Introduction During the coronavirus disease-19 (COVID-19) outbreak in spring 2020, people may have been reluctant to seek medical care fearing infection. We aimed to assess the number, characteristics and in-hospital course of patients admitted for acute cardiovascular diseases during the COVID-19 outbreak.

Methods We enrolled all consecutive patients admitted urgently for acute myocardial infarction, heart failure or arrhythmias from 1 March to 31 May 2020 (outbreak period) and 2019 (control period). We evaluated the time from symptoms onset to presentation, clinical conditions at admission, length of hospitalization, in-hospital medical procedures and outcome. The combined primary end point included in-hospital death for cardiovascular causes, urgent heart transplant or discharge with a ventricular assist device.

Results A similar number of admissions were observed in 2020 (N = 210) compared with 2019 (N = 207). Baseline characteristics of patients were also similar. In 2020, a significantly higher number of patients presented more than 6 h after symptoms onset (57 versus 38%, P < 0.001) and with signs of heart failure (33 versus 20%, P = 0.018), required urgent surgery (13 versus 5%, P = 0.004) and ventilatory support (26 versus 13%, P < 0.001). Hospitalization duration was longer in 2020 (median 10 versus 8 days, P = 0.03). The primary end point was met by 19 (9.0%) patients in 2020 versus 10 (4.8%) in 2019 (P = 0.09).

Conclusion Despite the similar number and types of unplanned admissions for acute cardiac conditions during the 2020 COVID-19 outbreak compared with the same period in 2019, we observed a higher number of patients presenting late after symptoms onset as well as longer and more complicated clinical courses.


Keywords: acute cardiovascular care, arrhythmias, cardiology, coronavirus disease-19, heart failure, myocardial infarction, outcome

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Introduction

On 21 February 2020, the first cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection were diagnosed in northern Italy. The first Italian patient who died for 2019 coronavirus disease (COVID-19) on 22 February 2020 was admitted to the Azienda Ospedaliera – Padua University hospital, Veneto region. During the subsequent days, the number of people infected by the SARS-CoV-2 and the number of hospital beds occupied by patients with COVID-19 increased exponentially. At the same time, the general population was warned by public authorities not to misuse the emergency services due to the possible overload of hospital capacity and risk of infection spreading. On 1 March, the national government issued several social distancing measures affecting northern Italian regions including Veneto. A national lock down was imposed on 8 March and continued until the beginning of May. At the end of May, the situation improved and the number of patients admitted to ICUs for COVID-19 was ≈10% of the peak value.

Previous reports from Italy and other countries showed a decline in the number of unplanned admissions for acute cardiovascular diseases such as acute coronary syndromes and arrhythmias during the first weeks of
the outbreak. Although multiple possible explanations have been proposed, it is plausible that a proportion of patients refrained from seeking medical care in the hospital fearing infection. However, data on the characteristics and in-hospital course of patients admitted over a longer period are lacking. It may be hypothesized that delayed presentation resulting from the reluctance to seek prompt medical aid may have translated into worse short-term outcome.

The aim of the study was to compare the number, characteristics, delay from symptoms onset to presentation, clinical course and outcome of patients admitted to the cardiology department of a large university hospital in the Veneto region, northern Italy during the first 3 months of the COVID-19 epidemic (1 March–31 May 2020) and during the corresponding period in 2019.

**Methods**

**Setting**

The study was conducted at the cardiology department of the Azienda Ospedaliera – University of Padova, a third-level teaching hospital in the Veneto region, northern Italy. The cardiology department includes a 16-bed cardiology ICU and a 44-bed ward. The Azienda Ospedaliera – University of Padova hospital catchment area includes the city of Padova and its suburbs (≈350 000 inhabitants). Moreover, during nighttime, weekends and bank holidays it is also the hub center for patients with ST-segment elevation myocardial infarction (STEMI) or unstable non-STEMI (NSTEMI) with indications for immediate coronary angiography of a larger area including ≈675 000 inhabitants.

Admissions to our cardiology department may be planned or unplanned: the former were suspended because of the epidemics in March and April 2020 and resumed in May. Except for STEMI or unstable NSTEMI patients, who may be admitted directly from the emergency medical system or bespoke hospitals, all other unplanned admissions come from the local emergency department (ED). After the COVID-19 epidemic started, the hospital management mandated that all patients admitted to the cardiology department must be screened for SARS-CoV-2 infection with pharyngeal swabs and transferred to dedicated ‘COVID units’ in case of positive results. This decision was adopted to reduce the risk of dissemination among fragile patients with cardiovascular diseases. The organization of the STEMI reperfusion network, including referral criteria, working hours and catchment area, remained unchanged; during primary coronary angioplasty medical personnel prudentially wore protective equipment as the results of the pharyngeal swab could not be waited for.

**Inclusion criteria**

The study included all consecutive patients who were admitted to our cardiology department in March, April and May 2020 (epidemic period) and 2019 (control period) with the following acute cardiovascular diseases: acute myocardial infarction (AMI), either STEMI or NSTEMI; acute heart failure unrelated to AMI; and arrhythmias including arrhythmic cardiac arrest (unrelated to AMI), sustained ventricular tachycardia, second- or third-degree atrioventricular block, symptomatic sinus node dysfunction or symptomatic low ventricular rate atrial fibrillation/flutter.

Patients with other acute cardiovascular conditions such as nonarrhythmic cardiac arrest, chest pain without troponin release, endocarditis, pericarditis, pulmonary embolism, syncope of unknown origin or supraventricular arrhythmias were not included as many are admitted to internal medicine wards or general ICUs rather than the cardiology department, depending on availability of beds. Patients transferred from other hospitals with conditions other than STEMI or unstable NSTEMI with indications for immediate coronary angiography were also not included, because in 2020 a number of nonemergency transfers became necessary due to limited bed availability in some centers.

The study was approved by the local review board. Because of the retrospective observational nature of the study, consent was waived.

**Variables of interest**

All patients’ files are stored electronically in the hospital management software. We reviewed all electronic health records and collected information about age, sex, main diagnosis at admission, history of cardiovascular diseases or interventions, and comorbidities. From the ED reports, we evaluated symptoms complained of by patients on admission, time from symptom onset to first medical contact, first recorded values of heart rate and systolic blood pressure, Killip class and admission ECG. Symptom onset was defined as the self-reported time when the patient started to complain of new symptoms or acute worsening of chronic symptoms. The Killip class classifies the presence of heart failure into four different categories: first, no signs of heart failure; second, mild-to-moderate heart failure (S3 gallop, basal pulmonary rales, elevated jugular venous pressure); third, frank pulmonary edema; and fourth, cardiogenic shock. We also evaluated the report of the bedside echocardiography that is routinely performed within a few hours to all patients admitted urgently. Finally, we collected information about the medical procedures that the patients underwent during hospitalization, the length of hospitalization and the outcome.

**Definition of outcomes**

The primary end point of the study was a composite of cardiac death during index hospitalization, urgent heart transplant that was performed during index hospitalization and discharge with a ventricular assist device that was
implanted during index hospitalization. Brain death following cardiac arrest of cardiac origin was classified as cardiac death. The secondary end point was all-cause death.

**Statistical analysis**
Categorical differences among groups were evaluated by the \( \chi^2 \) test or the Fisher exact test, as appropriate. Continuous data are expressed as median with 25–75th percentiles because normality could not be assumed for any variable. Differences among continuous variables were compared using the Mann–Whitney \( U \) test. A two-tailed probability value of 0.05 was considered statistically significant. All analyses were performed using SPSS 23 (SPSS Inc, Chicago, Illinois, USA).

**Results**
During the study period of 1 March–31 May 2020, 210 unplanned admissions were observed (mean 2.3/day), compared with 207 during the control period of March–May 2019 (mean 2.3/day). In March 2020, we observed a lower number of admissions compared with 2019 (60 versus 76, -27%), and in April (74 versus 61, +18%) and May (76 versus 70, +6%) a higher number. All patients admitted in 2020 tested negative for SARS-CoV-2. In three cases of severe heart failure secondary to acute myocarditis, further tests to exclude COVID-19-related myocarditis including antibodies and viral genome search in endomyocardial biopsy samples were carried out with negative results.

Table 1 shows the baseline characteristics and reason for admissions of the study patients. There were no differences in terms of age, sex, previous history of cardiovascular diseases or interventions and comorbidities between the two periods. AMI was the most frequent reason for admission both in 2020 and 2019, with a similar proportion of STEMI and NSTEMI. There were a nonsignificantly higher number of patients admitted for acute heart failure unrelated to AMI in 2020 compared with 2019.

Table 2 compares signs and symptoms, delays from symptoms onset to first medical contact and clinical presentation between patients admitted during the coronavirus disease-19 epidemic in 2020 and in the corresponding 2019 period.
conditions at presentation between the two study periods. In 2020, a significantly higher proportion of patients presented for dyspnea and more than 6 h after symptom onset (Fig. 1). All eight patients who presented more than 1 month after symptoms onset in 2020 were admitted in April and May, whereas in 2019 there were two patients presenting very late after symptoms onset in March, three in April and one in May. Signs of heart failure at admission (Killip class ≥2) were more often observed in 2020. No differences between main ECG and echocardiographic abnormalities were observed between the two periods.

Table 3 shows the medical procedures that patients underwent in 2019 and 2020. Compared with 2019, a significantly higher proportion of patients admitted in 2020 required unplanned surgery, ventilatory support and blood transfusion.

Table 4 shows the duration and outcome of hospitalization in 2019 and 2020. Median hospitalization duration was longer in 2020 than in 2019. There was a nonsignificant trend toward a higher number of patients meeting the primary end point in 2020 (Fig. 2). The proportion of patients who met the primary end point and presented more than 6 h after symptoms onset was 10/19 (53%) in 2020, 5/9 (55%) in 2019.

Prevalence of patients presenting more than 6 h after symptoms onset in 2019 and 2020 according to type of acute cardiovascular condition. AMI, acute myocardial infarction; ARR, arrhythmias; HF, heart failure.

Table 3 Medical procedures undergone by patients admitted during the coronavirus disease-19 epidemic in 2020 and in the corresponding 2019 period

| Procedure                        | 2020, N = 210 | 2019, N = 207 | P  
|----------------------------------|--------------|--------------|-----
| Percutaneous interventions       | 104 (50%)    | 100 (48%)    | 0.80 |
| PTCA                             | 100 (48%)    | 98 (48%)     | 0.96 |
| TAVR                             | 2 (1%)       | 1 (0.5%)     | 1.0  |
| Mitral clip                      | 2 (1%)       | 1 (0.5%)     | 1.0  |
| Cardiac rhythm device implantation| 41 (20%)    | 34 (16%)     | 0.42 |
| Pacemaker                        | 29 (14%)     | 28 (14%)     | 0.93 |
| ICD                              | 12 (6%)      | 6 (3%)       | 0.16 |
| Unplanned surgery                | 27 (13%)     | 10 (5%)      | 0.004|
| Cardiac surgery                  | 22 (10%)     | 8 (4%)       | 0.008|
| Vascular surgery                 | 2 (1%)       | 1 (0.5%)     | 1.0  |
| Other surgery                    | 7 (3%)       | 1 (0.5%)     | 0.07 |
| Ventilatory support              | 54 (26%)     | 26 (13%)     | <0.001|
| Noninvasive ventilation          | 30 (14%)     | 15 (7%)      | 0.021|
| Invasive ventilation             | 33 (16%)     | 15 (7%)      | 0.007|
| Circulatory support              | 48 (22%)     | 37 (18%)     | 0.30 |
| Inotropic infusion               | 47 (22%)     | 36 (17%)     | 0.24 |
| IABP                             | 5 (3%)       | 2 (1%)       | 0.45 |
| ECMO                             | 10 (5%)      | 4 (2%)       | 0.17 |
| Kidney replacement therapy (CVVH)| 10 (5%)      | 4 (2%)       | 0.17 |
| Blood transfusion                | 16 (8%)      | 6 (3%)       | 0.033|
| None of the above                | 33 (16%)     | 52 (25%)     | 0.017|

CVVH, continuous venovenous hemofiltration; Extracorporeal Membrane Oxygenation; IABP, intra-aortic balloon pump; ICD, implantable cardioverter defibrillator; PTCA, percutaneous transluminal coronary angioplasty; TAVR, transaortic valve replacement.

Table 4 Hospitalization length and outcomes of patients admitted during the coronavirus disease-19 epidemic in 2020 and in the corresponding 2019 period

| Outcome                        | 2020, N = 210 | 2019, N = 207 | P  
|--------------------------------|--------------|--------------|-----
| Hospitalization length         |              |              |     |
| Days in ICU                    | 4 (2–5)      | 3 (1–5)      | 0.012|
| Days in hospital               | 10 (6–19)    | 8 (5–15)     | 0.027|
| Outcomes                       |              |              |     |
| Primary end point              | 19 (9.0%)    | 10 (4.8%)    | 0.09 |
| Cardiac death                  | 17           | 10           |     |
| Urgent heart transplant        | 1            | –            |     |
| Discharged with VAD            | 1            | –            |     |
| All-cause death                | 18 (8.6%)    | 14 (6.8%)    | 0.46 |

VAD, ventricular assist device.
2020 versus 3/10 (30%) in 2019. All-cause in-hospital mortality was similar in 2019 and 2020. Five patients died of noncardiac causes: one of stroke (in 2019), two of sepsis (both in 2020) and two of intracranial bleeding (one in 2019 and one in 2020).

In the subgroup of patients with STEMI, time from symptom onset to first medical contact was less than 3 h in 52/72 (72%) cases in 2019 versus 33/64 (51%) in 2020 ($P = 0.01$). The primary end point was met by 8/64 (12.5%) patients in 2020 versus 3/72 (4.2%) in 2019 ($P = 0.12$): 5/8 presented more than 3 h after symptom onset in 2020 versus 0/3 in 2019.

**Discussion**

The study aimed to evaluate the number, characteristics, clinical course and outcome of unplanned admissions for acute cardiovascular conditions (AMI, heart failure and arrhythmias) to the cardiology department of a large university hospital of northern Italy during the 2020 COVID-19 outbreak and during the corresponding 2019 period. The main findings were that the number, causes and baseline characteristics of patients admitted in 2020 and 2019 were similar; patients admitted during the outbreak significantly more often presented late after symptom onset and with signs of heart failure; hospitalization duration was longer in 2020 and ventilatory support and unplanned surgery were needed more often; there was a nonsignificant trend toward a worse in-hospital outcome in 2020 compared with 2019, as evaluated by a composite end point including cardiac death, urgent heart transplant during the index hospitalization and discharge after ventricular assist device implantation (Fig. 3).

**Trends in admissions for cardiovascular diseases during the coronavirus disease-19 epidemic**

Soon after the beginning of the COVID-19 epidemic in 2020, analyses of epidemiological data that were reported during the daily press conference of the Italian Civil Protection Department revealed that elderly patients with preexisting cardiovascular diseases were at highest risk of mortality. Moreover, many infection clusters occurred in hospitals, both among patients and healthcare personnel. Finally, health authorities discouraged the population from visiting the ED unless strictly necessary to leave medical resources available for patients with COVID-19. For all these reasons, individuals with cardiac symptoms may have refrained from seeking timely medical attention.

A 1-week nationwide survey conducted in March 2020 and collecting data from 54 Italian hospitals found a $\approx 50\%$ reduction in admissions for AMI compared with the same week in 2019. The decrease was more pronounced for NSTEMI than for STEMI. The case fatality rates markedly increased compared with the previous year: from 4.1 to 13.7\% among patients admitted for STEMI and from 1.7 to 3.3\% among those with NSTEMI. Although multiple possible explanations have been proposed, it was noteworthy that data were homogeneous in northern and southern regions, the latter much less affected by the COVID-19 epidemic. This suggests that the main reason for the decrease in AMI
admissions was the reluctance of patients with less severe symptoms to seek medical care, thus selecting those with worse clinical conditions and higher risk of in-hospital mortality. Other Italian studies reported a decrease in admissions for acute coronary syndromes and bradycardias in the first weeks of the COVID-19 outbreak.\textsuperscript{2,3} By pooling the data of 10 cardiology departments in the Veneto region of Italy, we observed a decrease in the rate of hospitalization for NSTEMI and for bradycardia requiring pacemaker implantation during the 6 weeks after the outbreak started.\textsuperscript{4,5} Similar observations were reported by investigations conducted in other countries.\textsuperscript{6–10}

In our study that focused on three categories of acute cardiovascular conditions (AMI, heart failure and arrhythmias) and extended the observation period to 3 months, we also found a reduction in unplanned admissions in the first month of the epidemic, which was however followed by a rebound in the second and third months.

**Characteristics and outcome of patients with acute cardiovascular diseases admitted during the coronavirus disease-19 outbreak**

Most previous studies lacked detailed information on the characteristics and outcome of patients with acute cardiovascular diseases that were admitted during the COVID-19 outbreak. In our center, we observed similar disease distribution and baseline characteristics of patients admitted urgently to the cardiology department during the 2020 epidemic compared with 2019. However, in 2020 patients presented later after symptom onset, more often complained of dyspnea and showed signs of heart failure. Similarly to reports from other countries,\textsuperscript{12–14} we found that the delayed presentation was evident also among STEMI patients, which is a time-critical condition, with a 21\% decrease in patients who were admitted within 3 h after symptom onset. These data may suggest that patients who initially refrained from seeking medical attention presented to the hospital later and in worse clinical condition. The hypothesis that some patients were unwilling to go to the hospital at the beginning of the outbreak but were subsequently forced by worsening symptoms may also explain the decrease in the number of admissions in March followed by a parallel increase in April and May: of note, all eight patients with time from symptom onset of more than 1 month observed in 2020 were admitted in April and May.

Hospitalizations of patients admitted in 2020 were longer and more complicated: a higher proportion of patients required unplanned surgery, ventilatory support and blood transfusions. Although it did not reach statistical significance, the incidence of the primary end point of in-hospital cardiovascular death, discharge after heart transplant or implantation of a ventricular assist device almost doubled in 2020 compared with 2019 and was nearly three times higher among STEMI patients.

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Interpretation of results
Multiple factors may have contributed to our study findings. In our hospital, there has never been a shortage of beds; on the contrary, availability in the cardiology department increased because of the suspension of planned admissions. The emergency medical system and the STEMI network continued to work normally during the entire epidemic period. Distribution of diseases and characteristics of patients who were admitted during the two study periods were similar. All patients admitted in 2020 tested negative for SARS-CoV-2 infection so that it is unlikely that concomitant COVID-19 contributed to increased hospital complications (in particular the need for ventilatory support) and adverse outcome. It is plausible that delayed presentation, probably secondary to the fear of contracting the infection in the hospital setting, was the most likely explanation underlying the different clinical course and outcome that characterized patients admitted in 2020 compared with those admitted in 2019. The fact that all three STEMI patients who met the end point in 2019 presented early after symptoms onset versus only 3/8 in 2020 suggests that delayed presentation played a role in the trend toward a worse outcome observed in this subgroup.

Conclusion
Our data suggested that, during the COVID-19 epidemic that struck Italy in 2020, a proportion of patients with acute cardiovascular diseases were unwilling to seek timely medical care. This was associated with worse clinical conditions at admissions, longer and more complicated clinical course and a trend toward worse outcome. We hypothesize that this may be the result of the widespread perception that hospitals were places at high risk of infection.

In the unfortunate event that other epidemic waves will occur in the future, better communication strategies by public health authorities may be needed to promote timely presentation of individuals with acute cardiovascular conditions. At the same time, patients need to feel reassured that all measures have been taken to limit the possibility of contracting SARS-CoV-2 infection while admitted.

Conflicts of interest
There are no conflicts of interest.

References