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Training/Practice
Contemporary Issues in Cardiology Practice

Decrease and Delay in Hospitalization for Acute Coronary Syndromes During the 2020 SARS-CoV-2 Pandemic

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ABSTRACT
The diffusion of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) forced the Italian population to restrictive measures that modified patients’ responses to non-SARS-CoV-2 medical conditions. We evaluated all patients with acute coronary syndromes admitted in 3 high-volume hospitals during the first month of SARS-CoV-2 Italian-outbreak and compared them with patients with ACS admitted during the same period 1 year before. Hospitalization for ACS significantly modified patients’ responses to non-SARS-CoV-2 medical conditions, including acute coronary syndrome (ACS). Because ACS is a life-threatening condition, with outcomes strictly dependent on prompt recognition and treatment, under- or misdiagnosis and late or missed treatment might be deleterious. In the current study, we report data from high-volume hospitals from 3 variably affected regions—Piedmont, Marche, and Tuscany—to evaluate changes in rate of hospitalization for ACS during the first month of the SARS-CoV-2 Italian outbreak.

Methods
This is a multicentre, observational, retrospective study involving 3 high-volume centres distributed in northern and central Italy. Epidemiologic data of consecutive patients with ACS admitted in March 2019, and March 2020 were anonymously extracted and entered into a dedicated database. Data

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decreased from 162 patients in 2019 to 84 patients in 2020. In 2020, both door-to-balloon and symptoms-to-percutaneous coronary intervention were longer, and admission levels of high-sensitive cardiac troponin I were higher. They had a lower discharged residual left-ventricular function and an increased predicted late cardiovascular mortality based on their Global Registry of Acute Coronary Events (GRACE) scores.

collections included procedural results and in-hospital outcomes.

The “case period” was set in the month of March because it was when the severe social containing measures were adopted. The rate of ACS-related hospitalization during March 2020 was compared with the rate in the control period (March 2019). Subanalyses comprised the rate of ACS type (ST-elevation myocardial infarction [STEMI], non—ST-elevation myocardial infarction [NSTEMI] and STEMI with a time-to-reperfusion delay > 24 hours), the delay between admission to percutaneous coronary intervention (PCI) and symptoms to PCI. Risk of NSTEMI was stratiﬁed using the Thrombolysis in Myocardial Infarction (TIMI) score. Time to reperfusion, basal admission, and peak high-sensitivity troponin level, as well as left-ventricular ejection fraction (LVEF) at discharge and in hospital mortality were also collected and compared. Patients signed informed consents for data collection, and the study was conducted according to the Declaration of Helsinki.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as numbers and percentages. Distributions of continuous variables were examined for skewness and were logarithmically transformed as appropriate. Continuous variables with normal distribution were compared using the unpaired Student’s t-test. Nonparametric continuous variables were compared using the U Mann-Whitney test. Categorical variables were compared using the χ² test. Incidence rate (IR) for ACS related hospitalization was calculated by dividing the number of cumulative events by the number of days for both time periods. A P value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 26 (IBM Corporation, Armonk, NY).

Results

Patient characteristics are shown in Table 1. A total of 246 ACS-patients were included in the study (162 patients with ACS admitted in March 2019, and 84 patients with ACS admitted in March 2020). During the case period, a total of 84 hospital admissions for ACS were observed, accounting for an IR of 2.7 admissions per day vs an IR of 5.2 admissions per day observed in the control period (odds ratio [OR], 0.52; 95% conﬁdence interval [CI], 0.39-0.67; P < 0.001). Of the 84 patients with ACS in 2020, 26 were positive for COVID-19; of these, 5 patients were already hospitalized for interstitial pneumonia, whereas—in the remaining 21 cases—the diagnosis of COVID-19 infection was an incidental finding from the routine COVID reverse transcription polymerase chain reaction (RT-PCR) assay of a nasal swab performed immediately at admission before cardiac catheterization.

There were no significant differences in patient clinical characteristics or risk factors in the 2 groups. In March 2019, NSTEMI was a more frequent admission diagnosis (57.4% vs 39.3%, P < 0.01) and symptom to PCI was signiﬁcantly shorter (18.8 ± 20 vs 36.9 ± 38.4 hours, P < 0.001). In the STEMI subgroup, door-to-balloon and symptoms-to-balloons were signiﬁcantly higher in March 2020 (66 ± 17 vs 40 ± 12 minutes, P < 0.001 and 5.8 ± 3.1 hours vs 3.9 ± 2.2 hours, P < 0.001 [Fig. 1]) with a delay from symptoms to wiring for STEMI PCI > 24 hours more frequently in March 2020 (17.8% vs 4.3%, P < 0.001). The Global Registry of Acute Coronary Events (GRACE) score was signiﬁcantly higher in 2020 (126 ± 27 vs 116 ± 26, P < 0.001), and more patients were in the higher European Society of Cardiology (ESC) tertile predictive of higher in-hospital and 6-month mortality (GRACE score above 140: 33.3% vs 18.5, P < 0.01, and GRACE score above 118: 59.6 vs 44.4%, P < 0.05).

In-hospital clinical outcome is summarized in Table 2. Admission and peak high sensitivity troponin were signiﬁcantly higher in 2020 (5138 ± 9408 vs 1142 ± 4017 ng/L, P < 0.001, 13,681 ± 10,936 vs 9143 ± 13,825 ng/L, P < 0.01 [Fig. 1]). Presence of an LVEF < 40% at discharge was more frequent in March 2020 (42.8% vs 24.7%, P < 0.01). No statistical difference in in-hospital mortality was observed between the 2 groups.

Discussion

The SARS-CoV-2 epidemic was associated with a signiﬁcant decrease in the rate of hospitalization for ACS, a reduction not justiﬁed by a possible biological explanation. Viral infections and ACS share the development of a peak during winter as clearly shown by epidemiologic studies and meta-analyses that suggest a signiﬁcant increase in ACS-STEMI in patients affected by seasonal ﬂu when compared with the remaining population.4 5 6 SARS-CoV-2 infection shares many similarities with other coronavirus infections such as SARS-CoV and MERS-CoV, both responsible for increase in acute cardiovascular events rate in infected patients.7 Patients with SARS-CoV-2 infections also develop general proinflamatory and hypercoagulative status, explaining the frequent in-hospital acute coronary events observed.7 The opposite phenomenon of a paradoxical reduction observed can...
Table 1. Patients clinical characteristics and acute clinical outcome

| Group 2019 | Group 2020 | P value | Group I 2019 | Group II 2020 | P value |
|-----------|------------|---------|--------------|---------------|---------|
|           | 162 patients | 84 patients |              | 162 patients | 84 patients |         |
| AGE       | 69.9 ± 32.6 | 68.3 ± 30.9 | ns | 59 (36.4%) | 34 (40.5%) | ns |
| SEX       | M:113/F:49  | M:62/F:22 | ns | 7 (4.3%)     | 15 (17.8%) | < 0.001 |
| COPD      | 35 (21.6%)  | 7 (8.3%)  | < 0.01       | 93 (57.4%)   | 33 (39.3%) | < 0.01 |
| HYPER   | TENSION   | 108 (66.7%)  | 65 (77.4%)  | 3 (1.9%)     | 2 (2.4%)    | < 0.01 |
| DIABETES | 48 (29.6%)  | 31 (36.9%) | ns | Door to balloon (STEMI) 40 ± 12 minutes | 66 ± 17 minutes | < 0.001 |
| SMOKING  | 85 (52.5%)  | 34 (40.5%) | ns | Symptoms to PCI (STEMI) 3.9 ± 2.2 hours | 5.8 ± 3.1 hours | < 0.001 |
| DYSLIPIDE | MA        | 100 (61.7%)  | 58 (69%)    | Symptoms to PCI (NSTEMI) 18.8 ± 20 hours | 36.9 ± 38.4 hours | < 0.001 |
| BMI > 30 | 36 (22.3%)  | 23 (27.4%) | ns | hs-cTnI (basal) 1142 ± 10.4017 | 13,681 ± 10.936 | < 0.01 |
| KNOWN CAD | 41 (25.3%)  | 31 (36.9%) | ns | hs-cTnI (peak) 9143 ± 12,852 | 13,681 ± 10.936 | < 0.01 |
| AF        | 18 (11.1%)  | 6 (7.1%)   | ns | LVEF 49.9 ± 9.4 | 45.9 ± 12 | < 0.05 |
| CKD       | 21 (13%)    | 12 (14.3%) | ns | LVEF < 40% 24.7% | 42.8% | < 0.01 |
| GRACE SCORE | 116 ± 26   | 126 ± 27   | < 0.01       | Death 1.8%     | 4.7% | ns |

Other ACS (Tako-Tsubo syndrome or myocardial infarction with nonobstructive coronary arteries (MINOCA)). AF, atrial fibrillation; ACS, acute coronary syndrome; BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; GRACE, Global Registry of Acute Coronary Events; hs-cTnI, high-sensitivity cardiac troponin I (lab range 0-58 ng/L); LVEF, left-ventricular ejection fraction; NSTEMI, non-ST-elevation myocardial infarction; rr, recommended reperfusion; PCI, percutaneous coronary intervention; rr, recommended reperfusion; STEMI, ST-elevation myocardial infarction.
improved the statistical power of our findings, but the reduction of hospitalizations for ACS during the first 3 months of the Italian lockdown has been confirmed by our recently published large North Italian registry.\(^1\)

"Stay home" is an important message to contain spreading of the virus, but this message should be tempered by a clear exclusion of chest pain and other medical emergencies that still require rapid in-hospital treatment.

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**Figure 1.** Graph bar shows the difference in door-to-balloon, symptoms-to-percutaneous coronary intervention, basal and peak in high-sensitivity troponin I between the 2 groups. *P < 0.001. **P < 0.01