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Impact of the COVID-19 pandemic on hospitalizations for acute coronary syndromes: a multinational study

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Summary

Background: COVID-19 has challenged the health system organization requiring a fast reorganization of diagnostic/therapeutic pathways for patients affected by time-dependent diseases such as acute coronary syndromes (ACS).

Aim: To describe ACS hospitalizations, management, and complication rate before and after the COVID-19 pandemic was declared.

Design: Ecological retrospective study. Methods: We analyzed aggregated epidemiological data of all patients > 18 years old admitted for ACS in twenty-nine hub cardiac centers from 17 Countries across 4 continents, from December 1st, 2019 to April 15th, 2020. Data from December 2018 to April 2019 were used as historical period.

Results: A significant overall trend for reduction in the weekly number of ACS hospitalizations was observed (20.2%; 95% confidence interval CI [1.6, 35.4] P = 0.04). The incidence rate reached a 54% reduction during the second week of April (incidence rate ratio: 0.46, 95% CI [0.36, 0.58]) and was also significant when compared to the same months in 2019 (March and April, respectively IRR: 0.56, 95%CI [0.48, 0.67]; IRR: 0.43, 95%CI [0.32, 0.58] p < 0.001). A significant increase in door-to-balloon, door-to-needle, and total ischemic time (p <0.04 for all) in STEMI patents were reported during pandemic period. Finally, the proportion of patients with mechanical complications was higher (1.98% vs. 0.98%; P = 0.006) whereas GRACE risk score was not different.

Conclusions: Our results confirm that COVID-19 pandemic was associated with a significant decrease in ACS hospitalizations rate, an increase in total ischemic time and a higher rate of mechanical complications on a international scale.

Introduction

Since the first reported cases from the Chinese city of Wuhan in December of 2019, Coronavirus Disease 2019 (COVID-19) has grown to a pandemic infecting more than 87 million individuals and causing more than 1.8 million deaths as of the beginning of January 2021.[1–2] Healthcare systems have been challenged due to the COVID-19 pandemic, which has led to a complete reorganization of all the acute care diagnostic and therapeutic pathways.

The combination of overwhelmed health care systems and the strict social containment measures may have had an impact on the illness threshold at which the patients with other diseases than COVID-19 seek for medical care. Previous reports from Hong Kong observed that the time of first medical contact of patients with acute coronary syndrome (ACS) increased since late January 2020, compared to a 12-month period preceding the pandemic onset.1 Additionally, the total number of hospitalizations, diagnostic and therapeutic procedures performed for ACS decreased after the COVID-19 outbreak in several country reports.[3–8]

As cardiovascular disease represents the leading cause of death worldwide,[9] identifying how the care of patients with ACS could be affected by the COVID-19 pandemic is of paramount importance. This study aims to describe the clinical characteristics, temporal trends, treatment, complications and outcomes in ACS hospitalizations before and after the onset of the COVID-19 pandemic at a multinational level.

Materials and methods

Study design and participants

The study was conducted through the network of Young Community from the Association for Acute Cardiovascular Care

(ACVC) of the European Society of Cardiology. All participant centers were regional hub hospitals for the treatment of ACS with either primary percutaneous coronary intervention (pPCI) or fibrinolysis before and after the onset of the COVID-19 pandemic.

All adult patients (≥18 years old) admitted for ACS [including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) and unstable angina] were included in this study. Data were retrospectively retrieved from patients' medical history records and hospital discharge files. The protocol was approved by the ethical committee from the principal investigator's institution and complies with the principles of the Declaration of Helsinki. Due to the ecological nature of the data, informed consent was waived.

Data collection

Data of patients consecutively admitted for ACS from 1 December 2019 to 15 April 2020 were considered for the study. Additionally, the period from 1 December 2018 to 30 April 2019 was considered as historical comparison period. Data were aggregated and expressed in monthly rates for December 2019–February 2020 and in weekly rates for the period after 1 March 2020. For the historical comparison, monthly aggregation was used.

Clinical characteristics, temporal trends in ACS hospitalization rates, chosen treatment strategy, time to treatment, complications and in-hospital outcomes were collected from all patients fulfilling the inclusion criteria during the study period in each center and aggregated in a central database.

Study period definition

We defined the pandemic period after 11 March 2020, according to the World Health Organization (WHO) declaration of the COVID-19 pandemic,[3] and compared trends with the 14 preceding weeks (1 December 2019–10 March 2020). To account for potential seasonal trends, we compared monthly ACS hospitalization rates in the observed timeframe with historic controls from the previous year (i.e. March 2020 vs. March 2019). Finally, to account for potential geographical and temporal dispersion of the COVID-19 outbreak, the date of the declaration of national emergency for each country was considered in a sensitivity analysis to define the onset of the pandemic period.

Assessment of the outcomes

The primary outcome of the study was the comparison between ACS weekly admission rates in pre-pandemic and pandemic periods. Additionally, we compared ACS monthly rates of pre-pandemic and pandemic periods with the historical comparison. Secondary outcomes included the proportion of patients treated by percutaneous coronary intervention (PCI), total ischemic time, as well as door-to-balloon/door-to-needle times (for patients with STEMI) and GRACE score. Rate of mechanical complications was also analyzed.

Primary PCI was defined as a percutaneous coronary intervention procedure performed during the first 12 h since symptoms onset. Ischemic time was defined as the total time, in minutes, between symptom onset and the guidewire crossing or lytic IV injection. Door to balloon and door to needle were defined as time from hospital presentation to guidewire crossing or lytic IV injection, respectively.[10] Mechanical complications were recorded as a composite frequency that included acute severe mitral regurgitation, ventricular septal defect and cardiac rupture/tamponade.

Statistical analysis

The weekly average rate was calculated by dividing the ACS events with the week considered (i.e. 14 weeks from 1 December 2019 to 11 March 2020). The relative differences in weekly rates between the pandemic and pre-pandemic periods were estimated using generalized linear regression models with a Poisson distribution, and we used robust estimation of variance and accounted for clustering of the data by center. A joinpoint regression analysis was performed to assess fluctuating trends over time in the weekly ACS rates after the WHO pandemic declaration. This analysis aimed to identify both an overall percentage change during the post-pandemic period and any timepoint in which the trend in ACS rates significantly changed (from 1 week to another). For both analyses, an overall percentage change during those periods were reported.

We compared the mean GRACE scores, time to treatment and total ischemic time by type of ACS. Door-to-balloon, door-to-needle times (for STEMI) and treatment used (by type of ACS) were compared between pre-pandemic and pandemic periods using paired *t*-tests. To compare the proportion of patients who underwent PCI and developed mechanical complications, we performed chi-squared tests. A two-sided P values <0.05 was considered significant and used in all analyses. Data were analyzed using the statistical software STATA SE version 15 (StataCorp LLC, College Station, TX, USA). Joinpoint regression analyses were performed with the Joinpoint Regression Program version 4.8.0.1, April 2020, provided by the Statistical Research and Applications Branch, National Cancer Institute. Artwork was done with GraphPad Prism 6.

Results

A total of 29 centers from 17 countries were enrolled in the study. A complete list of participant centers is included in Supplementary Appendix A. Across the three study periods, a total of 16 117 patients with ACS were admitted to the participant centers (pre-pandemic period = 5923; pandemic period = 1444; historical control period = 8750). Table 1 shows the absolute admissions through each study period according to individual diagnosis (ST elevation ACS and/non-ST elevation ACS).

Primary outcome

When compared to the pre-pandemic period, a significant overall trend for reduction of 20.2% in the weekly number of ACS hospitalizations was observed during the pandemic period (95% confidence interval CI [1.6, 35.4], $P=0.04$) (Figure 1). The maximal reduction in the incidence rate was 54% during the second week of April compared with the pre-pandemic period [incidence rate ratio (IRR): 0.46, 95% CI [0.36–0.58], $P<0.001$]. Additionally, we observed relevant reductions as compared with historical period (Figure 2) which reached statistical significance for the months of March and April 2020 when compared to the same months in 2019 (respectively IRR: 0.56, 95%CI [0.48, 0.67]; IRR: 0.43, 95% CI [0.32–0.58] $P<0.001$). A world map including the participant countries and their relative ACS reduction is included in Supplementary Appendix B.

To account for the difference in ACS hospitalization rates between WHO pandemic declaration and the date of national emergency declaration of each of the participating countries, a sensitivity analysis was conducted, and the results are summarized in Table 2. This alternative model confirmed the reductions in ACS weekly admissions, up to a 63% decrease during

Table 1. Absolute number of patients admitted through the enrolled centers according to the three study periods

	Historical control: December 2018–April 2019	Pre-pandemic period: 1 December 2019–11 March 2020	Pandemic period: 12 March 2020–15 April 2020
Total ACS	8750	5923	1444
Non-ST-elevation ACS (NSTEMI and UA)	5215	3605	712
ST-elevation ACS	3535	2318	713

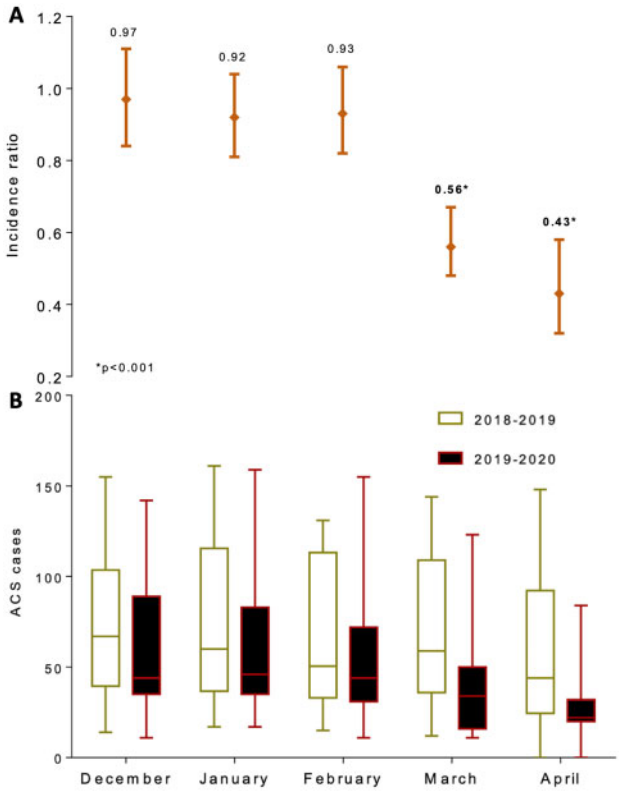

Figure 1. ACS admissions during the pre- and pandemic periods compared to previous year historical data. **(A)** Incidence rate ratios for ACS admissions during the pre-pandemic and pandemic periods compared with historical control. **(B)** Whisker and box plot of the total ACS admissions during the pre-pandemic and pandemic periods compared with historical control. Pre-pandemic period was defined as 1 December 2019–11 March 2020; pandemic period was defined as 12 March–15 April. Historical control comprises the same periods from 2018 and 2019 matched dates. The data for April 2020 were imputed from those obtained for the first two weeks.

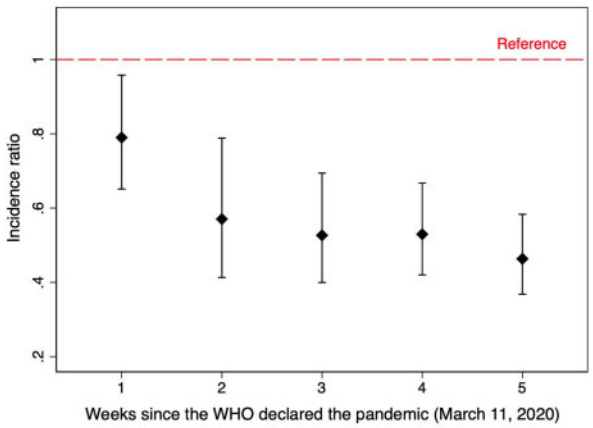

Figure 2. Incidence rate ratios for the weekly rate of ACS hospitalizations after the first WHO COVID-19 pandemic declaration. Reference line indicates the average weekly ACS hospitalizations for the 14 weeks preceding the pandemic period.

Table 2. Sensitivity analysis: IRR for ACS weekly admissions

	IRR	95% CI	*P* value
Weekly average, 1 December 2019—Declaration of emergency, 2020	Reference		
Week 1 after COVID-19 pandemic	0.57	0.41–0.79	0.017
Week 2 after COVID-19 pandemic	0.59	0.45–0.78	0.001
Week 3 after COVID-19 pandemic	0.49	0.39–0.62	<0.001
Week 4 after COVID-19 pandemic	0.60	0.49–0.74	<0.001
Week 5 after COVID-19 pandemic	0.37	0.28–0.49	<0.001

The pandemic period was defined for each country from the date of the declaration of emergency.

the fifth week after the pandemic onset as defined at a country-level (IRR for the fifth week: 0.37, 95% CI [0.28–0.49], $P < 0.001$). A table including the date of national emergency declaration for each country is included in Supplementary Appendix C.

Secondary outcomes

A significant reduction of patients undergoing pPCI was observed (81.8% pre-pandemic vs. 76.2% pandemic, difference: -5.6%, $P = 0.041$), with no significant difference in the proportion of patients undergoing systemic fibrinolysis (11.8% pre-pandemic vs. 14.7% pandemic, difference: +2.8%, $P = 0.56$). A significant delay was reported in total ischemic time (relative difference +22.7 min; $P = 0.02$), door-to-balloon (relative difference +11.2; $P = 0.04$) and door-to-needle times (relative difference +48.3 min; $P < 0.004$). No significant differences were noted in the rate of NSTEMI patients undergoing either PCI (70.3% pre-pandemic vs. 73.6% pandemic, difference: +3.0%, $P = 0.29$) or CABG (8.3% pre-pandemic vs. 12.1% pandemic, difference: +4.8%, $P = 0.43$). No significant difference between pre-pandemic and pandemic was found in mean GRACE scores both in STEMI (129.7; 95% CI [119.6–139.8] vs. 130.1, 95% CI [117.3–142.8]; $P = 0.91$) and NSTEMI patients (123.2, 95% CI [112.3–134.1]) vs. 121.1, 95% CI [102.7–139.6]; $P = 0.78$).

Twenty-two centers provided data on mechanical complications. The proportion of patients who developed any mechanical complication during the pandemic period was higher when compared with the pre-pandemic period (1.98% [23/1161] vs. 0.98% [41/4143], $P = 0.006$). When compared to the historical control, a similar pattern was observed (1.98% [23/1161] vs. 1.17% [30/2547], $P = 0.057$), but the difference was not statistically significant.

Discussion

Our study reports a significant decrease in hospitalizations for ACS after the WHO COVID-19 pandemic declaration in several countries worldwide. Furthermore, among patients with STEMI, a lower rate of pPCI with significant increase in patient and system-related delays and a higher rate of mechanical complications were observed.

A disruption in the diagnostic/therapeutic pathway of acute diseases, including ACS, has been reported during previous infectious disease outbreaks.[11] Furthermore, previous studies during SARS-CoV-1 outbreak reported changes in ACS hospitalization rates with substantial decreases in cardiac catheterizations,[12] which were likely explained by restrictions in the use of health care services affecting the access for some potentially seriously ill patients.

It was therefore expected that COVID-19 pandemic would result in a significant reduction in emergency department and hospital admissions with related procedures. According to data from a STEMI registry and reports from Europe, a steep decline in the admissions after the COVID-19 lockdown has been observed,[5–8] which is consistent with our results on a wider perspective.

De Filippo *et al.*[5] reported the results of a retrospective multicentric analysis of consecutive patients admitted for ACS at 15 hospitals from Italy after national COVID-19 outbreak, demonstrating a reduction of 26% in the number of admissions when compared with the previous months, and a reduction of 30% when compared the previous year. Similarly, in another report comprising ~10% of the Italian population, a significant decline in the rates of PCI both for NSTEMI and STEMI was observed.[6] Likewise, a reduction of 38% in STEMI prevalence has been also observed in the USA after the national COVID-19 outbreak.[4] An increased complication rate was also observed in a nationwide survey, although limited to a 1-week enrollment.[7]

The reasons behind the decline of procedure rates and prolonged times to treatment may be several. Dyspnea and chest pain are common overlapping symptoms of both, overt ischemia and COVID-19, which makes the differential diagnosis more challenging[13,14] and potentially leads to prolonged reperfusion times. Additionally, besides the reluctance of patients seeking care, the infection and prevention control measures may have played a role in prolonging the patient's clinical evaluation and procedure organization.[15]

Outcomes of patients presenting with ACS have progressively improved over the last decades also due to the institution of dedicated networks.[16] Delayed reperfusion time may be the explanation of a higher mechanical complication rate. For the same reason, the incidence of chronic heart failure with adverse remodeling might be expected to increase in the near future among patients who survive the acute setting. Furthermore, a concerning increase is out-of-hospital cardiac arrest, as a higher number of cases has also been observed during the COVID-19 pandemic.[17]

Finally, it is interesting to note that the reduction of ACS hospitalization was observed in the vast majority of countries involved in the present study, including those initially less affected by the COVID-19 pandemic. These results highlight the need for health care awareness and strategies for emergency network reorganization to ensure rapid, easy and safe access to patients with time-dependent illness.

Limitations

Our study has limitations. First, data from the participant centers may not be representative for their country. Thus, our findings may not reflect a true decrease in the looking for medical attention in patients with ACS as those patients may have sought attention elsewhere. Additionally, due to the ecologic nature of the present study, we did not stratify patients on clinical phenotype, and we were not able to provide clinical characteristics among patients in different study periods.

Conclusions

Our results confirm that COVID-19 pandemic onset was associated with a significant decrease in ACS hospitalizations rate, an increase in total ischemic time and time to treatment in STEMI and a higher rate of mechanical complications. Actions to improve the patients' awareness and quality of care of patients with ACS during the COVID-19 pandemic are advocated.

Supplementary material

Supplementary material is available at *QJMED* online.

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Conflict of interest. None declared.

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