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# Acute Coronary Syndrome in the Era of SARS-CoV-2 Infection: A Registry of the French Group of Acute Cardiac Care

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## ABSTRACT

**Background:** In this study, we aimed to report clinical characteristics and outcomes of patients with and without SARS-CoV-2 infection who were referred for acute coronary syndrome (ACS) during the peak of the pandemic in France.

Since December 2019, the world has been facing an outbreak of an emerging coronavirus SARS-CoV-2 (severe acute respiratory syndrome related to coronavirus-2) with a wide spectrum of presentations and associated mortality of 2%-3%.<sup>1,2</sup> The disease is characterized first by a viral replication phase (early infection) followed by a host inflammatory

## RÉSUMÉ

**Contexte :** Notre étude avait pour but d'établir les caractéristiques cliniques et les résultats de patients infectés ou non par le SRAS-CoV-2 qui ont été orientés en raison d'un syndrome coronarien aigu (SCA) pendant la phase aiguë de la pandémie en France.

response phase related to a cytokine storm, which might be accompanied by thrombotic events. For example, pulmonary embolism is frequent among patients with SARS-CoV-2-associated pneumonia, with predominantly bilateral vascular defects, which might suggest a prothrombotic state.<sup>3,4</sup> Data in the literature indicate a cardiac involvement in 20% of severe SARS-CoV-2 infections, which translates into worsened outcome. Underlying pathophysiological mechanisms remain poorly understood and might involve coronary thrombosis and/or acute viral and immunoinflammatory myocarditis.<sup>5-7</sup> The recent case series by Bangalore et al., in which 18 patients presented with SARS-CoV-2 infection and ST-segment elevation on electrocardiogram, showed a surprisingly high in-hospital mortality rate (ie, 72%), contrary to the reported event rates for acute coronary syndrome (ACS) in recent literature (between 4% and 12%).<sup>8,9</sup> Also in the case series of

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**Methods:** We included all consecutive patients referred for ST-elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI) during the first 3 weeks of April 2020 in 5 university hospitals (Paris, south, and north of France), all performing primary percutaneous coronary intervention.

**Results:** The study included 237 patients ( $67 \pm 14$  years old; 69% male), 116 (49%) with STEMI and 121 (51%) with NSTEMI. The prevalence of SARS-CoV-2-associated ACS was 11% ( $n = 26$ ) and 11 patients had severe hypoxemia on presentation (mechanical ventilation or nasal oxygen  $> 6$  L/min). Patients were comparable regarding medical history and risk factors, except a higher prevalence of diabetes mellitus in SARS-CoV-2 patients (53.8% vs 25.6%;  $P = 0.003$ ). In SARS-CoV-2 patients, cardiac arrest on admission was more frequent (26.9% vs 6.6%;  $P < 0.001$ ). The presence of significant coronary artery disease and culprit artery occlusion in SARS-CoV-2 patients respectively, was 92% and 69.4% for those with STEMI, and 50% and 15.5% for those with NSTEMI. Percutaneous coronary intervention was performed in the same percentage of STEMI (84.6%) and NSTEMI (84.8%) patients, regardless of SARS-CoV-2 infection, but no-reflow (19.2% vs 3.3%;  $P < 0.001$ ) was greater in SARS-CoV-2 patients. In-hospital death occurred in 7 SARS-CoV-2 patients (5 from cardiac cause) and was higher compared with noninfected patients (26.9% vs 6.2%;  $P < 0.001$ ).

**Conclusions:** In this registry, ACS in SARS-CoV-2 patients presented with high a percentage of cardiac arrest on admission, high incidence of no-reflow, and high in-hospital mortality.

**Méthodologie :** Nous avons inclus dans l'étude tous les patients consécutifs qui ont présenté un infarctus du myocarde avec sus-décalage du segment ST (STEMI) ou sans sus-décalage du segment ST (NSTEMI) au cours des 3 premières semaines d'avril 2020 et qui ont été orientés vers 5 hôpitaux universitaires (situés à Paris, ainsi que dans le sud et le nord de la France), tous en mesure de réaliser des interventions coronariennes percutanées primaires.

**Résultats :** L'étude comprenait 237 patients (âge :  $67 \pm 14$  ans; proportion d'hommes : 69 %); 116 (49 %) présentaient un STEMI et 121 (51 %), un NSTEMI. La prévalence d'un SCA associé à une infection par le SRAS-CoV-2 s'établissait à 11 % ( $n = 26$ ), et 11 patients étaient en hypoxémie grave (nécessitant une ventilation artificielle ou l'administration d'oxygène par voie nasale à un débit de plus de 6 l/min) à leur arrivée. Les patients présentaient des antécédents médicaux et des facteurs de risque comparables, à l'exception du fait que la prévalence du diabète était plus élevée chez les patients infectés par le SRAS-CoV-2 (53,8 % vs 25,6 %;  $p = 0,003$ ). Ces derniers avaient plus souvent subi un arrêt cardiaque à leur admission (26,9 % vs 6,6 %;  $p < 0,001$ ). Chez les patients infectés par le SRAS-CoV-2, une coronaropathie importante et une occlusion de l'artère coupable ont été observées chez respectivement 92 % et 69,4 % des patients présentant un STEMI, et chez 50 % et 15,5 % des patients présentant un NSTEMI. Une intervention coronarienne percutanée a été effectuée dans les mêmes proportions chez les patients subissant un STEMI (84,6 %) que chez ceux présentant un NSTEMI (84,8 %), sans égard à la présence ou à l'absence d'une infection par le SRAS-CoV-2, mais les cas de non-reperfusion (*no-reflow*) ont été plus fréquents chez les patients infectés que chez les autres patients (19,2 % et 3,3 %, respectivement;  $p < 0,001$ ). Sept patients infectés par le SRAS-CoV-2 sont morts à l'hôpital (5 de cause cardiaque), ce qui représente un taux de mortalité plus élevé que chez les patients non infectés (26,9 % vs 6,2 %;  $p < 0,001$ ).

**Conclusions :** Dans le cadre de cette étude, le SCA survenu chez les patients infectés par le SRAS-CoV-2 était associé à un fort pourcentage d'arrêt cardiaque à l'admission, à une fréquence élevée de cas de non-reperfusion et à un taux élevé de mortalité hospitalière.

Stefanini et al. from Italy, in approximately 40% of patients with COVID-19 and ST-elevation myocardial infarction (STEMI), a culprit lesion was not identifiable using coronary angiography.<sup>10</sup> Therefore, we aimed to investigate the clinical characteristics and outcome of patients with myocardial infarction and SARS-CoV-2 infection among French hospitals during the peak of the SARS-CoV-2 pandemic in France.

## Methods

### Population

All patients referred for ACS to the cardiac catheterization laboratory during the first 3 weeks of April (from April 1-22, 2020) were screened. All patients with myocardial infarction (STEMI or non-STEMI [NSTEMI]) who underwent coronary angiogram were included in the study. Myocardial infarction was defined as rise and/or fall of troponin values with at least 1 value above the 99th percentile and clinical evidence of acute myocardial ischemia (symptoms of myocardial ischemia, new ischemic electrocardiogram changes, development of pathological Q waves, imaging

evidence of new loss of viable myocardium, or new regional wall motion abnormality in a pattern consistent with an ischemic etiology, or identification of a coronary thrombus using coronary angiography).<sup>11</sup> STEMI was diagnosed when ST-segment elevation  $\geq 1$  mm was seen in at least 2 contiguous leads in any location on the index or qualifying electrocardiogram, or when presumed new left bundle-branch block or documented new Q waves were observed. In the absence of ST-segment elevation, patients who met the inclusion criteria were considered to have NSTEMI. We excluded patients medically treated without coronary angiogram documentation. The study was conducted by the French Group of Cardiac Intensive Care Network in accordance with European Society of Cardiology guidelines and French law. Data were collected from 3 regions of France with high (Paris,  $n = 2$  centres), moderate (north of France,  $n = 1$  centre), and low (south of France,  $n = 2$  centres) prevalence of SARS-CoV-2 infection. Investigator centres were 5 university hospitals with high experience in percutaneous coronary intervention (PCI). Although all consecutive patients were screened, data collection was retrospective.

**Table 1. Baseline characteristics of the patients according to SARS-CoV-2 infection status**

	All (N = 237)	SARS-CoV-2 (n = 26)	Non-SARS-CoV-2 (n = 211)	P
Medical history and demographic characteristics				
Inclusion centre				<b>0.034*</b>
North	34 (14)	3 (11.5)	31 (14.7)	
Paris	75 (32)	14 (53.8)	61 (28.9)	
South	128 (54)	9 (34.6)	119 (56.4)	
Age, years	66.6 ± 13.8	62.7 ± 13.3	67 ± 13.8	0.13
Male sex	163 (68.8)	19 (73.1)	144 (68.2)	0.62
Body mass index	27 ± 4.7	28 ± 4.15	26.2 ± 4.7	0.07
Active smoking	72 (30.4)	5 (19.2)	67 (31.7)	0.19
Arterial hypertension	117 (49.4)	15 (57.7)	102 (48)	0.36
Diabetes	68 (28.7)	14 (53.8)	54 (25.6)	<b>0.003</b>
Dyslipidemia	90 (38)	11 (42.3)	79 (37.4)	0.63
eGFR < 50 mL/min/m <sup>2</sup>	20 (8.4)	4 (15.4)	16 (7.6)	0.17
Respiratory disease	21 (8.9)	4 (15.4)	17 (8.1)	0.21
Clinical presentation and procedural aspects				
STEMI	116 (49)	17 (65.4)	99 (46.9)	0.0761
Nonobstructive coronary arteries	21 (8.9)	5 (19.2)	16 (7.6)	<b>0.0489</b>
Cardiac arrest at presentation	21 (8.9)	7 (26.9)	14 (6.6)	<b>0.0005</b>
Thromboaspiration	22 (9.3)	3 (11.5)	19 (9)	0.67
Persistent no-reflow	12 (5.1)	5 (19.2)	7 (3.3)	<b>0.0004</b>
D-dimer, ng/mL <sup>†</sup>	270 [1-752]	1340 [414-2983]	270 [1-500]	<b>&lt; 0.01</b>
C-reactive protein, mg/L	4 [2-19]	53 [19-127]	3 [2-8]	<b>&lt; 0.0001</b>
Patient outcome				
In-hospital death	20 (8.4)	7 (26.9)	13 (6.2)	<b>0.0003</b>
In-hospital cardiac arrest	24 (10.1)	12 (46.2)	12 (5.7)	<b>&lt; 0.0001</b>
Cardiogenic shock or heart failure	46 (19.4)	10 (38.5)	36 (17.1)	<b>0.0091</b>

Data are presented as n (%), mean ± SD, or mean [25%-75% quartile]. Bold values represent  $P < 0.05$ .

C-reactive protein, C-reactive protein; eGFR, estimated glomerular filtration rate by Modification of Diet in Renal Disease (MDRD) equation; STEMI, ST-elevation myocardial infarction.

\*  $P$  value is given for contingency tables.

† Available in only 74 patients (15 with and 59 without SARS-CoV-2 infection).

## Diagnosis of SARS-CoV-2 during ACS

SARS-CoV-2 infection status was systematically investigated in all suspected cases. A first clinical evaluation was conducted by the emergency structure (emergency department, French emergency medical system [SAMU] or in the cardiac intensive care unit) before admission in the catheterization laboratory. Criteria for suspecting SARS-CoV-2 infection were: (1) any recent or current clinical sign compatible with SARS-CoV-2 infection (fever, dyspnea, cough, flu symptoms); and (2) a recent contact (< 15 days) with a patient with a confirmed SARS-CoV-2 infection. In patients with suspected infection, reverse transcriptase polymerase chain reaction (RT-PCR) on nasopharyngeal sample was performed. Chest computed tomography imaging was performed at the discretion of the attending physician in association with RT-PCR to confirm or exclude the diagnosis of SARS-CoV-2 infection. Only patients with definite infection diagnosis according to RT-PCR or chest computed tomography imaging were included in the “ACS with SARS-CoV-2 infection” group.

## Management of ACS

All study centres routinely perform primary PCI and ACS according to current guidelines regardless of SARS-CoV-2 infection status.<sup>9,12</sup> However, patients with confirmed or suspected SARS-CoV-2 infection were treated in a dedicated catheterization lab space and subsequently admitted in a dedicated SARS-CoV-2 intensive care unit. Procedural aspects

were recorded, including infarct-related artery, type and localization of culprit lesion, use of thromboaspiration, PCI, antiplatelet glycoprotein IIb/IIIa antibody (GP IIb/IIIa inhibitors) and post-revascularization Thrombolysis In Myocardial Infarction (TIMI) flow. Coronary reperfusion was assessed using the TIMI grade score, in which grade 0 signifies absence of any antegrade flow, grade 1 indicates contrast penetration with incomplete filling of the distal coronary bed, grade 2 slow antegrade flow and filling of the distal territory, and grade 3 complete perfusion. The presence of angiographic no-reflow was defined as the delayed progression or lack of contrast medium through the artery after patency restoration with PCI.<sup>13</sup> Data collection was on the basis of the investigator’s evaluation.

## Management of SARS-CoV-2 infection

Specific treatment of SARS-CoV-2 infection was not standardized and depended on local practice and research protocols. Briefly, most of the participating centres used a combination of antiviral treatment (hydroxychloroquine or retrovirus inhibitor [lopinavir/ritonavir or remdesivir]), inflammation inhibitors (anti-interleukin 6, anti-interleukin 1, or corticosteroids) and empirical antibiotic treatment. Patients with confirmed SARS-CoV-2 pneumonia who required oxygen support and/or mechanical ventilation were systematically empirically treated with amoxicillin/clavulanate or ceftriaxone with macrolides.

**Table 2. Characteristics of patients with STEMI according to SARS-CoV-2 infection status**

	All (N = 116)	SARS-CoV-2 (n = 17)	Non-SARS-CoV-2 (n = 99)	P
Age, years	66.3 ± 13.8	63.4 ± 13.2	66.8 ± 13.9	0.34
Male sex	79 (68)	12 (70)	67 (67)	0.81
Cardiac arrest at presentation	18 (15.5)	6 (35)	12 (12.1)	<b>0.015</b>
Time to revascularization	4 [2-48]	3 [2-48]	4 [2.1-48]	0.77
Nonobstructive coronary arteries	5 (4.3)	4 (23.5)	1 (1.1)	<b>&lt; 0.001</b>
Infarct-related artery				0.76*
Left main	1 (0.9)	0 (0)	1 (1.1)	
Left anterior descending	43 (38.7)	5 (38.4)	38 (38.8)	
Left circumflex	23 (20.7)	4(30.8)	19 (19.4)	
Right coronary artery	44 (39.6)	4 (30.8)	40 (40.8)	
Type of culprit lesion				0.08*
Acute occlusion	80 (72)	12 (92)	68 (69.4)	
Stenosis > 50%	31 (27.9)	1 (7.7)	30 (30.6)	
Coronary anatomy				<b>0.037*</b>
Single-vessel disease	47 (42)	9 (69.2)	38 (38.8)	
Multivessel disease	64 (57.6)	4 (30.7)	60 (61.2)	
Procedural aspects				
Thromboaspiration	18 (16.2)	3 (23.1)	15 (15.3)	0.48
Stent PCI	94 (84.6)	10 (76.9)	84 (85.4)	0.41
Any PCI (balloon or stent)	97 (87.4)	11 (84.6)	86 (87.8)	0.75
Anti-GP IIb/IIIa use	12 (10.8)	3 (23.1)	9 (9.2)	0.13
Persistent no-reflow	8 (7.2)	4 (30.8)	4 (4.1)	<b>0.0004</b>
Outcome (all STEMI patients)				
In hospital death	15 (12.9)	7 (41.2)	8 (8.1)	<b>0.0001</b>
In-hospital cardiac arrest	16 (13.8)	9 (52.9)	7 (7.1)	<b>&lt; 0.001</b>
Cardiogenic shock or heart failure	30 (25.8)	8 (47.1)	22 (22.2)	<b>0.003</b>
Mechanical complications	4 (3.4)	1 (5.9)	3 (3)	0.56
LVEF on discharge, %	47 ± 13	47 ± 12	47 ± 15	0.95
Peak Hs troponin, ng/L	3225 [1086-6030]	1650 [686-3572]	3520 [1177-6608]	<b>0.038</b>
C-reactive protein, mg/L	4 [2-23]	31 [3-128]	4 [2-8]	<b>0.026</b>

Data are presented as n (%), mean ± SD, or mean [25%-75% quartile]. Bold values represent  $P < 0.05$ .

GP, glycoprotein; Hs, high-sensitivity; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

\*  $P$  value is given for contingency tables.

## Clinical outcomes

The primary end point was in-hospital death. Secondary end points included in-hospital cardiac arrest, cardiogenic shock or heart failure, mechanical complications, and discharge left ventricular ejection fraction (LVEF).

## Statistical analyses

SPSS 25 software (IBM Corp, Armonk, NY) was used for the statistical analyses. Nominal and categorical variables were expressed as frequency and percentages and compared using a  $\chi^2$  test. Continuous variables were expressed as mean ± SD and/or in median and quartile (25%-75%), as appropriate. Comparisons between groups were performed with a Student  $t$  test, a  $Z$  test, or 1-way analysis of variance if the validity conditions were met. If necessary, the normal distribution was assessed using a Kolmogorov-Smirnov test or a normality  $\chi^2$  test. If the normal distribution was not verified, continuous variables were compared using Kruskal-Wallis or Mann-Whitney test. A  $P$  value  $< 0.05$  was considered statistically significant.

## Results

From April 1-22, 2020, two hundred thirty-seven patients (mean age, 67 ± 14 years; 69% male; Table 1) were included in the registry, of whom 49% (n = 116) were admitted for

STEMI and 51% (n = 121) for NSTEMI. SARS-CoV-2 infection was reported in 26 patients (17 with STEMI and 9 with NSTEMI). Patients with SARS-CoV-2 were more frequently diabetic (54% vs 26%;  $P = 0.003$ ) and tended to have greater body mass index (28 ± 4 vs 26 ± 5;  $P = 0.07$ ; Table 1). The rate of ACS with SARS-CoV-2 infection was higher for Paris (19%) compared with the other centres (9% in the north of France and 7% in the south of France). Most patients with ACS with SARS-CoV-2 infection (54%) were directly admitted from home and 14 of 26 patients had unknown SARS-CoV-2 infection status on admission. Median time delay between first SARS-CoV-2 symptoms and ACS was 10 days (interquartile range, 6-15) and the SARS-CoV-2 pneumonia status during hospitalization period was graded as nonsevere ( $O_2$  flow  $< 6$  L/min) for 15 patients (58%) and severe for 11 (42%) patients, 8 of whom required invasive mechanical ventilation. Characteristics of SARS-Cov-2 patients are detailed

. Overall, patients with ACS and SARS-CoV-2 infection had more severe clinical presentation with a higher incidence of cardiac arrest at admission (27% vs 7%;  $P = 0.03$ ), higher C-reactive protein (53 mg/L [19-127 mg/L] vs 3 mg/L [2-8 mg/L];  $P < 0.001$ ) and D-dimer levels (1340 ng/mL [414-2983] vs 270 ng/mL [0-500 ng/mL];  $P < 0.001$ ), post procedure no-reflow (19% vs 3%;  $P < 0.001$ ), greater in-hospital mortality (27% vs 7%;  $P = 0.003$ ), and in-hospital cardiac arrest (46% vs 6%;  $P < 0.001$ ).

**Table 3. Characteristics of patients with NSTEMI according to SARS-CoV-2 infection status**

	All (N = 121)	SARS-CoV-2 (n = 9)	Non-SARS-CoV-2 (n = 112)	P
Age, years	66.8 ± 13.9	61.6 ± 14.8	67.2 ± 13.8	0.24
Male sex	84 (69)	7 (78)	77 (69)	0.58
Cardiac arrest at presentation	3 (2.5)	1 (11.1)	2 (1.8)	0.08
Nonobstructive coronary arteries	16 (13.2)	1 (11.1)	15 (13.4)	0.85
Infarct related artery				0.61*
Left main	6 (5.7)	0 (0)	6 (6.2)	
Left anterior descending	44 (41.9)	5 (62.5)	39 (40.2)	
Left circumflex	24 (22.8)	1 (12.5)	23 (23.7)	
Right coronary artery	31 (29.5)	2 (25)	29 (29.9)	
Type of culprit lesion				<b>0.021*</b>
Acute occlusion	19 (18)	4 (50)	15 (15.5)	
Stenosis > 50%	81 (77)	3 (37.5)	78 (80.4)	
Stenosis < 50%	5 (4.7)	1 (12.5)	4 (4.1)	
Coronary anatomy				0.77*
Single-vessel disease	31 (29.5)	2 (25)	29 (29.9)	
Multivessel disease	37 (35.2)	6 (75)	69 (71.1)	
Procedural aspects				
Thromboaspiration	4 (3.8)	0 (0)	4 (4.1)	0.56
Stent PCI	89 (84.8)	7 (87.5)	80 (82.5)	0.72
Any PCI (balloon or stent)	92 (87.6)	7 (87.5)	83 (85.6)	0.88
Anti-GP IIb/IIIa use	5 (4.7)	2 (25)	3 (3.1)	<b>0.049</b>
Persistent no-reflow	4 (3.8)	1 (12.5)	3 (3.3)	0.19
Outcome (all NSTEMI patients)				
In-hospital death	5 (4.1)	0 (0)	5 (4.5)	0.52
In-hospital cardiac arrest	8 (6.6)	3 (33.3)	5 (4.5)	<b>0.007</b>
Cardiogenic shock or heart failure	16 (13.2)	2 (22.2)	14 (12.5)	0.41
LVEF on discharge, %	52 ± 11	48 ± 10	53 ± 11	0.24
Median peak Hs troponin, ng/L	443 [131-1269]	605 [311-2631]	441 [120-1256]	0.26
Median C-reactive protein, mg/L	3.3 [2-15]	68.1 [46-115]	3.0 [2-8]	<b>&lt; 0.001</b>

Data are presented as n (%), mean ± SD, or mean [25%-75% quartile]. Bold values represent  $P < 0.05$ .

C-reactive protein, C-reactive protein; GP, glycoprotein; Hs, high-sensitivity; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention.

\*  $P$  value is given for contingency tables.

## STEMI

The initial admission pathway for STEMI was the French emergency structure (SAMU,  $n = 80$ ; 72%), emergency department ( $n = 13$ ; 12%), and in- or interhospital transfer ( $n = 18$ ; 16%; [Table 2](#)). All patients underwent primary PCI and no thrombolytic therapy was administered. Time delay from symptom onset to reperfusion was 4 hours [0-48], with no difference between Paris (median, 3 hours [2-9]) and the other centres and between SARS-CoV-2 and no SARS-CoV-2 infection (3 hours [2-48] vs 4 hours [2-48];  $P = 0.62$ ). However, cardiac arrest or severe ventricular arrhythmia at admission was more prevalent in patients with SARS-CoV-2 infection (35% vs 12%;  $P = 0.015$ ; [Table 2](#)). Aspirin was administered in 100% of STEMI patients irrespective of SARS-CoV-2 status. Administration of P2Y12 inhibitors (82% vs 92%), heparin (82% vs 92%;  $P = 0.1$ ), and GP IIb/IIIa inhibitors (84.6 vs 87.8;  $P = 0.75$ ) did not differ in SARS-CoV-2 infected and noninfected patients. Normal coronary angiogram was reported in 4 of 17 (24%) patients with STEMI and SARS-CoV-2 infection. In patients with significant coronary artery disease ( $n = 17$ ), 9 of 17 (53%) had single-vessel disease. Complete culprit artery occlusion was more frequently observed in STEMI patients with than without SARS-CoV-2 infection (98% vs 69%;  $P < 0.05$ ). PCI was similarly performed regardless of infection status (85% in SARS-CoV-2 vs 88% in non-SARS-CoV-2 infection;  $P = 0.75$ ) but angiographic no-reflow was more frequently

observed after PCI in patients with SARS-CoV-2 infection (31% vs 4%;  $P < 0.001$ ). Despite lower peak troponin levels and similar LVEF, cardiac arrest (53% vs 7%;  $P < 0.0001$ ) and heart failure during the hospitalization (47% vs 22%;  $P = 0.003$ ) were more frequent in patients with STEMI and SARS-CoV-2 infection. Finally, the mortality rate was greater in STEMI patients with than without SARS-CoV-2 infection (41% vs 8%;  $P < 0.001$ ). The causes of death in STEMI patients with SARS-CoV-2 infection were cardiac arrest ( $n = 3$ ), refractory arrhythmia ( $n = 1$ ), and pneumonia related to SARS-CoV-2 ( $n = 1$ ).

## NSTEMI

SARS-CoV-2 infection was reported in 9 of 121 (7.4%) patients admitted for NSTEMI. Patients with NSTEMI with and without SARS-CoV-2 infection had similar age and sex distribution ([Table 3](#)). Similar to the STEMI population, cardiac arrest on presentation tended to be more frequent in patients with SARS-CoV-2 infection (11% vs 2%;  $P = 0.08$ ). No differences were observed in ACS treatment between the SARS-CoV-2 and non-SARS-CoV-2 group (89% vs 92% for aspirin; 78% vs 80% for P2Y12 inhibitors; and 67% vs 77% for heparin). However, GP IIb/IIIa inhibitors were used more frequently in patients with NSTEMI with than without SARS-CoV-2 (25% vs 3%;  $P = 0.05$ ). Nonobstructive coronary artery disease was reported in only 1 NSTEMI patient

with SARS-CoV-2 infection. In NSTEMI patients with significant coronary lesions, occlusion of the culprit artery was more frequent in patients with SARS-CoV-2 infection (50% vs 16%;  $P = 0.015$ ). PCI rate was similar in the 2 groups. Cardiac troponin levels and LVEF were similar in the 2 groups. In-hospital cardiac arrest (33% vs 5%;  $P = 0.007$ ) was more frequent in patients with NSTEMI and SARS-CoV-2 infection but no death was reported in patients with NSTEMI and SARS-CoV-2 infection (Table 3).

### Myocardial infarction with nonobstructive coronary arteries

Myocardial infarction with nonobstructive coronary arteries ( $n = 21$ ) was reported in 5 of 26 (19%) patients with and 16 of 211 (7.6%) patients without SARS-CoV-2 infection ( $P < 0.0001$ ). Of the 5 patients with SARS-CoV-2 infection, 1 had NSTEMI and 4 had STEMI presentations. Specific etiology was identified in 2 patients (1 takotsubo syndrome and 1 of embolic origin from native aortic valve thrombosis). The 2 deaths in the myocardial infarction with nonobstructive coronary arteries group occurred exclusively in patients with SARS-CoV-2 infection, both as the result of acute respiratory distress syndrome.

### In-hospital death

Mortality rates were higher in patients with ACS and SARS-CoV-2 infection (26.9% vs 13%;  $P = 0.0003$ ). In univariate analysis, clinical and angiographic factors associated with in-hospital death were SARS-CoV-2 infection (odds ratio [OR], 5.6 [95% confidence interval (CI), 1.99-15.7];  $P = 0.0011$ ), no-reflow (OR, 15 [95% CI, 4.2-52.8];  $P < 0.001$ ), cardiac arrest on presentation (OR, 7.8 [95% CI, 2.68-22.68];  $P = 0.002$ ), STEMI (OR, 3.4; [95% CI, 1.2-9.8];  $P = 0.02$ ), and diabetes (OR, 2.7 [95% CI, 1.085-6.9];  $P = 0.03$ ). In multivariate analysis, independent variables were diabetes, no-reflow and cardiac arrest on presentation whereas SARS-CoV-2 was not because SARS-CoV-2 was the only variable associated with no-reflow (OR, 6.3 [95% CI, 1.7-23];  $P = 0.05$ ) and cardiac arrest on presentation.

### Discussion

This multi centre registry conducted in April during the SARS-CoV-2 epidemic plateau in France showed a significant prevalence of SARS-CoV-2 infection in ACS patients (19% for Paris, 11% for overall). ACS with concomitant SARS-CoV-2 infection was characterized by a more severe initial clinical presentation with greater percentage of cardiac arrest on admission, occluded culprit lesion, and no-reflow after PCI. This resulted in a higher in-hospital mortality and increased complications.

### STEMI and SARS-CoV-2

In a comparison of STEMI patients with and without SARS-CoV-2 infection, there was no significant difference in time from symptom onset to revascularization. Also, compared with the data of the French registry on ACS, French Registry of Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction (FAST-MI), the pandemic did not

seem to influence the median time from symptom onset to revascularization (4 hours vs 3.8 hours).<sup>14</sup> This lack of difference was probably because of the efficient reinforcement of the SAMU during the epidemic crisis. In terms of coronary anatomy, SARS-CoV-2 patients had myocardial infarction with nonobstructive coronary arteries more frequently but most had obstructive coronary artery disease with a high prevalence of an acutely occluded culprit artery in STEMI and NSTEMI patients. This might explain the high proportion of cardiac arrest in this population.

### SARS-CoV-2 and thrombotic burden

The high incidence of no-reflow phenomenon after PCI suggests a high thrombotic burden in the culprit lesion and raises the question of GP IIb/IIIa inhibitors use with or without cytokine inhibitors to block the cytokine storm and the inflammation-related coagulopathy. Our data are in agreement with the retrospective study performed by Choudry et al., showing that COVID-19 infection in patients with STEMI was associated with a higher thrombus burden, increased need to use GP IIb/IIIa inhibitors, and mortality.<sup>15</sup> The main hypothesis to explain this phenomenon is the procoagulant state induced by SARS-CoV-2 infection due to endothelial and/or platelet dysfunction and associated with disseminated intravascular coagulation secondary to severe inflammation. Such a hypothesis is also consistent with recent literature data on various thrombotic events and complications among SARS-CoV-2 patients.<sup>16,17</sup>

### SARS-CoV-2 and mortality

Consistently, patients with STEMI and SARS-CoV-2 infection had a dramatically higher in-hospital mortality (42.1%) than patients with STEMI without SARS-CoV-2 infection (8.1%). These rates are also higher than those reported in the FAST-MI registry (approximately 2.8%)<sup>18</sup> because patients with ACS with early death were excluded from the FAST-MI registry. It might be tempting to consider that the excess mortality in patients with ACS and concomitant SARS-CoV-2 infection is driven by the respiratory infection but our present registry shows that hemodynamic complications (cardiac arrest and heart failure) were highly prevalent in the SARS-CoV-2 group and that independent variables associated with death were cardiac arrest at presentation and no-reflow. Almost half (43%;  $n = 3$  of 7) of the deaths in the SARS-CoV-2 group had nonsevere respiratory infection and died of cardiovascular complications.

Altogether, these data underline the importance of referring most patients with ACS and SARS-CoV-2 infection to coronary angiogram, because the a large proportion of patients with STEMI and concomitant SARS-CoV-2 infection had a significant coronary lesion that could be treated with PCI. These findings are also consistent in the NSTEMI population because 90% of patients in the SARS-CoV-2 group had significant coronary disease with a high proportion of culprit artery occlusion. The low proportion of NSTEMI in SARS-CoV-2 patients is possibly related to the fact that SARS-CoV-2 patients with NSTEMI are underreported and usually not referred for a coronary

angiogram. An increase in cardiac biomarkers has been considered a sign of myocardial injury related to systemic inflammation, cytokine storm, or other immunologic mechanisms. However, because of the high rate of significant coronary thrombosis, coronary angiogram should be systematically considered, especially in patients with hemodynamic instability.

## Limitations

Although significant data from multiple centres were gathered in this registry in a very short period of time, the sample size remains small. Larger studies are needed to precisely describe the relationship between SARS-CoV-2 infection, ACS occurrence, and prognosis. Moreover, the prevalence of SARS-CoV-2-related ACS might be overestimated for 2 reasons. First, some of the participating hospitals were reference centres for the SARS-CoV-2 infection, in regions with high SARS-CoV-2 prevalence during the study period. Second, published data from regions with a high SARS-CoV-2 prevalence suggest a significant decrease in ACS-related hospitalizations during the pandemic.<sup>19</sup> The effect of SARS-CoV-2 in the overall ACS prevalence in the corresponding population was beyond the scope of this study.

## Conclusion

SARS-CoV-2 infection is frequent in patients managed for ACS (11%) especially in regions with high prevalence of SARS-CoV-2 infection. Patients with SARS-CoV-2 infection and ACS have a high prevalence of occluded artery and no-reflow phenomenon, which suggests high thrombotic burden that could explain, in part, higher rates of in-hospital complications and mortality. Further studies are needed to elucidate the mechanisms and the optimal management of coronary thrombosis in SARS-CoV-2 patients.

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