

## Editorial

## Direct and indirect effects of COVID-19 on acute coronary syndromes: Can we pick the worst?



Martino Pepe<sup>a</sup>, Giacomo Frati<sup>b,c</sup>, Giuseppe Biondi-Zoccai<sup>b,d,\*</sup>, Nicola Corcione<sup>e,f</sup>, Arturo Giordano<sup>e,f</sup>

<sup>a</sup> Cardiovascular Diseases Section, Department of Emergency and Organ Transplantation (DETO), University of Bari, Bari, Italy

<sup>b</sup> Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy

<sup>c</sup> IRCCS NEUROMED, Pozzilli, Italy

<sup>d</sup> Mediterranea Cardiocentro, Naples, Italy

<sup>e</sup> Unità Operativa di Interventistica Cardiovascolare, Pineta Grande Hospital, Castel Volturno, Italy

<sup>f</sup> Unità Operativa di Emodinamica, Santa Lucia Hospital, San Giuseppe Vesuviano, Italy

### *To lose patience is to lose the battle*

Mahatma Gandhi

Since December 2019, COronaVirus Disease-2019 (COVID-19) due to Severe Acute Respiratory Syndrome-CoronaVirus-2 (SARS-CoV-2) has rapidly evolved into a global pandemic, carrying a double threat: the high morbidity and mortality of the COVID-19 itself and the shift of attention and resources away from other diseases [1].

A substantial reduction of hospital admissions for acute coronary syndromes (ACS) has been reported in Italy as well as elsewhere during the first (and so far the hardest) COVID-19 outbreak [2]. Fear of in-hospital contagion, overload of emergency medical systems (EMS), and restructuring of healthcare organizations are the conjectured hypotheses to explain the decrease of ACS admissions [3]. Some effects of the national lockdown such as the reduction of air pollution, the low level of physical activity, and a more relaxed lifestyle have been also assumed to have beneficially influenced ACS incidence (Fig. 1) [4,5]. Yet, the dark side of the moon is still elusive, as outcome data of patients with ACS who did not access medical care are very challenging to obtain. Conversely, clinical features and short-term prognosis of patients hospitalized for ACS in the middle of the pandemic are of great interest and are showing up.

In this issue, D'Ascenzo and colleagues report results of a multicenter registry including all-consecutive patients admitted for ACS to 18 Northern Italy hospitals from February 20th to May 3rd, 2020 [6]. The study population also included 67 patients affected by COVID-19. Clinical characteristics and in-hospital outcome of the “case period” cohort were compared with patients admitted for ACS during a “same-year control period” (January 1st to February 19th, 2020) and a “previous-

year control period” (February 20th to May 3rd, 2019). In the pandemic context a significantly higher rate of all-cause death was observed relative to the control time intervals. Remarkably, this difference was entirely driven by the higher mortality of COVID-19 patients. As a confirmation, the authors demonstrated, by mean of a multivariable regression analysis, that being admitted for ACS during the “case period” was not associated per se with increased mortality.

This novel piece of evidence is far from obvious, as with the objective of limiting the spread of SARS-CoV-2 infection and continuing the provision of timely access to care for patients with ACS, traditional networks have been quickly reorganized by centralizing urgent activities into few *macrohubs* centers with the remaining hospitals acting as *spoke centers* [7]. Along these lines, the main findings of the paper by D'Ascenzo and coauthors support the hypothesis that the restructuring of healthcare systems, which also required the reassessment of the EMS and the adoption of new in-hospital care pathways, proved effective and favorably impacted on the difficult management of a time dependent disease like ACS. Moreover, several recent pieces of evidence suggest a strong interaction between COVID-19 infection and cardiac damage: from one side, COVID-19 positive patients with previous cardiovascular diseases faced a worse prognosis and, from the other, acute myocardial injury proved to be a common finding in COVID-19 patients [8].

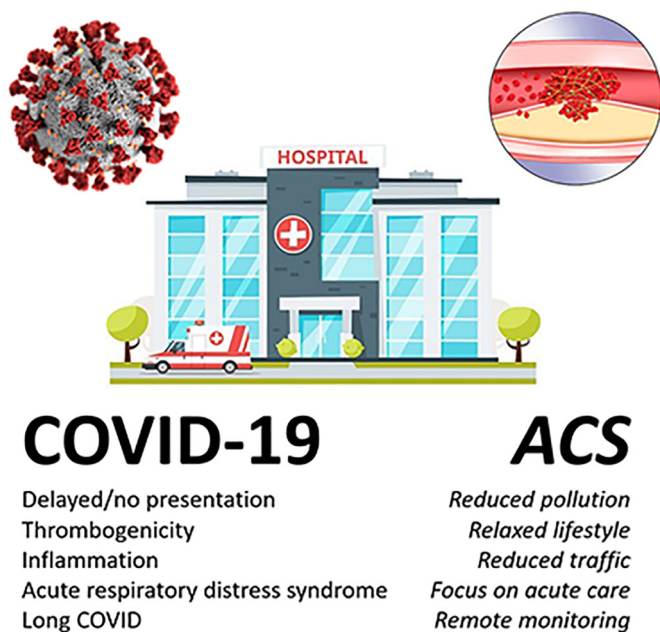
The pathogenesis of cardiac involvement in COVID-19 remains currently under investigation. The most supported mechanisms to explain the high incidence of ACS in COVID-19 patients are cytokine storm and augmented blood thrombogenicity due to the hyperactivation of the immune system, which could contribute to the destabilization of atherosclerotic plaques in the epicardial vessels, as well as hypoxia

DOI of original article: <https://doi.org/10.1016/j.ijcard.2021.03.063>.

\* Corresponding author at: Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Corso della Repubblica 79, 04100 Latina, Italy.  
E-mail address: [giuseppe.biondizoccai@uniroma1.it](mailto:giuseppe.biondizoccai@uniroma1.it) (G. Biondi-Zoccai).

<https://doi.org/10.1016/j.ijcard.2021.04.036>

0167-5273/© 2021 Elsevier B.V. All rights reserved.



**Fig. 1.** Interplay between different patient, physician, and management factors on the diagnosis and treatment of patients with acute coronary syndromes (ACS) in the COronaVirus Disease-2019 (COVID-19) era.

consequent to respiratory failure and hemodynamic instability which might have contributed to the non-negligible increase of type 2 acute myocardial infarction cases among COVID-19 patients [8].

In line with the current literature, D'Ascenzo and colleagues reported higher rates of in-hospital all-cause death in patients suffering from both ACS and COVID-19 infection; furthermore, these patients more frequently faced arrhythmic episodes, cardiogenic and septic shock, and were more often treated with invasive and non-invasive ventilation. The idea that these findings could merely be the “sum” of the effects of two coexisting diseases seems in our opinion an oversimplification. Recent evidences suggest indeed the presence in COVID-19 patients of a higher susceptibility to myocardial infarction-related mechanical and arrhythmic complications (such as ventricular arrhythmias and cardiac arrest) and of a greater myocardial damage, especially in the setting of ST elevation-segment myocardial infarction, as attested by lower left ventricle ejection fraction and increased troponin levels. The proposed underlying causes for the worse outcome of ACS patients with COVID-19 are several: exacerbation of myocardial ischemia due to the hypoxic state, abnormal host immune response, electrolyte imbalance, intravascular volume depletion, and sides effects of COVID-19 related drugs. Indeed, it remains to be seen whether escalating to invasive management strategies is warranted in ACS associated with acute COVID-19 [9,10].

In summary, this intriguing paper by D'Ascenzo et al. allows some relevant considerations: firstly, patients with both COVID-19 and ACS faced worse prognosis, as expected and confirmed by most of the recent literature; secondly, the outcome of patients with “ACS only” who accessed North Italian hospitals during the first peak of the pandemic was not affected by either the healthcare reorganization and the reallocation of the resources. Nevertheless, the reduction of hospital admissions for ACS during the COVID-19 outbreak has been assessed as a matter of fact and, as mentioned above, partly attributed to the fear of

in-hospital infection. Despite data on in-hospital COVID-19 contagion being scant and very challenging to interpret in view of the long and variable incubation period of the disease, the choice to exchange a potential infectious risk for the concrete risk of rejecting the treatment for a life-threatening disease like ACS seems not supported by the current evidences. The danger of this choice can be poignantly summarized by the saying “*jumping out of the frying pan into the fire!*” Since the specialized scientific literature is out of layman's reach and we are nowadays still in the middle of the third wave of COVID-19, we firmly believe that noteworthy and reassuring messages such those brought by this important paper would deserve to be conveniently publicized by mass media.

#### Funding

None.

#### Declaration of Competing Interest

Giuseppe Biondi-Zoccai has consulted for Cardionovum, Innovheart, Meditrial, Opsens Medical, and Replycare.

#### References

- [1] G. Biondi Zoccai, G. Landoni, R. Carnevale, E. Cavarretta, S. Sciarretta, G. Frati, SARS-CoV-2 and COVID-19: facing the pandemic together as citizens and cardiovascular practitioners, *Minerva Cardioangiol.* 68 (2020) 61–64.
- [2] S. De Rosa, C. Spaccarotella, C. Basso, M.P. Calabrò, A. Curcio, P.P. Filardi, M. Mancone, G. Mercurio, S. Muscoli, S. Nodari, R. Pedrinelli, G. Sinagra, C. Indolfi, Società Italiana di Cardiologia and the CCU Academy investigators group, Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era, *Eur. Heart J.* 41 (2020) 2083–2088.
- [3] M. Pepe, C. Maroun-Eid, R. Romero, R. Arroyo-Espiguero, I. Fernández-Rozas, A. Aparisi, V.M. Becerra-Muñoz, M. García Aguado, G. Brindicci, J. Huang, E. Alfonso-Rodríguez, A.F. Castro-Mejía, S. Favretto, E. Cerrato, P. Albiol, S. Raposeiras-Roubin, O. Vedia, G. Feltes Guzmán, A. Carrero-Fernández, C. Perez Cimarra, L. Buzón, J.L. Jativa Mendez, M. Abumayyaleh, E. Romagnoli, G. Frati, Zoccai G. Biondi, P.L. Nestola, G. Biondi-Zoccai, I.J. Núñez-Gil, Clinical presentation, therapeutic approach, and outcome of young patients admitted for COVID-19, with respect to the elderly counterpart, *Clin. Exp. Med.* (2021) 1–20.
- [4] A. Giordano, G. Biondi-Zoccai, G. Frati, A.L. Bartorelli, Management of Structural Heart Disease and Acute Coronary Syndromes in the COVID-19 Pandemic, *Curr. Atheroscler. Rep.* 22 (2020) 29.
- [5] F. Versaci, A. Gasparone, A. Danesi, F. Ferranti, M. Mancone, E. Mariano, F.L. Rotolo, C. Musto, I. Proietti, A. Berni, C. Trani, S.C. Sergi, G. Speciale, G. Tanzilli, F. Tomai, A.D. Di Giosa, G. Marchegiani, S. Calcagno, E. Romagnoli, G. Frati, Zoccai G. Biondi, Impact of temporary traffic bans on the risk of acute coronary syndromes in a large metropolitan area, *Panminerva Med.* 62 (2020) 252–259.
- [6] F. D'Ascenzo, O. De Filippo, A. Borin, L. Barbieri, M. Adamo, N. Morici, A. Truffa Giachet, M. Iannaccone, G. Crimi, L. Gaido, P.P. Bocchino, C.A. Privato, G. Campo, D. Trabattoni, A. Chieffo, N. Gaibazzi, F. Angelini, A. Rubboli, A. Rognoni, G. Musumeci, F. Ugo, S. Gili, B. Cortese, P. Vadalà, V. Dusi, G. Gallone, G. Patti, G.M. de Ferrari, Impact of COVID-19 pandemic and infection on in hospital survival for patients presenting with Acute Coronary Syndromes: a multicenter registry, *Int. J. Cardiol.* (2021) <https://doi.org/10.1016/j.ijcard.2021.03.063> PMID: 33794235; PMCID: PMC8006512.
- [7] G.G. Stefanini, E. Azzolini, G. Condorelli, Critical organizational issues for cardiologists in the COVID-19 outbreak: a frontline experience from Milan, Italy, *Circulation* 141 (2020) 1597–1599.
- [8] Y. Sandoval, J.L. Januzzi Jr., A.S. Jaffe, Cardiac troponin for assessment of myocardial injury in COVID-19: JACC review topic of the week, *J. Am. Coll. Cardiol.* 76 (2020) 1244–1258.
- [9] A.G. Marullo, E. Cavarretta, G. Biondi Zoccai, M. Mancone, M. Peruzzi, F. Piscioneri, P. Sartini, F. Versaci, A. Morelli, F. Miraldi, G. Frati, Extracorporeal membrane oxygenation for critically ill patients with coronavirus-associated disease 2019: an updated perspective of the European experience, *Minerva Cardioangiol.* 68 (2020) 368–372.
- [10] L. Cabrini, W. Ageno, S. Balbi, F. Baruzzi, E. Candeloro, C. Capra, F. Carimati, B. Castiglioni, V. Conti, R. De Ponti, D. Franchi, G. Gini, A. Giorgianni, M. Sartorelli, G. Landoni, D. Locatelli, L. Maffioli, R. Pradella, P. Severgnini, M. Tozzi, M. Versino, G. Zocchi, A. Zoli, Caring for acute coronary syndrome and other time-sensitive medical emergencies during the coronavirus disease 2019 pandemic in Northern Italy: report from a hub centre, *Minerva Cardioangiol.* (2020 Dec 1) <https://doi.org/10.23736/S0026-4725.20.05384-0> Epub ahead of print.