EDITORIAL

# Myocardial infarction with nonobstructive coronary arteries in the era of COVID-19

Giampaolo Niccoli, Filippo L. Gurgoglione

Division of Cardiology, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy

**RELATED ARTICLE**

by Bil et al

Myocardial infarction with nonobstructive coronary arteries (MINOCA) is a disease defined as the evidence of myocardial infarction (MI) according to the fourth universal definition of MI,[1] together with the absence of obstructive coronary artery stenosis on coronary angiography.[2] MINOCA is a heterogeneous conundrum of clinical conditions with different pathophysiology, natural history, and prognosis.[3] COVID-19 has revolutionized our lives, as it is capable of causing multisystem complications, including a large variety of cardiac disorders.[4] Of note, a close link between COVID-19 and a predisposition to the development of MINOCA has been supported by multiple reports.[5,6] However, there are no clear data as to whether the patients with MINOCA treated in the era of COVID-19 differ from those treated before the pandemic in terms of clinical characteristics and outcomes.

In this issue of *Polish Archives of Internal Medicine*, Bil et al[7] attempted to answer this question by means of comparing the clinical characteristics, management, and prognosis of 3178 patients with MINOCA enrolled in the Polish Registry of Acute Coronary Syndromes (PL-ACS) before (2019) and during the COVID-19 pandemic (2020). The large sample size of the PL-ACS is a major strength of the study, allowing the authors to compare significant clinical, epidemiological, and prognostic features.

From a clinical standpoint, in line with the literature,[8] the current study emphasized that MINOCA is a frequent cause of MI, accounting for nearly 6% of all MI cases. Of note, clinical characteristics were similar in the MINOCA patients treated before and during the COVID-19 pandemic, except for a slightly higher prevalence of hypercholesterolemia and a lower rate of a family history of cardiovascular disease in 2019 as compared with 2020.

From an epidemiologic point of view, this study provided robust evidence of the impact of the COVID-19 pandemic on the health care system, as reflected by a striking decrease in the number of both elective outpatient clinical visits and urgent medical procedures.[9] In particular, the authors reported an impressive 37.5% reduction in MI cases in 2020 as compared with 2019, along with a lower prevalence of MINOCA during the COVID-19 pandemic (2020) than in the year before its outbreak. At first glance, this finding is in contrast with recent reports showing a higher prevalence of MINOCA in patients with COVID-19, as compared with those without the disease.[5,6] Two major hypotheses, linked with patient clinical characteristics and health care system organization, might be advocated to explain these findings. On the one hand, the patients with MINOCA frequently presented with non–ST-segment elevation MI (NSTEMI), usually associated with milder symptoms than ST-segment elevation MI (STEMI), and they were less likely to report to the hospital due to the fear of contracting COVID-19. On the other hand, especially during the first wave of the pandemic, health care networks profoundly changed the usual management of patients with MI, often reserving mechanical coronary reperfusion for patients with suspected STEMI and favoring the pharmacological approach in those with NSTEMI.[10]

Of note, even though MINOCA has been considered a benign condition for a long time, a growing body of evidence shows that it is associated with a poor prognosis, with a similar rate of major adverse cardiovascular events at follow-up to that reported in patients with MI with obstructive coronary artery disease. In particular, the mortality rate at 1 year was 4.7% in the pivotal ACUITY trial[11] and 3.5% in a large metanalysis by Pasupathy et al.[12] In the current study, Bil et al[7] reported a mortality rate of 9.9% at 12 months in the overall MINOCA population. Some putative mechanisms may be implied to explain the excess mortality rate in the PL-ACS cohort, as compared with the aforementioned studies. First,

Correspondence to:
Giampaolo Niccoli, MD, PhD, FESC, Department of Cardiology, Azienda Ospedaliero-Universitaria di Parma, Via Gramsci 14, 43126 Parma, Italy, phone: +39 0521 702070, email: giampaolo.niccoli@unipr.it
**Received:** April 2, 2023.
**Accepted:** April 3, 2023.
**Published online:** May 23, 2023.
Pol Arch Intern Med. 2023; 133 (5): 16505
doi:10.20452/pamw.16505
Copyright by the Author(s), 2023

MINOCA is a heterogeneous syndrome, caused by distinct etiologies demanding a multimodality diagnostic approach and different management and therapeutic strategies. No identification of a precise mechanism underlying MINOCA in this cohort of patients probably precluded the implementation of a personalized therapy, leading to subsequent worse outcomes. Second, COVID-19 might have played a crucial role in aggravating the prognosis in this population, as revealed by the higher rate of in-hospital stroke, together with a trend toward worse 12-months prognosis in 2020, as compared with 2019 ($P$ = 0.09). From a mechanistic point of view, COVID-19 and MINOCA share common pathophysiologic foundations. In detail, endothelial cells, responsible for vascular homeostasis, are the main target of COVID-19,[13] and their damage results in the activation and dysfunction of the endothelium, which is also a crucial step toward the development of MINOCA.[2] Furthermore, COVID-19 has the potential to promote a proinflammatory and prothrombotic milieu, characterized by diffuse endotheliitis, inflammatory cell recruitment, and widespread thrombotic microangiopathy,[14] which are also the hallmarks of MINOCA.[2] Finally, COVID-19 has been linked to an enhanced risk of particular mechanisms of MINOCA, such as coronary artery plaque rupture, epicardial coronary spasm, and spontaneous coronary artery dissection.[15]

However, the vast majority of these considerations remains largely speculative, as the current study has some limitations. First, the PL-ACS did not provide information on the number of patients with MINOCA and concomitant COVID-19. Second, an extensive diagnostic workup aimed at elucidating the underlying mechanism of MINOCA in this cohort of patients was not performed. Third, relevant clinical end points, such as the rate of recurrent MI and rehospitalization for angina along with the need for percutaneous coronary interventions have not been evaluated at the follow-up.

In conclusion, the study by Bil et al[7] provided relevant epidemiologic information, confirming that MINOCA is a frequent cause of MI, associated with a high mortality rate at the 12-month follow-up. Furthermore, the authors demonstrated that during the COVID-19 pandemic, MINOCA events were less prevalent, but they were associated with a slightly worse prognosis as compared with the prepandemic period. However, the inherent limitations of the current study did not allow for drawing definitive conclusions. Future mechanistic and clinical studies are largely awaited to shed light on the link between MINOCA and COVID-19 pathophysiology, to delineate distinct MINOCA phenotypes in order to refine risk stratification in patients with this disease, and to identify novel therapeutic targets.

## ARTICLE INFORMATION

**DISCLAIMER** The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

**CONFLICT OF INTEREST** None declared.

**OPEN ACCESS** This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material, provided the original work is properly cited, distributed under the same license, and used for noncommercial purposes only. For commercial use, please contact the journal office at pamw@mp.pl.

**HOW TO CITE** Niccoli G, Gurgoglione FL. Myocardial infarction with nonobstructive coronary arteries in the era of COVID-19. Pol Arch Intern Med. 2023; 133: 16505. doi:10.20452/pamw.16505

## REFERENCES

1 Thygesen K, Alpert JS, Jaffe AS, et al; ESC Scientific Document Group. Fourth universal definition of myocardial infarction (2018). Eur Heart J. 2019; 40: 237-269.

2 Scalone G, Niccoli G, Crea F. Editor's Choice – Pathophysiology, diagnosis and management of MINOCA: an update. Eur Heart J Acute Cardiovasc Care. 2019; 8: 54-62.

3 Crea F, Montone RA, Niccoli G. Myocardial infarction with non-obstructive coronary arteries: dealing with pears and apples. Eur Heart J. 2020; 41: 879-881.

4 Xie Y, Xu E, Bowe B, Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. Nat Med. 2022; 28: 583-590.

5 Popovic B, Varlot J, Metzdorf PA, et al. Changes in characteristics and management among patients with ST-elevation myocardial infarction due to COVID-19 infection. Catheter Cardiovasc Interv. 2021; 97: E319-E326.

6 Manolis AS, Manolis AA, Manolis TA, Melita H. COVID-19 and acute myocardial injury and infarction: related mechanisms and emerging challenges. J Cardiovasc Pharmacol Ther. 2021; 26: 399-414.

7 Bil J, Kern A, Bujak K, et al. Clinical characteristics and 12-month outcomes of patients with myocardial infarction with nonobstructive coronary arteries before and during the COVID-19 pandemic. Pol Arch Intern Med. 2023; 133: 16405.

8 Tamis-Holland JE, Jneid H, Reynolds HR, et al. Contemporary diagnosis and management of patients with myocardial infarction in the absence of obstructive coronary artery disease: a scientific statement from the American Heart Association. Circulation. 2019; 139: e891-e908.

9 De Filippo O, D'Ascenzo F, Angelini F, et al. Reduced rate of hospital admissions for ACS during COVID-19 outbreak in Northern Italy. N Engl J Med. 2020; 383: 88-89.

10 Campo G, Fortuna D, Berti E, et al. In- and out-of-hospital mortality for myocardial infarction during the first wave of the COVID-19 pandemic in Emilia-Romagna, Italy: a population-based observational study. Lancet Reg Health Eur. 2021; 3: 100055.

11 Planer D, Mehran R, Ohman EM, et al. Prognosis of patients with non-ST-segment-elevation myocardial infarction and nonobstructive coronary artery disease: propensity-matched analysis from the Acute Catheterization and Urgent Intervention Triage Strategy Trial. Circ Cardiovasc Interv. 2014; 7: 285-293.

12 Pasupathy S, Air T, Dreyer RP, et al. Systematic review of patients presenting with suspected myocardial infarction and non obstructive coronary arteries. Circulation. 2015; 131: 861-870.

13 Xu SW, Ilyas I, Weng JP. Endothelial dysfunction in COVID-19: an overview of evidence, biomarkers, mechanisms and potential therapies. Acta Pharmacol Sin. 2023: 44: 695-709.

14 Kamel MH, Yin W, Zavaro C, et al. Hyperthrombotic milieu in COVID-19 patients. Cells. 2020; 9: 2392.

15 Atri D, Siddiqi HK, Lang JP, et al. COVID-19 for the cardiologist: basic virology, epidemiology, cardiac manifestations, and potential therapeutic strategies. JACC Basic Transl Sci. 2020; 5: 518-536.