American Heart Journal Plus: Cardiology Research and Practice 44 (2024) 100422

Contents lists available at ScienceDirect

American Heart Journal Plus: Cardiology Research and Practice

journal homepage: www.sciencedirect.com/journal/american-heart-journal-plus-cardiology-research-and-practice

Research Paper

The impact of coronavirus disease 2019 on acute coronary syndrome: Differences between epidemic waves

Vincenzo Sucato *, Giusy Sausa, Grazia Gambino, Alessandro D'Agostino, Salvatore Evola, Giuseppina Novo, Egle Corrado, Alfredo Ruggero Galassi

Division of Cardiology, University Hospital Paolo Giaccone, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (ProMISE), University of Palermo, Italy

ARTICLE INFO

Keywords:
COVID - 19
Acute coronary syndrome
Door-to-balloon
Emergency management
Percutaneous coronary intervention

ABSTRACT

Introduction: Since the beginning of the COronaVIrus Disease 2019 (COVID-19) pandemic, poor attention has been paid to the indirect effects of the pandemia on cardiovascular health system, in particular in patients with Acute Coronary Syndrome (ACS). The aims of this study is to compare possible epidemiological, clinical and management differences between the four epidemic waves in groups of patients hospitalized for ACS with a view to highlighting the burden of the pandemic on the management of this syndrome.

Materials and methods: In this retrospective observational study we included 98 patients admitted to Coronary Intensive Care Unit (CICU) for ACS between March 2020 and March 2022, who underwent revascularization procedure using percutaneous coronary angioplasty (PCI). The patients examined were divided into four groups representative of the four epidemic waves that affected our country.

Results: The rate of hospitalization for ACS increased progressively to a 178 % increase in the third wave compared to the first ($p = 0.003$), with an increase of 900 % if we consider only Non-ST-Elevation Myocardial Infarction (NSTEMI) (representing 54 % of the ACS diagnoses of the third group against 14.3 % in the first). Longer door-to-balloon times were recorded in the third wave for the increased presence of NSTEMI. The average hospital stay was lower in the third wave with 5 ± 2 days ($p = 0.007$) as well as mortality (5.1 % in the third wave; the highest in the fourth wave with 9.5 %).

Conclusions: The study show that the management of ACS suffered most from the indirect effects of the pandemic during the first wave, both because of the unpreparedness of hospital facilities and because of the fear of infection that has dissuaded people from asking for help.

1. Introduction

Since the beginning of the COronaVIrus Disease 2019 (COVID-19) pandemic, great attention has been paid to the cardiovascular implications induced by coronavirus infection. No less important, however, are the indirect effects of the virus on cardiovascular health which contributed to the increase in all-cause mortality recorded during the pandemic [4].

On the basis of data published in the literature, we wanted to analyze the quantitative and qualitative impact of the COVID-19 pandemic on hospitalizations in our Coronary Intensive Care Unit (CICU) in which are admitted all patients with ACS of our Hospital, in order to critically evaluate any differences that occurred between the different epidemic waves.

In particular, we focused our attention on epidemiological aspects such as the variation in the rate of hospitalizations for acute coronary syndrome in the different periods analyzed. Numerous studies have demonstrated a clear reduction in hospitalizations for acute myocardial infarction (AMI) in the first month of lockdown compared to the pre-pandemic period [5]. On the basis of these data, we aim to analyze whether the rate of hospitalizations for ACS has undergone variations between the different epidemic waves. Another parameter evaluated is the in-hospital mortality rate in patients hospitalized for acute coronary syndrome. International studies conducted during the first lockdown reported an indirect increase in mortality for patients hospitalized for ACS [13,14]. In order to investigate the influence that a possible delay in

* Corresponding author at: Division of Cardiology, University Hospital Paolo Giaccone, Palermo, Department of ProMISE, University of Palermo, Via del Vespro n 129, 90127 Palermo, Italy.
E-mail address: vincenzo.sucato@unipa.it (V. Sucato).

https://doi.org/10.1016/j.ahjo.2024.100422
Received 10 April 2024; Received in revised form 23 June 2024; Accepted 29 June 2024
Available online 3 July 2024

the most appropriate treatment could have on patient mortality, we paid attention to the "door-to-balloon" and "symptoms-to-balloon" times, which respectively reflect the efficiency of hospital management and the timeliness with which the patient requested help.

We also evaluated the coronary angiographic characteristics of these patients and the procedural characteristics of percutaneous coronary intervention (PCI).

Through the evaluation of these different parameters, we have tried to highlight the weight that the pandemic has had on the management of acute coronary syndrome, analyzing the impact on hospitals and on the use of hospital care by patients.

2. Materials and methods

In our retrospective observational study we included 98 patients hospitalized for ACS at the CICU between March 2020 and March 2022, underwent a revascularization procedure using PCI. The patients examined were divided into four groups representing the four epidemic waves that affected our country. The first group included all patients hospitalized for acute coronary syndrome from March 10, 2020 to June 10, 2020, a period assimilated to the entire duration of the first epidemic wave. The second group included patients hospitalized for acute coronary syndrome from October 1, 2020 to January 1, 2021, representative of the second wave. The third group included patients hospitalized for acute coronary syndrome from February 20, 2021 to May 20, 2021, representative of the third wave. Finally, all patients admitted from December 2021 to March 2022 were selected to represent the fourth wave.

We enrolled 98 patients (62 males and 36 females aged between 34 and 90 years). The first wave group includes 14 patients, all Caucasian, of which 9 men (64 %), with an average age of 60 years. The representative group of the second wave includes 24 patients, all Caucasian, of which 16 men (66 %), with an average age of 62 years. The third group includes 39 patients, all Caucasian, of which 24 men (61 %), with an average age of 62 years. The fourth group includes 21 patients, of which 20 Caucasians and one African, with 13 men (62 %) and an average age of 61 years.

In detail, we included in the study adult patients over 18 years of age, affected by ACS and who presented on coronary angiography, performed at the time of hospitalization, coronary arteries affected by stenoses >70 % of the vessel lumen (critical stenoses). Patients who did not undergo percutaneous transluminal coronary angioplasty, directed only to optimize medical therapy, were excluded.

Patients were considered to have ACS if they presented the clinical characteristics of unstable angina, NSTEMI (Non-ST elevation myocardial infarction) or STEMI (ST elevation myocardial infarction), diagnosed in the presence of a clinical, laboratory and instrumental context suggestive of ischemia myocardial, as indicated by the European Society of Cardiology (ESC) guidelines.

For each patient we calculated the time elapsed from the moment the patient experienced symptoms (typical or atypical chest pain, dyspnoea, syncope, cardiac arrest, worsening of pre-existing symptoms in a patient with previous ischemic heart disease) until arrival in the cath-lab (symptoms-to-balloon time) and the time elapsed from the first medical contact until arrival in the cath-lab (door-to-balloon time).

Prognostic scores were calculated for each patient: the Global Registry of Acute Coronary Events (GRACE) Risk score and the CRUSADE score. To analyze the procedural characteristics of PCI we considered the number of stents implanted, the access site, the procedure times, the volume of contrast agent, the number of vessels treated and the use of glycoprotein IIb/IIIA inhibitors. The rate of temporary pacemaker (PM) and aortic counterpulsator implantation was considered as a further indicator of intra-procedural complexity and complications. The angiographic results and the efficacy of recanalization were analyzed based on the degree of pre- and post-procedure TIMI (Thrombolysis in Myocardial Infarction) flow and the presence of "slow flow/no flow".

In order to obtain prognostic elements we evaluated the onset of short/medium term complications, including the development of effusion, ventricular aneurysm, reduction in Left Ventricular Ejection Fraction (LVEF<35 %), contrast-induced nephropathy and mechanical complications.

We calculated the in-hospital mortality rate for each group and the average length of stay in the ICU for surviving patients.

Given that each group includes all patients affected by ACS during a three-month period, it was possible to compare the rate of hospitalization for ACS between the four groups, evaluating the relative rates of STEMI and NSTEMI infarctions.

3. Results

The experience reported in this study comes from a large tertiary referral center. Pre-pandemic, our center managed a high clinical volume, with an average of 267 presentations of acute coronary syndrome (ACS) in two years. During the COVID-19 pandemic, we observed a significant reduction in the number of ACS presentations, which decreased to a value of 98 presentations in the in the twelve months representative of the first 4 epidemic waves.

Regarding the evaluation of the demographic characteristics of the examined population, the differences in age and sex between the four waves were not statistically significant.

Comparing the clinical characteristics and cardiovascular risk factors of patients belonging to the various groups, no statistically significant differences emerged except for the increase in smokers among patients of the third wave (89 % in the third, 50 % in the first, $p = 0.04$) [see Table 1].

For each group we calculated the number of STEMI and NSTEMI out of the total diagnoses. In the first group out of the total patients, there were 12 (85.7 %) diagnoses of STEMI and 2 (14.3 %) diagnoses of NSTEMI. In the second group 18 (75 %) diagnoses of STEMI and 6 (25 %) of NSTEMI. In the third group there were 18 (46 %) diagnoses of STEMI and 21 (54 %) of NSTEMI. In the fourth group 14 (66.6 %) diagnoses of STEMI and 7 (33.4 %) of NSTEMI. Considering the relationship between STEMI and NSTEMI diagnoses between the various waves, a statistically significant difference was evident between the percentage of STEMI (or NSTEMI) between the first and third waves ($p = 0.006$) and between the second wave and the third ($p = 0.02$). In the third wave, of the total acute myocardial infarctions, 54 % were NSTEMI while in the first wave they represented the 14.3 % of the total diagnoses of myocardial infarction [see Table 2].

Table 1
Comparison of clinical characteristics between the four groups.

	1° group (n = 14)	2° group (n = 24)	3° group (n = 39)	4° group (n = 21)	1° - 2°	1° - 3°	1° - 4°
Obesity n (%)	0 (0)	4 (16.6)	7 (17.9)	7 (33.3)	0,68	0,31	0,61
Hypertension n (%)	11 (78.6)	17 (70.8)	24 (61.5)	14 (66.6)	0,61	0,25	0,44
Diabetes n (%)	5 (35.7)	7 (29.3)	15 (38.5)	7 (33.3)	0,69	0,86	0,8
Dyslipidemia n (%)	10 (71.4)	17 (70.8)	29 (74.3)	15 (71.4)	0,97	0,84	0,95
Smoke n (%)	7 (50)	17 (70.8)	32 (82)	11 (52.3)	0,22	0,04	0,89
COPD n (%)	2 (14.3)	6 (25)	2 (5.1)	2 (9.5)	0,42	0,38	0,68
Family history of CVD n (%)	4 (28.6)	7 (29.3)	16 (41)	11 (52.3)	0,97	0,4	0,13
IRC n (%)	2 (14.3)	6 (25)	10 (25.6)	4 (19)	0,42	0,35	0,71
Personal history of CVD n (%)	2 (14.3)	5 (20.8)	13 (33.3)	6 (28.6)	0,61	0,13	0,31

Table 2
Comparison of STEMI rates between the four groups.

	1° group (n = 14)	2° group (n = 24)	3° group (n = 39)	4° group (n = 21)	1° - 2°	1° - 3°	1° - 4°	2° - 3°
STEMI n (%)	12 (85.7)	18 (75)	18 (46)	14 (66.6)	0,49	0,006	0,23	0,02
NSTEMI n (%)	2 (14.3)	6 (25)	21 (54)	7 (33.3)				

Comparing the rate of global hospitalizations for ACS (STEMI + NSTEMI/UA) between the four epidemic waves, a reduction in hospitalizations was recorded during the first wave. In the second wave the rate of hospitalizations for ACS in our ICU increased overall by 71 % (24 AMI) compared to the first wave, the increase proved to be statistically significant ($p = 0.02$), in particular there was a 50 % increase in STEMI diagnoses and 200 % increase in NSTEMI diagnoses.

Comparing the third wave with the first, there was an increase in hospitalizations for ACS of 178 %; the increase proved to be statistically significant ($p = 0.003$), with 50 % more STEMI and 900 % more NSTEMI.

From the comparison between the first and fourth waves (21 Acute Myocardial Infarction - AMI), the increase in hospitalizations for ACS was 50 %; statistical significance was reached ($p = 0.04$).

The analysis of the symptoms-to-balloon time revealed a shorter time in the first group but statistical significance was not reached.

The same was done for the door-to-balloon time. Also in this case the shorter time was recorded in the first wave but the only statistically significant difference was found by comparing the first and third waves ($p = 0.03$) [see Table 3].

Regarding the prognosis, the comparison shows a lower GRACE score and CRUSADE score in the third group compared to the other three but no difference proved to be statistically significant.

Analysis of some procedural characteristics, angiographic findings, and complications was included in the study. To evaluate the complexity of the angioplasty procedure we analyzed the type of access used for the procedure (femoral access or radial access), the number of drug-eluting stents (DES) used, the procedure times, the amount of contrast used and the possible use of glycoprotein IIB/IIA inhibitors. From the comparison between the different groups, the characteristics of the PCI were found to be little different, the only statistically significant difference ($p = 0.04$) was found in the use of glycoprotein IIb/IIIA inhibitors reduced in the third wave compared to the others, result explainable by the increased of NSTEMI relative percentage during this wave. The same reason can justify the reduction in the average amount of contrast agent used during the third wave, even if it did not reach statistical significance.

The peak value of high-sensitivity Troponin T was in the range of 30 to 32,300 ng/L; the mean peak value of troponin-T-hs was 16,165 ng/L.

The mean value of pre-revascularization LVEF was 47.64 % (within the range of 25–60 %); the mean value of post-revascularization LVEF was 49.74 % (within the range of 30–60 %).

The angiographic results were analyzed in terms of post-procedure TIMI flow and presence of the "slow flow/no flow" phenomenon. From the comparison between the various groups there were no major differences in terms of effectiveness of the procedure.

The comparison of in-hospital mortality between the various groups revealed a lower rate in the second and third waves but did not reach statistical significance. The only significant difference was the reduction in the average length of stay during the third wave compared to the others ($p = 0.007$) [see Table 4].

In terms of complications arising during hospitalization, the most evident, but still not significant, difference was the reduction in contrast nephropathy during the third wave.

Table 3
Comparison of "symptoms-to-balloon" and "door-to-balloon" time between the four groups.

	1° group	2° group	3° group	4° group	1° - 2°	1° - 3°	1° - 4°
Time symptoms-to-balloon (h)	17 ± 23	20 ± 22	26 ± 25	19 ± 20	0,74	0,31	0,82
Time door-to-balloon (h)	3,7 ± 6	3,8 ± 6	12 ± 14	6 ± 11	0,97	0,03	0,42

4. Discussion

Several national and international studies have demonstrated profound differences between the first months of lockdown and the same months of 2019 [1–3]. Through our study, although small in size, we have assessed how the pandemic has continued to influence the management of acute coronary syndromes even beyond the first months of national lockdown, looking for any differences between one wave and another both in terms of the response of healthcare facilities and of the impact on the use of care by citizens.

The first interesting data emerging from the analysis concerns the rate of hospitalizations for acute coronary syndrome in our CICU. From 10 March 2020 to 10 June 2020, the representative period of the first epidemic wave, only 14 cases of acute coronary syndrome were recorded, compared to the 24 recorded from 1 October 2020 to 1 January 2021, and the 39 from 20 February 2021 to 20 May 2021 and the 21 cases in the period between 10 December 2021 and 10 March 2022. The very low number of hospitalizations during the first wave is in line with what was reported by numerous studies such as that of Di Pasquale et al. [4] in which was recorded a reduction in hospitalizations for ACS compared to the same months of 2019 [10–13]. In our study the comparison was made between the various waves, reporting an increase of 71 % in the second wave compared to the first wave ($p = 0.02$), 178 % in the third ($p = 0.003$) and 50 % in the fourth ($p = 0.04$). Further evidence, already anticipated by a survey by the Italian Society of Cardiology (SIC) [5], was the much more marked reduction in the diagnoses of NSTEMI rather than STEMI. During the first wave in our ICU only two cases of NSTEMI were recorded, representing only 14.3 % of the total heart attack diagnoses. The percentage of NSTEMI/(STEMI+NSTEMI) reached 50 % during the second wave and 53 % during the third, decreasing to 33.3 % in the fourth. In the third wave, NSTEMIs were more frequent than STEMIs, the progressive increase in NSTEMIs was statistically significant both in the comparison between the first and third waves but also in the comparison between the second and third wave.

The reasons for this reduction in hospitalizations for ACS, especially during the first wave, are likely to be traced back to the climate of panic and uncertainty that pervaded citizens, leading to a reduction in the use of the emergency-urgency system also for pathologies that required immediate health interventions, following a widespread and sometimes disproportionate perception of contagion within hospital facilities, considered the epicenter of the contagion [15–19]. This would also explain the very low number of diagnoses of NSTEMI compared to STEMI, since it is probable that faced with more severe symptoms and signs during STEMI the patient was able to more easily overcome the initial reluctance in calling for help [6]. During the third wave, but partly already in the second, there was a greater turnout of citizens to hospital facilities and less reluctance in calling for help, partly due to the

Table 4
Comparison of in-hospital mortality and duration of hospitalization.

	1° group	2° group	3° group	4° group	1° - 2°	1° - 3°	1° - 4°
In-hospital mortality n (%)	1 (7,1)	1 (4,1)	2 (5,1)	2 (9,5)	0,45	0,39	0,24
Duration of hospitalization (days)	9 ± 4	10 ± 6	5 ± 2	8 ± 4	0,33	0.0.007	0,11

advent of the vaccination campaign which may have generated a greater sense of protection from the contagion and partly due to a gradual acceptance of the idea of having to live with the virus after more than a year of the pandemic.

Another significant data in line with previous evidence is the increase in symptom-to-balloon and door-to-balloon time which was recorded in all waves compared to the average pre-pandemic times as already demonstrated by Di Pasquale et al. [4] The fear of contagion has led patients to underestimate the symptoms and delay arriving at the emergency room or calling 118; lockdown policies have limited travel, especially for elderly people; furthermore, in some areas there has been difficulty in accessing emergency health services overloaded by the high number of patients affected by COVID-19 [7]. Also for the time elapsed from the first medical contact to PCI, there was an unexpected increase especially during the third wave with an average of 12 h, compared to the 3.5–3.8 h of the first two waves. The statistically significant data is explained by the greater quantity of NSTEMI diagnoses during this wave. Since these are generally less compromised patients, we can hypothesize a longer delay in calling for help compared to those who have experienced more severe symptoms, as well as a less urgency in carrying out revascularization procedures, giving priority to patients with a more severe condition. During the first wave, presentation times and hospital management times, although longer than in the pre-pandemic period, were the shortest of the four waves. One possible explanation is the increased presence of STEMI in this group of patients compared to subsequent waves. Patients with STEMI experiencing a more severe symptomatology probably have more easily overcome the reluctance and fear to go to hospital or alert the emergency system. In addition, the different timing for PCI in STEMI patients and the increased presence of STEMI in the first wave explains the shorter door-to-balloon time.

Regarding the characteristics of hospitalized patients, we can state that there were no differences regarding age, sex and the main cardiovascular risk factors except two noteworthy differences regarding obesity and smoking habits. In particular, a progressive increase in obese patients emerged in the waves following the first, going from 0 % to 33.3 % in the fourth wave. At the same time there was an increase in smokers, from 50 % in the first wave up to 82 % in the third with a statistically significant difference. Both findings can be explained by the unfavorable effects associated with the lockdown [25–27]. The restrictions imposed by various governments in order to contain the spread of the virus have led to a severe limitation on physical activity through a limitation of travel to those strictly essential, the closure of gyms and the cancellation of sporting events. It has also been shown that the lockdown, probably through the limitation of social contacts and recreational activities and the interruption of personal routine, can have an important psychological impact by acting as a trigger for post-traumatic stress, anxiety and depression which in some way may have contributed to the increase of psychotropic drugs' consumption and to the increase of smokers, as reported in a press release from National Institute of Health, with 1.3 million more smokers in May 2021 compared to January 2020 [8]. These statistics have shown that the increase in smokers, which began already in the early stages of lockdown, has continued even beyond the end of the same. Thus being able to speak of indirect long-term effects of lockdown.

Comparing the procedural characteristics of PCI we obtained almost comparable results in terms of access site (radial/femoral) and procedure times, with an average time of 60–64 min in all groups. The only difference that reached statistical significance ($p = 0.04$) was the reduction in the use of glycoprotein IIb/IIIA inhibitors during the third wave which affected only 28.2 % of patients compared to 57, 1 % of the first wave.

Despite these procedural differences, angiographic results were comparable across all four waves, achieving TIMI 3 flow in the majority of patients and maintaining optimal standards [20]. The mortality rate was higher in the fourth wave (9.5 %) and in the first (7.1 %) while in the third wave, in addition to a lower mortality rate (5.1 %) there was also a reduction in the average duration of hospitalization in the ward with an average of 5 days, reaching statistical significance ($p = 0.007$).

This data, like the previous ones, once again reflects the lower clinical complexity of a large part of the patients hospitalized during the third wave. Further favorable data emerged from the analysis of the incidence of complications arising during hospitalization. Cases of contrast nephropathy [9] were recorded in all groups with the highest number during the first wave (14.2 %) and the lowest (2.6 %) during the third, justified both by less complex procedures and by majority of less compromised patients. The worsening trend that occurred in the fourth wave, although not statistically significant, partly reflects the difficulties that the national healthcare system had to face during this period. The number of infections has never been so high, even within the wards, leading to serious shortages of medical and healthcare staff. Added to this was the collapse of the emergency-urgency network almost completely involved in COVID-19 emergencies [21–24]. The difficulties of the healthcare system have been highlighted, for example, as an increase in the time from the first medical contact to PCI during this latest wave. Furthermore, it is understandable that in this situation the fear of contagion has been rekindled, making people reluctant to seek help despite symptoms such as chest pain, explaining the reduction in the number of hospitalizations for ACS, especially for NSTEMI, compared to the third wave [25–27]. Finally, it cannot be excluded that the worsening of the prognosis may be partly the effect of the suspension, during the most months of the pandemic, of non-urgent cardiological services and follow-up of patients with or without pre-existing ischemic heart disease. No less important was the increase in sedentary lifestyle, obesity and smoking that were recorded over the two years and which inevitably worsen the cardiovascular profile of patients, thus being able to define them as “long-term indirect effects of the COVID-19 pandemic”.

As for the analysis of the direct effects of the COVID-19 pandemic on ACS, the main limitation was the small number of patients positive for SARS-Cov2 infection admitted to our CICU. In the selected population there were only 5 SARS-cov-2 positive patients (2 patient in the first wave e 3 in the fourth), all STEMI patients. Among these patients, despite presenting times similar to patients without infection, 3 patients had more complex procedures in terms of increased thrombotic load, increased use of glycoprotein IIb/IIIA inhibitors, longer procedures; outcomes were also worse with higher troponin-T-hs values and a longer stay in the Coronary Intensive Care Unit. Among these 5 patients, one death was recorded during the revascularization procedure.

It seems unlikely that the worsening of the prognosis was due to the time of presentation and hospital management which, moreover, were comparable to patients without SARS-Cov2 infection. In the protocol adapted in our center, in case of patient with ACS and concurrent SARS-cov-2 infection suspected or certain on the basis of antigen tests, priority was given to the revascularization procedure carried out with adequate personal protective equipment and followed by sanitization of the cath lab and isolation of the patient in rooms reserved for SARS-cov-2 positive patients. Thus the delay in the management of patients positive to COVID-19 is minimal compared to negative patients. Therefore it is reasonable to think that other factors concur in determining a worse

prognosis. However, the small number of patients did not allow us to generalise these observations.

5. Conclusions

Our study shows how the COVID-19 pandemic has continued to have negative indirect effects both on the national healthcare system and on patients' use of the emergency system. Acute coronary syndromes, the prototype of time-dependent pathologies, were most affected during the first wave both due to the unpreparedness of hospital structures and to the climate of panic that dissuaded people from asking for help. However, after an apparent return to normality recorded in the third wave, the situation worsened again in the last wave. Even if today the indirect effects of the COVID-19 pandemic are no longer recorded and the restrictive measures have almost been abolished, we continue to deal with the indirect effects of the lockdown such as the increase in cardiovascular risk factors and the dropout of patients from follow-up. Experience teaches us how essential it is to maintain adequate standards of care for the treatment of acute cardiovascular diseases, in particular time-dependent pathologies, even in situations that may put the healthcare system in difficulty. Equally essential is to raise awareness among the population towards the adoption of healthy lifestyles and adherence to cardiovascular screening and follow-up programmes.

6. Limitations of study

This study, being a monocentric study, has the limit of not being able to extend this evidence beyond the reality of the Policlinico Paolo Giaccone. To this limit is added the current lack in the literature of similar analyses with which to compare the results obtained because the only studies in the literature have focused on the comparison between the first pandemic wave and the pre-pandemic period, demonstrating longer door-to-ballon and symptoms-to-ballon times during the pandemic than in the pre-pandemic period, evidence also supported by our experience.

Ethical statement

All the authors confirm that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The manuscript is in line with the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals and aim for the inclusion of representative human populations (sex, age and ethnicity) as per those recommendations. The terms sex and gender should be used correctly.

CRediT authorship contribution statement

Vincenzo Sucato: Conceptualization. **Giusy Sausa:** Writing – original draft. **Grazia Gambino:** Data curation. **Alessandro D'Agostino:** Investigation. **Salvatore Evola:** Formal analysis. **Giuseppina Novo:** Writing – review & editing. **Egle Corrado:** Supervision, Data curation. **Alfredo Ruggero Galassi:** Supervision, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] S. De Rosa, C. Spaccarotella, C. Basso, et al., Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era, Eur. Heart J. 41 (22) (2020) 2083–2088. Jun 7.

[2] C.C. Tam, K.S. Cheung, S. Lam, et al., Impact of coronavirus disease 2019 (COVID-19) outbreak on ST-segment-elevation myocardial infarction care in Hong Kongm China, Circ. Cardiovasc. Qual. Outcomes 13 (2020) e006631.

[3] V. Ganyukov, V. Sucato, I. Vereshchagin, N. Kochergin, R. Tarasov, D. Shukevic, A. Shilov, I. Ganyukov, R. Kornelyuk, D. Diana, G. Vadala, A.R. Galassi, Outcome of extracorporeal membrane oxygenation support for high-risk percutaneous coronary intervention in non-ST-segment elevation acute coronary syndrome, J. Cardiovasc. Med. (Hagerstown) 22 (5) (2021) 423–424. May 1.

[4] Giuseppe Di Pasquale, Rossana De Palma, Daniela Fortuna, et al., Effetti indiretti della pandemia COVID-19 sulla mortalità cardiovascolare, G. Ital. Cardiol. 22 (3) (2021) 188–192.

[5] V. Sucato, F. Comparato, A. Ortello, A.R. Galassi, Myocardical Infarction with Non-Obstructive Coronary Arteries (MINOCA): pathogenesis, diagnosis and treatment, Curr. Probl. Cardiol. 49 (7) (2024) 102583.

[6] ISS, Sistema di sorveglianza integrata Covid- 19. Impatto dell' epidemia covid-19 sulla mortalita totale della popolazione residente. Anni 2020–2021 e Gennaio 2022. Report IS TAI. 2 Marzo, 2022.

[7] G.G. Secco, C. Locchi, R. Parisi, et al., Decrease and delay in hospitalization for acute coronary syndromes during the 2020 SARS-CoV-2 pandemic, Can. J. Cardiol. 36 (7) (2020) 1152–1155. Jul.

[8] Mattioli AV, Palmiero P, Manfrini O, et al. Mediterranean diet impact on cardiovascular diseases: a narrative review. J. Cardiovasc. Med. (Hagerstown) 2017 Dec;18(12):925–9359.

[9] Luca Fileti, Sabine Vecchioa, Carolina Moretti, et al., Impact of the COVID-19 pandemic on coronary invasive procedures at two Italian high-volume referral centers, J. Cardiovasc. Med. 21 (2020) 869–873.

[10] D.M. Weinberger, J. Chen, T. Cohen, et al., Estimation of excess deaths associated with the COVID-19 pandemic in the United States, March to May 2020, JAMA Intern. Med. 180 (2020) 1336–1344.

[11] S.H. Woolf, D.A. Chapman, R.T. Sabo, D.M. Weinberger, L. Hill, Excess deaths from COVID-19 and other causes, March–April 2020, JAMA 324 (2020) 510–513.

[12] S.H. Woolf, D.A. Chapman, R.T. Sabo, et al., Excess deaths from COVID-19 and other causes. March-July 2020, JAMA 324 (2020) 1562–1564.

[13] R.K. Wadhera, C. Shen, S. Gondi, S. Chen, D.S. Kazi, R.W. Yeh, Cardiovascular deaths during the COVID- 19 pandemic in the United States, JAm Coll Cardiol 77 (2021) 159–169.

[14] J. Wu, M.A. Mamas, M.O. Mohamed, et al., Place and causes of acute cardiovascular mortality during the COVID-19 pandemic, Heart 107 (2021) 113–119.

[15] V. Sucato, S. Evola, A. Quagliana, et al., Comparison of coronary artery flow impairment in diabetic and hypertensive patients with stable microvascular angina, Eur. Rev. Med. Pharmacol. Sci. 18 (23) (2014) 3687–3689.

[16] O. De Filippo, F. D' Ascenzo, F. Angelini, et al., Reduced rate of hospital admissions for ACS during Covid-19 outbreak in Northern Italy, N. Engl. J. Med. 383 (2020) 88–89.

[17] A.S. Bhatt, A. Moscone, E.E. McElrath, et al., Fewer hospitalizations for acute cardiovascular conditions during the COVID-19 pandemic, JAm Coll Cardiol 76 (2020) 280–288.

[18] G. Pessoa-Amorin, C. Camm, P. Gajendragadkar, et al., Admission of patients with STEMI since the outbreak of the COVID-19 pandemic: a survey by the European Society of Cardiology, Eur Heart J Qual Care Clin Outcomes 6 (2020) 210–216.

[19] S. Garcia, M.S. Albaghdadi, P.M. Meraj, et al., Reduction in ST-segment elevation cardiac catheterization laboratory activations in the United States during COVID-19 pandemic, JAm Coll Cardiol 75 (2020) 2871–2872.

[20] G. De Luca, M. Verdoia, M. Cercek, et al., Impact of COVID-19 pandemic on mechanical reperfusion for patients with STEMI, J. Am. Coll. Cardiol. 76 (2020) 2321–2330.

[21] M. Katsoulis, M. Gomes, A.G. Lai, et al., Estimating the effect of reduced attendance at emergency departments for suspected cardiac conditions on cardiac mortality during the COVID-19 pandemic, Circ Cardiovase Qual Outcomes 14 (2021) 705–708.

[22] E. Baldi, G. Sechi, C. Mare, et al., Lombardia CARe researchers. Out-of-hospital cardiac arrest during the Covid-19 outbreak in Italy, N. Engl. J. Med. 382 (2020) 496–498.

[23] V. Sucato, E. Corrado, C. Castellana, et al., Real-world use of ticagrelor and prasugrel in patients with NSTEMI undergoing percutaneous coronary intervention, J. Cardiovasc. Med. (Hagerstown) 18 (6) (2017) 450–451. Jun.

[24] W. Cheng, Z. Zhang, W. Cheng, et al., Associations of leisure-time physical activity with cardiovascular mortality: a systematic review and meta-analysis of 44 prospective cohort studies, Eur. J. Prev. Cardiol. 25 (2018) 1864–1872.

[25] S.K. Brooks, R.K. Webster, L.E. Smith, et al., The psychological impact of quarantine and how to reduce it: rapid review of the evidence, Lancet 395 (2020) 912–920.

[26] C. Rafanelli, R. Roncuzzi, Y. Milaneschi, et al., Stressful life events, depression and demoralization as risk factors for acute coronary heart disease, Psychother. Psychosom. 74 (2005) 179–184.

[27] P.D. L'Angiocola, M. Monti, COVID-19: the critical balance between appropriate governmental restrictions and expected economic, psychological and social consequences in Italy. Are we going in the right direction? Acta Biomed 91 (2020) 35–38.