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ORIGINAL STUDIES

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Patients with COVID-19 who experience a myocardial infarction have complex coronary morphology and high in-hospital mortality: Primary results of a nationwide angiographic study

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Abstract

Objectives: We aimed to explore angiographic patterns and in-hospital outcomes of patients with concomitant coronavirus disease-19 (COVID-19) and myocardial infarction (MI).

Background: Patients with COVID-19 may experience MI during the course of the viral infection. However, this association is currently poorly understood.

Methods: This is a multicenter prospective study of consecutive patients with concomitant COVID-19 and MI who underwent coronary angiography. Quantitative and qualitative coronary angiography were analyzed by two observers in an independent core lab.

Results: A total of 152 patients were included, of whom 142 (93.4%) had COVID-19 diagnosis confirmation. The median time between symptom onset and hospital admission was 5 (1–10) days. A total of 83 (54.6%) patients presented with ST-elevation MI. The median angiographic Syntax score was 16 (9.0–25.3) and 69.0% had multi-vessel disease. At least one complex lesion was found in 73.0% of patients, 51.3% had a thrombus containing lesion, and 57.9% had myocardial blush grades 0/1. The overall in-hospital mortality was 23.7%. ST-segment elevation MI presentation and baseline myocardial blush grades 0 or 1 were independently associated with

List of Abbreviations: COVID-19, coronavirus disease 2019; FFR, fractional flow reserve; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCR, polymerase chain reaction; QFR, quantitative flow ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; STEMI, ST-segment elevation myocardial infarction; Syntax, synergy between PCI with TAXUS and cardiac surgery; TIMI, thrombolysis in myocardial infarction.

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a higher risk of death (HR 2.75, 95%CI 1.30–5.80 and HR 3.73, 95%CI 1.61–8.61, respectively).

Conclusions: Patients who have a MI in the context of ongoing COVID-19 mostly present complex coronary morphologies, implying a background of prior atherosclerotic disease superimposed on a thrombotic milieu. The in-hospital prognosis is poor with a markedly high mortality, prompting further investigation to better clarify this newly described condition.

KEYWORDS
coronary angiography, coronavirus disease 2019, myocardial infarction

1 | INTRODUCTION

Initially diagnosed in China, coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) triggered a pandemic around the globe early in January 2020, leading the World Health Organization to declare a state of global emergency. The cardiovascular consequences of COVID-19 have been well documented.[1] Importantly, several studies showed a significant association between myocardial injury and poor outcomes in patients hospitalized with COVID-19.[2-4] Case reports of acute myocardial infarction (MI) in COVID-19 are available, including patients with a wide variety of symptom presentation and electrocardiogram changes, culminating in referral for coronary angiography.

While pathophysiologic mechanisms have been suggested,[3] including an imbalance between oxygen demand and supply, an intense inflammatory activity, a high thrombotic risk, and hemodynamic changes leading to atherosclerotic plaque instability, it is still not known whether MI in the context of a COVID infection shows similar angiographic patterns to ''regular'' acute coronary syndromes. Moreover, data are lacking on the prognosis of these patients. Therefore, we aimed to explore the angiographic characteristics and clinical outcomes of patients with COVID-19 presenting with MI, including ST-segment elevation MI (STEMI) and non-ST-segment elevation MI (NSTEMI), requiring coronary angiography, regardless of the need for percutaneous coronary intervention.

2 | METHODS

2.1 | Study design and participants

The present work is a multicenter, retrospective and prospective, observational cohort study. The retrospective cohort includes patients who were identified by investigators from the beginning of the pandemic in Brazil, and before the prospective study start date. The prospective cohort included patients who fulfilled inclusion criteria after the study start date. This study was approved by the National Research Ethics Committee and by the local Institution Review Boards of each site. The informed consent form was waived for the retrospective cohort and the inclusion of patients prospectively occurred after signature of the informed consent form.

We included consecutive patients presenting with suspected or confirmed COVID-19 and MI who underwent coronary angiography at 17 tertiary sites in Brazil from April 14, 2020 to June 28, 2020. The complete list of investigators is provided in the Data S1. The diagnosis of COVID-19 was confirmed by either a positive result of a SARS-CoV-2 polymerase chain reaction test on a nasopharyngeal swab or serologic tests. A suspected case of COVID-19 was defined as a patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath) and radiological evidence by chest computed tomography showing pulmonary lesions compatible with COVID-19. A suspected case was only included when an independent committee reviewed the case and concluded that COVID-19 was the primary diagnosis for the patient.

2.2 | Definition of MI

For the present study, types 1 and 2 MIs were considered, according to the Fourth International Definition of MI. For type 1 MI, the increase and/or decrease in troponin values were considered at least one value above the 99th percentile plus one of the following criteria: (a) symptoms of acute myocardial ischemia; (b) new changes in the electrocardiogram suggestive of ischemia; (c) presence of Q waves in the electrocardiogram; (d) evidence of loss of viable myocardium or new change in mobility in the myocardial wall consistent with ischemic etiology; (e) identification of coronary thrombus at angiography or autopsy. For the diagnosis of type 2 MI, the same criteria above were considered, in addition to any evidence of an imbalance between oxygen supply and demand.

2.3 | Coronary angiography

The coronary angiograms were performed following standard procedures. The procedure could be performed using femoral or radial approach, following the internationally recommended standards for

protection against viral exposure. If necessary, and at the discretion of the local interventional team accompanying the case, percutaneous coronary intervention with stent implantation was performed as needed. All procedures were performed in accordance with national and international guidelines and equipments and devices used were left at the discretion of the operators and the institution where it was performed.

The coronary angiography films were analyzed by two observers in an independent core lab at the Heart Institute, InCor, University of Sao Paulo. In case of disagreement between the two observers, a third observer was invited for final opinion. These analyses were blinded to patients' baseline characteristics and clinical presentation.

The images were evaluated for the detection and location of luminal stenoses, as well as the morphological pattern of the lesions. The Synergy between PCI with TAXUS and cardiac surgery (SYNTAX) score was calculated using an electronic calculator available online (www.syntaxscore.com).[5]

Lesions were also categorized as complex or not using a classification previously described.[6,7] Lesions were considered complex if they caused at least 50% stenosis and had one or more of the following morphologic features: (a) an intraluminal filling defect consistent with thrombus, defined as abrupt vessel cutoff with persistence of contrast, or an intraluminal filling defect in a vessel within or adjacent to a stenotic region with surrounding homogeneous contrast opacification; (b) plaque ulceration, defined by the presence of contrast and hazy contour beyond the vessel lumen; (c) plaque irregularity (haziness), defined by irregular margins or overhanging edges; (d) impaired flow (thrombolysis in MI [TIMI] flow <3, except lesions characteristic of chronic total occlusion, identified as tapering lesions with multiple fine collaterals).

The thrombus burden was assessed using as previously described.[8] Anterograde coronary flow was classified according to the TIMI flow criteria from 0 to 3.[9] Myocardial blush grade has been defined previously as follows[10]: 0, no myocardial blush or contrast density; 1, minimal myocardial blush or contrast density; 2, moderate myocardial blush or contrast density but less than that obtained during angiography of a contralateral or ipsilateral non–infarct-related coronary artery; and 3, normal myocardial blush or contrast density, comparable with that obtained during angiography of a contralateral or ipsilateral non–infarct-related coronary artery.

Quantitative flow ratio (QFR; QAngioXA-3D, Medis Medical Imaging System, Leiden, The Netherlands) was assessed in all complex lesions with antegrade flow ≥2. QFR is an estimate of fractional flow reserve and is derived from 3-dimensional quantitative coronary angiography.[11] Two angiographic image projections acquired at ≥ 30° apart that presented the least foreshortening of the stenosis and minimum overlap of the main vessel and side branches were selected for

TABLE 1 Baseline characteristics according to survival status

	Overall *N* = 152	Survivors *N* = 116	Non-survivors *N* = 36	*p* value
Age (years)	64 ± 11	62 ± 12	68 ± 9	.013
Male sex	103 (67.8)	80 (69.0)	23 (63.9)	.354
Symptoms				
Cough	73 (48.0)	54 (45.6)	19 (52.8)	.322
Dyspneia	66 (43.3)	50 (43.1)	16 (44.4)	.518
Fever	65 (42.8)	51 (44.0)	14 (38.9)	.367
Chest pain	40 (26.3)	35 (30.2)	5 (13.9)	.038
Myalgia	15 (9.9)	11 (9.4)	4 (11.1)	.495
Fatique	12 (7.9)	11 (9.5)	1 (2.8)	.173
Anosmia	12 (7.9)	10 (8.6)	2 (5.6)	.426
Comorbidities				
Hypertension	117 (77.0)	89 (76.7)	28 (77.8)	.547
Diabetes	72 (47.4)	50 (43.1)	22 (61.1)	.045
Smoking	53 (34.9)	42 (36.2)	11 (30.6)	.340
Prior coronary disease	28 (18.4)	19 (16.4)	9 (25.0)	.178
Obesity	24 (15.8)	19 (16.4)	5 (13.9)	.475
Renal disease on dialysis	14 (9.2)	8 (6.9)	6 (16.7)	.08
Heart failure	12 (7.9)	8 (6.9)	4 (11.1)	.307
Atrial fibrillation	2 (1.3)	1 (0.9)	1 (2.8)	.419
Cancer	8 (5.3)	6 (5.2)	2 (5.6)	.605
Chronic obstructive pulmonar disease	6 (3.9)	5 (4.3)	1 (2.8)	.564
Prior stroke	4 (2.6)	2 (1.7)	2 (5.6)	.238

TABLE 2 Baseline characteristics according to presentation as NSTEMI or STEMI

	Overall (152)	NSTEMI (69)	STEMI (83)	*p* value
Age (years)	65 (57–72)	65 (59–73)	65 (55–72)	.397
Male sex	103 (67.8)	44 (63.8)	59 (71.1)	.216
Symptoms				
Cough	73 (48.0)	41 (59.4)	32 (10.7)	.008
Dyspneia	66 (43.3)	39 (56.5)	27 (32.5)	.002
Fever	65 (42.8)	35 (50.7)	30 (36.1)	.050
Chest pain	40 (26.3)	22 (31.9)	18 (21.7)	.108
Myalgia	15 (9.9)	9 (13.0)	6 (7.2)	.178
Fatique	12 (7.9)	8 (11.6)	4 (4.8)	.108
Anosmia	12 (7.9)	5 (7.2)	7 (8.4)	.516
Comorbidities				
Hypertension	117 (77.0)	56 (81.2)	61 (73.5)	.178
Diabetes	72 (47.4)	35 (50.7)	37 (44.6)	.277
Smoking	53 (34.9)	26 (37.7)	27 (32.5)	.311
Prior coronary disease	28 (18.4)	20 (29.0)	8 (9.6)	.002
Obesity	24 (15.8)	11 (15.9)	13 (15.7)	.568
Renal disease on dialysis	14 (9.2)	12 (17.4)	2 (2.4)	.002
Heart failure	12 (7.9)	8 (11.6)	4 (4.8)	.108
Atrial fibrillation	2 (1.3)	1 (1.5)	1 (1.2)	.703
Cancer	8 (5.3)	3 (4.4)	5 (6.0)	.466
Chronic obstructive pulmonar disease	6 (3.9)	3 (4.4)	3 (3.6)	.568
Prior stroke	4 (2.6)	2 (2.9)	2 (2.4)	.617

Abbreviations: NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

analysis. The lumen contour was delineated automatically and manual correction performed as appropriate. A 3D anatomical vessel model without side branches was derived from the software and QFR computation was performed using a specific flow model: contrast-flow QFR as previously described.

2.4 | Data collection and follow-up

Data on demographic characteristics, medical history, clinical presentation, laboratory results, treatments, and clinical outcomes were assessed through medical records and collected in a case report form by local investigators. Participants had their data collected until hospital discharge and/or death. No intervention was carried out through this study. The registry utilized a web-based case report form, and remote electronic data monitoring was performed in all cases, to actively search and correct missing and/or inconsistent information.

2.5 | Clinical outcomes

We describe in-hospital events, including all-cause death, acute respiratory distress syndrome, and need for mechanical ventilation.

2.6 | Statistical analysis

Categorical variables were reported as percentages and continuous variables as mean ± standard deviation (SD) or median (interquartile range [IQR]) according to their distribution. Normality was assessed with the Kolmogorov–Smirnov test. Independent samples *T* or Kruskal–Wallis tests was used for comparison between groups. Multivariable analyses were conducted with a Cox regression model for the occurrence of all-cause death, using all variables shown in Tables 1 and 2. The set of variables with a p value ≤ .10 in the univariate regression analyses was included in the multivariable regression analyses. Forward selection was used, and the entry and stay criteria were set to 0.05. The results were considered significant with p values <.05. Analyses were conducted using the statistical software ver. 16.0 (SPSS Inc., Chicago, IL).

3 | RESULTS

3.1 | Study population

A total of 152 participants were included, of whom 142 (93.4%) had COVID-19 diagnosis confirmation. The remaining 10 cases were

TABLE 3 Angiographic characteristics according to survival status

	Overall *N* = 152	Survivors *N* = 116	Non-survivors *N* = 36	*p* value
Syntax score, (IQR)	16.0 (9.0–25.3)	16.0 (9.0–23.5)	19.8 (9.0–31.5)	.75
Diseased territories, *n*(%)				.14
None	19 (12.5)	12 (10.3)	7 (19.4)	
Single vessel disease	28 (18.4)	21 (18.1)	7 (19.4)	
Two vessel disease	37 (24.3)	33 (28.4)	4 (11.1)	
Three vessel disease	68 (44.7)	50 (43.1)	18 (50.0)	
Patients with at least one complex lesion, *n*(%)	111 (73.0)	87 (75.0)	24 (66.7)	.39
Thrombus containing lesion, *n*(%)	78 (51.3)	60 (51.7)	18 (50.0)	1.0
Thrombus burden, *n*(%)				.05
0,1,2	90 (59.2)	64 (55.2)	10 (27.8)	
3,4,5	62 (40.8)	52 (44.8)	26 (72.2)	
Haziness, *n*(%)	60 (39.5)	49 (42.6)	11 (31.4)	.32
Ulcer, *n*(%)	17 (11.2)	15 (13.0)	2 (5.7)	.36
TIMI flow, *n*(%)				.11
0, I, II	86 (56.6)	62 (53.4)	24 (66.7)	
III	66 (43.4)	54 (46.6)	12 (33.3)	
Myocardial blush, *n*(%)				
0, I	88 (57.9)	61 (52.5)	27 (75.0)	.02
II, III	64 (42.1)	55 (47.4)	9 (25.0)	
Lesions > 50% per patient, (IQR)	3.00 (2.00–4.00)	3.00 (2.00–4.00)	3.00 (2.00–4.00)	.81
3D quantitative coronary angiography of acute lesions				
Reference diameter, ± SD	2.6 ± 0.62	2.6 ± 0.60	2.8 ± 0.84	.20
% stenosis, (IQR)	90.5 (71.1–100.0)	90.5 (71.1–100.0)	94.2 (72.2–100.0)	.75
Lesion length, mm (IQR)	21.7 (14.1–33.9)	20.5 (14.1–29.5)	33.3 (11.3–38.9)	.54
Minimal lumen diameter, mm (IQR)	0.2 (0.0–0.80)	0.2 (0.0–0.80)	0.1 (0.0–0.7)	.89
Plaque volume, mm^3 (IQR)	56.3 (30.8–90.1)	53.0 (30.0–78.2)	95.7 (43.2–157.1)	.10
Quantitative flow ratio of non-occluded vessels ± SD	0.53 ± 0.25	0.53 ± 0.25	0.43 ± 0.31	.26

defined as suspect cases that fulfilled inclusion criteria for clinical symptoms and chest tomography results. Demographical and clinical characteristics are presented in Table 1, stratified by survivors and non-survivors. Overall, the mean age was 64 ± 11 years and 67.8% were male. The median time between symptom onset and hospital admission was 5 (1–10) days and median time between hospital admission and coronary angiography was 1 (0–7) day. Overall, 54.6% presented with STEMI and 45.4% with NSTEMI. The most common symptoms of COVID-19 were cough (48.0%), dyspnea (43.3%), and fever (42.8%). Chest pain occurred in 26.3%. Overall, 77.0% had hypertension, 47.4% diabetes, 34.9% were prior or current smokers, 18.4% had prior coronary artery disease, and 15.8% were obese. A total of 18 (11.8%) patients had cardiogenic shock or heart failure at hospital presentation. Regarding oxygen need at admission, 47.4% were on room air, 33.6% used oxygen by nasal cannula, and 11.8% needed mechanical ventilation. Baseline characteristics according to presentation as STEMI or NSTEMI are displayed in Table 2.

3.2 | Angiographic characteristics

The angiographic findings according to survival status are presented in Table 3. Median Syntax score was 16.0 (IQR 9.0–25.3). Overall, 69% had multi-vessel disease and 44.7% presented three vessel disease. A total of 19 patients (12.5%) did not show significant obstructive coronary artery disease. Overall, haziness was found in 39.5% and ulcers in 11.2%. The median QFR was 0.53 ± 0.25. Thrombus burden grades 3, 4, or 5 were more frequent among non-survivors than among survivors (72.2 vs. 44.8%; $p = .05$), as was myocardial blush grades 0 or I (75.0 vs. 52.2%; $p = .02$).

Angiographic characteristics of patients with STEMI and NSTEMI are presented in Table 4. At least one complex lesion was found more frequently in STEMI patients than in NSTEMI patients (80.7 vs. 63.8%; $p = .03$). Thrombus containing lesions were also more common among those with STEMI, as compared with NSTEMI (66.3 vs. 33.3%; $p < .01$). Thrombus burden grades 3, 4, or 5 were present in 59.0% of STEMI patients and 18.7% of NSTEMI patients ($p < .01$). A total of

TABLE 4 Angiographic characteristics according to clinical presentation

	Overall *N* = 152	STEMI *N* = 83	NSTEMI *N* = 69	*p*
Syntax score, (IQR)	16 (9–25.25)	17.8 (10.0–25.5)	14.5 (6.0–22.0)	.17
Diseased territories, *n*(%)				
None	19 (12.5)	9 (10.8)	10 (14.5)	.48
Single vessel disease	28 (18.4)	19 (22.9)	9 (13.0)	
Two vessel disease	37 (24.3)	20 (24.1)	17 (24.6)	
Three vessel disease	68 (44.7)	35 (42.2)	33 (47.8)	
Patients with at least one complex lesion, *n*(%)	111 (73.0)	67 (80.7)	44 (63.8)	.03
Thrombus containing lesion, *n*(%)	78 (51.3)	55 (66.3)	23 (33.3)	<.01
Thrombus burden, *n*(%)				<.01
0	74 (48.7)	28 (33.7)	46 (66.7)	
1	13 (8.6)	5 (6.0)	8 (11.6)	
2	3 (2.0)	1 (1.2)	2 (2.9)	
3	5 (3.3)	2 (2.4)	3 (4.3)	
4	20 (19.7)	23 (27.7)	7 (10.1)	
5	27 (17.8)	24 (28.9)	3 (4.3)	
Haziness, *n*(%)	60 (39.5)	28 (33.7)	32 (47.8)	.09
Ulcer, *n*(%)	17 (11.2)	10 (12.0)	7 (10.4)	.80
TIMI flow, *n*(%)				<.01
0	63 (41.4)	46 (55.4)	17 (24.6)	
I	7 (4.6)	5 (6.0)	2 (2.9)	
II	16 (10.5)	6 (7.2)	10 (14.5)	
III	66 (43.4)	26 (31.3)	40 (58.0)	
Myocardial blush, *n*(%)[a]				<.01
0	69 (45.4)	52 (62.7)	17 (25.4)	
I	19 (12.5)	8 (9.6)	11 (16.4)	
II	19 (12.5)	8 (9.6)	11 (16.4)	
III	43 (28.3)	15 (18.1)	28 (41.8)	
Lesions>50% per patient, (IQR)	3.00 (2.00–4.00)	3.00 (2.00–3.00)	3.00 (2.00–4.00)	.41
3D quantitative coronary angiography of acute lesions				
Reference diameter, ± SD	2.6 ± 0.62	2.6 ± 0.64	2.6 ± 0.61	.95
% stenosis, (IQR)	90.5 (71.1–100.0)	100.0 (80.4–100.0)	72.9 (61.4–82.1)	<.01
Lesion length, mm (IQR)	21.7 (14.1–33.9)	21.7 (15.6–36.5)	21.2 (14.0–33.0)	.78
Minimal lumen diameter, mm (IQR)	0.2 (0.0–0.80)	0.0 (0.0–0.5)	0.6 (0.5–1.0)	<.01
Plaque volume, mm^3 (IQR)	56.3 (30.8–90.1)	47.4 (31.6–67.2)	63.1 (30.8–93.9)	.29
qFR ± SD[a]	0.53 ± 0.25	0.49 ± 0.26	0.52 ± 0.27	.72

[a]qFR, Quantitative flow ratio of non-occluded vessels; TIMI, thrombolysis in myocardial infarction.

72.3% of STEMI patients and 41.8% of NSTEMI patients had myocardial blush grades 0 or 1 ($p < .01$).

3.3 | Clinical outcomes

Overall, median hospitalization days was 14 (6–31). Need for mechanical ventilation occurred in 30.3%, acute respiratory distress syndrome in 28.3% and cardiogenic shock in 16.5%. The overall in-hospital mortality was 23.7%, reaching 75.0 and 44.4%, among those who needed mechanical ventilation and those who presented with cardiogenic shock, respectively.

3.4 | Predictors of in-hospital death

In the univariate analysis, age, prior coronary artery disease, presentation as STEMI, reduced TIMI and myocardial blush grades were associated with a higher risk of death (Table 5). In the multivariate analysis, presentation as STEMI and myocardial blush grades 0/1 were

TABLE 5 Univariate and multivariate predictors of in-hospital death

	Univariate			Multivariate		
Variables	**HR**	**95% CI**	***p***	**HR**	**95% CI**	***p***
Age	1.02	0.99–1.06	.131			
Prior coronary disease	1.92	0.88–4.18	.097			
STEMI	3.36	1.63–6.92	.001	2.75	1.30–5.80	.008
Baseline TIMI 3 flow	0.38	0.19–0.79	.010			
Myocardial blush 0/1	4.27	1.90–9.60	<.001	3.73	1.61–8.61	.002

Abbreviations: STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction.

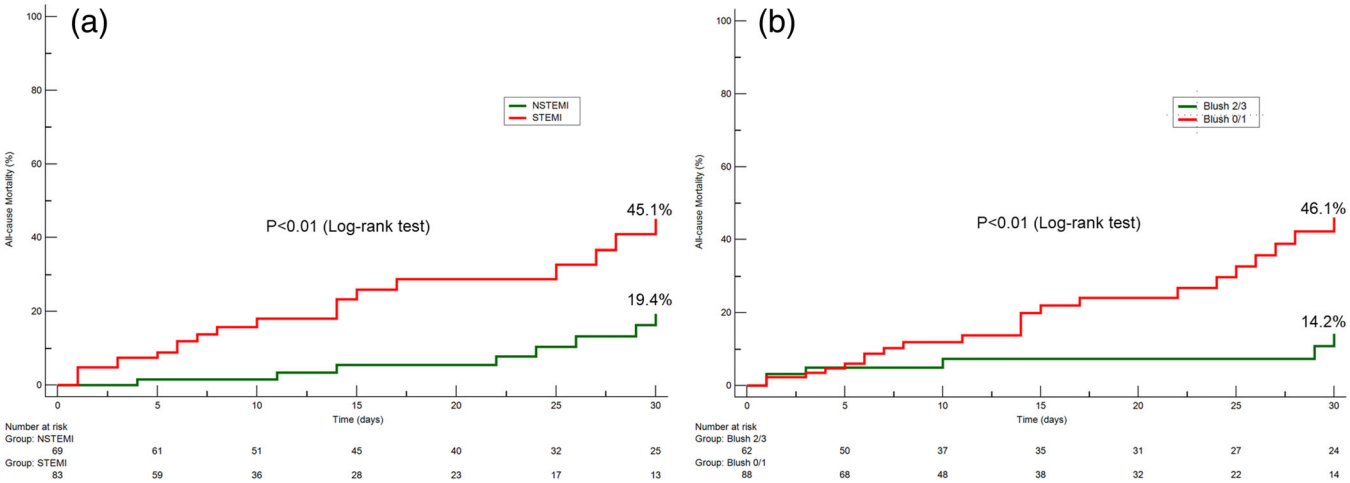

FIGURE 1 Survival curves according to clinical presentation and myocardial blush grades. NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction

identified as independent predictors of in-hospital mortality (HR 2.75, 95% CI 1.30–5.80 and HR 3.73, 95% CI 1.61–8.61, respectively) (Figure 1).

4 | DISCUSSION

To the best of our knowledge, our multicenter national study presents the largest cohort of COVID-19 patients with detailed angiographic evaluation for MI, including both STEMI and NSTEMI. The majority of patients had severe coronary artery disease that extended to multiple territories. The overall mortality was high and was related to poor myocardial perfusion (ST-segment elevation and blush 0/1).

COVID-19 infection has been associated with myocardial injury and cardiovascular events, especially in patients admitted to intensive care units.[12,13] A case series of 18 STEMI patients in New York City reported that half of them underwent coronary angiography.[14] Among them, up to 67% had obstructive coronary artery disease. Similarly, a report from northern Italy included 28 COVID-19 patients with STEMI who underwent coronary angiography and showed that culprit lesions were not identified in approximately 40.0% of patients.[15] In our cohort, the occurrence of MI without obstructive coronary disease was only 12.5%, rate that is substantially lower than those found in previous studies. In this setting, myocardial injury might have occurred secondary to direct viral tissue invasion, exacerbated inflammatory response and/or hypoxemia.[1]

The United Kingdom experience with 115 STEMI patients observed a higher prevalence of multi-vessel thrombosis and a trend toward higher thrombus burden among COVID-19 patients (n = 39) as compared with the non-COVID population (n = 76).[16] In our cohort, including both STEMI and NSTEMI patients, about half of them had thrombus containing lesions and thrombus burden grades 3, 4, or 5 were observed in approximately 40%. Additionally, significant coronary artery disease was present in the vast majority of the cases, including a fairly high rate of two- and triple-vessel disease. A patient-level pooled analysis from a convenience sample of eight independent, international randomized STEMI clinical trials, non–infarct-related artery disease involved one vessel in 29.6% and in 18.8% involved two vessels.[16] Our analysis demonstrated much more complex coronary artery disease (CAD) in COVID-19 patients, of whom 44.7% presented with three-vessel disease.

In a more detailed assessment of CAD complexity, we demonstrated a relatively much higher SYNTAX score, when compared with the SYNTAX score of previous studies including patients with acute coronary syndromes.[17] Singbal et al. demonstrated that a cutoff value of 12 for SYNTAX score is related with higher mortality (95% CI

1.18–7.64; p = .02) after 12 months.[18] Importantly, in our study the overall median SYNTAX score was 16 (9–25.25), demonstrating the severity of CAD in these patients.

Previous studies demonstrated the presence of at least one complex lesion (with thombus, ulcer, haziness, or impaired flow) in about 80% of patients presenting acute coronary syndromes and in only 31.8% of patients with stable CAD.[7] Our analysis found complex lesions in 73% of patients, being more frequent among those with STEMI versus NSTEMI (80.7 vs. 63.8%; p = .03). Conversely, MI with nonobstructive coronary arteries (MINOCA) was found in 12.5% of patients in the present study. This finding is similar to acute coronary syndromes studies of patients without COVID-19. In the variation in recovery: role of gender on outcomes of young AMI patients (VIRGO) trial, of 2,690 patients undergoing coronary angiography, 88.4% had obstructive CAD and 11.1% had MINOCA.[19] The percentage of STEMI and NSTEMI (52.1 and 47.9%, respectively) in VIRGO study was similar to our study (54.6 and 45.4%).

Although limited to case reports and small case series, the mortality rates of MI in COVID-19 patients is high.[14,15,20] In our study, including a larger number of patients, we observed a 23% mortality rate in our cohort and a 30% rate of invasive mechanical ventilation, which is comparable with other series of critically ill patients with COVID-19. Noteworthy, those patients presenting with cardiogenic shock and needing mechanical ventilation had an even higher mortality rate. Gupta et al reported a 35% mortality rate in a multicenter registry in the United States including 2,215 COVID-19 patients.[21] In their large experience, the presence of CAD increased the risk of death in 47%. Collectively, these findings suggest that COVID-19 patients with MI should be early stratified and aggressively treated according to clinical guidelines since they may present with complex coronary anatomy, high thrombus burden, and an increased risk of death.

4.1 | Limitations

Our findings should be interpreted in light of some limitations. First, we included patients with COVID-19 and MI, therefore we did not have a control group. Since several reports showed that the incidence of MI during the pandemic was lower than the one from other periods of time,[22] we believe that including a control group with non-COVID MI patients may not truly represent the overall MI population. Second, even though the majority of patients in our cohort had COVID-19 diagnosis confirmation, 6.6% tested negatively. Still, these few cases fulfilled pre-specified inclusion criteria for a suspected case of COVID-19 based on clinical symptoms and chest tomography imaging findings and were adjudicated by an independent committee which concluded that COVID-19 was still the main diagnosis for those patients. Third, our number of clinical events was somewhat low, which limited the analysis of predictors of death. However, to our knowledge, our study comprises the largest cohort of COVID-19 patients undergoing coronary angiography so far.

5 | CONCLUSIONS

Patients who have a MI in the context of ongoing COVID-19 mostly present complex coronary morphologies, implying a background of prior atherosclerotic disease superimposed on a thrombotic milieu. The in-hospital prognosis is poor with a markedly high mortality, prompting further investigation to better clarify this newly described condition.

CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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