosis and reduce the long-term benefits of the intervention (for example, increased incidence of in-stent restenosis).[11] The procedural medical environment is stressful for both the performer and the subject. It was observed that the clinical findings at the time of admission were significantly worse in the group of patients admitted after midnight, but similar results were observed in terms of endpoints. We think that this situation can be explained by the fact that the referral chain works more comfortably at night, the operator is away from the stress of the routine angiography program and the whole team works in a more comfortable

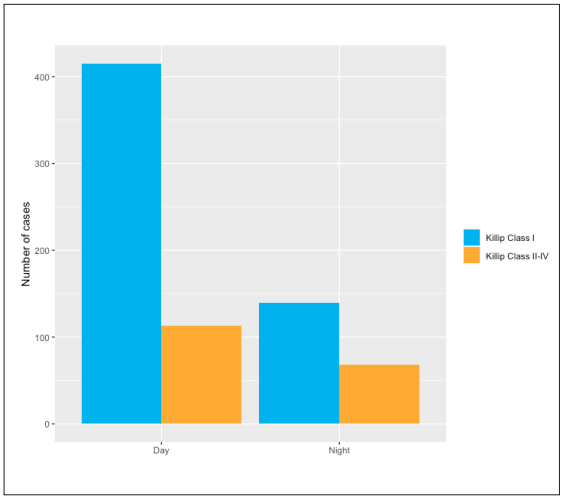

Figure 3. Killip I and Killip II-IV classification of daytime (06:00 to <18:00) and nighttime (18:00 to <24:00) patients.

environment. During the periprocedural period, the patient's stress responses can be both beneficial and harmful. Periprocedural patient stress is a difficult factor that can enhance survival and recovery, but can be harmful, for unknown reasons.[11] We think that the arrival of patients in different time periods causes positive and

Table 3. Complications and clinical outcomes during follow-up period by admission interval.

	24:00 to <06:00 (n=67)	06:00 to <12:00 (n=200)	12:00 to <18:00 (n=328)	18:00 to <24:00 (n=140)	*P* value
Myocardial blush grade					
Grade 0	1 (1.5)	7 (3.5)	11 (3.4)	5 (3.6)	
Grade 1	2 (3)	3 (1.5)	13 (4)	1 (0.7)	.746
Grade 2	5 (7.5)	18 (9)	29 (8.8)	11 (7.9)	
Grade 3	59 (88)	172 (86)	275 (83.8)	123 (87.9)	
No-reflow	8 (11.9)	28 (14)	53 (16.2)	17 (12.1)	.625
Minor bleeding	2 (3)	2 (1)	4 (1.2)	2 (1.4)	.569
Major bleeding	1 (1.5)	1 (0.5)	1 (0.3)	1 (0.7)	.437
Recurrent myocardial infarction	3 (4.5)	5 (2.5)	4 (1.2)	2 (1.4)	.253
New-onset stroke	1 (1.5)	3 (1.5)	6 (1.8)	0	.440
Hospitalization due to heart failure	6 (9)	8 (4)	18 (5.5)	9 (6.4)	.465
Hospitalization time (days)	4 (2)	4 (2)	4 (2)	4 (1)	.583
In-hospital mortality	10 (14.9)	25 (12.5)	34 (10.4)	22 (15.7)	.382
1-year mortality	13 (19.4)	28 (14)	44 (13.4)	24 (17.1)	.507
5-years mortality	23 (34.3)	43 (21.5)	75 (22.9)	36 (25.7)	.168

Data are expressed as number (percentage of time group total) or median (interquartile range).

Table 4. Multivariable logistic and Cox proportional hazards regression analysis of mortality by time period.

Time of admission	In-hospital mortality		1-year mortality		5-year mortality	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
24:00 to <06:00	Reference		Reference		Reference	
06:00 to <12:00	0.568 (0.198-1.632)	.507	0.990 (0.400-2.449)	.944	0.652 (0.370-1.149)	.529
12:00 to <18:00	0.811 (0.394-1.669)		0.889 (0.374-2.113)		0.724(0.425-1.234)	
18:00 to <24:00	0.628 (0.320-1.231)		1.079 (0.422-2.758)		0.751 (0.415-1.361)	

negative compensatory results of operator and patient stress factors.

Circadian regulatory factors exhibit a prothrombotic trend during daylight hours.[12] The patient's history and physiological circadian rhythms can interact in a complex way, which may lead to different results than expected. A meta-analysis including 30 STEMI studies and 19 sudden cardiac death studies showed that more than a quarter of morning STEMIs and about a quarter of sudden cardiac death could be attributed to the risk of excess in the morning.[13] In our population, the incidence of malignant arrhythmia was similar in all the admission time intervals, but the rates of presentation with cardiac arrest were higher in the patients admitted at night. In a short-term follow-up study, the authors reported that STEMI patients who were admitted at night (between 24:00 and 06:00) had the worst 1-month mortality.[14] In contrast to this study, another study found that time of onset was important to outcome in STEMI patients after balancing clinical risk factors. We did not observe a significant relationship between time and hospital mortality.[15] In another recent study, it was reported that time of day on symptom onset was not associated with infarct size or long-term mortality in STEMI patients undergoing PCI.[16] We surmise that the lack of mortality differences in our study was due to the effect of compensatory circadian factors on the endpoints. No significant difference in mortality was observed in our patient groups regardless of follow-up period.

In conclusion, short- and long-term all-cause mortality in patients admitted during the day was similar to that observed in patients admitted for PCI for STEMI at night. While patients presented with pulmonary edema and cardiogenic shock more frequently at night, strangely, no-reflow was observed during the day after the procedure. Although patients with STEMI presented with worse clinical conditions at night, similar results were observed between both groups in clinical outcomes.

The results of this single-center retrospective study may be partially affected by referral biases. We think that the low number of major and minor bleeding events was due to retrospective data collection. We think the actual bleeding rates are higher. Since our clinic is a tertiary health care clinic, inclusion of other clinics where patients are typically admitted for coronary angiography might have resulted in more "real world" results. In other words, the promising results of this study may not be easy to replicate in unfavorable referral conditions, as patients often arrive at different times.

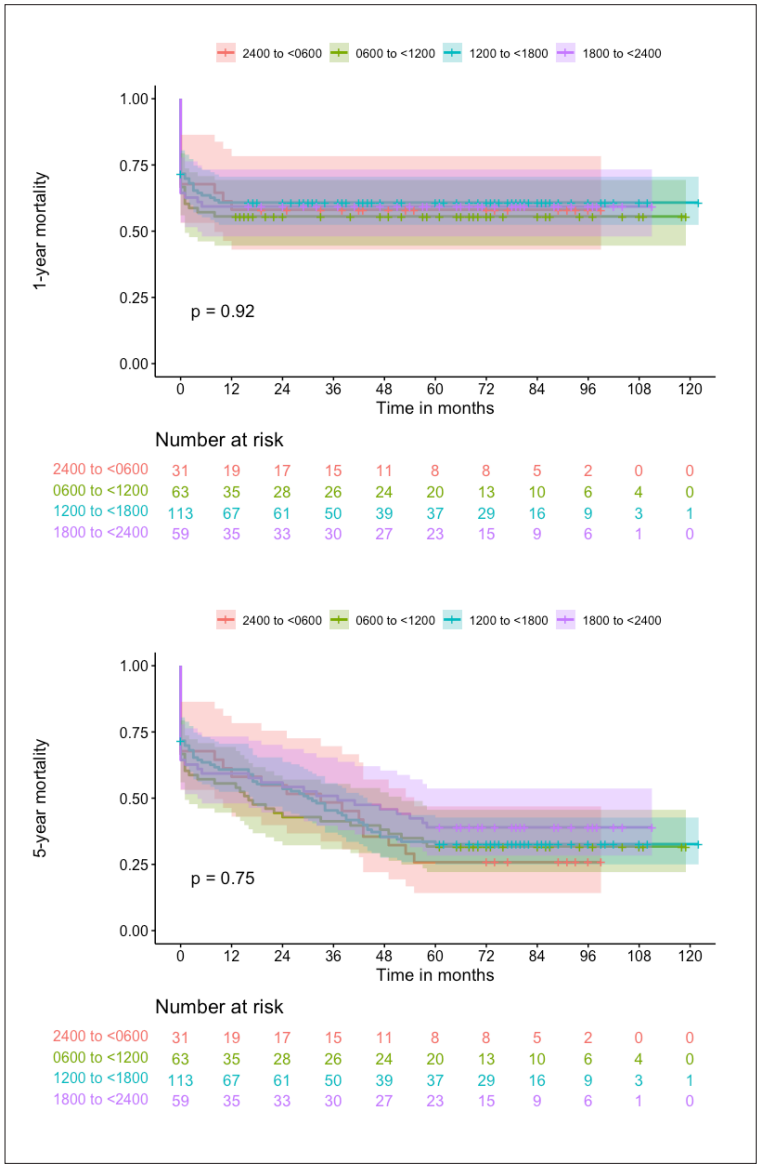

Figure 4. Kaplan-Meier 1-year (top) and 5-year (bottom) survival curve for each of the four time periods.

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