Impact of COVID-19 outbreak on prevalence, clinical presentation and outcomes of ST-elevation myocardial infarction

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Aims The aim of this study was to report the prevalence, clinical features and outcomes of patients with ST-elevation myocardial infarction (STEMI) hospitalized during the Corona-Virus Disease 2019 (COVID-19) outbreak compared with those admitted in a previous equivalent period.

Methods and results Eighty-five patients admitted for STEMI at a high-volume Italian centre were included. Patients hospitalized during the COVID-19 outbreak (21 February–10 April 2020) (40%) were compared with those admitted in pre-COVID-19 period (3 January–20 February 2020) (60%). A 43% reduction in STEMI admissions was observed during the COVID-19 outbreak compared with the previous period. Time from symptom onset to first medical contact (FMC) and time from FMC to primary percutaneous coronary intervention (PPCI) were longer in patients admitted during the COVID-19 period compared with before [148 (79–781) versus 130 (30–185) min; P = 0.018, and 75 (59–148)] versus 45 (30–70) min; P < 0.001]. High-sensitive troponin T levels on admission were also higher. In-hospital mortality was 12% in the COVID-19 phase versus 6% in the pre-COVID-19 period. Incidence of the composite endpoint, including free-wall rupture, severe left ventricular dysfunction, left ventricular aneurysm, severe mitral regurgitation and pericardial effusion, was higher during the COVID-19 than the pre-COVID-19 period (19.6 versus 41.2%; P = 0.030; odds ratio = 2.87; 95% confidence interval 1.09–7.58).

Conclusion The COVID-19 pandemic had a significant impact on the STEMI care system reducing hospital admissions and prolonging revascularization time. This translated into a worse patient prognosis due to more STEMI complications.

Materials and methods

Study population The population includes consecutive patients admitted for STEMI at Civil Hospitals of Brescia (Lombardy, Italy) between 3 January 2020 and 10 April 2020. Patients hospitalized during the COVID-19 outbreak, from the first diagnosed COVID case in Italy on 21 February to 10 April, were compared with patients admitted during the COVID-19 outbreak. However, data about the impact of the COVID-19 pandemic on reperfusion timing and its possible effect on patient prognosis are less described.

Our aim is to report the prevalence, clinical features and in-hospital outcomes of STEMI patients treated during the COVID-19 outbreak compared with those managed during an equivalent previous period at a single high-volume Italian centre at the epicentre of the infection.
the pre-COVID outbreak period, between 3 January and 20 February 2020. The two considered periods had an equivalent duration of 7 weeks. All patients underwent coronary angiography and possibly PPCI at our catheterization laboratory, which is a high-volume centre (>200 PPCI per year). In addition, following the regional health system reorganization due to the COVID-19 pandemic, our catheterization laboratory has become a hub centre for four additional hospitals performing 40–100 PPCI per year each since 8 March 2020. The present study has been approved by the Local Ethics Committee (Comitato Etico di Brescia).

Data collection and definitions
Demographic, clinical, laboratory and procedural data as well as data about clinical presentation, such as STEMI location, Killip class,19 SBP and heart rate on admission were collected from medical records. Time from symptom onset to first medical contact (FMC) and time from FMC to PPCI were also collected for all patients.3,4 Laboratory data analysed included blood cell count, serum creatinine, C-reactive protein, high-sensitive troponin T (hs-TnT) (baseline and peak) and creatine kinase myocardial band (CK-MB) (baseline and peak). Cardiac markers were measured every 6 h for 48 h after the baseline value assessment (time zero), and then every 12 h.

Regarding the procedure, vascular access, culprit vessel, number of vessels diseased, initial and final Thrombolysis In Myocardial Infarction (TIMI) flow grade, thrombus burden and slow flow or no flow occurrence after stent implantation were reported. The definition of TIMI flow grade was based on visual assessment of the rate of contrast opacification of the culprit vessel according to the grading scale proposed by the TIMI study group.20 Thrombus burden was classified on the basis of the TIMI thrombus grade scale evaluated after wire deployment and before balloon inflation and/or stent positioning.21 Procedural time, defined as the time between the patient coming to and leaving from the catheterization laboratory, fluoroscopy time and contrast medium amount were also collected.

Outcomes
Intrahospital death and its cause, and need for inotropic and/or mechanical supports [i.e. intra-aortic balloon pump (IABP), and extracorporeal membrane oxygenation (ECMO)] were reported. A composite end point including all the major acute and subacute STEMI complications (free-wall rupture, ventricular septum defect, papillary muscle rupture, severe ischaemic mitral regurgitation, severe left ventricular dysfunction and pericardial effusion) was analysed. These latter were ascertained by echocardiography. Finally, incidences of bleeding requiring blood transfusion, acute kidney injury (AKI), defined as increase of baseline serum creatinine of at least 0.3 mg/dl, as well as length of hospital stay, and length of ICU stay, were reported.

Statistical analysis
The normal distribution of continuous variables was explored with Kolmogorov–Smirnov and the Shapiro–Wilk tests. Continuous variables following a normal distribution are reported as mean ± standard deviation (SD) and were compared using the Student’s t-test, whereas those not following a normal distribution are presented as median and interquartile range (IQR) and were compared with the Mann–Whitney U test. Categorical variables are reported as counts and percentages and were compared using the χ² or Fisher exact tests, as appropriate.

The relative risk of composite end point was calculated by logistic regression and results reported as odds ratio (OR) and corresponding 95% confidence interval (95% CI).

For all analyses, a two-sided P value less than 0.05 was considered to be significant. All statistical analyses were performed using the SPSS software, version 21 (SPSS Inc, Chicago, Illinois, USA).

Results
Baseline characteristics
A total of 85 patients were hospitalized for STEMI during the observation period: 51 (60%) during the pre-COVID-19 period and 34 (40%) during the COVID-19 outbreak. A 33% decrease in the number of STEMI presentations was observed during the COVID-19, compared with the pre-COVID-19 phase. This reduction reached 43% after excluding cases coming from additional spoke centres after our catheterization laboratory became a hub centre for four additional hospitals (Fig. 1). During the pre-COVID-19 period, an average number of seven STEMI presentations per week was observed, with a little week-to-week variability. In the COVID-19 period, there was a...
decline in STEMI admissions during the first 3 weeks, reaching a minimum number, and then a slow and modest upturn during the last 3 weeks (Fig. 2).

Demographic features and clinical characteristics of the population stratified by the period of presentation are reported in Table 1. No differences were observed in patients admitted during the period before the COVID-19 outbreak compared with those hospitalized during the COVID-19 pandemic. The time between symptoms onset and FMC was significantly longer in patients admitted during the COVID-19 period than in those admitted before [148 (IQR: 79–781) versus 130 (IQR: 30–185) min; \(P = 0.018\)]. Similar results were found for the time between FMC and PPCI [75 (IQR: 59–148) versus 45 (IQR: 30–70) min; \(P < 0.001\)] (Fig. 3). Even excluding patients coming from additional spoke centres, both time between symptoms and FMC and time between FMC and PPCI were significantly longer during the pandemic [148 (IQR: 135–772) versus 130 (IQR: 30–185) min; \(P = 0.021\), and 68 (IQR: 55–115) versus 45 (30–70) min; \(P < 0.001\)].

During the COVID-19 period, six patients presented 12 h after symptom onset (versus two in the pre-COVID period) and four patients had a late presentation (>24 h of symptom onset). They all underwent PPCI due to ongoing symptoms and signs suggestive of ischaemia or haemodynamic instability. The location of the STEMI and Killip class was equally distributed among patients admitted during the two different periods (Table 1). Compared with patients hospitalized during the pre-COVID period, those admitted during the COVID-19 outbreak had higher levels of baseline hs-TnT [341 (103–1986) versus 122 (52–493) ng/l; \(P = 0.05\)]. Instead, no significant differences were observed between the two groups with respect to peak hs-TnT, baseline CK-MB and peak CK-MB (Fig. 4). The platelets count on

![Distribution of STEMI admissions during the observation period. A steep decrease in STEMI admissions occurred during the first weeks of the COVID-19 period followed by a slow and modest upturn.](image-url)
admission was significantly higher among patients admitted during the COVID period than the others. A similar trend was noted for CRP levels (Table 2).

Among patients admitted during the COVID-19 outbreak, six had concomitant COVID-19 diagnosis confirmed by positive results of PCR testing of a nasopharyngeal swab.

Procedural data
No patients received thrombolysis. Radial access was used in most of the cases. The left anterior descending coronary artery was the most frequent culprit vessel, and multivessel disease was noted in one-third of patients. Thrombosis degree and TIMI flow were equally distributed between the two groups. A trend towards a higher rate of stent thrombosis was noted in patients treated during the COVID period than in the others. Moreover, patients admitted during the COVID period were more likely to receive GPI in bailout than the control group. Final TIMI flow, procedural and fluoroscopy time, and contrast amount were similar between the two groups (Table 2).

Outcomes
A numerical increase in in-hospital mortality occurred during the COVID-19 period versus before: 12 versus 6% (Table 3). Three patients admitted during the pre-COVID-19 period died because of irreversible cerebral damage owing to out-of-hospital cardiac arrest. Among patients hospitalized during the COVID-19 period, two died of free-wall rupture, one of cardiogenic shock followed by multiorgan failure and one, with concomitant COVID-19 pneumonia, of septic shock.

Hospital-stay length, bleeding requiring blood transfusions and AKI were similar between the two groups (Table 3). Inotropic supports and/or IABP and/or ECMO were needed in 25% of patients in the pre-COVID-19 period and in 38% of individuals hospitalized during the COVID-19 pandemic.

The incidence of the composite end point was significantly higher among patients admitted during the COVID-19 outbreak than those hospitalized before (41.2 versus 19.6%; \( P = 0.030 \); Fig. 5). The COVID-19 pandemic significantly increased the relative risk of STEMI complications (OR for the composite end point: 2.87; 95% CI 1.09–7.58; \( P = 0.033 \)). Excluding patients coming from additional spoke centres, the incidence of composite outcome was similarly higher in the COVID period, even if it did not reach statistical significance (34.5 versus 19.6%; \( P = 0.140 \)).

Discussion
This study investigates the impact of the COVID-19 outbreak on the prevalence, clinical presentation and outcomes of patients hospitalized for STEMI. The main findings of our analysis are the following. First, there was a 43% reduction in STEMI admissions during the COVID-19 outbreak compared with a period of the same duration before. Second, the reperfusion time, including patient and healthcare system delay, was significantly increased during the COVID-19 period compared with a period of the same duration before. Second, the reperfusion time, including patient and healthcare system delay, was significantly increased during the COVID-19 period compared with the pre-COVID-19 time. Third, patients admitted during the COVID-19 outbreak had an almost three-fold increased risk of developing STEMI complications.

Our data showing a meaningful reduction in STEMI admissions (43%) during the COVID-19 outbreak are in line with those reported worldwide, ranging from 30 to 48%.\(^{11-17}\) Thus, we do not confirm a more recent study from Massachusetts reporting no significant reduction in STEMI volume during the COVID-19 pandemic.\(^{22}\) Compared with a multicentre nationwide study conducted in Italy, our results showed a higher reduction in STEMI admissions (43 versus 26.5%).\(^{18}\) Brescia was one of the major hotspots for COVID-19 in Italy and this could explain such a difference. Our catheterization
laboratory, which was already a hub centre for many spoke hospitals before the COVID-19 emergency, has become the hub centre for four additional spoke centres since 8 March 2020. The reduction of 43% in STEMI admissions was calculated excluding five patients coming from these additional spoke centres, which did not refer patients to our centre before. However, even including these additional STEMI admissions, the decrease during the COVID-19 pandemic was relevant: 33%.

A possible protective effect of the infection towards cardiovascular disease is unlikely. Indeed, recent data showed an increased risk of both venous and arterial thrombotic or thromboembolic events in COVID-19 patients.

Table 2 Procedural data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (n = 85)</th>
<th>Pre-COVID (n = 51)</th>
<th>COVID (n = 34)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culprit vessel LM, n (%)</td>
<td>3 (4)</td>
<td>2 (4)</td>
<td>1 (3)</td>
<td>0.810</td>
</tr>
<tr>
<td>Culprit vessel LAD, n (%)</td>
<td>45 (53)</td>
<td>25 (49)</td>
<td>20 (59)</td>
<td>0.375</td>
</tr>
<tr>
<td>Culprit vessel CX, n (%)</td>
<td>10 (12)</td>
<td>7 (14)</td>
<td>3 (9)</td>
<td>0.492</td>
</tr>
<tr>
<td>Culprit vessel RCA, n (%)</td>
<td>27 (32)</td>
<td>17 (33)</td>
<td>10 (29)</td>
<td>0.704</td>
</tr>
<tr>
<td>Multivessel coronary disease, n (%)</td>
<td>33 (39)</td>
<td>21 (41)</td>
<td>12 (35)</td>
<td>0.586</td>
</tr>
<tr>
<td>Radial access, n (%)</td>
<td>71 (84)</td>
<td>43 (84)</td>
<td>28 (82)</td>
<td>0.467</td>
</tr>
<tr>
<td>Baseline TIMI flow 0, n (%)</td>
<td>48 (56)</td>
<td>27 (53)</td>
<td>21 (62)</td>
<td>0.455</td>
</tr>
<tr>
<td>Baseline TIMI flow 1, n (%)</td>
<td>12 (14)</td>
<td>7 (14)</td>
<td>5 (15)</td>
<td>0.899</td>
</tr>
<tr>
<td>Baseline TIMI flow 2, n (%)</td>
<td>10 (12)</td>
<td>8 (16)</td>
<td>2 (6)</td>
<td>0.169</td>
</tr>
<tr>
<td>Baseline TIMI flow 3, n (%)</td>
<td>15 (18)</td>
<td>9 (18)</td>
<td>6 (18)</td>
<td>0.999</td>
</tr>
<tr>
<td>Thrombosis degree</td>
<td>4 (3–4)</td>
<td>3 (3–4)</td>
<td>4 (3–4)</td>
<td>0.186</td>
</tr>
<tr>
<td>Stent thrombosis, n (%)</td>
<td>5 (6)</td>
<td>1 (2)</td>
<td>4 (12)</td>
<td>0.060</td>
</tr>
<tr>
<td>Collateral circulation, n (%)</td>
<td>34 (40)</td>
<td>21 (41)</td>
<td>13 (38)</td>
<td>0.786</td>
</tr>
<tr>
<td>Thromboaspiration, n (%)</td>
<td>2 (2)</td>
<td>1 (2)</td>
<td>1 (3)</td>
<td>0.770</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa inhibitors, n (%)</td>
<td>22 (26)</td>
<td>9 (18)</td>
<td>13 (38)</td>
<td>0.034</td>
</tr>
<tr>
<td>TIMI flow 0 after PCI, n (%)</td>
<td>2 (2)</td>
<td>0 (0)</td>
<td>2 (6)</td>
<td>0.080</td>
</tr>
<tr>
<td>TIMI flow 1 after PCI, n (%)</td>
<td>3 (4)</td>
<td>1 (2)</td>
<td>2 (6)</td>
<td>0.337</td>
</tr>
<tr>
<td>TIMI flow 2 after PCI, n (%)</td>
<td>9 (11)</td>
<td>5 (10)</td>
<td>4 (12)</td>
<td>0.675</td>
</tr>
<tr>
<td>TIMI flow 3 after PCI, n (%)</td>
<td>71 (84)</td>
<td>45 (88)</td>
<td>26 (76)</td>
<td>0.354</td>
</tr>
<tr>
<td>Slow flow/no flow, n (%)</td>
<td>18 (21)</td>
<td>8 (16)</td>
<td>10 (29)</td>
<td>0.129</td>
</tr>
<tr>
<td>Procedural time (min)</td>
<td>50 (40–60)</td>
<td>50 (40–60)</td>
<td>55 (43–67)</td>
<td>0.097</td>
</tr>
<tr>
<td>Contrast dye (ml)</td>
<td>117 ± 45</td>
<td>117 ± 39</td>
<td>117 ± 53</td>
<td>0.964</td>
</tr>
<tr>
<td>Fluoroscopy time (min)</td>
<td>8 (5–13)</td>
<td>8 (5–12)</td>
<td>9 (5–15)</td>
<td>0.801</td>
</tr>
</tbody>
</table>

Continuous variables are reported as mean ± standard deviation (normal distributed) or as median and interquartile range (non-normally distributed). CX, circumflex artery; LAD, left anterior descending artery; LM, left main artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; TIMI, Thrombolysis In Myocardial Infarction.
patients and STEMI was described as a possible clinical manifestation of COVID-19 also in the absence of a culprit lesion. Moreover, only a limited proportion of our patients were infected (17% during the COVID-19 period). Therefore, the reduction in STEMI admissions can be explained only by the effects of the COVID-19 pandemic on people’s behaviour. In particular, the fear of acquiring the infection may have prevented patients with STEMI from calling emergency services or going to the hospital. Moreover, misinterpretation of STEMI-related symptoms (i.e. chest pain and dyspnoea) as being possibly due to COVID-19 may have also limited the appropriate diagnosis and treatment of some patients.

The analysis of the time course of STEMI admissions (Fig. 2) shows a reduction during the first 3 weeks after COVID-19 onset with, actually, an immediate response on the same days as COVID-19 related admissions started, followed by a slow and modest upturn in STEMI presentations in the last 3 weeks. Even if week-to-week variability might be random, the decline is clear after the outbreak and it reaches a minimum number of admitted patients never reached before. The following upturn may be due to a better patient and health worker awareness of the COVID-19 pandemic.

The second important effect of the COVID-19 pandemic on the STEMI care system is the delay in diagnosis and treatment. Tam et al. found a large delay in coronary reperfusion during the COVID-19 outbreak in a small series of seven patients hospitalized for STEMI at a single Chinese centre. The median time between the symptoms onset and FMC was 318 min, while the median door-to-balloon time was 110 min. However, the number of patients included was too limited to perform statistical comparisons. A few more data are available confirming this worrisome aspect of the STEMI management during the COVID-19 era.

Reperfusion timing in STEMI is an index of quality of care that needs to be periodically evaluated. It includes two aspects: patient delay, for example time from symptoms onset to FMC, and system delay, for example time from FMC to PCI. In our cohort, both intervals were significantly delayed during the COVID-19 period. Accordingly, cardiac marker levels, in particular hs-TnT, were higher on admission during the outbreak period than the previous one. Patient delay during the COVID-19 emergency had likely the same causes as the reduction in admissions, for example patients’ fear of infection by coming to the hospital and in-hospital delays for differential diagnosis with COVID-19. A further delay in the catheterization laboratory is due to the need for adopting several precautionary measures (i.e. personal protective equipment).

Lastly, the management of STEMI presenting with out-of-hospital cardiac arrest could be difficult during a pandemic era.
higher proportion of patients presenting with cardiac arrest during the pre-COVID-19 period (seven patients, 14%) compared with those admitted during the outbreak (two patients, 6%). This suggests that there was a proportion of patients who never arrived at the catheterization laboratory due to misinterpretation of the cause of the cardiac arrest or due to an overloaded emergency system, causing delayed transportation.

Except for cardiac arrest, almost all other STEMI complications were more common during the COVID-19 period than during the pre-COVID-19 period. Use of GPI in bailout, which could be a surrogate for a more complicated procedure, was more common during the COVID-19 period. Moreover, higher platelet count, CRP and incidence of stent thrombosis were observed during the pandemic. These findings may be attributed to the presence of patients with the infection in the group admitted during the COVID-19 period, which as known can present with a huge pro-thrombotic inflammatory system activation. Most importantly, the composite end point, including mechanical complications of STEMI, such as free-wall rupture, severe left ventricular dysfunction, left ventricular aneurysm, severe mitral regurgitation and pericardial effusion, was significantly higher in patients admitted during the COVID-19 outbreak than in the others. Consistently, an increase in both fatality and complication rates was reported by De Rosa et al. (risk ratio (RR) = 3.3, 95% CI 1.7–6.6; \( P < 0.001 \) and RR = 1.8, 95% CI 1.1–2.8; \( P = 0.009 \), respectively). All the components of this composite end point are strongly associated with a poor prognosis, even at long-term follow-up. Angiographic findings, culprit coronary arteries and baseline characteristics of our two groups were quite similar, except for the timing of presentation (time from symptom onset to FMC, and time from FMC to PPCI), suggesting that the main cause of the different outcome is the delay in STEMI diagnosis and treatment during the COVID-19 pandemic. In this regard, recent recommendations reported the possible role of fibrinolysis in treating STEMI patients during the COVID-19 outbreak. Decisive measures should be adopted and efforts are needed to encourage patients with STEMI to call emergency services, implement emergency services and improve out- and in-hospital STEMI management, even during the pandemic, in a timely way in order to maintain a short time to reperfusion so that PPCI may remain the revascularization method of first choice.

**Limitations**

Our study presents some limitations. It is a report from a single, even if high-volume, centre. This makes the population homogeneous but limited. In fact, the small sample size and the reduced number of events limit the statistical comparison between the two periods. Furthermore, our results could be biased by seasonal and month-to-month variability. However, other studies comparing the COVID-19 period with both the same period in 2019 and the previous period of 2020 showed a similar reduction in STEMI admissions.

**Conclusion**

The COVID-19 outbreak had a significant impact on the STEMI care system. It was associated with a reduced rate of STEMI admissions and longer time to revascularization leading to a worse patient outcome with a high incidence of major STEMI complications.

**Acknowledgements**

None declared.

**Conflicts of interest**

There are no conflicts of interest.

**References**


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