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ORIGINAL ARTICLE

Characteristics of ST-Elevation Myocardial Infarction during the SARS-CoV-2 Outbreak

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Abstract

Background: The SARS-CoV-2 outbreak has led to radical transformation in social, economic, and healthcare systems. This may lead to profound indirect consequences on clinical presentation and management of patients with ST-segment–elevation myocardial infarction.

Objectives: The objective of this study was to describe the characteristics, management, and outcomes of patients admitted with acute myocardial infarction with ST-segment elevation (STEMI), in two tertiary reference hospitals during the SARS-CoV-2 outbreak and compare them with patients admitted in the previous year.

Methods: We analyzed data from a multicenter STEMI registry from reference centers in the South Region of Brazil from March 2019 to May 2021. The beginning of the COVID-19 outbreak was considered to be March 2020 and compared to the same period in 2019. Only patients with STEMI submitted to primary percutaneous coronary intervention (PCI) were included in the analysis. Mortality rates were compared with chi-square test. All hypothesis tests had a two-sided significance level of 5%.

Results: A total of 1169 patients admitted with STEMI were enrolled in our registry, 635 of whom were admitted during the pandemic period. The mean age of our sample was 61.6 (± 12.4) years, and 66.7% of patients were male. Pain-to-door time and door-to-balloon time were longer during the pandemic period. However, there was no difference in mortality rates or major adverse cardiovascular outcomes (MACE).

Conclusions: We observed a stable incidence of STEMI cases in our registry during the SARS-CoV-2 outbreak with higher pain-to-door time and door-to-balloon time, without any influence on mortality rates however.

Keywords: COVID-19; Pandemics; Myocardial Infarction; Mortality; Percutaneous Coronary Intervention.

Introduction

The ongoing pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections led to more than 101,371,256 cases and 2,817,659 deaths globally by January 28, 2021.[1] Although many infections have mild and self-limiting symptoms, around 15% of adults develop severe pneumonia requiring supplementary oxygen treatment, and approximately 5% progress to respiratory failure and require prolonged mechanical ventilation. When this occurs, there is a high rate of mortality and complications, overloading health systems, especially intensive care units.[2–4]

Social isolation has been recommended by the World Health Organization as the main measure to avoid contagion. To avoid unnecessary circulation, most hospitals have cancelled elective procedures, maintaining only urgency and emergency care. One of the concerns about the social isolation recommendation was that people with potentially life-

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Central Illustration: Characteristics of ST-Elevation Myocardial Infarction during the SARS-CoV-2 Outbreak

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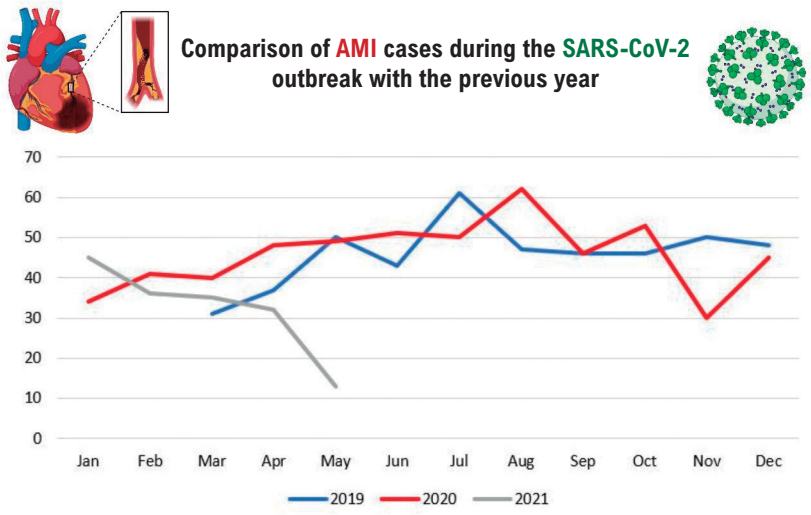

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Comparison of AMI cases during the SARS-CoV-2 outbreak with the previous year. Figure created with BioRender.com
AMI: Acute myocardial infarction

threatening conditions, such as acute myocardial infarction, would take more time to seek medical assistance due to fear of exposure to the virus.

After some time, many countries have loosened isolation measures, trying to find a balance between contagion rate and maintenance of the local economy. Also, the long duration of the pandemic and the large number of people who have recovered from SARS-CoV-2 infection contributed to the decrease in isolation measures. To date, with the approval of vaccines, the rates of contagion and severe cases have decreased. All these measures changed medical assistance globally, and the impact on health care is uncertain and may differ in different countries.

The present analysis aimed to describe the characteristics, management, and outcomes of patients admitted with acute myocardial infarction with ST-segment elevation (STEMI), in two tertiary reference hospitals during the SARS-CoV-2 outbreak and compare them with patients admitted in the previous year.

Methods

Data, study design, and population

This prospective registry included patients admitted with STEMI and treated with primary percutaneous coronary intervention (PCI) in two tertiary hospitals (Hospital de Clinicas de Porto Alegre [HCPA], a general hospital, and Instituto de Cardiologia do Rio Grande do Sul [IC-FUC], a cardiology center) in the South Region of Brazil between the years of 2019 and 2021. During the SARS-CoV-2 outbreak, HCPA was considered a center for treatment of patients with COVID-19; therefore, there was a recommendation by the Health Secretary to avoid referring patients with STEMI to HCPA to preserve intensive care unit beds during the first three months, approximately. The beginning of the COVID-19 outbreak was considered to be March 2020 and compared to the same period in 2019.

Patients eligible for inclusion were consecutive adults (≥ 18 years of age) admitted with STEMI, based on the presence of typical chest pain at rest associated with ST-segment elevation or abnormalities that met the diagnostic criteria for STEMI according to current guidelines.[5] Only patients with STEMI submitted to primary PCI were included in the analysis. This study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the Institutional Research and Ethics Committee, and written informed consent was obtained from all individual participants included in the study. Medications and PCI strategies were based on current guidelines and performed according to the operator's choice.[5]

Data from medical records were transferred into standardized case report forms. Data collected included baseline clinical characteristics, medical history, procedure characteristics, reperfusion strategy, initial and final thrombolysis in myocardial infarction (TIMI) flow grade, and discharge therapies. In-hospital outcomes were also recorded in the case report form.

Outcomes

The primary outcome of our study was in-hospital mortality. The secondary outcome was in-hospital major adverse cardiovascular outcomes (MACE), defined as in-hospital mortality, new myocardial infarction, stent thrombosis, and non-fatal stroke.

Definitions

Stroke was defined as a new, sudden-onset focal neurologic deficit, of a presumably cerebrovascular cause, which was irreversible (or resulting in death), without other readily identifiable causes.

Successful primary PCI was defined as final TIMI 3 flow and residual stenosis < 30%. Cardiac arrest was considered when occurring during primary PCI and requiring resuscitation procedures (i.e., ventilation, chest compression, defibrillation). Chronic kidney disease was defined as kidney damage or glomerular filtration rate < 60 mL/min/1.73 m² for 3 months or more, irrespective of cause.[6] A positive family history of cardiovascular disease was defined as a self-reported diagnosis that occurred (age of onset < 55 years for men and < 65 years for women) in first-degree relatives (parents, siblings, or children).[7]

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median and interquartile range based on the presence of symmetrical and asymmetrical distribution, respectively. Normality was assessed by the Shapiro-Wilk test. Categorical variables were expressed as relative and absolute frequencies. Differences between groups were compared using unpaired Student's t-test or Mann–Whitney test, as appropriate. The chi-square test or Fisher's exact test was used for categorical variables. All hypothesis tests had a two-sided significance level of 5%. Data were analyzed using SPSS Statistics (version 26.0.0; IBM Company).

Results

Baseline clinical characteristics

Between March 2019 and May 2021, 1169 consecutive patients admitted with STEMI and referred for primary PCI were enrolled in our registry. There was a total of 635 STEMI cases during the pandemic period. The mean age of our sample was 61.6 (± 12.4) years, and 66.7% of patients were male. The baseline characteristics of patients who were admitted during the pandemic period are detailed in **Table 1** with a comparison of the previous year.

Compared to the pre-pandemic year, patients admitted during the COVID-19 outbreak were younger, and they had less previous myocardial infarction, positive family history of cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease.

Data regarding procedural characteristics were similar, with radial access being used in the majority of cases, and the left anterior descending artery was the most frequent culprit vessel. There was a higher incidence of angiographic success. The pain-to-door time and door-to-balloon time were longer during the pandemic period. However, there was no difference in mortality rates or MACE (**Table 2**).

During the pandemic, the incidence of cases was similar to the previous year. (**Central Illustration**). However, when analyzing the incidence of cases according to centers, there was a higher volume referred to the Cardiology Hospital during the period that the General Hospital was considered a reference for COVID-19 referral (**Figure 1**).

Discussion

In a cohort of STEMI patients admitted to two tertiary reference hospitals, we observed a stable incidence of STEMI cases during the pandemic. Although median pain-to-door time and door-to-balloon time were longer, overall mortality rates remained unchanged. Data on assistance modifications and changes in demographic profiles of patients seen during the pandemic are scarce, especially in Brazil.

One of the major concerns with lockdown and isolation measures was that patients would avoid seeking medical assistance, leading to a delay in the diagnosis and treatment of potentially lethal conditions, such as acute

Table 1 – Baseline demographic characteristics

	2019 (n = 534)	2020-2021 (n = 635)	p
Age (SD)	62.3 (±11.9)	60.9 (±12.8)	0.02
Male sex	352 (65.9)	428 (67.8)	0.49
Hypertension	326 (61.0)	385 (60.8)	0.93
Diabetes	169 (31.6)	176 (27.8)	0.14
Smoking (previous or current)	309 (57.9)	56 (56.1)	0.54
Previous MI	101 (19.1)	82 (12.9)	0.04
Previous stroke	39 (7.4)	31 (4.9)	0.07
Family history of CAD	86 (16.3)	69 (11.0)	0.01
Heart failure	30 (5.7)	33 (5.2)	0.72
COPD	61 (11.5)	28 (4.4)	0.0001
Chronic kidney disease	24 (4.5)	14 (2.2)	0.02
Anterior MI	244 (45.7)	297 (46.8)	0.69
Cardiac arrest	26 (12.1)	60 (9.4)	0.25
Killip III or IV	53 (9.9)	59 (9.4)	0.73
Pain-to-door, minutes (IQR)	278 (180-447)	300 (195-468)	0.04
Door-to-balloon, minutes (IQR)	66 (48 - 90)	71 (54 - 90)	0.02
Procedural Characteristics			
TIMI flow pre-procedure			0.08
0	130 (71.0)	103 (77.4)	
1	38 (20.8)	15 (11.3)	
2	10 (5.5)	7 (5.3)	
3	5 (2.7)	8 (6.0)	
Angiographic success	499 (95.0)	609 (97.8)	0.01
Previous PCI	98 (18.6)	65 (10.3)	<0.0001
Previous CABG	14 (2.7)	15 (2.4)	0.75
Previous fibrinolysis	15 (2.8)	12 (1.9)	0.29
Radial access	428 (82.5)	538 (85.7)	0.14
Culprit vessel			0.52
LAD artery	252(47.5)	306(48.8)	
Circumflex artery	51 (9.6)	72 (11.5)	
RC artery	208 (39.2)	223 (35.6)	
No reflow	15 (2.8)	18 (2.8)	0.97

Values are expressed as mean (SD), median (IQR), or n (%). CABG: coronary artery bypass graft; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; IQR: interquartile range; LAD: left anterior descending; MACE: major adverse cardiovascular event; MI: myocardial infarction; PCI: percutaneous coronary intervention; RC: right coronary; SD: standard deviation.

Table 2 – Incidence of outcomes during COVID-19 pandemic and previous year

Outcomes	2019 (n = 534)	2020-2021 (n = 635)	p
In-hospital death	46 (9.3)	48(9.1)	0.90
In-hospital MACE	53 (10.7)	59(11.1)	0.81
30-day death	49(9.9)	56(10.6)	0.72
30-day MACE	61(12.3)	68(12.8)	0.79

Values are expressed as n (%). MACE: major adverse cardiovascular event.

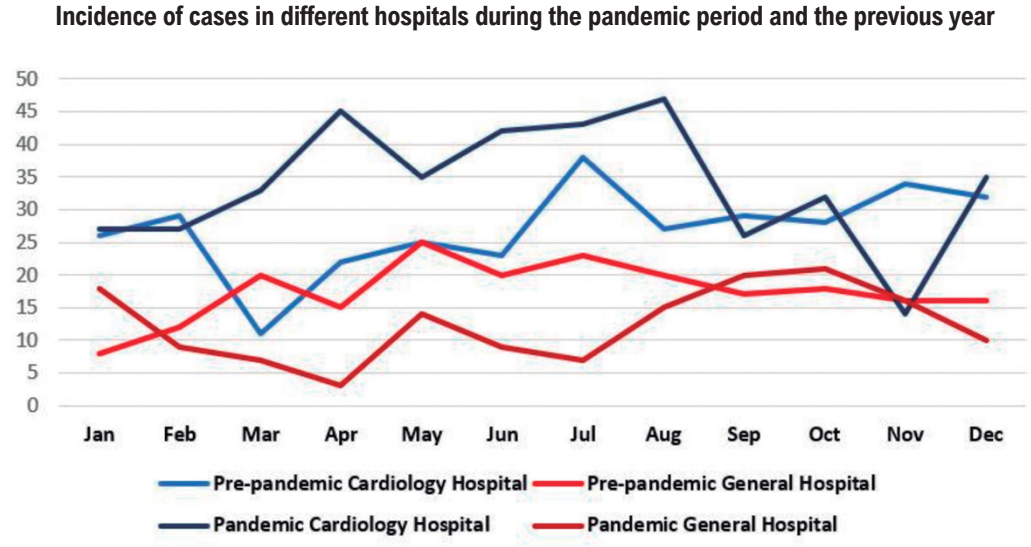

Figure 1 – Incidence of cases in different hospitals during the pandemic period and the previous year

myocardial infarction. In the United States, reductions of 33.1% and 21.1% were observed in hospital admissions for acute myocardial infarction in Abril and June, respectively, compared to the same period of 2019.[8] The same pattern was observed in Italy and United Kingdom, especially in the beginning of the pandemic.[9–11] Interestingly, a study from Singapore showed an increase in the incidence of acute myocardial infarction from February to April 2020, from 15.3% to 17.5%, compared to the same period in 2019.[12] The only study performed in Brazil so far showed a 15% decrease in hospital admissions for cardiovascular causes between March and May 2020 compared to 2019. However, the decrease in STEMI was only 4%, less than that reported in international series.[13] In our study, there was a notable decrease in STEMI admissions in our center that was designated to be a reference for COVID-19 treatment, during the first months of the pandemic, with a simultaneous increase of STEMI cases referred to the Cardiology Center. However, overall, we observed a stable incidence of STEMI admissions.

Regarding patients' profile during the pandemic, a meta-analysis performed by Furnica et al. observed a younger age and a higher comorbidity burden for acute coronary syndromes (arterial hypertension, diabetes mellitus, smoking, dyslipidemia, and known coronary artery disease).[14] In our study as well, younger patients were affected during the pandemic, with fewer comorbidities however. This could be explained by the increased risk of thromboembolism in

patients with COVID-19, whose exact mechanism remains unclear (e.g., endothelial dysfunction, hypercoagulability, and/or increased platelet activity).[15] However, given the inherent nature of our observational study, this imbalance could be due to a survival bias, since older patients may be less likely to survive until hospital admission.

Data in the literature are inconsistent regarding the door-to-balloon and pain-to-door times. No differences in the time from onset of symptoms to first medical contact and door-to-balloon time were observed in Germany, and no difference was observed in ischemia time compared to previous years in Italy.[9,16] In contrast, in Lithuania, England, and another study from Italy, the median pain-to-door time was significantly higher during the pandemic (1885 versus 606 minutes, $p < 0.0001$; 153 versus 135 minutes, $p = 0.004$; and 15.0 versus 2.0 hours; $p < 0.01$, respectively), as was door-to-balloon time (332 versus 194 minutes, $p = 0.03$; 48 versus 37 minutes, $p < 0.001$; and 60 versus 40 minutes; $p = 0.22$, respectively).[17–19] Similar results were found by De Luca,[20] in a worldwide multicenter analysis with 16000 patients, observing an increase in total ischemia time (225 versus 196 minutes, $p < 0.001$). In our analysis, we observed an increase in pain-to-door time, probably due to people's fear of exposure to the virus in health facilities. Door-to-balloon time was also higher, probably due to isolation precautions that occurred in all health centers. The impact of delayed presentation is a major concern for patients with STEMI. This may lead to a significantly worse left ventricular ejection fraction and a higher future morbidity and mortality.

Interestingly, few places found differences in STEMI mortality during pandemics compared to previous years. An Italian study performed by De Rosa et al.[10] observed an increase from 4.1% to 13.7%; ($p < 0.001$). De Luca et al.[20] observed higher in-hospital (6.5% versus 5.3%; $p < 0.001$) and 30-day (8% versus 6.5%, $p = 0.001$) mortality during the pandemic. Data from Lithuania, United Kingdom, England, and Italy showed no significant differences.[11,17–19] In Brazil, a non-significant 9% reduction in STEMI mortality was observed ($p = 0.08$).[13] Likewise, our study did not observe a difference in mortality or MACE rates during the in-hospital period or in 30 days. Although short-term worsening of outcomes is not evident, the long-term impact is uncertain. As speculated above, these changes observed in STEMI assistance, such as longer door-to-balloon time, may reflect higher rates of patients with heart failure, re-hospitalizations, and probably higher long-term mortality.

Some strengths and limitations should be highlighted. First, we performed an observational study from a COVID-19 tertiary reference hospital and a cardiology tertiary reference hospital with high volumes of STEMI. While the available data in the literature show a brief period at the beginning of the pandemic, our analysis reflects most of the year 2020 and 2021. However, our data should be interpreted with caution since countries have different health systems and different economic situations. Furthermore, isolation measures were adopted in different ways and at different times, which may directly interfere with the results obtained.

Conclusions

We observed a stable incidence of STEMI cases in our registry during the SARS-CoV-2 outbreak, with higher pain-to-door time and door-to-balloon time, without any influence on mortality rates however.

Author Contributions

Conception and design of the research and writing of the manuscript: Machado GP, Araujo GN; acquisition of data: Beltrame R, Theobald A, Niches MS, Fracasso JF, Custodio J, Cardoso CP, Tietz PHT, Reichert GB, Schmidt MM, Milan V; analysis and interpretation of the data and statistical analysis: Machado GP; critical revision of the manuscript for intellectual content: Araujo GN, Quadros AS, Wainstein M.

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 of the Hospital de Clinicas de Porto Alegre under the protocol number 2015-0557. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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