COVID-19 impact on ST-elevation myocardial infarction incidence rate in a Italian STEMI network: a U-shaped curve phenomenon

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\textbf{Background} Public health emergencies such as the COVID-19 outbreak may impact on the incidence rate of ST-elevation myocardial infarction (STEMI) in severely affected areas. However, this phenomenon demands attention also in areas where media and patients were focused on the COVID-19 pandemic, but the healthcare system was not overwhelmed by the huge number of COVID-19 patients.

\textbf{Methods and results} In this observational study, we compared the incidence rate of all consecutive STEMI patients admitted at the University Hospital of Trieste, Italy, during March and April 2020 with the same 2 months of the previous 5 years (2015–2019). Patient characteristics were compared between 2020 and 2019.

The incidence rate of STEMI admission in March–April 2020 was lower than those in March–April 2015–2019, 36 vs. 56 cases per 100 000 inhabitants/year [relative risk (RR) 0.65, 95% confidence interval (95% CI) 0.42–0.96, \(P = 0.045\)]. Considering that the incidence rates were constant in the past years (\(P = 0.24\)), the turnaround in 2020 is most likely due to the COVID-19 outbreak. Interestingly, this reduction was a dynamic phenomenon with a U-shaped curve during the 2-month period. System-of-care times were similar between 2020 and 2019; however in 2020, patients presented more frequently signs of heart failure compared to 2019 (Killip class \(\geq 2\) in 68\% vs. 29\%, \(P = 0.003\)).

\textbf{Conclusion} During the COVID-19 outbreak, we observed a marked reduction in the STEMI incidence rate. This U-shaped phenomenon demands attention because a potential cause for the decrease in STEMI incidence may include the avoidance of medical care. Public campaigns aiming to increase awareness of ischemic symptoms may be needed during community outbreak.

\textbf{Keywords: COVID-19, myocardial infarction, pandemic, primary percutaneous intervention, SARS-CoV-2, ST-elevation myocardial infarction}

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\textbf{Introduction} The potential impact of public health emergencies such as virus disease outbreaks on the incidence rate of ST-elevation myocardial infarction (STEMI) demands attention. On 11 March 2020, the WHO declared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak a pandemic. Patients with SARS-CoV-2 infection can develop coronavirus disease 2019 (COVID-19)\textsuperscript{3} and Italy was among the first heavily affected countries by COVID-19,\textsuperscript{2} and adopted stringent lockdown measures in the entire nation as of 11 March 2020.

A reduction in hospital admissions for acute coronary syndromes (ACS) has been perceived globally\textsuperscript{3}; however, the evaluation of variation in primary percutaneous intervention (pPCI) rates for STEMI during the COVID-19 outbreak is important especially in areas where media and patients were focused on the COVID-19 pandemic, but the healthcare system was not overwhelmed with a huge number of patients requiring mechanical ventilation or intensive care, and where no changes occurred during the lockdown period in the management of STEMI patients and in the hub-spoke model of care.

Therefore, we investigated the impact of the COVID-19 outbreak on the incidence rate of STEMI admissions at the University Hospital of Trieste, a city located in northeastern Italy, and the capital of the Friuli-Venezia Giulia region. Although the most affected area in Italy has been the north of the country, this area has been less affected than other northern regions by the COVID-19 pandemic with 3025 (250 per 100 000 inhabitants) and 1438 (417 per 100 000 inhabitants) confirmed cases as of 30 April 2020 in the Friuli-Venezia Giulia and Trieste-Gorizia province, respectively.\textsuperscript{4} In our hospital, during March–April 2020, out of 2716 total admissions, 321 COVID-19 patients...
were admitted. In the Cardiology Unit, we had five COVID-19 cases. On 28 March 2020, we registered the maximum simultaneous presence of COVID-19 patients: 115 COVID-19 patients out of 632 hospital beds.

Materials and methods
The University Hospital of Trieste is the only catheterization laboratory in the province of Trieste and Gorizia and covers a total population of about 350 000 inhabitants. We analysed the incidence rate of all consecutive STEMI admissions for pPCI at the University Hospital of Trieste during 2 months (March and April 2020) of the COVID-19 outbreak, and compared this incidence rate of admission with those in the same 2 months of the previous 5 years (2015–2019). Moreover, we compared the clinical characteristics of STEMI patients admitted between March–April 2020 and March–April 2019. STEMI diagnosis was defined according to STEMI guidelines. This study complies with the Declaration of Helsinki.

Statistical analysis
The incidence rate of STEMI admissions from 2020 and the previous 5 years (2015–2019) was modelled by fitting a Poisson regression model allowing for overdispersion. An interaction term was added to estimate the interaction effect between the number of weeks and the dummy variable representing the year 2020. A cubic regression spline was used to model the nonlinear effect over the weeks.

Continuous variables were expressed as mean ± standard deviation or as median with interquartile range depending on the distribution shape. Differences between 2020 and 2019 STEMI populations for continuous variables were compared using the Mann–Whitney U test. Categorical variables were expressed as counts and percentages and assessed by Chi-square test or Fisher exact test, as appropriate. Statistical analysis was performed using R statistical software version R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

Results
The incidence rate of STEMI admissions in March–April 2020 was lower than those in March–April 2015–2019, at 36 vs. 56 cases per 100 000 inhabitants/year [relative risk (RR) 0.65, 95% confidence interval (95% CI) 0.42–0.96, \( P = 0.045 \)]. Incidence rates have been constant in recent years (\( P = 0.24 \)). However, in 2020, a turnaround was observed, most likely due to the COVID-19 pandemic (Fig. 1).

Interestingly, this reduction was a dynamic phenomenon with a U-shaped curve during the 2-month period; the incidence rate was not significantly different between

<table>
<thead>
<tr>
<th>Week</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 1–8</td>
<td>1.12</td>
<td>0.61–2.05</td>
</tr>
<tr>
<td>March 9–16</td>
<td>0.68</td>
<td>0.46–1.01</td>
</tr>
<tr>
<td>March 17–24</td>
<td>0.41</td>
<td>0.24–0.71</td>
</tr>
<tr>
<td>March 25–31</td>
<td>0.27</td>
<td>0.12–0.63</td>
</tr>
<tr>
<td>April 1–8</td>
<td>0.27</td>
<td>0.12–0.62</td>
</tr>
<tr>
<td>April 9–16</td>
<td>0.41</td>
<td>0.24–0.69</td>
</tr>
<tr>
<td>April 17–24</td>
<td>0.66</td>
<td>0.44–0.98</td>
</tr>
<tr>
<td>April 25–30</td>
<td>1.07</td>
<td>0.57–2</td>
</tr>
</tbody>
</table>

Incidence rates of STEMI admission per 100 000 inhabitants/year in March–April from 2015 to 2020.

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2015–2019 and 2020 during the first, the second and last weeks of the explored period, while during all the remaining weeks, 2020 showed a significantly lower incidence rate per admissions than 2015–2019 (Table 1, Fig. 2).

Comparison between 2019 and 2020 STEMI populations is reported in Table 2. Age and risk factors were not different between 2019 vs. 2020. However, in 2020, STEMI patients presented more...
frequently signs of heart failure (Killip class ≥2 in 68% vs. 29%, \( P = 0.003 \), in 2020 vs. 2019, respectively) and received a higher percentage, although not significant, of circulatory support (intra-aortic balloon pump or extracorporeal membrane oxygenation) (9.5 vs. 5% in 2020 vs. 2019, respectively). In-hospital mortality was not different between the 2 years (4.7% in 2019 vs. 4.8% in 2020).

It has to be noted that pain to first medical contact (FMC) time, FMC-to-balloon time, ECG-to-balloon time and ischemia time were all similar between 2020 and 2019 (Table 2, Fig. 3).

At the time of the procedure, none of the patients admitted for STEMI had a diagnosis of COVID-19 made by real time reverse transcriptase–polymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swabs. Pharmacological reperfusion was not used during the studied period.

Interestingly, in the province of Trieste, the incidence rate of out of hospital cardiac arrest (OHCA) with resuscitation attempt was lower in March–April 2020 compared with March–April 2019, 2.79 vs. 5.57 cases per 100 000 inhabitants, respectively (RR 0.5, 95% CI 0.25–0.97; \( P = 0.04 \)).

**Discussion**

During the COVID-19 outbreak, we observed a marked reduction in the incidence rate of STEMI admissions in our institution. Reduction in admissions is in line with contemporary findings, wherein a reduction in STEMI activations was reported by US\(^6\) and Spain\(^7\) cardiac catheterization laboratories. Although admissions for acute myocardial infarction were reduced during the COVID-19 pandemic also in Italy,\(^8\) our study, differently from previously, evaluated STEMI admission rates during an extended period of 2 months of the COVID-19 pandemic, and in an Italian region affected but not overwhelmed by COVID-19 sick patients. Moreover, no significant changes in the system of care of STEMI occurred, except for the identification of a dedicated laboratory for the treatment of suspected or confirmed COVID-19 patients, and the presence of clinical staff who have been trained and competent in the use of personal protective equipment. This privileged point of observation together with the extended study period allowed the following relevant findings to be observed.

First, the decline in the incidence rate of STEMI admissions was a dynamic phenomenon with a U-shaped curve.
and with a peak of the reduction in STEMI admissions corresponding to the early phase of lockdown (when probably the perception of the risk of infection was higher). Conversely, during the late phase, a subsequent normalization of the incidence rate of STEMI admissions was observed. Considering that the incidence rates were constant in our institution in recent years ($P = 0.24$), the turnaround in 2020 is most likely due to the COVID-19 outbreak. Moreover, the number of PCIAs performed in Italy has steadily grown over the last decade with the trend driven by a striking increase in the number of pPCIAs for patients with STEMI.¹⁹

The causes for the lower incidence of STEMI admissions are likely multifactorial: it may include patient fear of contracting an infection from the healthcare system. Indeed, the national and media diffused the news that the infection was largely spread across hospitalized patients and healthcare personnel due to the lack of personal protection equipment in the earlier phases. As a consequence, chest pain might be underestimated or misestimated by patients. Importantly, in our area, we can exclude that one of the reasons could have been a weakened of the emergency medical services due to sick staff or systemic overload. This is confirmed by the fact that in 2020 system of care times were no longer compared with those in 2019. Moreover, it is possible that the absence of traffic during transportation coupled with the reduction in elective procedures (which allowed a free cathlab to be available more frequently for emergency procedures) may have counterbalanced by the potentially longer time to perform an emergent procedure in a dedicated cathlab with appropriate personal protective equipment.

Second, during the COVID-19 outbreak, patients admitted for STEMI presented with a higher prevalence of heart failure symptoms than those in 2019. Interestingly, despite the higher percentage of Killip class at least 2, lengths of stay were similar in 2019 and 2020. Possible explanations for this finding are hospital efforts to maintain bed availability and patient preference for early discharge due to concern about the risk of contracting SARS-CoV-2. Considering that a fundamental prognostic factor such as patient delay¹⁰–¹³ was not increased, it is possible that patients with more severe myocardial infarction presentation did not avoid seeking medical help. However, those patients with the involvement of a large territory or higher thrombus burden are at high risk of reduced microvascular reperfusion¹⁴ and heart failure presentation.¹⁵ Conversely, it is possible that a proportion of patients with less painful infarction did not seek care for fear of contracting an infection during hospitalization. However, even less severe infarction, if left untreated, may cause sudden death or may develop mechanical complications; indeed, in March–April 2020, we admitted two patients with mechanical complications for subacute myocardial infarction and very late presentation. From this perspective, mass public education efforts are needed for reassuring patients that healthcare services remain operational and safe. Our findings have also important implications because public campaigns aiming to increase awareness of ischemic symptoms should be reinforced during pandemic events. Elderly and diabetic patients demand particular attention for the higher rates of comorbidities that they present.¹⁶

However, we cannot determine to what extent the observed difference reflects changes in population behaviours (in terms of seeking medical assistance) vs. a possible true reduction in STEMI incidence rates as the potential result of low physical stress and widespread prevalence of the resting state during the quarantine, or the health beneficial effect of reduced air pollution. Finally, in the province of Trieste, we also observed a lower incidence rate of OHCA in March–April 2020; however, further research is needed to evaluate the potential effects of COVID-19 on OHCA, also considering the different trends of variation,¹⁷–²⁰ which seem related to the COVID-19 incidence rate in each region.

**Limitations**

Our research is subject to limitations. The results of this study are from a single STEMI network and our findings should be interpreted in light of the common limitations of a registry-based cohort studies. Moreover, the similar mortality rate in 2019 and 2020, despite a higher percentage of patients with Killip class at least 2 in 2020, should be cautiously interpreted due to the small size of our population and the short follow-up. It has to be considered that part of the data were collected during a pandemic emergency. Despite no environmental alerts being recorded between those months in 2015–2019 and 2020, the use of a 2-month period for data collection still represents a source of potential bias. Finally, as this is an observational study, we just describe a phenomenon. No demonstration of cause can be drawn from this study.

**Conclusion**

During COVID-19 lockdown, we observed a marked reduction in the incidence rate of STEMI admissions. The findings of this study demand attention by the scientific and healthcare communities. Avoidance of medical care may be a potential cause of the decrease in admissions for STEMI. Thus, public campaigns aiming to increase awareness of ischemic symptoms may be necessary during infectious disease outbreaks.

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Conflicts of interest
There are no conflicts of interest.

References