

## ORIGINAL ARTICLE

## Acute Myocardial Infarction and Primary Percutaneous Coronary Intervention at Night Time

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### Abstract

**Background:** Primary percutaneous coronary intervention is the preferred treatment in ST-elevation myocardial infarction. At night period, the delay until performing primary percutaneous coronary intervention may be determinant to prognosis worsening.

**Objective:** To analyze the results of primary percutaneous coronary intervention performed at day and night periods.

**Methods:** Cohort study that included patients admitted with ST-elevation myocardial infarction who underwent primary percutaneous coronary intervention from December 2013 until December 2016 in a ST-elevation myocardial infarction reference hospital of a metropolitan region in Brazil, followed from admission to hospital discharge or death, compared according to time of primary percutaneous coronary intervention (night or day). Statistical analysis comprehended the Chi-square test, the Fisher test, the Student's t-test and the analysis of variance, with significance level of 5%.

**Results:** 446 patients were submitted to primary percutaneous coronary intervention, 159 (35.6%) at night time and 287 (64.4%) at day time. No differences were found between the two groups concerning clinical baseline characteristics. Door-to-balloon time ( $101 \pm 81$  minutes vs.  $99 \pm 78$  minutes;  $p = 0,59$ ) and onset-to-balloon time ( $294 \pm 158$  minutes vs.  $278 \pm 174$  minutes;  $p = 0,32$ ) did not differ between the groups. The incidence of combined major adverse cardiac events (15.1% vs. 14.3%;  $p = 0,58$ ) and in-hospital mortality (9.4% vs. 8.0%;  $p = 0,61$ ) were similar between the groups, as well as length of hospital stay ( $6.0 \pm 4$  days vs.  $4.9 \pm 4$  days;  $p = 0,91$ ).

**Conclusion:** Primary percutaneous coronary intervention at night time showed similar results as the procedure performed at day time, without significant increase of in-hospital adverse events, length of stay or mortality. (Int J Cardiovasc Sci. 2018;31(5)513-519)

**Keywords:** Myocardial Infarction; Percutaneous Coronary Intervention; Cohort Studies; Night Care.

### Introduction

In the treatment of ST-segment elevation myocardial infarction (STEMI), mechanical coronary reperfusion through primary percutaneous coronary intervention (PPCI) has an important position and its efficacy has been demonstrated and proven in large studies.<sup>1-3</sup> In addition to attaining target vessel patency in more than 90% of cases, it is able to increase survival and reduce the rates of reinfarction and cerebrovascular accident

(CVA) related to chemical thrombolysis.<sup>3-6</sup> PPCI is a class I indication for treatment of the STEMI within the first 12 hours of evolution, when available in a timely manner and performed in qualified centers.<sup>7-9</sup>

Access to PPCI is not always easy to achieve, and its unavailability can lead to severe delays and the ineffective treatment of STEMI, with significantly more severe clinical outcomes. The nocturnal period is particularly complex in this context, and previous studies suggest

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that hospital admission at night culminates in higher mortality rates, when compared to the daytime period.

However, several factors seem to be related to impediments to this access experienced at night, and Brazilian cities have structural problems; plus the fact that emergency care systems usually depend on the on-call Interventional Cardiology professionals, which may prolong the delay until the definitive treatment of STEMI is implemented.<sup>10</sup>

Data evaluating the treatment of STEMI in the nighttime period in Brazil are scarce. To date, there have been no outcome-related analyses in Hemodynamic Services with on-duty Interventional Cardiologists. Therefore, the aim of this study was to evaluate the results of PPCI performed during the daytime and nighttime periods in a cardiology referral center, which has a regular, on-duty interventional cardiologist, together with a specialized nursing team.

## Methods

A prospective observational, single-center cohort study was developed, which included patients with a diagnosis of STEMI of any wall submitted to PPCI within the first 12 hours of the clinical presentation in a tertiary cardiology institution in the municipality of Vitória, state of Espírito Santo, Brazil, between December 2013 and December 2016.

The inclusion criteria were the clinical and electrocardiographic diagnoses of IAMCSST, and the indication for treatment by PCI by the attending physician, corroborated by the interventional cardiologist. Exclusion criteria were IAMCSST with more than 12 hours of evolution, diagnosis of nonconfirmed or doubtful IAMCSST, patients not submitted to PPCI immediately after coronary angiography,

The inclusion criteria were the clinical and electrocardiographic diagnoses of STEMI, and the indication of PPCI treatment by the attending physician, corroborated by the interventional cardiologist. The exclusion criteria were STEMI with more than 12 hours of evolution, nonconfirmed or uncertain diagnosis of STEMI, patients not submitted to PPCI immediately after the coronary angiography, patients younger than 18 years of age or refusal to sign the Free and Informed Consent Form (FICF) or to participate in the study through prospective data collection. All patients were interviewed at hospital admission and followed

until hospital discharge. The study was approved by the local Research Ethics Committee, according to the Declaration of Helsinki.

The patients included in the study were compared according to the period of admission at the Hemodynamics service, regardless of the day of the week, specifically at night time, from 7:00 p.m. to 6:59 a.m.; and daytime, from 7 am to 6:59 p.m. The clinical variables evaluated were age, gender, arterial hypertension, diabetes mellitus, dyslipidemia, smoking status, chronic renal failure, prior PCI, previous myocardial revascularization surgery, disease severity at admission described by the Killip-Kimball classification, use of glycoprotein IIb / IIIa inhibitors during PPCI and treatment delay time (door-to-balloon time and pain-to-balloon time).

The primary endpoint of the study consisted in combined Major Adverse Cardiac Events (MACE) - death from any cause in the in-hospital phase, new nonfatal AMI or CVA during hospitalization. The secondary outcomes included all-cause death, CVA and new AMI alone, successful PPCI and hospital length of stay in days. At the analysis of hospitalization time, only those patients who were discharged to their homes were considered, excluding those who died during the hospitalization period.

All STEMI cases treated at the referral institution had spontaneous demand or were transferred after initial treatment and recognition of the clinical picture at another institution. The emergency nature of the PPCI procedure was followed in all patients, and they were taken to the interventional laboratory as soon as possible after communicating with the emergency unit team. The service had a regular on-duty interventional cardiologist, including at non-commercial hours, operating 24 hours a day.

According to the institution's STEMI care protocol, patients received a loading dose of 200 to 300 mg of acetylsalicylic acid and 300 to 600 mg of clopidogrel or 180 mg of ticagrelor. All patients received full heparinization with unfractionated heparin in the interventional laboratory (70 to 100 U/kg). The patients were taken to undergo the procedure as soon as the interventional laboratory was available after conduct confirmation by the interventional cardiologist. After the PPCI procedure, dual antiplatelet therapy was maintained systematically in all patients.

The total time of myocardial ischemia in STEMI until the PPCI was performed (pain-to-balloon time) was

routinely recorded in the service by the emergency room and interventional laboratory medical staff, as well as the door-to-balloon time (delay from admission at the referral service emergency unit until the implementation of PPCI).

### Statistical analysis

The data obtained were stored in a Microsoft Office Excel spreadsheet for subsequent descriptive and comparative analysis according to the time of the treatment at the Hemodynamics Service.

In the descriptive analysis of the data, the categorical variables were expressed as absolute and percentage frequencies, and the continuous variables as mean and standard deviation. The data were considered as having a normal distribution through the Shapiro-Wilk's test. For comparisons, the statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), version 20.0, for Windows, and comprised Pearson's chi-square test, Fisher's exact test, the unpaired Student's t-test, and one-way ANOVA, with p values <0.05 being considered statistically significant.

### Results

During the assessed period, 522 patients were identified and referred for cardiac catheterization as a matter of urgency, of which 446 (85.4%) were diagnosed with STEMI and submitted to PPCI during the first 12 hours since symptom onset, comprising the assessed sample. Of these, the procedure was performed in the nighttime period in 159 (35.6%), and 287 (64.4%) in the daytime period.

When comparing the Nighttime and Daytime Groups, no differences were observed regarding the basal clinical characteristics (Table 1). When analyzing the severity of the STEMI clinical presentation through the Killip-Kimball classification, we observed a predominance of class I in both groups, with no statistically significant difference for the classification when comparing the Nighttime and Daytime Groups, as shown in Table 2.

The means of the door-to-balloon and pain-to-balloon times did not differ statistically between the Nighttime and Daytime Groups. Table 3 shows the time delays until the performance of PPCI.

There was no difference regarding the mean number of stents per patient, number of drug-eluting stents, mean stent diameter and length in the two groups. The administration of acetylsalicylic acid and clopidogrel

**Table 1 - Basal clinical characteristics, according to the time of admission at the Hemodynamics service**

Characteristic	Nighttime group	Daytime group	p value
Male gender, n (%)	123 (77.3)	207 (72.1)	0.09
Age, years ± SD	58.9 ± 11.8	60.2 ± 12.4	0.08
Arterial hypertension, n (%)	153 (96.2)	240 (83.6)	0.06
Diabetes mellitus, n (%)	40 (25.1)	74 (25.8)	0.68
Dyslipidemia, n (%)	60 (37.7)	90 (31.3)	0.24
Smoking, n (%)	61 (38.3)	95 (33.1)	0.12
Chronic renal failure, n (%)	13 (8.1)	31 (10.8)	0.33
Previous PCI, n (%)	10 (6.2)	20 (6.9)	0.4
Previous CABG, n (%)	4 (2.5)	6 (2.1)	0.89

*Statistical tests used: Pearson's chi-square test, Fisher's exact test and unpaired Student's t-test. SD: standard deviation; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting.*

**Table 2 - Severity of the acute myocardial infarction clinical presentation through the Killip-Kimball classification**

Killip-Kimball class	Nighttime group n (%)	Daytime group n (%)	p value
I	121 (76.1)	239 (83.2)	
II	12 (7.5)	21 (7.3)	0.06
III	6 (3.8)	3 (1.0)	
IV	18 (11.3)	24 (8.3)	

*Statistical tests used: one-way Analysis of Variance (ANOVA).*

or ticagrelor was similar between the Nighttime and Daytime Groups. During the PPCI procedures, there was a higher rate of use of glycoprotein IIb / IIIa inhibitors at nighttime, with similar procedure success rates in both periods. The characteristics related to the PPCI procedures are described in table 4.

The PPCI procedure success rate did not show a significant difference when the time schedules were compared (91.1% in the Nighttime Group vs. 93.3% in the Daytime Group, p = 0.38). The mean time of

**Table 3 - Mean times delays until the performance of the primary percutaneous coronary intervention**

Time delays	Nighttime group	Daytime group	p value
Door-to-balloon time, minutes $\pm$ SD	101 $\pm$ 81	99 $\pm$ 78	0.59
Pain-to-balloon time, minutes $\pm$ SD	294 $\pm$ 158	278 $\pm$ 174	0.32

Statistical tests used: unpaired Student's t-test. SD: standard deviation.

hospitalization among patients who were discharged to their homes was  $6.0 \pm 4.3$  days in the Nighttime Group and  $4.9 \pm 4.0$  days in the Daytime one ( $p = 0.91$ ).

Regarding the in-hospital evolution after the PPCI, similar mortality rates were observed in both groups. No cases of CVA were diagnosed in the total sample. In-hospital outcomes and their comparison between the Nighttime and Daytime Groups are shown in table 5.

## Discussion

The non-business hours represent a challenge to medical assistance in the presence of STEMI, a diagnosis that requires rapid decisions and availability of several links in an urgency and emergency network. In this study, we demonstrated that it is possible to attain satisfactory results in the Brazilian scenario, with times of delay and incidence of similar adverse events among the PPCI performed in the nighttime and daytime periods.

National and international guidelines have strong recommendations for the implementation of effective STEMI treatment systems, with necessary adaptations and regionalizations.<sup>8,11,12</sup> This includes the integration of several links in the chain of care, especially the pre-hospital level and the availability of a referral service with Interventional Cardiology and PPCI training, aiming at increasing survival of patients with STEMI.<sup>13-15</sup> Nonetheless, the nighttime period usually has an on-call Interventional Cardiology team, and the increase in the time of delay can greatly affect the prognosis.

Keeping the Interventional Cardiology team on duty at the referral centers is an attractive strategy to reduce the delay until the coronary reperfusion is performed and to extend the possibility of effective treatment to patients with STEMI. The applicability of PPCI within the recommended time, that is, within 90 minutes of

**Table 4 - Characteristics of the primary percutaneous coronary intervention procedures, according to the time of admission at the Hemodynamics service**

Characteristic	Nighttime group	Daytime group	p value
Acetylsalicylic acid, n (%)	154 (96.8)	281 (97.9)	0.19
Clopidogrel / ticagrelor, n (%)	150 (94.3)	276 (96.1)	0.32
Glycoprotein IIb/IIIa inhibitors, n (%)	43 (27.0)	54 (18.8)	0.04
Treated vessels (territory)			
Anterior descending artery, n (%)	76 (47.8)	130 (45.3)	0.61
Right coronary artery, n (%)	52 (32.7)	103 (35.9)	0.49
Circumflex artery, n (%)	28 (17.6)	61 (21.3)	0.35
Left main coronary artery, n (%)	5 (3.1)	6 (2.1)	0.19
Access route			
Femoral, n (%)	144 (90.6)	245 (85.3)	0.11
Radial, n (%)	15 (9.4)	42 (14.6)	0.11
Pré-dilation	132 (83.0)	256 (89.2)	0.06
Post-dilation	38 (23.9)	82 (28.6)	0.28
Number of stents, total (mean stents per patient $\pm$ SD)	215 (1.3 $\pm$ 0.4)	349 (1.2 $\pm$ 0.6)	0.9
Drug-eluting stents, n (%)	7 (3.2)	19 (5.4)	0.33
Stent nominal diameter	2.98 $\pm$ 0.41	3.09 $\pm$ 0.49	0.93
Stent nominal length	23.4 $\pm$ 7.3	20.5 $\pm$ 8.1	0.91
Procedural success, n (%)	151 (94.9)	278 (96.8)	0.31

Statistical tests used: Pearson's chi-square test, Fisher's exact test, unpaired Student's t-test and one-way Analysis of Variance. SD: standard deviation.

admission to the emergency unit is, in itself, a challenge in the context of the urgency and emergency network,<sup>16,17</sup> and the nighttime period discloses even greater difficulties. To ensure a well-functioning and qualified

**Table 5 - Comparison of in-hospital outcomes between the Nighttime and Daytime Groups after the primary percutaneous coronary intervention**

Outcome	Nighttime group n (%)	Daytime group n (%)	P value
Combined MACE*	24 (15.1)	41 (14.3)	0.58
Death	15 (9.4)	23 (8.0)	0.61
New non-fatal AMI*	9 (5.6)	19 (6.6)	0.15

*Statistical tests used: Pearson's chi-square test. \* Death from all-cause in the in-hospital phase, new non-fatal AMI or CVA during hospitalization. MACE: major adverse cardiovascular events; AMI: acute myocardial infarction.*

system is of utmost importance for health strategy policies, since about 50% of STEMI cases occur outside regular business hours.<sup>18</sup>

Studies consistently suggest that PPCI may have different results, according not only to the total time of myocardial ischemia,<sup>17,19,20</sup> but also the time when it is performed.<sup>21-26</sup> Nighttime or weekends may show a PPCI procedure failure rate up to 81% higher,<sup>21</sup> a door-to-balloon time up to 21.3 minutes longer,<sup>24</sup> time from the electrocardiogram to arrival in the Hemodynamics unit 20.7 minutes longer<sup>24</sup> and mortality in 30 days up to 121% higher,<sup>21</sup> when compared to the business hours. In our study, the only statistically significant difference between the Nighttime and Daytime Groups was the rate of glycoprotein IIb/IIIa inhibitor use. The main hypothesis for this finding is the greater anxiety by the operator to optimize the anterograde coronary flow and to resolve the finding of intracoronary thrombi at nighttime.

A Brazilian study showed that the delay associated with nocturnal PPCI was 18 minutes (102 ± 98 minutes vs. 84 ± 66 minutes,  $p < 0.01$ ). The in-hospital mortality rate was 10.2% vs. 7.6%, and the one-year mortality rate was 12.6% vs. 9.5% (PPCI at nighttime vs. daytime), both showing no statistical significance.<sup>25</sup> The differences in results between the Nighttime and Daytime Groups in comparison to the data in our study can be explained by the presence of a regular on-duty interventionist cardiologist in our service, not one on-call regimen.

We demonstrated that the strategy of having an on-duty Interventional Cardiology team at nighttime can shorten the delay in STEMI treatment at these times.

Although this point is only one of the necessary care links, there is an increase in the possibility of performing PPCI in a timely manner, being able to reach the recommended goals even at non-business hours and to avoid an increase in mortality. In a study by Nguyen et al.,<sup>27</sup> the use of the 24-hour on-duty presence of the interventionist cardiologist led to a reduction of 57% in the door-to-balloon time, with a mean absolute reduction of 71 minutes, and a 54% reduction in hospital length of stay.

The mean door-to-balloon time over 90 minutes observed in the present study was probably due to avoidable in-hospital delays and to the immaturity of the care system at the time, which still relied on the wait for non-medical staff who were on-call due to contractual issues. Also, the result reflects the practical difficulty of reaching the time goals recommended for STEMI treatment in our country. However, the nighttime schedule did not interfere in the total delay, demonstrating the feasibility of attaining adequate reperfusion times, aiming to improve the quality of care, with no harm to the patient as a result of the time of day when the event occurs.

### Limitations

Although the present study is relevant, some limitations should be mentioned. The single-center characteristic limits the extrapolation of results to other populations. Clinical follow-up restricted to the in-hospital period, despite having the power to demonstrate differences between the two groups, underestimates the real impact of the time when the PPCI was performed on the results, by not evaluating outcomes in the medium or long term. Potentially relevant data, such as kidney dysfunction and hemorrhagic complications during the in-hospital evolution were not collected and evaluated in this study. The times used to divide the groups do not always accurately represent the business and non-business hours, which were the object of our study due to the potential difference regarding the speed and quality of medical care. As the study included only patients actually submitted to PPCI in a timely manner, some patients that were not transferred or were not diagnosed with STEMI were not analyzed, restricting the results to outcomes after the PPCI, and not all patients with STEMI.

### Conclusion

The results of the primary percutaneous coronary interventions performed in the nighttime and daytime

periods were comparable, showing similar mortality rates and incidence of major adverse cardiovascular events between the two groups. With logistic optimization and the prioritizing of immediate care in STEMI cases, it is possible to overcome the accessibility, availability and information barriers, which are extremely common in Brazilian metropolitan regions, especially at nighttime.

### Author contributions

Conception and design of the research: Barbosa RR, Cesar FB, Bayerl DMR, Serpa RG, Veloso WUG, Cesar RA, Reseck PAR. Acquisition of data: Barbosa RR, Cesar FB, Mauro VF. Analysis and interpretation of the data: Barbosa RR. Statistical analysis: Barbosa RR. Writing of the manuscript: Barbosa RR. Critical revision of the manuscript for intellectual content: Barbosa RR, Bayerl DMR, Reseck PAR. Supervision / as the major investigator: Barbosa RR.

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