ORIGINAL ARTICLE

Clinical characteristics and 12-month outcomes of patients with myocardial infarction with nonobstructive coronary arteries before and during the COVID-19 pandemic

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KEY WORDS

acetylcholine, coronary spasm, major adverse cardiovascular events, microcirculation dysfunction, MINOCA

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ABSTRACT

INTRODUCTION SARS-CoV-2 infection is associated with an increased risk of thromboembolic complications. Thromboembolism is one of the possible causes of myocardial infarction with nonobstructive coronary arteries (MINOCA).

OBJECTIVES We aimed to compare the characteristics and 12-month clinical outcomes of patients with MINOCA treated before and during the COVID-19 pandemic.

PATIENTS AND METHODS We retrospectively analyzed data of 51 734 patients with acute myocardial infarction registered in the nationwide Polish Registry of Acute Coronary Syndromes database in 2019 and 2020. The final study group included 3178 patients with MINOCA. We compared the baseline characteristics, management strategies, and 12-month clinical outcomes of the MINOCA patients treated before (2019) and during the COVID-19 pandemic (2020).

RESULTS The rate of MINOCA was higher in 2019 than in 2020 (6.3% vs 5.9%; $P = 0.03$). The only difference between the groups was a higher hypercholesterolemia rate before the pandemic (33.9% vs 28.2%; $P < 0.001$). In-hospital stroke was observed more frequently during the pandemic (0% vs 0.3%; $P = 0.01$), whereas other in-hospital complications were similar between the groups. Most patients were discharged on aspirin (85.6%), a β-blocker (73.1%), an angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (70.2%), and a statin (62.7%), but only 50.6% of the participants received a $P2Y_{12}$ inhibitor. There was no difference in 12-month all-cause mortality between the patients with MINOCA treated before and during the pandemic (9.2% vs 11%; $P = 0.09$).

CONCLUSIONS We observed a lower percentage of MINOCA cases and higher in-hospital stroke rates in the MINOCA patients treated during the COVID-19 pandemic (2020). The possible association between worse clinical outcomes of the MINOCA patients treated during the pandemic and the increased risk for thromboembolic complications of SARS-CoV-2 infection needs further evaluation.

WHAT'S NEW?

Patients with myocardial infarction with nonobstructive coronary arteries (MINOCA) still pose a challenge to modern catheterization laboratories because determining the real cause of MINOCA is often difficult. COVID-19 is associated with increased thromboembolic risk, and thromboembolism is one of the causes of MINOCA. We analyzed over 50 000 patients with acute myocardial infarction treated before and during the COVID-19 pandemic (2019 vs 2020). The rate of MINOCA was higher in 2019 than in 2020, but the patients' characteristics did not differ significantly, except for the higher rate of hypercholesterolemia before the pandemic. In-hospital complications were similar between the groups, with the exception of in-hospital stroke, which occurred more often during the pandemic. In the 12-month follow-up, we did not observe higher mortality among the MINOCA patients treated during the pandemic. The main novelty of our study stems from providing the most recent characteristics and outcomes of Polish patients with MINOCA.

INTRODUCTION Myocardial infarction (MI) with nonobstructive coronary arteries (MINOCA) is a heterogeneous syndrome evoked via several different pathophysiological pathways. It is defined by the presence of clinical or laboratory evidence of MI and no significant coronary artery stenosis (lesions with diameter stenosis <50%).[1]

In recent years, focus on patients with MINOCA has increased. The prevalence of MINOCA among all MI cases is estimated to range between 5% and 15%.[2] Unfortunately, this syndrome is related to various conditions that are challenging to identify, such as coronary microcirculatory dysfunction, epicardial coronary spasm, or plaque erosion.[3] It is possible that inflammation also has an impact on the MINOCA prevalence.[4] Quesada et al[5] recently reported that the prevalence of ST-segment elevation MI (STEMI) with no culprit lesion on angiography among patients with COVID-19 was 21%. MINOCA is no longer perceived as a benign disorder, and cardiologists acknowledged that patients with this syndrome are characterized by long-term outcomes similar to those observed in individuals with obstructive coronary artery disease. In a recent Italian study,[6] the rate of cardiac death was lower in the MINOCA group than in individuals with obstructive coronary artery disease (4.2% vs 8.4%; $P = 0.03$); however, there were no significant differences with respect to other end points, such as recurrent MI (17.3% vs 25.4%; $P = 0.18$), ischemic stroke (9.5% vs 3.7%; $P = 0.12$), or all-cause mortality (14.1% vs 20.7%; $P = 0.26$) during a median follow-up of 19.9 years.[6] Other studies also confirmed these findings.[7,8]

SARS-CoV-2 infection is associated with an increased risk of thromboembolic complications. In some patients, thromboembolic processes may be responsible for the development of MINOCA.[9] Other possible causes of MINOCA in the patients with COVID-19 include myocarditis,[10] stress cardiomyopathy in the setting of severe illness,[11] coronary artery plaque rupture, epicardial coronary spasm, spontaneous coronary artery dissection, and nonischemic cardiomyopathy.[12] However, the potential influence of the COVID-19 pandemic on the rate and clinical outcomes of MINOCA remains unknown.

The present study aimed to compare the characteristics and 12-month clinical outcomes of patients with MINOCA treated before and during the COVID-19 pandemic.

PATIENTS AND METHODS **Data source** We retrospectively analyzed data from the Polish Registry of Acute Coronary Syndromes (PL-ACS)—a national, multicenter registry that collects information on patients hospitalized with ACS in Poland.[13] PL-ACS is a joint venture of the Silesian Center of Heart Diseases in Zabrze and the Polish Ministry of Health, managed in cooperation with the National Health Fund (NHF). The registry was established in October 2003. In 2004, it was harmonized with the European Cardiology Audit and Registration Data Standards (CARDS). The present analysis involved consecutive patients included in the registry in 2019 and 2020. At that time, a total of 141 hospitals submitted data to the registry. The data were collected prospectively using electronic case report forms which included, among others, information on the medical history, comorbidities, initial presentation, results of coronary angiography, in-hospital treatment, and in-hospital outcomes. Data on posthospitalization all-cause mortality, including the date of death, were obtained from the NHF. The approval of an ethics committee was not required due to the retrospective design of the analysis.

Study population All patients with a principal diagnosis of STEMI and non-STEMI (NSTEMI) according to the current guidelines of the European Society of Cardiology were considered for analysis. The exclusion criteria comprised age below 18 years at the time of hospitalization, a history of percutaneous coronary intervention (PCI) or coronary artery bypass grafting, as well as out-of-hospital cardiac arrest or heart failure on admission (Killip class 3 or 4). Only the patients who underwent cardiac catheterization were included in the analysis. The final cohort consisted of patients hospitalized for acute myocardial infarction (AMI) without obstructive coronary lesions (<50% diameter stenosis).

Statistical analysis The MINOCA patients included in this analysis were stratified into 2 groups according to the year of admission (2019 vs 2020). Categorical variables were presented as numbers and percentages and were compared using the χ^2 test or Fisher exact test, as appropriate. The normality of data distribution was assessed with the Shapiro–Wilk test. Since all quantitative variables were non-normally distributed, they were expressed as medians and interquartile ranges (IQRs), and the differences between the groups were compared using the Mann–Whitney test. The cumulative 12-month mortality was depicted using the Kaplan–Meier curves. The log-rank test was used

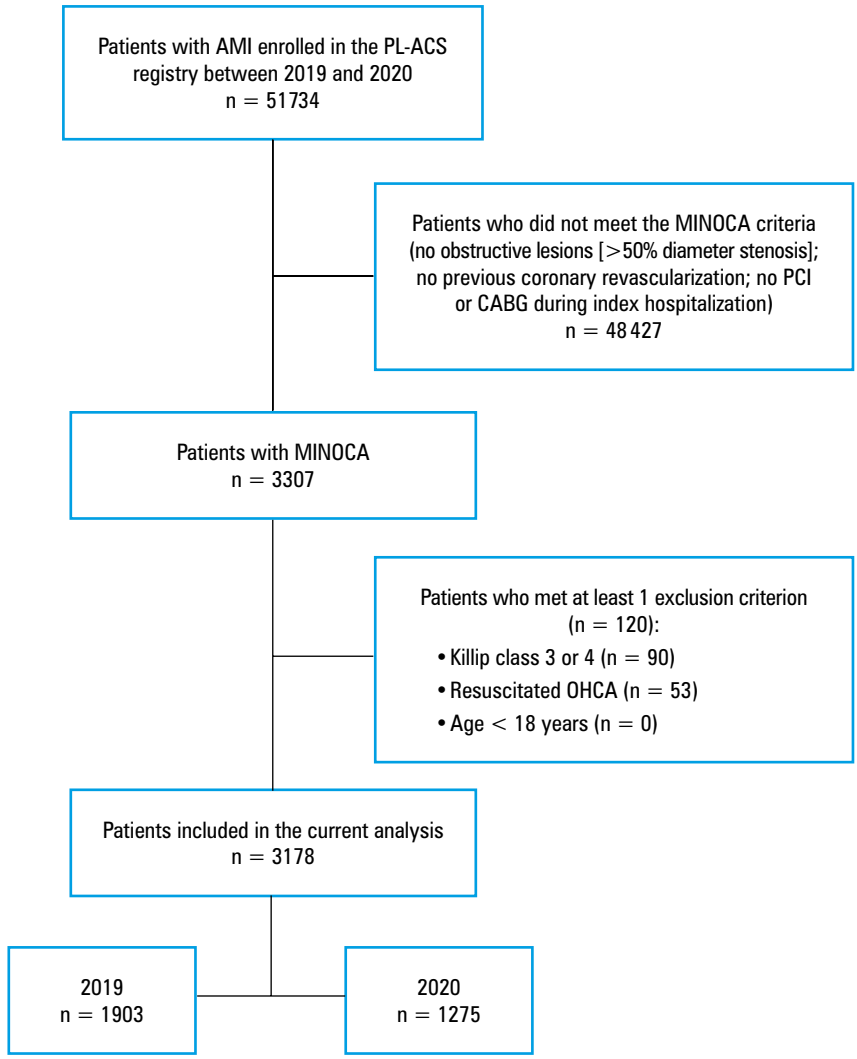

FIGURE 1 Study flowchart

Abbreviations: AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; MINOCA, myocardial infarction with nonobstructive coronary arteries; PCI, percutaneous coronary intervention; PL-ACS, Polish Registry of Acute Coronary Syndromes; OHCA, out-of-hospital cardiac arrest

to compare the 12-month mortality rates between the groups. Moreover, the Cox regression analysis was performed to identify independent factors associated with all-cause mortality at 12 months. Baseline characteristic variables (including demographics, medical history, comorbidities, and initial presentation) that reached a *P* value of less than 0.1 in the univariable model were included in the multivariable analysis. The final multivariable model was obtained using the backward variable selection method. The level of significance was set at a *P* value below 0.05 (2-tailed). All statistical analyses were performed using Statistica version 13.3 (TIBCO Software, Palo Alto, California, United States) and R software (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS **Baseline characteristics** We retrospectively analyzed data of 51 734 patients with AMI included in the nationwide PL-ACS registry in 2019 and 2020. A working diagnosis of MINOCA was made in 3307 patients (6.4% of all AMI patients). After excluding individuals younger than 18 old and those after out-of-hospital cardiac arrest, we finally evaluated 3178 patients with MINOCA (6.1% of the total AMI group) (FIGURE 1). The rate of MINOCA was higher in 2019 (1903/28 115; 6.3%) than in 2020 (1275/20 441; 5.9%; *P* = 0.03).

The median age of the study population was 68 years (IQR, 59.5–76.1), and 56.1% of the patients were women. The most common comorbidities were hypertension (66.3%), a history of smoking (52.2%, including 25.7% of current smokers), hypercholesterolemia (31.6%), type 2 diabetes (18.4%), and atrial fibrillation (13.7%). There were no differences between the groups (MINOCA 2019 vs MINOCA 2020) apart from the rate of hypercholesterolemia (33.9% vs 28.2%; *P* <0.001) and family history of cardiovascular diseases (5% vs 7%; *P* = 0.02) (TABLE 1).

Types of myocardial infarction at presentation Most patients presented with NSTEMI (90.7%), and

TABLE 1 Baseline characteristics of the patients with myocardial infarction with nonobstructive coronary arteries treated before (2019) and during the COVID-19 pandemic (2020)

Parameter		MINOCA patients			*P* value
		Total (n = 3178)	2019 (n = 1903)	2020 (n = 1275)	
Male sex		1396 (43.9)	843 (44.3)	553 (43.4)	0.61
Age, y		68 (59.5–76.1)	67.8 (59.2–76.4)	68.2 (59.9–76)	0.38
BMI, kg/m^2		27.7 (24.7–31.1)	27.7 (24.5–31.1)	27.7 (24.8–31.1)	0.8
Family history of CVD		177 (5.8)	91 (5)	86 (7)	0.02
Smoking	Current smoking	713 (25.7)	414 (25.2)	299 (26.4)	0.26
	Former smoking	736 (26.5)	422 (25.7)	314 (27.7)	
	Never-smoking	1326 (47.8)	805 (49.1)	521 (45.9)	
Hypercholesterolemia		922 (31.6)	589 (33.9)	333 (28.2)	<0.001
Hypertension		2048 (66.3)	1240 (67.2)	808 (65.1)	0.22
Diabetes or prediabetes	Type 2 diabetes	575 (18.4)	355 (19)	220 (17.4)	0.46
	Type 1 diabetes	19 (0.6)	12 (0.6)	7 (0.6)	
	Impaired fasting glucose	54 (1.7)	27 (1.4)	27 (2.1)	
	Impaired glucose tolerance	33 (1.1)	18 (1)	15 (1.2)	
	None	2448 (78.2)	1455 (77.9)	993 (78.7)	
Chronic kidney disease (eGFR <60 ml/min/1.73 m^2)		168 (5.3)	101 (5.3)	67 (5.3)	0.95
Previous myocardial infarction		195 (6.2)	120 (6.3)	75 (5.9)	0.63
Atrial fibrillation		435 (13.7)	257 (13.5)	178 (14)	0.7
Heart failure		242 (7.7)	135 (7.1)	107 (8.5)	0.17
Previous stroke		159 (5)	94 (4.9)	65 (5.1)	0.85
Peripheral artery disease		114 (3.6)	67 (3.5)	47 (3.7)	0.81

Data are presented as number (percentage) or median (interquartile range).

Abbreviations: BMI, body mass index; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; others, see **FIGURE 1**

chest pain was the most common symptom (81%). The median duration of symptoms before admission to the PCI center was 8.2 hours (IQR, 3.9–24.9), and the median door-to-catheter time was 3.7 hours (IQR, 1–13.3). Interestingly, these variables did not differ between the analyzed periods, that is, before and during the pandemic. More details are presented in **TABLE 2**.

In-hospital course The overall all-cause in-hospital death rate was 1.4%, with no significant differences between the groups. However, in-hospital stroke was more frequently observed during the pandemic (0% vs 0.3%; *P* = 0.01). The frequency of other in-hospital complications was similar between the groups. Most participants were discharged on aspirin (85.6%), a β-blocker (73.1%), an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (70.2%), and a statin (62.7%), but only 50.6% of the patients received a $P2Y_{12}$ inhibitor (**TABLE 3**).

Follow-up outcomes and predictive factors The data on 12-month all-cause mortality were available for 3177 patients (99.9%). At the 12-month follow-up, the all-cause mortality rate in the whole study population was 9.9% (n = 315). There was no difference in the 12-month all-cause mortality in the patients with MINOCA treated before and during the pandemic (9.2% vs 11%; *P* = 0.09) (**FIGURE 2**). In the multivariable analysis, we identified the following predictive factors for all-cause death: male sex (hazard ratio [HR], 2.09; 95% CI, 1.43–3.05; *P* <0.001), age (HR, 1.07; 95% CI, 1.05–1.09; *P* <0.001), chronic kidney disease (HR, 2.07; 95% CI, 1.27–3.38; *P* = 0.004), peripheral artery disease (HR, 1.96; 95% CI, 1.1–3.47; *P* = 0.02), chest pain as the predominant symptom before admission (HR, 0.61; 95% CI, 0.42–0.88; *P* = 0.009), systolic blood pressure on admission (HR, 0.99; 95% CI, 0.986–0.9998; *P* = 0.04), heart rate on admission (HR, 1.01; 95% CI, 1.002–1.02; *P* = 0.02), STEMI on admission (HR, 2.10; 95% CI, 1.17–3.79), and ejection fraction (HR, 0.98; 95% CI, 0.97–0.997; *P* = 0.02) (**TABLE 4**).

DISCUSSION

To our best knowledge, this is so far the largest all-comers population study providing data on the occurrence of MINOCA in patients treated before and during the COVID-19 pandemic. MINOCA is a challenging disease associated with significant morbidity and mortality. The concomitance of COVID-19 and MINOCA increases the risk of subsequent adverse events. It was reported that patients with MI and COVID-19 presented significantly higher morbidity and mortality than the patients with MI who did not suffer

TABLE 2 Characteristics of myocardial infarction with nonobstructive coronary arteries

Parameter		MINOCA			*P* value
		Total (n = 3178)	2019 (n = 1903)	2020 (n = 1275)	
MINOCA presentation	STEMI	294 (9.3)	180 (9.5)	114 (8.9)	0.62
	NSTEMI	2884 (90.7)	1723 (90.5)	1161 (91.1)	
Predominant symptoms before admission	Chest pain	2574 (81)	1579 (83)	995 (78)	0.01
	Dyspnea	370 (11.6)	195 (10.2)	175 (13.7)	
	Fatigue	56 (1.8)	32 (1.7)	24 (1.9)	
	Syncope	33 (1)	22 (1.2)	11 (0.9)	
	Other symptoms	111 (3.5)	57 (3)	54 (4.2)	
	No symptoms	34 (1.1)	18 (0.9)	16 (1.3)	
First medical contact	PCI-capable center (self-referral)	281 (8.8)	196 (10.3)	85 (6.7)	<0.001
	PCI-capable center (by EMS)	895 (28.2)	517 (27.2)	378 (29.7)	
	Non-PCI center	1534 (48.3)	930 (48.9)	604 (47.4)	
	Cardiology outpatient clinic	266 (8.4)	131 (6.9)	135 (10.6)	
	Primary health care center	200 (6.3)	128 (6.7)	72 (5.7)	
Duration of symptoms before admission to a PCI center, h		8.2 (3.9–24.9)	8.2 (4–24.3)	8.2 (3.8–26.2)	0.62
Door-to-catheter time, h		3.7 (1–13.3)	3.7 (1–13.6)	3.7 (1–13)	0.76
Killip classification	Class 1	2905 (91.4)	1742 (91.5)	1163 (91.2)	0.75
	Class 2	273 (8.6)	161 (8.5)	112 (8.8)	
Rhythm on ECG	Sinus	2823 (88.9)	1693 (89)	1130 (88.8)	0.89
	Paced	29 (0.9)	19 (1)	10 (0.8)	
	AF/AFI	245 (7.7)	143 (7.5)	102 (8)	
	Other	78 (2.5)	47 (2.5)	31 (2.4)	
QRS changes on ECG	LBBB	143 (4.5)	95 (5)	48 (3.8)	0.26
	RBBB	129 (4.1)	82 (4.3)	47 (3.7)	
	Other QRS changes	513 (16.1)	298 (15.7)	215 (16.9)	
	No QRS changes	2393 (75.3)	1428 (75)	965 (75.7)	
ST-T changes on ECG	ST-segment elevation	312 (9.8)	187 (9.9)	125 (9.8)	0.34
	ST-segment depression	725 (22.8)	432 (22.8)	293 (23)	
	T-wave inversion	419 (13.2)	247 (13)	172 (13.5)	
	Other ST-T changes	1059 (33.4)	616 (32.5)	443 (34.7)	
	No ST-T changes	658 (20.7)	416 (21.9)	242 (19)	
LVEF, %		55 (45–60)	55 (45–60)	54 (45–60)	0.26

Data are presented as number (percentage) or median (interquartile range).

Abbreviations: AF, atrial fibrillation; AFI, atrial flutter; ECG, electrocardiography; LVEF, left ventriculr ejection fraction, EMS, Emergency Medical Service; LBBB, left bundle branch block; NSTEMI, non–ST-segment elevation myocardial infarction; RBBB, right bundle branch block; STEMI, ST-segment elevation myocardial infarction; others, see **FIGURE 1**

from COVID-19.[14] However, our study showed that the percentage of MINOCA was higher in 2019 than in 2020 (6.3% vs 5.9%; *P* = 0.03). The all-cause in-hospital death rate was 1.4%, with no significant differences between the groups. At the 12-month follow-up, the all-cause mortality rate was 9.9% (n = 315). There was no difference in the 12-month all-cause mortality between the patients with MINOCA treated before and during the pandemic, only a trend toward a worse outcome in the patients treated in 2020 was observed (9.2% vs 11%; *P* = 0.09). Notably, the dramatic situation and the reduction in the number of ACS patients presenting to hospitals at the beginning of 2020, which resulted in an increase in mortality, might have largely contributed to the outcomes. The rate of MINOCA was at the lower range of the percentage of cases reported in other studies.[6,15-17] In our analysis, we observed a striking decrease in the number of MI cases by 37.5% (28 115 in 2019 vs 20 441 in 2020), which was also noted in other national registries.[18] The database endorsed by the Association of Cardiovascular Interventions of the Polish Cardiac Society and operated daily by the Jagiellonian University Medical College showed that the COVID-19 pandemic had had an enormous impact on interventional cardiology in Poland. A substantial decrease in the number of coronary angiography and PCI procedures across various indications, as well as underuse of modern imaging and physiological assessment techniques were observed. In comparison with 2019, 2020 brought a substantial decrease (by 25%) in the total number of reported

TABLE 3 In-hospital course and complications

Parameter	MINOCA			*P* value
	Total (n = 3178)	2019 (n = 1903)	2020 (n = 1275)	
Complications				
Cardiogenic shock	6 (0.2)	3 (0.2)	3 (0.2)	0.62
Pulmonary edema	2 (0.1)	1 (0.1)	1 (0.1)	0.78
Acute mitral regurgitation	5 (0.2)	2 (0.1)	3 (0.2)	0.37
Free wall rupture	6 (0.2)	4 (0.2)	2 (0.2)	0.73
Ventricular septal rupture	3 (0.1)	2 (0.1)	1 (0.1)	0.81
Major bleeding	23 (0.7)	14 (0.7)	9 (0.7)	0.92
Outcomes				
In-hospital stroke	4 (0.1)	0	4 (0.3)	0.01
In-hospital recurrent MI	2 (0.1)	1 (0.1)	1 (0.1)	0.78
In-hospital cardiac arrest	19 (0.6)	8 (0.4)	11 (0.9)	0.11
All-cause in-hospital death	46 (1.4)	22 (1.2)	24 (1.9)	0.09
Noncardiovascular death	6 (0.2)	3 (0.2)	3 (0.2)	0.62
Medications at discharge				
Aspirin	2708 (85.6)	1626 (85.9)	1082 (85.1)	0.55
$P2Y_{12}$ inhibitor	1607 (50.6)	994 (52.2)	613 (48.1)	0.02
OAC	434 (13.7)	247 (13)	187 (14.7)	0.17
ACEI or ARB	2231 (70.2)	1352 (71)	879 (68.9)	0.20
β-Blocker	2313 (73.1)	1396 (73.7)	917 (72.1)	0.30
Statin	1993 (62.7)	1201 (63.1)	792 (62.1)	0.57

Data are presented as number (percentage).

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; MI, myocardial infarction; OAC, oral anticoagulant; others, see **FIGURE 1**

coronary angiographies (172 521 vs 130 662), as well as of PCI procedures (101 716 vs 82 349).[14,19] This was also observed in other countries where COVID-19 impacted the unplanned hospitalization rates. Wang et al[20] reported a significant decrease in the overall hospitalization rate (–182 per 100 000), as well as a decline in the rate of unplanned hospitalizations (–39 per 100 000) and hospitalizations due to AMI (–1.32 per 100 000), stroke (–1.51 per 100 000), and heart failure (–8.7 per 100 000). The causes of these findings are multifactorial, and we should mention at least the following: patients' fear of COVID-19 contraction, an excess of prepandemic hospitalizations, as well as pandemic mitigation measures, such as cancellation of nonurgent procedures and treatments. Also, the MINOCA symptoms might not be as severe and persistent as those of acute MI with total occlusion; therefore, it is possible that more patients decided not to report to emergency departments. Moreover, most patients did not present with STEMI, and when SARS-CoV-2 infection was confirmed, coronary angiography was often postponed, and COVID-19 could have been the cause of death. This also might have led to the fewer registered cases of MINOCA.

Previous studies showed increased rates of mortality and complications from acute MI and stroke during the pandemic, as compared with the preceding years.[21-23] Thus, we expected to note an increase in in-hospital mortality rates from urgent, non–COVID-19–related conditions, such as acute MI and stroke. However, we did not find

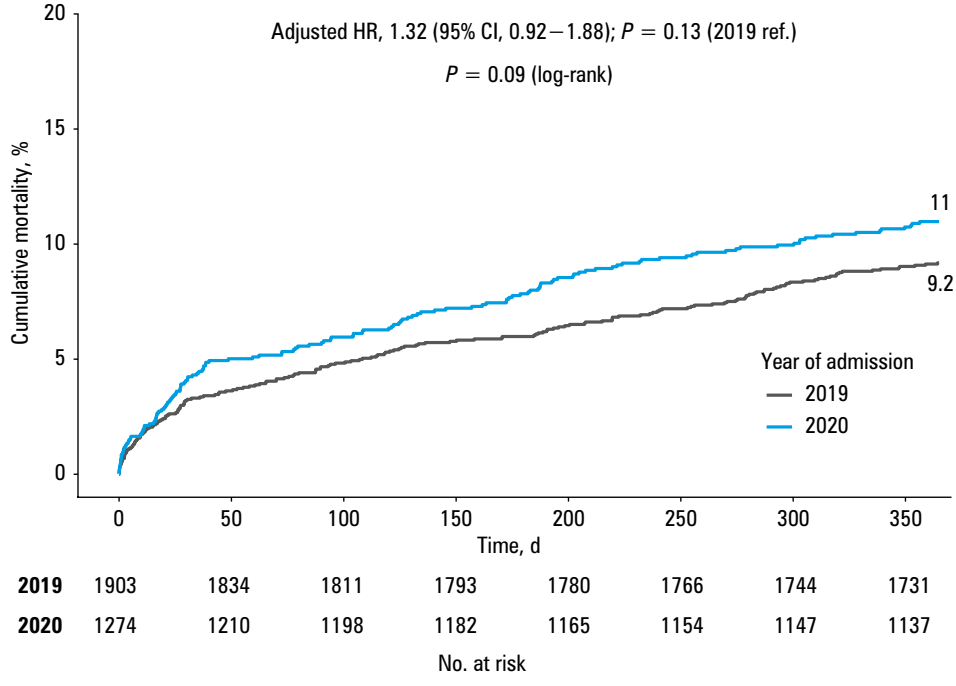

FIGURE 2 Kaplan–Meier curves showing all-cause mortality rates in the patients with myocardial infarction with nonobstructive coronary arteries. Hazard ratio (HR) with a corresponding 95% CI refers to the effect of admission in 2020 (vs 2019) on all-cause mortality at 12 months in the multivariable Cox regression model.

TABLE 4 Factors associated with 12-month all-cause mortality: results of univariable and multivariable Cox regression analyses

Variable	Univariable model		Multivariable model	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Male sex	1.27 (1.02–1.59)	0.03	2.09 (1.43–3.05)	<0.001
Age (per 1-year increase)	1.06 (1.05–1.07)	<0.001	1.07 (1.05–1.09)	<0.001
BMI (per 1 kg/m^2 increase)	0.97 (0.94–1)	0.02	–	–
Family history of heart disease	0.85 (0.5–1.42)	0.53	–	–
Current smoking (vs former or never smoking)	0.72 (0.54–0.97)	0.03	–	–
Hypercholesterolemia	0.89 (0.69–1.15)	0.37	–	–
Hypertension	0.82 (0.65–1.04)	0.10	–	–
Diabetes	1.61 (1.25–2.07)	<0.001	–	–
Chronic kidney disease	3.18 (2.31–4.38)	<0.001	2.07 (1.27–3.38)	0.004
Previous myocardial infarction	1.22 (0.8–1.87)	0.36	–	–
Atrial fibrillation	1.90 (1.46–2.47)	<0.001	1.47 (0.93–2.34)	0.10
Heart failure	2.42 (1.79–3.27)	<0.001	–	–
Previous stroke	1.67 (1.11–2.51)	0.01	–	–
Peripheral artery disease	2.67 (1.8–3.96)	<0.001	1.96 (1.1–3.47)	0.02
Chest pain as the predominant symptom before admission	0.57 (0.45–0.73)	<0.001	0.61 (0.42–0.88)	0.009
PCI-capable center as a first medical contact	1.04 (0.83–1.31)	0.73	–	–
Duration of symptoms before admission to PCI center (per 1-hour increase)	1 (1–1)	0.97	–	–
Killip class 2 (vs class 1)	2.59 (1.95–3.45)	<0.001	–	–
Systolic blood pressure on admission (per 1 mm Hg increase)	0.988 (0.983–0.993)	<0.001	0.993 (0.99–0.9998)	0.04
Heart rate on admission (per 1 bpm increase)	1.01 (1.01–1.02)	<0.001	1.01 (1.002–1.02)	0.02
Rhythm other than sinus	1.52 (1.12–2.06)	0.007	0.64 (0.36–1.15)	0.14
LBBB or RBBB	1.51 (1.07–2.11)	0.02	–	–
STEMI (vs NSTEMI)	2.07 (1.53–2.79)	<0.001	2.10 (1.17–3.79)	0.01
Ejection fraction (per 1% increase)	0.96 (0.95–0.97)	<0.001	0.98 (0.97–0.997)	0.02
Hospital admission in 2020 (vs 2019)	1.21 (0.97–1.51)	0.09	1.32 (0.92–1.88)	0.13

Abbreviations: see TABLES 1 and 2

evidence of significant changes in the percentage of in-hospital mortality or the mean length of hospital stay after the implementation of COVID-19 containment measures, as compared with the prepandemic period.

Nevertheless, we must stress that despite relatively few MINOCA cases, mechanical complications have been observed, such as ventricular septal or free wall rupture. This is in accordance with previous reports and our recent systematic review on MINOCA complications.[24] The literature search revealed 5 cases of intraventricular septal rupture, 3 cases of free wall rupture with pericardial effusion or cardiac tamponade, and 3 cases of bleeding complications (intracerebral or intestinal bleeding). Moreover, the rates of ventricular arrhythmia ranged from 2% to 13.8%, and the in-hospital death rate ranged from 0.9% to 6.4%.[25]

In the present study, the mortality rate among patients with MINOCA was around 10%, depending on the year of admission. On the other hand, in the recently published largest available MINOCA database, the 12-month mortality rate was approximately 3.5%.[8] The difference might have been associated with worse diagnostic methods in Poland, mainly based on echocardiography and coronary angiography, and rarely supported by intravascular imaging and cardiac magnetic resonance. Another reason might be poor long-term monitoring of patients with ACS,[26] since, as previously shown, the patients with close follow-up are characterized by better outcomes in Poland.[27] In our study, the 12-month outcomes tended to be worse for the MINOCA patients treated in 2020, with male sex, age, chronic kidney disease, peripheral artery disease, and STEMI on admission as the most important factors associated with a poor prognosis.

Partially, as mentioned above, it may be due to impaired access to medical care after discharge, but also to the thrombotic risk associated with COVID-19. Early studies regarding SARS-CoV-2 described a correlation between coagulation parameter derangement and worse patient outcomes. Furthermore, postmortem examination of patients who died from COVID-19 demonstrated direct viral infection of the endothelial cells evoking diffuse endothelialitis, microcirculatory dysfunction, and widespread thrombotic microangiopathy. These abnormalities could be prognostic markers of thrombotic complications rather than of bleeding events.[28] Literature data show that patients hospitalized for COVID-19

are characterized by an increased risk of venous thromboembolism (pulmonary embolism and deep vein thrombosis), as well as higher rates of arterial thromboembolism (MI, systemic arterial embolism, stroke, or acute limb ischemia).[29-31]

The present study has some limitations. The first one is its observational design. Second, the follow-up data were taken from the NHF, so we did not have access to detailed information on the causes of death or other end points, such as recurrent MI or repeated coronary angiography. Moreover, the lack of data on cardiac magnetic resonance, intracoronary imaging, microcirculation resistance, and provocative spasm testing prevented us from dividing the patients into subgroups based on the pathophysiological mechanisms. Finally, we did not have information on SARS-CoV-2 infection in the analyzed group of patients with MINOCA.

In conclusion, we observed a lower percentage of MINOCA cases and higher in-hospital stroke rates in the patients with MINOCA treated during the COVID-19 pandemic (2020). The possible association between worse clinical outcomes of the MINOCA patients treated during the pandemic and thromboembolic complications of SARS--Cov-2 infection needs further evaluation.

ARTICLE INFORMATION

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