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# Delay Times and Clinical Outcomes in Acute Myocardial Infarction: Comparison of Periods before and during the COVID-19 Pandemic

## —Myocardial Infarction and the Pandemic

**Clarice Teixeira Silva Araújo[1], Arnon Salviato Mameri[2], Thúlio Carrera Guarçoni Venturini[3], Marcus Tadeu Aguilar Constantino Matos[2], Igor Morais Araujo Lopes[2], Luiz Gustavo Ribeiro de Carvalho Murad[4], Cleberson Duartes Ovani[5], Guilherme Vassalo Morais[2], Fernanda Venturini de Castro[2], Danielle Lopes Rocha[6], Lucas Crespo de Barros[2], Rodolfo Costa Sylvestre[2], Luiz Fernando Machado Barbosa[2], Roberto Ramos Barbosa[2*]**

[1]Internal Medicine, Universidade Federal do Espírito Santo (UFES), Vitória, Brazil
[2]Hospital Santa Casa de Misericórdia de Vitória, Vitória, Brazil
[3]Hospital Santa Rita de Cássia, Vitória, Brazil
[4]Hospital Estadual Dr. Jayme Santos Neves, Serra, Brazil
[5]Grupo Kora Saúde, Vitória, Brazil
[6]Hospital Estadual Infantil e Maternidade Alzir Bernardino Alves (HIMABA), Vila Velha, Brazil
Email: claricetsaraujo@gmail.com, arnonmameri@gmail.com, thuliocarreragv@hotmail.com, marcusaguilar_@hotmail.com, igorlopes_morais@hotmail.com, luizmurad@gmail.com, cdovani@gmail.com, moraisvassalo@gmail.com, fernandaventurini31297@gmail.com, daniellelopesrocha@hotmail.com, lucascrespodebarros88@gmail.com, rodolfosylvestre_1993@hotmail.com, uip@terra.com.br, *roberto.cardio@gmail.com

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## Abstract

**Introduction:** At the beginning of the COVID-19 pandemic, a drop in the number of patients treated for cardiac emergencies raised concern about cardiovascular mortality in that period. An increase in care delay for patients with ST-segment elevation myocardial infarction (STEMI) may have affected clinical outcomes. **Objectives:** 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:** Retrospective observational study that included patients with STEMI undergoing PPCI from December 2018 to July 2021. The COVID-19 pandemic cases were divided into two groups: pandemic I—from March to August 2020; and pandemic II—from September 2020 to July 2021. Patients were compared according to the period of hospitalization. Primary outcomes were delay times in assistance and clinical outcomes (acute kidney injury [AKI], post-procedural vascular complications and in-hospital mortality). **Results:** 108 patients were

included, 39 (36.1%) in the pre-pandemic period, 13 (12.1%) in pandemic I and 56 (51.8%) in pandemic II. Time from onset of symptoms to arrival at the service and door-to-balloon time did not differ significantly among groups. Vascular complications were more frequent during the pandemic (I and II) than in the pre-pandemic period (2.5% pre-pandemic vs 15.4% pandemic vs 12.5% pandemic II; p = 0.03). AKI incidence was similar in all three periods. There was a non-significant increase in in-hospital mortality during the COVID-19 pandemic. **Conclusion:** In patients with STEMI, there was an increase in vascular complications and a trend toward increased mortality during the COVID-19 pandemic. Delay times to admission and reperfusion did not differ significantly between before and during the pandemic.

## Keywords

Myocardial Infarction, Primary Percutaneous Coronary Intervention, Coronary Reperfusion, Pandemic, COVID-19

## 1. Introduction

Acute ST-segment elevation myocardial infarction (STEMI) represents one of the most severe clinical presentations of atherosclerotic cardiovascular disease and is one of the leading causes of death worldwide. Interventional Cardiology plays an essential role in the diagnosis and treatment not only of STEMI, but also of stable coronary disease and other types of acute coronary syndrome (ACS), helping to stratify risk and offer proper treatment. Primary percutaneous intervention (PPCI), when available, is the preferred option for coronary reperfusion, if offered within 90 minutes after confirmation of STEMI, as well as for patients with contraindication for fibrinolysis or in the presence of cardiogenic shock. [1]

At the onset of the COVID-19 pandemic, several countries reported a substantial drop in the number of patients who attended the Cardiac Emergency Department and a reduced number of cardiac procedures. [2] The reduction in admissions during the COVID-19 pandemic is a serious concern, since patients with symptoms indicative of acute myocardial ischemia benefit from in-hospital evaluation and effective treatment in a timely manner. [3] In addition to the reduction and delay in admissions due to fear of contact with the virus in the hospital environment, studies show that COVID-19 itself promotes prothrombotic effects in the vasculature that may predict a poor prognosis for ACS. [4] These features may lead to a serious health problem concerning STEMI mortality and costs.

The failure of early hospital admission of patients with STEMI to receive early reperfusion therapy, added to the cardiovascular effects of a COVID-19 infection, results in complications and preventable deaths. [5] [6] However, these data are poorly described and must be assessed in different regions and health systems. Thus, the present study aimed to analyze the clinical profile, delay times

and clinical evolution of patients with STEMI who underwent PPCI in the state of Espírito Santo, Brazil, in the periods before and during the COVID-19 pandemic.

## 2. Methods

### 2.1. Study Design

This is a single-center observational retrospective study, carried out from June 2019 to July 2021, that included patients diagnosed with STEMI who underwent urgent PPCI in a public reference service. Comparisons were made between the pre-pandemic period (December 2018 to February 2020) and the COVID-19 pandemic groups. The COVID-19 pandemic period was divided into two groups, observing the different moments of health care for other conditions. The interval from March to August 2020 was called pandemic I, and pandemic II was the interval from September 2020 to July 2021. Data were collected from the moment of admission to hospital discharge or death, using the patient's electronic medical records.

### 2.2. Population

Patients diagnosed with STEMI who underwent urgent cardiac catheterization, with or without PPCI, were included. Patients with a final clinical diagnosis other than STEMI or undergoing fibrinolysis or those who underwent elective cardiac catheterization after initial care were excluded. Patients who were subsequently transferred to other institutions before hospital discharge had no completion of their data and were also excluded.

### 2.3. Analyzed Variables and Outcomes

The number of procedures performed in each period was evaluated monthly. The clinical variables analyzed were age, sex, severity of the clinical condition according to the Killip classification, previous diagnoses of arterial hypertension, diabetes mellitus, dyslipidemia, chronic renal failure and current and previous smoking. The outcomes analyzed were delay time from the onset of symptoms to arrival at the reference service (in minutes)—pain-to-door time, delay time from the first consultation to the hemodynamics procedure (in minutes)—door-to-balloon time, total hospitalization time (in days), occurrence of acute kidney injury (AKI) after the procedure, vascular complications after the procedure and in-hospital death.

The pain-to-door time was considered from the onset of symptoms reported by the patient or family until the time of arrival recorded in the emergency room of the reference service. The door-to-balloon time was considered from arrival at the emergency department of the reference institution until the performance of PPCI in the Interventional Cardiology department of the same institution. Vascular complications were considered as any reports of local complications at the vascular access site of cardiac catheterization, as long as they

were recorded in the medical record. These could even be minor bleeding without complications, but that generated medical and nursing care. AKI after cardiac catheterization and PPCI was defined as an increase in serum creatinine levels above 0.3 mg/dL or more than 50% above baseline, within 48 hours after the procedure. The length of stay was counted in complete days from the day of arrival at the reference institution, regardless of the hospital outcome of discharge or death.

### 2.4. Statistical Analysis

Comparisons were made between the pre-pandemic, pandemic I and pandemic II groups. Categorical variables were described as absolute frequency and percentage. Continuous variables were described as mean and standard deviation when they had normal distribution, and as median and interquartile range when they had abnormal distribution. For comparative analyses, the chi-square test, the Fisher test, the ANOVA test and the Student t-test were used, with p-values lower than 0.05 being considered statistically significant.

### 2.5. Ethical Aspects

This study followed all ethical principles according to the declaration of Helsinki and the recommendations of Resolution 466 of 2012 of the National Health Council. The study project was previously approved by the Ethics Committee for Research with Human Beings of the institution, under the number of approval 4,179,508.

## 3. Results

Data from 108 patients diagnosed with STEMI and undergoing urgent PPCI were included in this research. Of the procedures performed, 39 (36.1%) occurred in the pre-pandemic period, 13 (12.1%) in pandemic I and 56 (51.8%) in pandemic II. The monthly variation in the number of PPCI procedures performed over the analyzed period is shown in Figure 1.

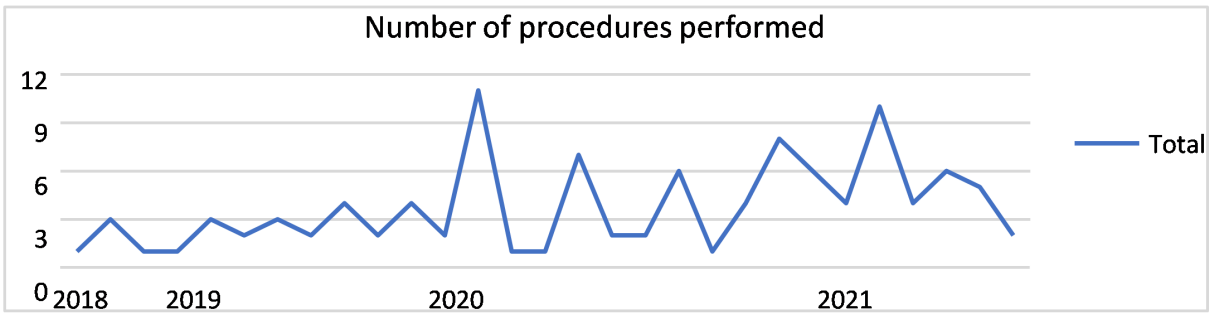


**Figure 1.** Primary percutaneous coronary intervention procedures performed per month during the analyzed periods.

There was a predominance of males in cases treated with PPCI in all three periods. Regarding the severity of the initial clinical presentation in the three

groups, the Killip I classification was the most common in all periods. A higher frequency of presentation in Killip II was observed during pandemic I compared to the other periods, in addition to a trend towards a higher prevalence of arterial hypertension. The baseline clinical characteristics of the included patients are presented in Table 1.

Table 1. Baseline clinical characteristics of patients with ST-segment elevation myocardial infarction with primary percutaneous coronary intervention according to the analyzed period.

| | Pre-Pandemic (n = 39) | Pandemic I (n = 13) | Pandemic II (n = 56) | p |
|---|---|---|---|---|
| Female, n (%) | 12 (30.8%) | 4 (30.8%) | 19 (33.9%) | 0.94 |
| Male, n (%) | 27 (69.2%) | 9 (69.2%) | 37 (66.1%) | 0.94 |
| Hypertension, n (%) | 28 (71.8%) | 12 (92.3%) | 39 (69.6%) | 0.24 |
| Diabetes mellitus, n (%) | 9 (23.1%) | 6 (46.2%) | 24 (42.9%) | 0.10 |
| Dyslipidemia, n (%) | 14 (35.9%) | 6 (46.2%) | 18 (32.1%) | 0.63 |
| Current smoking, n (%) | 16 (41.0%) | 4 (30.8%) | 15 (26.8%) | 0.34 |
| Previous smoking, n (%) | 5 (12.8%) | 2 (15.4%) | 3 (5.4%) | 0.33 |
| Chronic renal failure, n (%) | 1 (2.6%) | 0 | 1 (1.8%) | 0.83 |
| Killip I, n (%) | 33 (84.6%) | 6 (46.2%) | 44 (78.6%) | 0.05 |
| Killip II, n (%) | 3 (7.7%) | 5 (38.5%) | 6 (10.7%) | 0.02 |
| Killip III, n (%) | 2 (5.1%) | 1 (7.7%) | 1 (1.8%) | 0.31 |
| Killip IV, n (%) | 1 (2.6%) | 1 (7.7%) | 5 (8.9%) | 0.38 |
| Age (years), average ± SD | 61.8 ± 9.4 | 64.4 ± 10.9 | 58.9 ± 10.1 | 0.12 |

Note: SD = standard deviation. Pre-pandemic period: from December 2018 to February 2020; Pandemic I period: from March to August 2020; Pandemic II period: from September 2020 to July 2021.

Delay times until medical care (pain-to-door and door-to-balloon times) did not differ significantly among groups, as well as the length of hospital stay. However, procedure-related vascular complications were more frequent in the pandemic I period. Besides, there was a trend towards higher in-hospital mortality in the pandemic I and II periods compared to the pre-pandemic period. Delay times, clinical outcomes and mortality are shown in Table 2.

**Table 2.** Delay times, clinical outcomes and in-hospital mortality in ST-segment elevation myocardial infarction with primary percutaneous coronary intervention according to the analyzed period.

| | Pre-Pandemic (n=39) | Pandemic I (n=13) | Pandemic II (n=56) | p |
|---|---|---|---|---|
| Pain-to-door time (minutes), average ± SD | 313.7 ± 284.8 | 344.6 ± 212.4 | 387.6 ± 240.8 | 0.12 |
| Door-to-balloon time (minutes), average ± SD | 64.1 ± 43.2 | 63.8 ± 29.3 | 67.9 ± 37.5 | 0.73 |
| Vascular complications, n (%) | 1 (2.5%) | 2 (15.4%) | 7 (12.5%) | 0.03 |
| Acute kidney injury, n (%) | 5 (12.8%) | 2 (15.4%) | 6 (10.7%) | 0.88 |
| Length of stay (days), average ± SD | 12.1 ± 21.7 | 8.7 ± 6.9 | 12.5 ± 14.1 | 0.41 |
| In-hospital death, n (%) | 16 (5.1%) | 4 (23.1%) | 15 (21.4%) | 0.07 |

Note: SD = standard deviation. Pre-pandemic period: from December 2018 to February 2020; Pandemic I period: from March to August 2020; Pandemic II period: from September 2020 to July 2021.

## 4. Discussion

In this study, no decline in ICPP procedures was observed in the first months of the pandemic, as reported in other studies. During the initial phase of the COVID-19 pandemic, there was an estimated 38% reduction in nine interventional centers in the United States of America, while Xiang *et al.* [7] reported a 62% reduction in the number of PPCI procedures performed in China during the pandemic. In turn, 73 centers reported a 40% reduction in the number of these procedures in Spain. [8] It is believed that this reduction was mainly due to patients' fear of being contaminated by the viral infection in the hospital. However, the balance observed in our incidence can be attributed to two factors: 1) the fact that it is a regional reference service that did not interrupt care for cardiac emergencies at any time, maintaining the flow of transfers for emergency cases; 2) the possible increase in cardiovascular emergencies related to COVID-19.

Although COVID-19 protocols may delay screening, diagnosis, and transfer of patients with cardiovascular emergencies, we did not observe a significant increase in pain-to-door and door-to-balloon times. It is also suspected that the fear of infection by COVID-19 may have delayed the search for medical care by patients. Contrary to our results, a study carried out in Hong Kong showed, during the pandemic, a significant increase in pain-to-door time (pre-pandemic 82 minutes vs pandemic 318 minutes) and door-to-balloon time (pre-pandemic 84 minutes vs pandemic 110 minutes). [9] The reasons for the delay in care are numerous, such as ambulance services that are occupied with COVID-19 cases and relocation of professionals from the Cardiology and Interventional Cardiology departments to areas of the hospital with greater demand, such as Intensive Care Units. The pre-hospital delay, in turn, could increase due to access difficulties and fear of patients and family members coming into contact with the virus.

Some balance may have occurred in this casuistry, as patients treated during the pandemic period I tended to present greater clinical severity and higher baseline cardiovascular risk. It is inferred, therefore, that patients with less severe conditions may have chosen not to seek medical attention.

Whilst the greater clinical severity in the pandemic I period did not result in a higher incidence of AKI, vascular complications were more frequent during the pandemic. A systematic review with meta-analysis performed with 2266 patients showed an increase in the number of patients undergoing PCI with AKI and vascular complications during the COVID-19 pandemic. [10] This result can be explained by the hypercoagulation characteristics and prothrombotic effects of the virus. Although the involvement of the virus with the vasculature is still not fully understood, mechanisms attributed to vascular injury were the activation of immune receptors in pre-existing atherosclerotic plaques, increasing the likelihood of plaque displacement, and the activation of cytokines, resulting in dysfunction with consequent vasoconstriction and thrombosis of the endothelium. [11]

Regarding in-hospital mortality during the pandemic, we observed an increase compared to the pre-pandemic period, but without statistical significance. More worrisome seems to be the fact that, in pandemic II, there was no reduction in mortality to pre-existing levels, even after the initial phase of the pandemic, considered more complex. Studies carried out in Italy [12] and China [7] observed a significant increase in in-hospital mortality of patients with STEMI admitted since the beginning of the pandemic. However, in regions less affected by the pandemic, no effect on mortality was detected. [13] Another possible justification is that, at the beginning of the pandemic, patients with less severe STEMI often avoided going to the hospital for fear of contamination. Hence, STEMI medical care was targeted to more severe patients, who had a higher risk of death. In pandemic II, in turn, a lack of control of cardiovascular risk factors and a deleterious psychosocial effect of the pandemic could explain the cases of higher complexity and mortality.

## Study Limitations

Despite being relevant, this study has some limitations. As this is an observational and retrospective study, some possible biases must be considered. Patients who underwent fibrinolysis were not included, as the delay considered in cases of success after fibrinolysis is different from PPCI cases and could contaminate the results. The pain-to-door time did not distinguish patients who sought the reference institution directly from those who were treated at first emergency service and subsequently transferred. Therefore, it is uncertain whether or not there was, with the onset of the pandemic, a greater delay in the search for medical care by the patient or by the health teams in the care of STEMI. Deaths from non-cardiac causes, mainly from complications of COVID-19, although closely related to the initial cardiac event, were not properly accounted for. Finally, the sample size is small and the study only maps the care situation in different periods, not having the power to demonstrate cause and effect. However, the re-

sults obtained are important and can help protocols and medical decisions in times of health crisis.

## 5. Conclusion

The present study demonstrated that the COVID-19 pandemic period was not associated with a reduction in the number of patients with STEMI treated by PPCI; however, there was an increase in vascular complications and a trend toward an increase in in-hospital mortality. The delay time until attendance at the service and the door-to-balloon time did not differ significantly between the pre-pandemic, pandemic I and pandemic II groups. In Pandemic I, a trend towards greater initial clinical severity and higher prevalence of arterial hypertension was observed, but without statistical significance.

## Conflicts of Interest

The authors declare no conflicts of interest related to this manuscript.

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