

## ORIGINAL ARTICLE

# Delay Times in Acute Myocardial Infarction Care: Comparison Between Periods Before and During the COVID-19 Pandemic

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## Abstract

**Background:** The success of acute myocardial infarction with ST-segment elevation (STEMI) treatment is time-dependent, requiring prompt access, diagnosis, and immediate medical intervention. The COVID-19 pandemic has significantly impacted the care of patients with STEMI.

**Objective:** To analyze delay times and clinical outcomes of patients with STEMI undergoing primary percutaneous coronary intervention (PPCI) before and during the COVID-19 pandemic.

**Methods:** This retrospective observational study included patients with STEMI undergoing PPCI from June 2019 to July 2022. The COVID-19 pandemic period was divided into 3 time groups. Pandemic I referred to the interval from March to August 2020, pandemic II from September 2020 to July 2021, and pandemic III from August 2021 to July 2022. Delay times, clinical characteristics, and in-hospital mortality were analyzed. The chi-square, Fisher's exact, Student's t and one-way ANOVA tests were applied, with p values less than 0.05 being considered statistically significant.

**Results:** Comparing the periods, the total ischemic time to PPCI was 346.3 versus 448.4 versus 398.4 versus 348.4 minutes ( $p = 0.47$ ); onset-to-door time 253.1 versus 421.1 versus 377.4 versus 370.6 minutes ( $p = 0.42$ ); first medical contact (FMC)-to-balloon time 243.9 versus 313.0 versus 239.5 versus 279.4 minutes ( $p = 0.38$ ); and door-to-balloon time 71.8 versus 76.8 versus 58.03 versus 88 minutes ( $p = 0.9$ ). Mortality significantly increased in pandemic I compared to pre-pandemic (29.4% versus 5.0%,  $p = 0.01$ ), with a marginal difference compared to pandemic II and III combined (12.2%,  $p = 0.05$ ).

**Conclusion:** There was a trend toward increased onset-to-door time and FMC-to-balloon time in STEMI care during the pandemic compared to the pre-pandemic period, although not statistically significant. Higher mortality in STEMI was observed in the first months of the COVID-19 pandemic.

**Keywords:** myocardial infarction; percutaneous coronary intervention; covid-19; mortality.

## Introduction

Success in treating acute myocardial infarction with ST-segment elevation (STEMI) is time-dependent, requiring access to emergency services, prompt identification of the problem, and immediate medical intervention.<sup>1</sup> This cardiovascular event is one of the most severe

pathologies, with high mortality and varying sequelae depending on the delay time to intervention.<sup>2</sup> Only 20% of patients with acute chest pain reach the emergency department within 2 hours of symptom onset.<sup>3</sup>

At the onset of the COVID-19 pandemic, patients with significant risk factors for cardiovascular diseases faced difficulties seeking medical attention due to the increased

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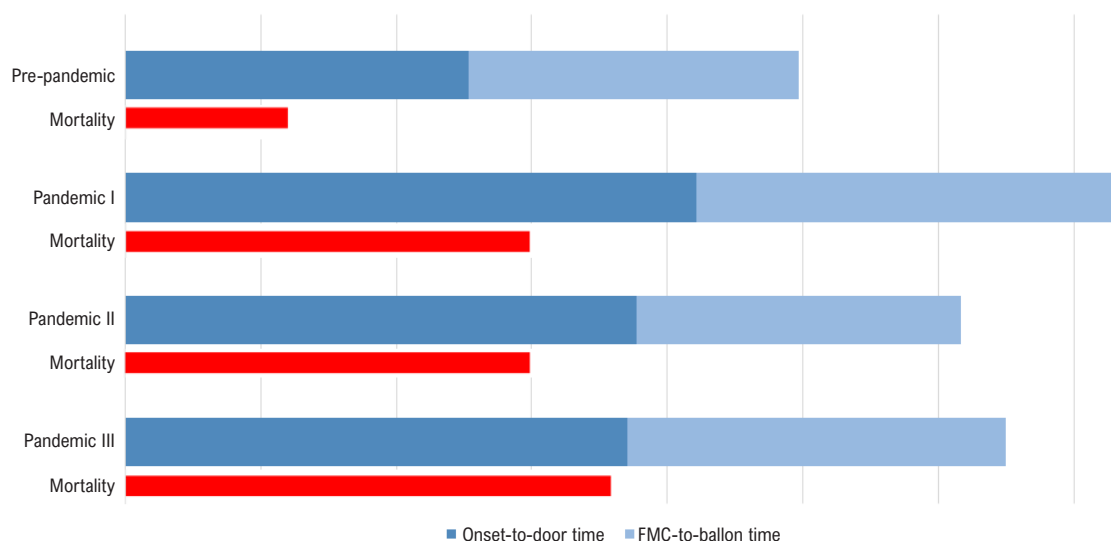
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### Central Illustration: Delay Times in Acute Myocardial Infarction Care: Comparison Between Periods Before and During the COVID-19 Pandemic

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Time taken to seek emergency care after the onset of pain and from the FMC to percutaneous treatment in patients with acute myocardial infarction with STEMI according to period of the COVID-19 pandemic (times shown in minutes), in addition to the relationship with the mortality rate of each period

risk of severe virus infection. Fear of COVID-19, the implementation of lockdowns, and a shift in healthcare priorities influenced the entire chain of organization for cardiovascular emergencies.<sup>4</sup> Additionally, it is important to note the potential exacerbating effect of COVID-19 on cardiovascular diseases and the psychological impact generated by isolation.

The lack of knowledge about the changes brought about by COVID-19 in cardiovascular diseases can have a negative impact on already known complications. Thus, new studies are needed to understand how the pandemic has modified healthcare, aiming for constant improvements in service. The objective of this study was to analyze the clinical profile, delay times, and clinical outcomes of patients with STEMI undergoing primary percutaneous coronary intervention (PPCI) before and during the COVID-19 pandemic.

## Methods

### Study Design

This retrospective, observational, single-center study was conducted from June 2019 to July 2022, involving patients diagnosed with STEMI undergoing urgent PPCI. Comparisons were made between the pre-pandemic

period (June 2019 to February 2020) and the pandemic period (March 2020 to July 2022).

The COVID-19 pandemic period was divided into 3 time groups, considering different moments of healthcare attention for other conditions. Pandemic I referred to the interval from March to August 2020, pandemic II from September 2020 to July 2021, and pandemic III from August 2021 to July 2022.

Comparative analyses were conducted according to the different pandemic periods. The first comparative analysis was between patients treated in the pre-pandemic period versus pandemic I. To assess patient care during the pandemic, another comparison was made between the combined periods of pandemic II and III versus pandemic I.

### Inclusion criteria

We included all patients diagnosed with STEMI who underwent urgent cardiac catheterization followed by PPCI in the Interventional Cardiology Department.

### Exclusion criteria

The following were excluded: patients with onset-to-door time and door-to-balloon time not documented in the

medical records; patients with a clinical presentation initiated more than 12 hours before hospital admission; and patients who received fibrinolytics as first therapy for coronary reperfusion.

### Variables analyzed and outcomes

A retrospective collection of clinical data was conducted from the time of admission to hospital discharge or death through the electronic records of included patients. The analyzed variables included age, sex, clinical presentation, arterial hypertension, diabetes mellitus, dyslipidemia, chronic kidney failure, and smoking status. The outcomes examined encompassed in-hospital mortality, success of the PPCI procedure, acute renal failure, delay time from symptom onset to PPCI (delta T), delay time from symptom onset to the first visit to the referral hospital (onset-to-door time), delay time from the first medical contact (FMC) at the originating facility to PPCI (FMC-to-balloon time), delay time from medical attention at the referral hospital to PPCI (door-to-balloon time), total hospitalization time, and periprocedural complications (no reflow, atrioventricular block, cardiogenic shock, acute stent thrombosis, cardiac arrest, and death during procedure).

### Statistical analysis

Categorical variables were described as absolute frequency and percentage. Continuous variables were described as mean and standard deviation when normally distributed, and as median and interquartile range when non-normally distributed. The Kolmogorov-Smirnov test was used to determine the normality of the data. For comparative analyses, the chi-square test, Fisher's exact test, unpaired Student's *t* test, and one-way ANOVA were applied, with *p* values less than 0.05 considered statistically significant. The analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 23.0. No post hoc tests related to one-way ANOVA were used.

### Ethical considerations

This study adhered to the guidelines outlined in Resolution 466/2012 of the Brazilian National Health Council and received approval from the Institutional Review Board for Human Research, with approval number 4,179,508.

## Results

A total of 157 patients were initially included. Ten patients were excluded for undergoing cardiac catheterization in a non-urgent fashion (1 excluded during the pre-pandemic period and 9 during the pandemic period). Thus, the final sample consisted of 147 patients, comprising 40 (27.2%) in the pre-pandemic period, 17 (11.5%) in pandemic I, and 90 (61.2%) in pandemics II and III combined. Only 5 patients were concurrently diagnosed with COVID-19 during the STEMI episode (4 cases in pandemic I and 1 in pandemic II). Overall, 100 patients (68.0%) had a prior diagnosis of arterial hypertension, and a higher prevalence of this risk factor was observed among patients affected during pandemic I. There was no significant difference in the prevalence of other risk factors between the compared periods (Table 1).

There was a trend towards an increase in delta T (time from symptom onset to PPCI), onset-to-door time, and FMC-to-balloon time during pandemic I; however, statistical significance was not reached. On the other hand, door-to-balloon time exhibited a more uniform behavior across the analyzed periods (Figure 1).

Throughout the pandemic, there was a decrease in the occurrence of cardiopulmonary arrest during the PPCI procedure, following an initial increase in this outcome during pandemic I. In-hospital mortality increased significantly from the pre-pandemic period to pandemic I. The intraprocedural complications and clinical outcomes are detailed in Table 2.

## Discussion

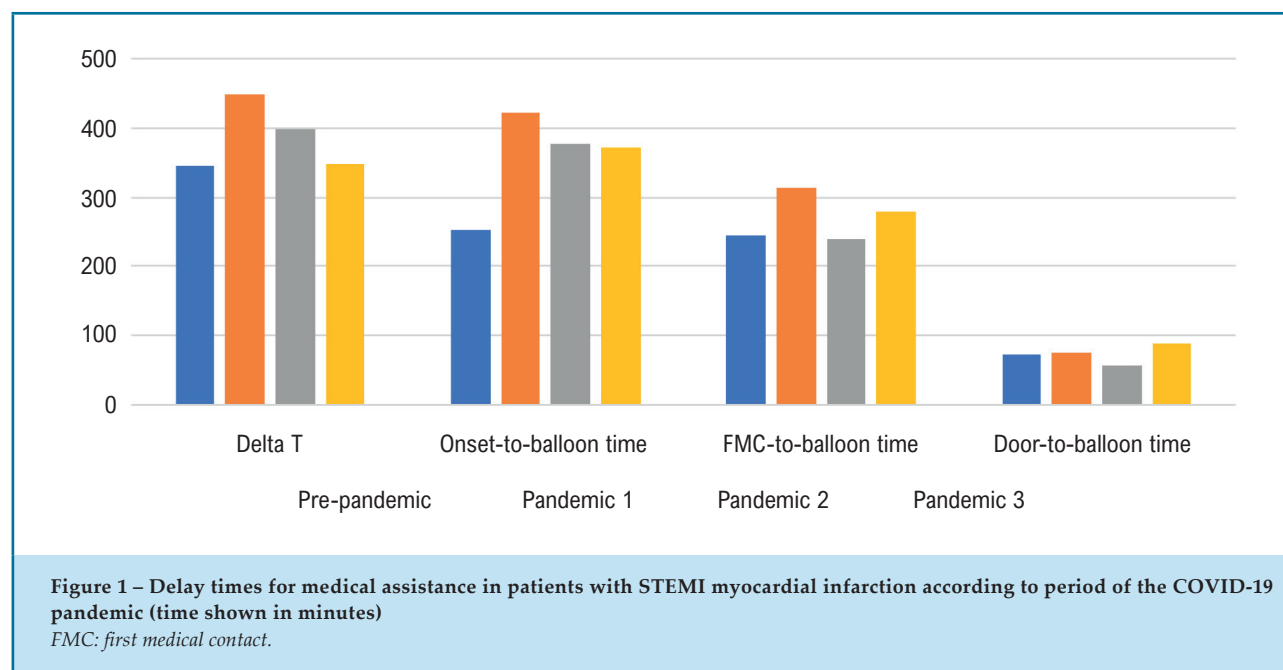
This study assessed the impact of the COVID-19 pandemic on delay times and clinical outcomes of patients with STEMI undergoing urgent cardiac catheterization and PPCI. It is well established that delay time until reperfusion significantly influences the clinical outcomes of these patients, and prolonged delays are associated with a higher likelihood of complications. We observed a trend toward increased delay times, particularly delta T, onset-to-door time, and FMC-to-balloon time during the initial COVID-19 outbreak compared to the pre-pandemic period, along with a significant increase in mortality. Several indirect and direct effects have been advocated to explain the increased in-hospital mortality associated

**Table 1 – Clinical characteristics of patients with STEMI myocardial infarction according to period of the COVID-19 pandemic**

Clinical variables	Pre-pandemic	Pandemic I	Pandemic II	Pandemic III	p value (p1 / p2)*
Male, n (%)	28 (70%)	11 (64.7%)	19 (65.5%)	43 (70.4%)	0.6 / 0.7
Female, n (%)	12 (30%)	6 (35.3%)	10 (34.4%)	18 (29.5%)	0.6 / 0.7
Age, n	62.2	65.9	58.9	60.4	0.9 / 0.9
Arterial hypertension, n (%)	29 (72.5%)	16 (94.1%)	20 (68.9%)	35 (57.3%)	0.05 / 0.004
Diabetes mellitus, n (%)	10 (25%)	7 (41.1%)	11 (37.9%)	18 (29.5%)	0.2 / 0.1
Dyslipidemia, n (%)	14 (35%)	6 (35.2%)	9 (31%)	15 (24.5%)	0.9 / 0.46
Chronic kidney failure, n (%)	1 (2.5%)	0	1 (3.4%)	3 (4.9%)	0.7 / 0.49
Current smoking, n (%)	17 (42.5%)	5 (29.4%)	9 (31%)	13 (21.3%)	0.15 / 0.2
Previous smoking, n (%)	5 (12.5%)	1 (5.8%)	2 (6.8%)	9 (14.7%)	0.31 / 0.28

\*p1: Comparison of clinical variables between pre-pandemic and pandemic I; p2: Comparison between pandemic I and the sum of pandemic II and pandemic III.

\*p: chi-square test and Fisher's exact test.



with SARS-CoV-2 positivity in patients presenting with STEMI. Among the indirect effects, the fear of contagion may have affected patients' willingness to present to hospital, resulting in a substantial delay in cardiac catheterization laboratory activations. Similar findings were observed in other studies, as a longer door-to-balloon time in SARS-CoV-2-positive patients with STEMI, reflecting the in-hospital delay. This has been attributed, especially during the first part

of the pandemic, to the different triaging systems for STEMI patients suspected of COVID-19, to the use of COVID-19-dedicated pathways, and to the time spent donning personal protective equipment.<sup>5</sup>

The prolongation of these times may be linked to factors such as patients delaying seeking hospital services from the onset of symptoms due to fear of contamination, as well as delays in the healthcare system's response. Although the reason for the delay

**Table 2 – Intraprocedural complications and clinical outcomes in patients with STEMI myocardial infarction according to period of the COVID-19 pandemic**

Complications and outcomes	Pre-pandemic	Pandemic I	Pandemic II	Pandemic III	p value (p1 / p2)*
No reflow, n (%)	2 (5%)	3 (17.6%)	1 (3.4%)	6 (9.83%)	0.12 / 0.14
Acute stent thrombosis, n (%)	0	1 (5.8%)	0	0	0.29 / 0.15
Atrioventricular block, n (%)	0	0	0	4 (6.5%)	NA / 0.49
Cardiogenic shock, n (%)	0	0	2 (6.8%)	1 (1.6%)	NA / 0.59
Cardiorespiratory arrest during procedure, n (%)	1 (2.5%)	3 (17.6%)	2 (6.8%)	1 (1.6%)	0.06 / 0.04
Death during procedure, n (%)	0	1 (5.88%)	0	0	0.29 / 0.15
Procedure success, n (%)	37 (92.5%)	14 (82.3%)	28 (96.5%)	58 (95%)	0.18 / 0.06
Acute renal failure, n (%)	6 (15%)	3 (17.6%)	3 (10.3%)	2 (3.2%)	0.28 / 0.09
In-hospital death, n (%)	2 (5%)	5 (29.4%)	5 (17.2%)	6 (9.8%)	0.01 / 0.05

\*p1: Comparison of clinical variables between pre-pandemic and pandemic I; p2: Comparison between pandemic I and the sum of pandemic II and pandemic III. \*p: chi-square test and Fisher's exact test.

was not investigated in this study, these data suggest challenges in adapting to manage the system amidst the global outbreak.<sup>6</sup> One of the findings of our study was the high percentage of procedures performed during weekends and after business hours: 82.5% in the pre-pandemic period, 64.6% in pandemic I, 89.2% in pandemic II, and 70.4% in pandemic III. According to a meta-analysis, patients who presented outside of business hours were less likely to undergo PPCI within 90 or 120 minutes after FMC. A longer delay was observed from chest pain to the first contact with medical services until coronary angiography was performed. PPCI for STEMI performed outside working hours may be associated with higher periprocedural mortality compared to procedures performed during regular working hours. The longer delay in transferring patients outside business hours may partially account for this finding.<sup>7</sup>

During the early phase of the pandemic, there was an estimated 38% reduction in procedures across 9 interventional centers in the United States.<sup>8</sup> Xiang et al. reported a 62% reduction in the number of procedures performed in China during the pandemic, and a 40% reduction was noted in an analysis of 73 centers in Spain.<sup>8,9</sup> Reporting this analysis to our environment, it can be said that there was a decrease in elective cardiological procedures, which could therefore provide an increase in the treatment of acute cases.<sup>10</sup>

Another possibility is that later presentation during pandemic I led to more severe clinical conditions, hence a higher risk of complications and death. Patients who initially refrained from seeking medical attention, likely due to the fear of contracting the infection in the hospital setting, probably presented to the hospital later and in a worse clinical condition.<sup>11</sup> Additionally, it is possible that, at the beginning of the pandemic, many patients with less severe clinical presentations avoided seeking medical attention due to fear of COVID-19,<sup>12</sup> thus selecting more severe patients actually treated during this period. Regarding the healthcare system, the protocols adopted by hospitals to minimize the chances of coronavirus spread may have resulted in delays in the transfer and diagnosis processes of STEMI.

The door-to-balloon time remained stable in the various analyzed periods, indicating the team's attention to STEMI care protocols at the institution. Public education and systems-level changes might be crucial in minimizing total myocardial ischemia time and improving healthcare of patients with STEMI during the COVID-19 pandemic.<sup>13</sup> However, concerning the increase in in-hospital deaths, occurrences of cardiopulmonary arrest, and complications during PPCI, one may conclude that they likely represent a consequence of delays in other points of care, including the patients' delay in seeking



urgent care, as well as the poorer clinical condition (Central Illustration). A shorter time until opening the culprit artery in STEMI remains crucial for reducing mortality and preserving myocardial viability.<sup>14</sup>

The higher proportion of patients with COVID-19 is another presumed cause of increased severity in STEMI at the beginning of the pandemic. It is known that the virus has direct cardiovascular effects, with myocardial injury occurring in 8% to 12% of COVID-19 cases. Direct myocardial injury, systemic inflammation, imbalance between myocardial oxygen supply and demand, hypercoagulability, and endothelial dysfunction seem to be the most common mechanisms responsible for cardiac injuries.<sup>15</sup> The high incidence of acute renal failure during this period may also be partially driven by the repercussions of the viral infection. A systematic review with meta-analysis<sup>16</sup> conducted with 2,266 patients showed increased rates of acute renal failure and vascular complications among patients undergoing PPCI during the COVID-19 pandemic. However, the direct action of the COVID-19 virus does not seem to have been the primary cause of the worse outcomes in pandemic I, as fewer than a quarter of patients had a confirmed diagnosis of the infection. Thus, the main reason we find to explain this outcome is the worse clinical setting and, probably, higher incidence of contrast-induced nephropathy.

We must acknowledge some study limitations, mainly the small sample size and the retrospective nature, which hinder a broader analysis and comparison of outcomes during different periods. Possible information biases are inherent to this type of study, especially regarding the time of onset of clinical symptoms. These characteristics, along with the dynamic nature of sanitary conditions in different locations throughout the COVID-19 pandemic, limit the generalizability of these data. Although the study representativeness is single-center, it is essential to note that it was conducted at a local reference service, receiving the majority of its STEMI patients referred by the Mobile Emergency Care Service, which may significantly impact delay times and generate influence from multiple non-measurable variables.

## Conclusion

There was a trend towards an increase in delta T, onset-to-door time, and FMC-to-balloon time during

the pandemic compared to the pre-pandemic period, reflecting greater delays at various levels of assistance for STEMI before reaching the referral service. There was a significant increase in in-hospital mortality for STEMI at the onset of the pandemic, with a tendency to decrease over time, but not returning to pre-pandemic levels. This study is of great relevance to reaffirm the importance of minimizing delays in the diagnosis and treatment of STEMI and to highlight the impact that the COVID-19 pandemic had on patients in the context of this disease.

## Author Contributions

Conception and design of the research: Barbosa RR; acquisition of data: Muzi RR, Bragatto IC, Marianelli C, Sylvestre RC; analysis and interpretation of the data: Lott LP; statistical analysis: Barbosa RR; writing of the manuscript: Lott LP, Trevizani Neto V, Muzi RR, Bragatto IC, Marianelli C, Paganini LN, Borges LMF, Vieira EG, Baptista GC, Calil OA; critical revision of the manuscript for intellectual content: Barbosa RR, Barros LC, Serpa RG, Barbosa LFM.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

## Sources of Funding

There were no external funding sources for this study.

## Study Association

This study is not associated with any thesis or dissertation work.

## Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee on Animal Experiments of the CEP/Emescam under the protocol number 4.179.508.

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