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Intensive cardiac care unit admission trends during the COVID-19 outbreak in Italy: a multi-center study

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Received: 2 January 2021 / Accepted: 17 March 2021 / Published online: 25 March 2021 © Società Italiana di Medicina Interna (SIMI) 2021

Abstract

A significant decline in the admission to intensive cardiac care unit (ICCU) has been noted in Italy during the COVID-19 outbreak. Previous studies have provided data on clinical features and outcome of these patients, but information is still incomplete. In this multicenter study conducted in six ICCUs, we enrolled consecutive adult patients admitted to ICCU in three specific time intervals: from February 8 to March 9, 2020 [before national lockdown (pre-LD)], from March 10 to April 9, 2020 [during the first period of national lockdown (in-LD)] and from May 18 to June 17, 2020 [soon after the end of all containment measures (after-LD)]. Compared to pre-LD, in-LD was associated with a significant drop in the admission to ICCU for all causes (– 35%) and acute coronary syndrome (ACS; – 49%), with a rebound soon after-LD. The in-LD reduction was greater for women (– 49%) and NSTEMI (– 61%) compared to men (– 28%) and STEMI (– 33%). Length-of-stay, and in-hospital mortality did not show any significant change from to pre-LD to in-LD in the whole population as well as in the ACS group. This study confirms a notable reduction in the admissions to ICCUs from pre-LD to in-LD followed by an increment in the admission rates after-LD. These data strongly suggest that people, particularly women and patients with NSTEMI, are reluctant to seek medical care during lockdown, possibly due to the fear of viral infection. Such a phenomenon, however, was not associated with a rise in mortality among patients who get hospitalization.

Keywords Intensive cardiac care unit · COVID-19

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Introduction

Since the first confirmed case of COVID-19 in Italy (February 20, 2020), the National Healthcare System has been deeply stressed, due to limited capacity of intensive care unit (ICU) departments. To avoid a total collapse of the ICU system, the Italian Government imposed extraordinary and progressive restriction measures. On March 9, 2020, the whole Italian country, with more than 60 million people, was put under quarantine [1, 2]. During the lockdown period, some changes in the pattern of hospital admissions for acute cardiovascular conditions have been noted, in particular, but not only, for acute coronary syndrome (ACS) [3–6]. Similar observations have been replicated worldwide [7–10].

These studies have provided, however, scant information about the treatment of patients admitted, the in-hospital complications, and the relevance of patients' characteristics to the observed outcome variables. Moreover, the effects of the end of the containment measures have not been deeply investigated yet.

Consequently, we analyzed all consecutive admissions to the intensive cardiac care units (ICCUs) of six Italian centers, during three different periods of time: from February 8 to March 9, 2020 (before national lockdown; pre-LD), from March 10 to April 9, 2020 (during the first period of national lockdown; in-LD) and from May 18 to June 17, 2020 (soon after the end of all containment measures; after-LD).

Methods

Study population

We conducted a multi-center, observational study involving six cardiac referral centers, homogeneously located from the North to the South of Italy, and not primarily involved in COVID-19 admissions. All hospitals were hub centers of local networks for primary percutaneous coronary intervention (PCI). The main characteristics of the cardiac centers involved, in term of bed availability, population served, and number of admissions performed during the study periods, are showed in Table 1. All consecutive adult patients $(\geq 18 \text{ years old})$ admitted in ICCU, were included in the analysis. Information about main diagnoses, triage to ICCU (source of admission, and timing from symptom onset to hospitalization, in case of ST elevation myocardial infarction-STEMI), comorbidities, interventional procedures, and main in-hospital outcome (complications, length of stay— LOS and mortality), were extrapolated from the discharge summary and the electronic chart records. Patients, whose hospital course was complicated by cardiogenic shock and cardiac arrest, received a primary diagnosis consistent with the principal cause of the shock or arrest. We categorized admissions in three main groups, in relation to the primary diagnosis: acute coronary syndrome (ACS), acute heart failure (AHF), and non-ACS/AHF. To characterize the patient's illness severity we calculated the Charlson Comorbidity

Table 1 Hospital details and absolute number of patients admitted before, during and after the lockdown

| Hospital | City | Region | Geographical area | Number of beds in ICCU | Population served | Number of patients admitted during the whole study period | Pre-LD | In-LD | After-LD |
|---|-----------|-----------|----------------------|------------------------------|-------------------|--|--------|-------|----------|
| San Giovanni di Dio e Ruggi d'Aragona Hospital | Salerno | Campania | South | 8 | ≈ 1.107.000 | 197 | 78 | 30 | 89 |
| Mater Domini University Hospital | Catanzaro | Calabria | South | 11 | ≈ 450.000 | 94 | 51 | 18 | 25 |
| Santa Maria della Misericordia Hospital | Perugia | Umbria | Centre | 8 | ≈ 600.000 | 180 | 76 | 43 | 61 |
| Riuniti Hospital | Ancona | Marche | Centre | 9 | ≈ 645.000 | 45 | 15 | 9 | 21 |
| San Paolo and San Carlo Bor- romeo Hospital | Milano | Lombardia | North | 8 | ≈ 500.000 | 82 | 36 | 28 | 18 |
| Dell'Angelo Hospital | Mestre | Veneto | North | 8 | ≈ 300.000 | 208 | 63 | 79 | 66 |

Variables are expressed as absolute number

Pre-LD, in-LD and after-LD: before the lockdown, during the lockdown and after the lockdown period



Index (CCI), that is a useful tool for estimating prognosis in patients with multiple coexisting illnesses [11, 12].

The study design was compliant with the Helsinki Declaration and it was approved by the local institutional committee on human research of the proposing centre.

Statistical analysis

Categorical variables were presented as absolute number and percentage value. Numeric data were tested for normality and presented as mean (SD) or median (interquartile range [IQR]), as appropriate. A Chi-square test was performed for categorical variables, while a nonparametric analysis of variance (Kruskal–Wallis test) was used for comparison of continuous variables. Incidence rates and their ratios were calculated using Poisson regression analysis [13].

All statistical analyses were performed using IBM SPSS Statistics (V. 25 SPSS, Chicago, Illinois, USA) and a p value less than 0.05 was taken as significant.

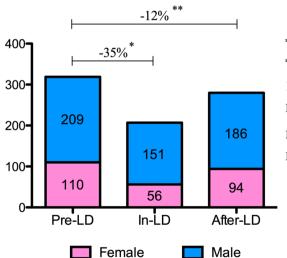
Results

Hospitalization rates, baseline patient characteristics and main in-hospital procedures

806 patients were admitted in the six ICCUs, during the whole study period; 319 before the lockdown (pre-LD), 207 during the lockdown (— 35% vs pre-LD, with an incidence rate ratio-IRR of 0.65), and 280 after the end of all containment measures (— 12% vs pre-LD, with an IRR of 0.88; Fig. 1). The reduction of hospitalization during the lockdown period was significantly higher in women (-49% vs pre-LD, with an IRR of 0.51) than in men (-28% vs pre-LD, with an IRR of 0.72; Fig. 1). For both gender categories, we observed a new increase in the hospitalization rate in the after-LD period (Fig. 1).

Of all hospitalizations, 498 (61.8%) had primary diagnoses of ACS, with 281 (56.4%) patients affected by STEMI and 217 (43.6%) by non-ST-elevation myocardial infarction/unstable angina (NSTEMI/UA). 63 (7.8%) patients were admitted due to AHF and 245 (30.4%) for other select cardiovascular conditions (non-ACS/AHF). Only one patient, admitted with primary diagnosis of pulmonary embolism, tested positive for SARS-CoV2. Differences in the hospitalization rates for the main admission

Absolute number of admission, stratified by gender, before (Pre), during (In-LD), and after Lockdown (LD)



*IRR: 0.65, 95% confidence interval [CI]: 0.54-0.77; p<0.001
**IRR: 0,88, 95% CI: 0,75-1,03; p=0,11,

IRR _{female} In-LD vs Pre-LD: 0.51; 95% CI: 0.37-0.70; p<0.001

IRR _{male} In-LD vs Pre-LD: 0.72; 95% CI: 0.59-0.89; p=0.002

IRR _{female} After-LD vs Pre-LD: 0.85; 95% CI: 0.65-1.12; p=0.26 IRR _{male} After-LD vs Pre-LD: 0.89; 95% CI: 0.73-1.08; p=0.25

Fig. 1 Absolute number of admission, stratified by gender, before (Pre), during (In-LD), and after Lockdown (LD)



diagnosis groups, during the three periods of interest, are presented in Fig. 2. Although the volume of hospitalizations was substantially lower during the lockdown period (Fig. 1), the relative distribution of primary admission diagnoses was substantially comparable (Fig. 2); ACS was, indeed, the most common cause of cardiovascular hospitalization (114; 55.1%) and STEMI was still the prevalent pattern of presentation (74; 64.9%). During the lockdown, however, we observed an important reduction in ACS admission (– 49% vs pre-LD, with an IRR of 0.54). Both STEMI and NSTEMI hospitalizations dropped in this phase, – 33%, and -61%, with an IRR of 0.67 and 0.39, respectively (Fig. 2).

An analytical description of the Non-ACS/AHF group, according to the period of hospitalization, is showed in the supplementary data (Table S1).

Demographic characteristics, source of admission, comorbidities, and main in-hospital procedures, stratified according to the period of admission, are showed in Table 2. The median age was 71 (60–79), and 32.3% of patients were women. There were no significant differences in ages, sex, source of admission and CCI; however, we detected a difference in the main interventional procedures, with a lower number of coronary angiography performed during the lockdown period (Table 2), and a progressive increase in the

percentage of patients undergoing to percutaneous coronary interventions during the three study periods (Table 2).

Finally, during the lockdown, invasive monitoring procedures (central venous catheter and arterial catheter insertion), significantly increased in comparison to the pre- and post-lockdown periods (Table 2).

In consideration of the strong impact of ACS in the definition of the hospital admission pattern during lockdown, and to better clarify the differences detected in the whole population, in the percentage of main interventional procedures, we analyzed demographic characteristics, source of admission, comorbidities and main in-hospital procedures for the ACS too (supplementary data: Table S2). Women with ACS were less frequently admitted during the lockdown (Table S2); we did not find differences in ages and CCI in ACS, similarly to the global study population. Interestingly, we did not observe differences in the percentage of coronary angiography in patients admitted for ACS, during the lockdown. The reduction that we showed for the whole population has, therefore, to be attributed to a low number of this procedure performed in the AHF and non-ACS/AHF groups. Surprisingly, we found higher percentages of PCI during lockdown (Table S2). The distribution of PCI for STEMI and NSTEMI/UA during the three periods, showed that the increment of PCI rate, is related to the number

Absolute number of hospitalization, stratified by main admission diagnosis group, before (Pre), during (In-LD), and after Lockdown (LD)

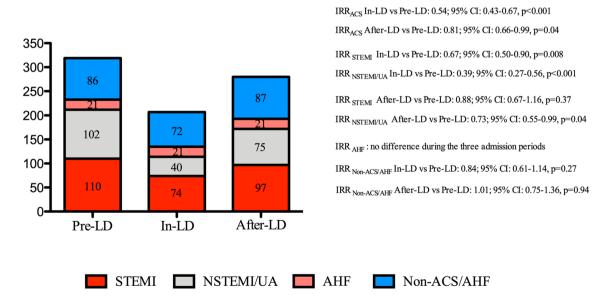


Fig. 2 Absolute number of hospitalization, stratified by main admission diagnosis group, before (Pre), during (In-LD), and after Lockdown (LD)



Table 2 Descriptive statistics stratified to the admission period

| Demographic characteristics and source of admission | Whole study period | Pre-LD | In-LD | After-LD | p value |
|--|--------------------|------------|------------|------------|---------|
| Age | 71 (60–79) | 72 (60–80) | 70 (62–79) | 70 (58–79) | 0.620 |
| Female gender | 260 (32.3) | 110 (34.5) | 56 (27.1) | 94 (33.6) | 0.173 |
| Self-presentation to the emergency department | 238 (29.6) | 104 (32.8) | 53 (25.6) | 81 (29) | 0.441 |
| Admission from the emergency medical system | 358 (44.6) | 139 (43.8) | 95 (45.9) | 124 (44.4) | |
| Direct outside or inside hospital transfer | 207 (25.8) | 74 (23.3) | 54 (38.5) | 74 (26.5) | |
| Timing from symptom onset to hospitalization (only for S | TEMI) | | | | |
| 0–3 h | 131 (50.2) | 56 (53.3) | 38 (52.8) | 37 (44) | 0.12 |
| 4–6 h | 36 (13.8) | 15 (14.3) | 11 (15.3) | 10 (11.9) | |
| 6–12 h | 36 (13.8) | 14 (13.3) | 13 (18.1) | 9 (10.7) | |
| > 12 h | 58 (22.2) | 20 (19) | 10 (13.9) | 28 (33.3) | |
| Comorbidities | | | | | |
| Hypertension | 562 (69.7) | 226 (70.8) | 148 (71.5) | 188 (67.1) | 0.501 |
| Hyperlipidaemia | 423 (52.5) | 155 (48.6) | 128 (61.8) | 140 (50.2) | 0.007 |
| Diabetes not requiring insuline | 176 (21.9) | 65 (20.4) | 49 (23.7) | 62 (22.3) | 0.657 |
| Diabetes requiring insuline | 71 (8.8) | 31 (9.7) | 15 (7.2) | 25 (8.9) | 0.612 |
| Smokers | 257 (31.9) | 107 (33.5) | 57 (27.5) | 93 (33.2) | 0.296 |
| Familiar history of coronary artery disease | 122 (15.1) | 44 (13.8) | 24 (11.6) | 54 (19.3) | 0.045 |
| Chronic kidney disease | 161 (20) | 68 (21.3) | 39 (18.8) | 54 (19.3) | 0.737 |
| End stage chronic kidney disease needing renal replacement therapy | 24 (3) | 10 (3.1) | 5 (2.4) | 9 (3.2) | 0.857 |
| Coronary artery disease | 215 (26.7) | 88 (27.6) | 63 (30.4) | 64 (22.9) | 0.156 |
| History of heart failure | 121 (15) | 52 (16.3) | 31 (15) | 38 (13.6) | 0.647 |
| History of atrial fibrillation | 136 (16.9) | 54 (16.9) | 40 (19.3) | 42 (15.1) | 0.462 |
| Previous stroke | 71 (8.8) | 28 (8.8) | 27 (13) | 16 (5.7) | 0.019 |
| Chronic obstructive pulmonary disease | 95 (11.8) | 42 (13.2) | 25 (12.1) | 28 (10) | 0.482 |
| Peripheral artery disease | 127 (15.8) | 54 (16.9) | 31 (15) | 42 (15) | 0.761 |
| Anaemia | 88 (10.9) | 31 (9.7) | 29 (14) | 28 (10) | 0.253 |
| Malignancy | 82 (10.2) | 28 (8.8) | 15 (7.2) | 39 (13.9) | 0.031 |
| Neurological and/or psychiatric disorder | 90 (11.2) | 36 (11.3) | 27 (13) | 27 (9.6) | 0.498 |
| Charlson Comorbidity Index | 4 (3–6) | 5 (3–6) | 4 (3–6) | 4 (3–6) | 0.823 |
| In-hospital procedures | | | | | |
| Coronary angiography | 570 (71) | 243 (76.4) | 129 (62.6) | 198 (71) | 0.003 |
| Percutaneous coronary intervention | 425 (60.2) | 170 (54.8) | 108 (60) | 147 (68.1) | 0.01 |
| Intra-aortic balloon pump | 26 (3.2) | 13 (4.1) | 4 (1.9) | 9 (3.2) | 0.39 |
| Pericardiocentesis | 12 (1.5) | 5 (1.6) | 1 (0.5) | 6 (2.2) | 0.32 |
| Temporary pacing | 32 (4) | 7 (2.2) | 10 (4.8) | 15 (5.4) | 0.11 |
| Central venous catheter insertion | 126 (15.6) | 42 (13.2) | 45 (21.7) | 39 (13.9) | 0.02 |
| Arterial catheter insertion | 192 (23.8) | 64 (20.1) | 61 (29.5) | 67 (23.9) | 0.047 |
| Non-invasive ventilation | 71 (8.8) | 27 (8.5) | 16 (7.7) | 28 (10) | 0.66 |
| Invasive ventilation | 50 (6.2) | 23 (7.2) | 15 (7.2) | 12 (4.3) | 0.26 |
| Haemodialysis | 33 (4.2) | 10 (3.1) | 12 (5.8) | 11 (3.9) | 0.32 |

Differences among the three main admission periods, for the whole study population. Categorical variables are presented as absolute number and percentage value. Numeric data are expressed as mean (SD) or median (interquartile range [IQR]), as appropriate. A Chi-square test was performed for categorical variables, while a non-parametric analysis of variance (Kruskal–Wallis test) was used for comparison of continuous variables among the three groups

Pre-LD, in-LD and after-LD: before the lockdown, during the lockdown and after the lockdown period

of procedures performed in the NSTEMI/UA subgroup



(supplementary data: Fig. S1).

In-hospital clinical course

Data on the length of stay and in-hospital mortality were available in 100% of patients (Table 3). Medians, for the whole study period, were 3 (2–4) and 7 (4–12), respectively, for ICCU and hospital LOS. Overall, there were 55 deaths observed during the whole study period, with a mortality rate of 6.8%. In the whole population and ACS group, we did not observe any difference in LOS and hospital mortality during the three admission periods. Separate analysis for STEMI and NSTEMI revealed a lower mortality rate, for STEMI, in the after-LD, and progressive shorter LOS and prolonged LOS, respectively for STEMI and NSTEMI, during LD and after-LD (Table 3).

In term of complications, we found a trend characterized by a higher rate of cardiovascular and non-cardiovascular complications during the lockdown period with a successive drop of both complications soon after the end of all containments measures (Table 4). This trend has been noted for the following cardiovascular and non-cardiovascular complications: pulmonary edema, atrial fibrillation requiring (pharmacological or electrical) cardioversion, acute kidney injury requiring renal replacement therapy, stroke, delirium, and blood loss requiring blood transfusion. Only pneumonitis

showed a constant rate reduction during the three period of interest (Table 4).

Similar trends but only for cardiovascular complications, were detected for the ACS subgroup, in particular for STEMI. No differences in the rate of complications were observed for NSTEMI patients (supplementary data; Table S3).

Discussion

In the present study, we confirm a significant reduction of global hospitalization for acute cardiovascular condition during the national lockdown in Italy, followed by a rebound soon after the end of all restriction measures. This observation is mostly related to an important drop in the hospitalization rate for acute coronary syndrome (– 49%), that is comparable to previous national and international report findings [14, 15]. We also confirm that the major reduction in ACS hospitalization is related to NSTEMI admission, as previously reported in literature [4, 6, 9, 14, 16].

In comparison to previous studies [4], we did not find any differences in AHF admission. Centers involved in our study are all tertiary centers for primary PCI, and five out of six have cardiac surgery availability on site; these characteristics may have moved away from these centers patients with primary diagnosis of acute heart

Table 3 LOS and in-hospital mortality according to the admission period

| Variables | Whole study period | Pre-LD | In-LD | After-LD | p-value |
|-----------------------|--------------------|-----------|-----------|----------|---------|
| ICCU LOS | 3 (2–4) | 2 (1–4) | 2 (1–5) | 3 (2–4) | 0.11 |
| Hospital LOS | 7 (4–12) | 7 (4–13) | 7 (5–11) | 6 (4–11) | 0.45 |
| In-hospital mortality | 55 (6.8) | 26 (8.2) | 15 (7.2) | 14 (5) | 0.3 |
| ACS | | | | | |
| ICCU LOS | 3 (2–4) | 2 (1–4) | 3 (2–4) | 3 (2–4) | 0.66 |
| Hospital LOS | 6 (4–10) | 6 (4–11) | 6 (4–9) | 6 (4–10) | 0.58 |
| In-hospital mortality | 28 (5.6) | 15 (7.1) | 8 (7) | 5 (2.9) | 0.16 |
| STEMI | | | | | |
| ICCU LOS | 3 (2–4) | 3 (2–5) | 3 (2–4) | 3 (1–4) | 0.054 |
| Hospital LOS | 6 (4–10) | 7 (5–11) | 6 (5–9) | 6 (4–9) | 0.27 |
| In-hospital mortality | 21 (7.5) | 12 (10.9) | 7 (9.5) | 2 (2.1) | 0.04 |
| NSTEMI/UA | | | | | |
| ICCU LOS | 2 (1–4) | 2 (1–3) | 2 (1–5) | 3 (2–4) | 0.001 |
| Hospital LOS | 6 (4–9.5) | 5 (4–10) | 5,5 (4–9) | 6 (4–10) | 0.88 |
| In-hospital mortality | 7 (3.2) | 3 (2.9) | 1 (2.5) | 3 (4) | 0.88 |

Outcome differences among the three main admission periods

Categorical variables are presented as absolute number and percentage value. Numeric data are expressed as mean (SD) or median (interquartile range [IQR]), as appropriate

A Chi-square test was performed for categorical variables, while a non-parametric analysis of variance (Kruskal-Wallis test) was used for comparison of continuous variables among the three groups. ACS acute coronary syndrome, STEMI ST-elevation myocardial infarction, NSTEMI/UA Non-ST-elevation myocardial infarction/unstable angina, ICCU intensive cardiac care unit, LOS length of stay. Pre-LD, in-LD and after-LD: before the lockdown, during the lockdown and after the lockdown period



Table 4 In-hospital complications, according to the admission period

| Complications | Whole study period | Pre-LD | In-LD | After-LD | p-value |
|---|--------------------|------------|-----------|-----------|---------|
| Cardiovascular | 307 (38.1) | 117 (36.7) | 97 (46.9) | 93 (33.2) | 0.007 |
| Pulmonary edema | 192 (23.8) | 78 (24.5) | 59 (28.5) | 55 (19.6) | 0.07 |
| Cardiogenic shock | 59 (7.3) | 24 (7.5) | 13 (6.3) | 22 (7.9) | 0.79 |
| Major ventricular arrhythmias | 66 (8.2) | 32 (10) | 15 (7.2) | 19 (6.8) | 0.29 |
| High grade AV block requiring temporary pacing | 24 (3.0) | 6 (1.9) | 9 (4.3) | 9 (3.2) | 0.25 |
| Atrial fibrillation requiring cardioversion | 102 (12.7) | 36 (11.3) | 38 (18.4) | 28 (10) | 0.015 |
| Cardiac arrest | 48 (6) | 20 (6.3) | 12 (5.8) | 16 (5.7) | 0.95 |
| Non-cardiovascular | 135 (19.7) | 57 (18) | 43 (21) | 35 (12.5) | 0.04 |
| Acute kidney injury requiring renal replacement therapy | 26 (3.2) | 6 (1.9) | 11 (5.3) | 9 (3.2) | 0.09 |
| Sepsis | 40 (5) | 18 (5.6) | 11 (5.3) | 11 (3.9) | 0.6 |
| Pneumonitis and primary respiratory failure | 50 (6.2) | 27 (8.5) | 14 (6.8) | 9 (3.2) | 0.03 |
| Stroke | 16 (2) | 8 (2.5) | 7 (3.4) | 1 (0.4) | 0.04 |
| Delirium | 37 (4.6) | 13 (4.1) | 15 (7.2) | 9 (3.2) | 0.09 |
| Anaemization requiring blood transfusion | 49 (6.1) | 14 (4.4) | 19 (9.2) | 16 (5.7) | 0.08 |

Differences in hospital complications among the three main admission periods

Variables are presented as absolute number and percentage value. A Chi-square test was performed to detect any differences among the three admission periods

Pre-LD, in-LD and after-LD: before the lockdown, during the lockdown and after the lockdown period

failure in favor of patients with ACS or complex heart disease requiring structural or cardiac surgical intervention. Indeed, in our study cohort, structural heart disease represented the second most frequent diagnosis in the non-ACS/AHF group (Table S1), and an important drop in this admission diagnosis was observed during the lockdown period (Table S1). Patients admitted during lockdown have comparable demographic characteristics when compared to patients admitted before and after the restriction measures. No difference in the comorbidity burden, expressed by the Charlson comorbidity score, is evident in our analysis among patients admitted during the three study periods. Notably, we found a reduction of self-presentation to the emergency department during the lockdown, even if not significant from the statistical point of view, both for the whole population (Table 2), and for the ACS subgroup (Table S2). The causes underlying the reduction in global acute cardiovascular hospitalization driven, in our case, mainly by a significant drop in ACS hospitalization, is largely unknown. Effects of social distancing and lockdown, including less business-related stress, improved air quality, and a more sedentary lifestyle, may have played a role [17]. However, a more concerning reason for our observed findings, is that individuals with cardiac symptoms, may have refrained from seeking timely medical attention, due to fear of infection [18, 19]. The rapid increase in hospitalization, observed soon after the end of all restriction measures, and our observation of a trend reduction in self-presentation to the emergency department, seems to give more credit to this hypothesis.

Secondary outcome analysis in the whole population, and in the ACS subgroup, showed no difference, among the three period of interest, for in-hospital mortality and length of stay (Table 3). A possible explanation is that the excess of mortality clearly seen during the lockdown, and described in different reports [20–22], may be related to out-of-hospital deaths [23]. Recently, the contribution of community deaths, in the inflation of acute cardiovascular deaths observed during the lockdown, has been investigated in England and Wales [24]. The authors found that stroke and acute coronary syndrome accounted for the vast majority of acute cardiovascular deaths, but the number of deaths in hospital, due to these conditions, fell below that expected for the time of year and it increased in the community, and particularly in people's homes. This 'displacement of death', was attributed by the authors to the fact that people did not seek help or were not referred to hospital during the pandemic, a finding supported by the fact that the majority of acute cardiovascular deaths were not recorded as related to infection with COVID-19. The concept that with COVID-19, the deaths of large numbers of people, above all in the elderly, prevented the same individuals from having an acute myocardial infarction and attending hospital for its treatment, has been recently advocated by different Authors, too [25]. A nationwide survey conducted in March 2020 and collecting data from 54 Italian hospitals found that 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 [4]. However, this



observation was restricted to no more than a single week, shortly after the lockdown, with fewer than ten cases per center. When we looked specifically at ACS subgroups, we did not find increased in-hospital mortality during the lockdown. We observed a lower mortality for STEMI in the period soon after the end of all containment measures (Table 3), but this observation clearly needs to be investigated in larger studies. Also in terms of time from symptoms onset to hospitalization and PCI rates, we could not find any difference in STEMI population, in contrast to what recently showed in a European registry [26]. The discrepancy regarding mortality may be related to the fact that some studies performed in Italy suggest a different risk in relation to the specific week analyzed and to the geographical area of interest [21]; however, the findings of equal PCI trends during lockdown, and equal presentation times, strenghten the suspicion that the excess of mortality associated to the lockdown period might be dependent from out of hospital deaths.

Study strengths and limitations

This study examines trends in acute cardiovascular hospitalizations across large hospital centers, with high volume PCI. Despite it has been conducted during pandemic emergencies, which was challenging, missing values are present only for seven variables: time to symptom onset to hospitalization for STEMI in 7.1%, PCI for ACS in 1.8%, intra-aortic balloon pump in 0.2%, pericardiocentesis in 0.1%, and history of atrial fibrillation, hyperlipidaemia and diabetes requiring insulin in 0.1%. Our observation period is longer than previously reported and extended to the time when all restrictions measures were abolished. Despite these strengths, this analysis has some limitations. It is a retrospective study and we did not compare our admission trends with those of previous years. This analysis does not include emergency department presentations and, therefore, does not assess the total number of initial presentations to the hospital for acute cardiovascular conditions. Since we only analyzed the first month of lockdown, potential variations in admission rates might have occurred later during lockdown. However, other studies showed that mortality peak in Italy was achieved at the end of March [20, 21], a period, that has been extensively included in our analysis. Finally, although a subgroup analysis according to the three different regions of interest (North, Centre and South) would have been interesting in comparing areas with high and low COVID-19 incidence, our sample size was probably too small (i.e., only two cardiac centers for each region) to make clinical inferences based on statistical results.



Conclusion

Our study confirms a significant reduction in global hospitalization for acute cardiovascular conditions, particularly for ACS. Reduction in ACS hospitalization was greatest for NSTEMI. Importantly, we did not observe differences in term of hospital mortality and LOS both for the whole population and for the ACS group. Larger studies are needed in the current scenario characterized by a second pandemic COVID-19 wave, possibly with representation of the entire national Italian territory.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11739-021-02718-8.

Funding Not applicable.

Declarations

Conflict of interest The authors declare they have no conflict of interest

Human and animal rights All procedures performed in studies involving human participants were in accordance with ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent All participants provided informed consent prior to their participation.

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