

Original Article

The bimodal “rise and fall” ACS curve overlapping COVID-19 pandemic peaks

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Abstract: Background: The COVID-19 outbreak harmed acute coronary syndromes. During the national lockdown in Italy, the fear of post-admission contagion translated into significant delays in seeking medical help among STEMI (ST-elevation myocardial infarction) patients. Objective and methods: Our analysis aimed to assess the ACS (Acute Coronary Syndromes) admissions during the pandemic, together with time to presentation and clinical outcomes compared to 2019 in a cardiovascular hub in Milan. Data of ACS patients admitted during the pandemic year 2020 were extracted by the hospital’s database and compared to a historical cohort of patients admitted for the same clinical indications in 2019. Results: A total of 599 ACS cases were recorded in 2020 vs. 386 cases in 2019, with a net 55% increase, associated with late clinical presentations, a threefold increase in cardiogenic shock, and a more than two-fold higher mortality rate. Conclusions: The ultimate goal of this analysis is to preserve the life-saving focus on universal and prompt STEMI diagnosis and treatment, even in a time of dynamic global crisis.

Keywords: ACS, COVID-19 outbreak, STEMI, late presentation

Introduction

The COVID-19 spreading pandemic phase in March-April 2020 was associated with preliminary observations of reduction in prompt acute coronary syndromes admissions and delayed presentations, mainly related to people’s perception of the hospital being war zones, leading to severe mechanical complications and worse clinical outcome [1]. By the time this analysis was conceived, Italy was the first most involved Country in the world for infected patients, actually ranking eighth in number (3,793,033) of confirmed COVID-19 cases and sixth in infection-related fatalities (115,088) [2].

Our Institute was selected as one of the cardiovascular emergency hubs in Milan, with an internal pathway ensuring timely, high-level cardiac care to COVID-19 and COVID-19-free patients, allowing an effective in-hospital infection spread and exposure risk prevention. The current analysis was aimed to assess the ACS

admissions during the pandemic periods, together with time to presentation and clinical outcomes compared to 2019 in our Institute serving as a cardiovascular hub.

Methods

Patients’ selection

This single-center, prospective study from a public service healthcare in Milan included all consecutive patients with acute coronary syndromes admitted from January 1 to December 31, 2020 including the COVID-19 pandemic. ACS included STEMI, NSTEMI and myocardial infarction with nonobstructive coronary arteries (MINOCA), all defined according to the current European Society of Cardiology guidelines definitions [3, 4].

These data were compared with the historical cohort of patients admitted for the same indications in 2019, in terms of time from symptoms onset to hospital admission, clinical characteristics, and in-hospital outcomes.

ACS curve in COVID-19 outbreak

Table 1. Patients' clinical characteristics and presentation

	Jan 1-Dec 31, 2019 (386 ACS)	Jan 1-Dec 31, 2020 (599 ACS)	P value
STEMI, n (%)	224 (58)	328 (54.7)	ns
NSTEMI, n (%)	162 (42)	271 (45.3)	ns
Male, n (%)	305 (79)	498 (83)	ns
Mean age, years	66.7±12.4	66.9±11.7	ns
Diabetes, n (%)	39 (10)	68 (11.5)	ns
Smoking, n (%)	76 (19.7)	160 (27)	0.005
Hypertension, n (%)	162 (41.9)	245 (40)	ns
Dyslipidemia, n (%)	114 (29.5)	198 (33)	ns
Late presentation, n (%)	70 (18)	180 (30)	0.003
Time from symptoms onset to ER (hrs)	4.3±2.5	11±18.7	0.02
Time from ER to PCI (hrs)	0.5±0.8	0.58±2.6	ns
Death, n (%)	23 (6)	90 (15)	0.001

STEMI: ST-elevation Myocardial Infarction; NSTEMI: Non-ST-elevation Myocardial Infarction; ER: Emergency Room; PCI: Percutaneous Coronary Intervention; hrs: hours.

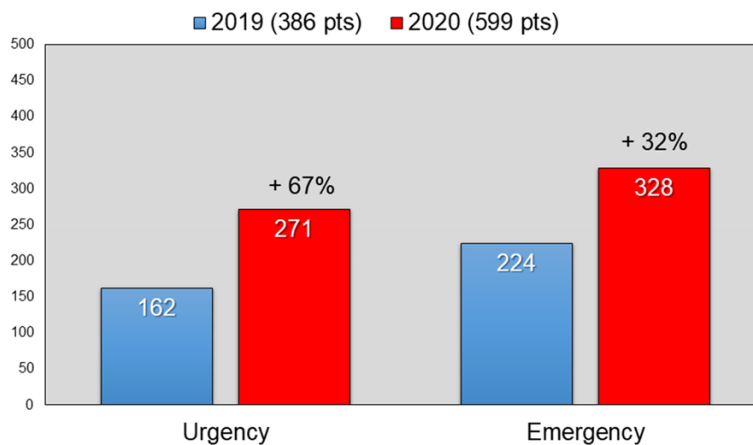


Figure 1. Cumulative increase in emergency (+32%) and urgency (+67%) interventional coronary procedures performed during Covid-19 pandemic outbreaks in 2020 compared to same periods in 2019.

Endpoints

Primary endpoints were the rate of ACS admissions, time to presentation from symptoms onset, and in-hospital mortality rate for ACS during the pandemic period vs. the control period in 2019.

Data collection

Epidemiological data of consecutive patients admitted for ACS were anonymously extracted from the hospital's database and checked for accuracy by the investigators. The informed consent was waived according to a specific FAQ "Data processing in clinical trials and medical research in the context of the COVID 19 health emergency", published by the Italian Data Pro-

tection Authority. The study was carried out in accordance with the Declaration of Helsinki and approved by the local Ethic research committee of Centro Cardiologico Monzino (R1255/20-CCM 1320).

Statistical analysis

Categorical variables were reported as number, percentage and compared by means of Pearson's Chi square test (or by Fisher exact test as appropriate). Statistical significance was set at p value < 0.05. All analyses were performed with SPSS 21 (IBM

Corporation, Armonk, NY, USA) and Jamovi version 1.2.27.0 (gamlj extension).

Results

Acute coronary syndromes and time to presentation

Patients' clinical presentation and characteristics are shown in **Table 1**. A total of 599 ACS cases were recorded in Covid-19 outbreak year vs. 386 cases in 2019, with a net 55% cumulative increase in emergency/urgency interventional coronary procedures (**Figure 1**).

Interestingly, ACS increase in 2020 reached the highest point with a bimodal presentation, paralleling the most contagious outbreak peri-

ACS curve in COVID-19 outbreak

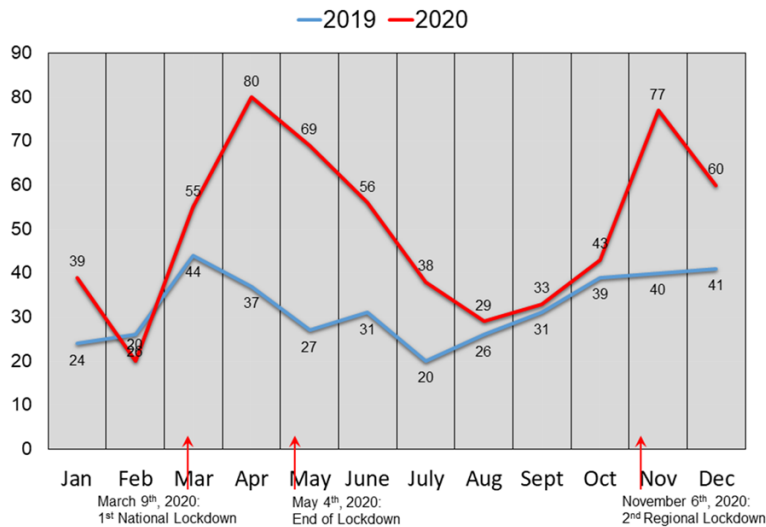


Figure 2. ACS increase in 2020 reached the highest point with a bimodal presentation, paralleling the most contagious outbreak periods (arrows).

ods (**Figure 2**). During the 2020 epidemic peak periods, admission times varied over a wider range (mean time 10 ± 16.9 hrs), and overall 30% of STEMI patients presented late (> 8 hrs) from symptoms onset, compared to 18% in 2019 ($P=0.003$). This delay to first medical contact translated in consequent worse clinical outcomes and fatal mechanical complications leading to higher in-hospital mortality (15% vs. 6% in 2019, $P=0.001$).

Discussion

Our group firstly reported the negative impact of the Covid-19 pandemic on ACS hospitalizations during national lockdowns in Milan, with several ensuing studies confirming similar patterns across the globe [5, 6]. According to a previous preliminary report [7], we observed a two-fold longer time from symptom onset to hospital presentation and almost a three-fold higher rate of cardiogenic shock during the COVID-19 outbreak in 2020 when compared with those during the previous year. Widespread fear and emotional stressors are known to precipitate acute coronary syndromes through abnormalities in autonomic tone that can increase platelet aggregation and plaque rupture [8]. Indeed, a cytokine storm associated with SARS-CoV-2 infection has been advocated to play a role in the development of severe lung involvement [9] and acute respiratory distress syndrome, as potent triggers for cardiovascular disease [10, 11]. The cytokine storm occurring in COVID-19 patients induces,

in concert with the imbalance of the endothelial functions, a massive cell activation with production of platelet-induced Tissue factor, which, together with a sustained platelet activation may be trigger for the hypercoagulable state during COVID-19 disease [12-14]. However, despite these hypothesis, SARS-Cov-2 nasopharyngeal swab or specific antibody (IgM/IgG) tests were found positive in 34 (5.7%) ACS patients only, while a higher ACS mortality rate was reported during this period without being fully explained by Covid-19 cases alone, as recently published [15, 16].

This paramount finding outlines that mechanisms other than the ACS itself are at work accounting for the increased overall mortality risk during the Covid-19 pandemic [17]. Anecdotal evidence suggested patients may have been behaving differently during the pandemic by delaying seeking help, resulting in a reduction in demand for emergency department and a rise in adverse outcomes [18], such as out-of-hospital cardiac arrest (OHCA). An increase in incidence of OHCA and number of patients declared deceased on scene has also been reported in France and England [19, 20], where disease prevalence has been particularly acute. On one hand, it should be acknowledged that patients' avoidance of seeking medical care may have led to an underestimation of the ACS-related adverse events and deaths occurring during the pandemic outbreak, as many of these events may have occurred out-of-hospital without a formal medical evaluation. Additionally, in areas severely affected by the pandemic increased incidence of OHCA, lower rates of successful resuscitation, and increased mortality have been reported. COVID-19 has significantly impacted patient outcomes through increased disease severity, decreased access to care, and the reshaping of emergency medical response and hospital-based health-care systems and policies [21, 22].

This reduction may have been fuelled by the lockdown and explained by changes in public

behaviour and the key government message to 'stay at home'.

Conclusions

These data reflect how the hospital's hub function required to reschedule daily activity accordingly, and rewrote criteria to prioritize patients also on regular admissions, resulting in a 20% reduced capability to address the demand of elective invasive procedures, only. Anyhow, this snapshot addresses important insights underlining the need of a healthcare system reassessment in COVID+, COVID-free, which should not forget to protect and reassure with dedicated spaces and paths, those patients in the need of time-sensitive treatments.

Disclosure of conflict of interest

None.

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