



ORIGINAL RESEARCH

Cardiology

Incidence, delays, and outcomes of STEMI during COVID-19 outbreak: Analysis from the France PCI registry

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Abstract

Objectives: The aim of this study was to assess the impact of the coronavirus disease 2019 (COVID-19) outbreak on incidence, delays, and outcomes of ST-elevation myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention (PPCI) in France.

Methods: We analyzed all patients undergoing PPCI <24 hours STEMI included in the prospective France PCI registry. The 2 groups were compared on mean monthly

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number of patients, delays in the pathway care, and in-hospital major adverse cardiac events (MACE: death, stent thrombosis, myocardial infarction, unplanned coronary revascularization, stroke, and major bleeding).

Results: From January 15, 2019 to April 14, 2020, 2064 STEMI patients undergoing PPCI were included: 1942 in the prelockdown group and 122 in the lockdown group. Only 2 cases in the lockdown group were positive for COVID-19. A significant drop (12%) in mean number of STEMI/month was observed in the lockdown group compared with prelockdown (139 vs 122, $P < 0.04$). A significant increase in “symptom onset to first medical contact” delay was found for patients who presented directly to the emergency department (ED) (238 minutes vs 450 minutes; $P = 0.04$). There were higher rates of in-hospital MACE (7.7% vs 12.3%; $P = 0.06$) and mortality (4.9% vs 8.2%; $P = 0.11$) in the lockdown group but the differences were not significant.

Conclusion: According to the multicenter France PCI registry, the COVID-19 outbreak in France was associated with a significant decline in STEMI undergoing PPCI and longer transfer time for patients who presented directly to the ED. Mortality rates doubled, but the difference was not statistically significant.

KEYWORDS

Acute coronary syndrom, COVID-19, Myocardial infarction, Percutaneous coronary intervention, STEMI

1 | INTRODUCTION

1.1 | Background

Acute ST-elevation myocardial infarction (STEMI) is the major cardiac emergency that most hospital cardiologists deal with daily. Rapid reperfusion of the culprit artery by primary percutaneous coronary intervention (PPCI) is recommended for optimal outcomes.^{1,2}

Emergency medical systems (EMS) are organized to minimize the time required to transfer patients to the catheterization laboratory (cath lab).³

1.2 | Importance

The coronavirus disease 2019 (COVID-19) outbreak has threatened European health care systems, potentially overshadowing other emergencies including STEMI. This has led to a change in the organization of the health care system for the management of patients without COVID-19. All non-emergency interventions have been downgraded and postponed. The Society for Cardiac Angiography and Interventions (SCAI) and the European Association of Percutaneous Cardiovascular Interventions (EAPCI) continue to recommend PPCI as the standard treatment of STEMI patients during the current pandemic.^{4,5} However, there are no data available on the effects of this strategy during a pandemic.

In many countries, a lockdown was imposed by the authorities in order to slow the progression of the virus and avoid hospital crowding. In France, the lockdown was implemented throughout the country. This situation may have discouraged patients from coming to the hospital. An impact on time from onset to first medical contact (FMC) for STEMI patients can be expected, but it may be influenced by opposing factors: overwhelmed EMSs would delay care, for example, but reduced intensity of road traffic would speed up transfer to care centers.

1.3 | Goal of this investigation

The aim of this study was to assess the impact of the COVID-19 outbreak on incidence, delays, and outcomes of STEMI in patients undergoing PPCI in France.

2 | METHODS

2.1 | Registry design

The prospective multicenter France PCI registry, started on January 1, 2014, collects all patients undergoing coronary angiography or coronary angioplasty at 16 interventional cardiology centers (ICC) participating in 3 different French regions (Centre Val de Loire, Auvergne Rhône Alpes, and Normandie; Figure 1). The basic methodology for the France PCI registry (originally named CRAC) has been previously

described. Out-of-hospital, clinical, and procedural data are collected prospectively by cardiologists at the time of the patient's admission to ICC and recorded in electronic reporting software (CardioReport; CVX Medical, Croissy-Beaubourg, France). The data are of high quality, 99.6% of completeness and with 89% of consistency.⁶ The registry is registered with clinicaltrials.org (NCT02778724).

The study was conducted according to contemporary clinical practice guidelines and French regulations (Advisory Committee on Information Processing in Material Research in the Field of Health no. 13.245). The French Persons Protection Committee (IRB00003888) approved the study protocol (no. 15–231). Data file collection and storage were approved by the French National Commission for Data Protection and Liberties (no. 2014–073). All patients were informed of the aims of the survey. All included patients gave their informed consent to participate before data collection.

2.1.1 | Selection of subjects

The current analysis included all consecutive patients undergoing PPCI for STEMI between January 15, 2019 and April 14, 2020. Four ICC centers that started their inclusion after January 15, 2019 and 1 center with incomplete data were excluded from the study. We also excluded fibrinolysis, late presentation STEMI (>24 hours), and patients without PPCI. The study population was divided into 2 groups: the prelockdown group (patients included before March 15, 2020, that

The Bottom Line

Societal “lockdowns” for coronavirus disease 2019 (COVID-19) have indirectly affected the care of other critical illness. In this analysis of 2064 patients from 16 hospitals in the France percutaneous coronary intervention (PCI) registry, COVID-19 lockdown resulted in a 12% reduction in monthly ST-elevation myocardial infarctions (STEMIs) but a more than 200-minute increase in STEMI symptom reporting delays. Major adverse cardiovascular events and mortality were slightly higher, but the differences were not statistically significant. These results illustrate the effects of COVID-19 societal lockdown upon STEMI care and outcomes.

is, date of national lockdown announcement) and the lockdown group (patients included from March 15 to April 14, 2020).

2.1.2 | Follow-up

Patient follow-up was conducted by local on-site research technicians in the participating centers. Data were anonymized before automatic and daily transfer to the central France PCI database. Regional data monitoring was coordinated by the France PCI clinical research asso-

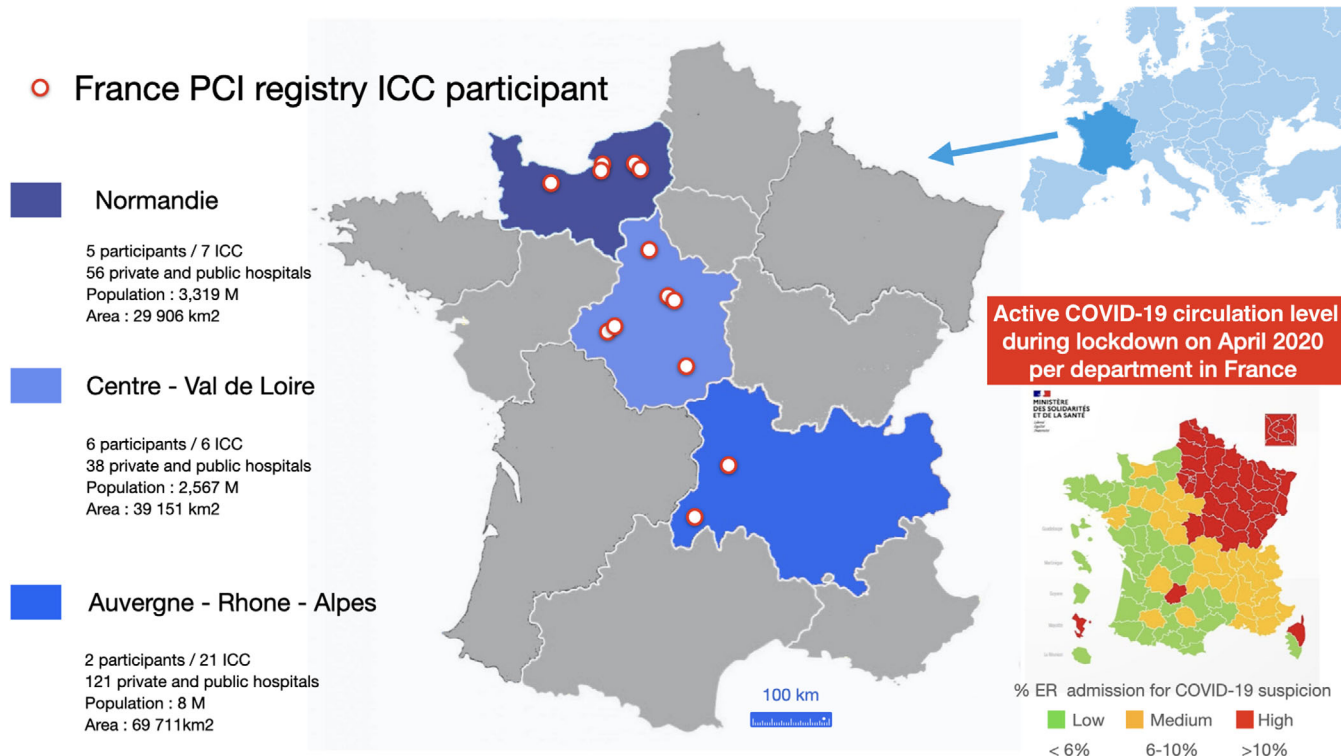


FIGURE 1 Participating centers in the France PCI percutaneous coronary intervention (PCI) registry. The 11 interventional cardiology centers (ICCs) included were located in 3 administrative regions in western France (Normandie, Centre Val de Loire, and Auvergne Rhône Alpes), which were less affected by the COVID-19 outbreak than the eastern part during lockdown on April 2020

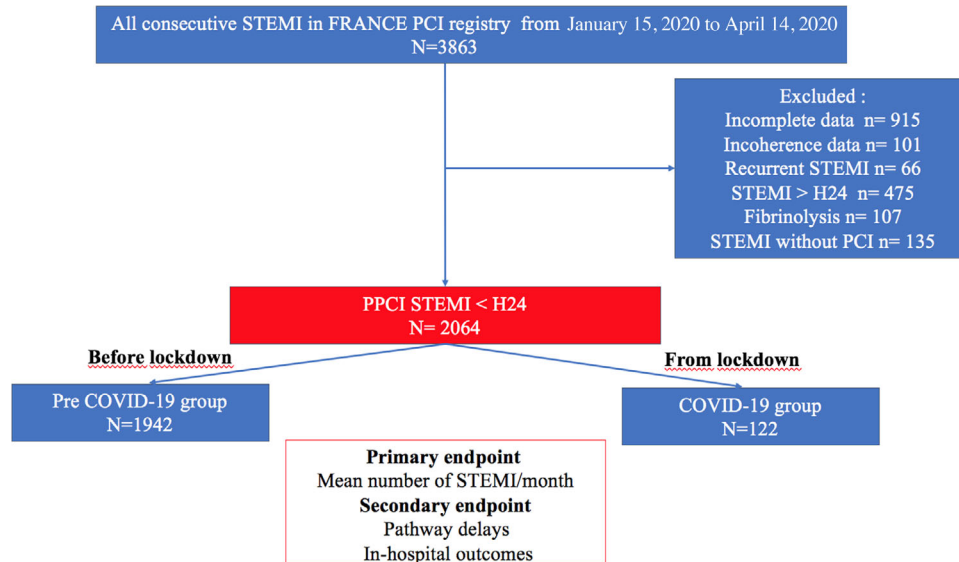


FIGURE 2 Flow chart. PCI, percutaneous coronary intervention; PPCI, primary percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction

ciate. External independent quality control (appropriate procedures, completeness, and consistency of data) was made periodically at each site by a multicenter research assistant.

2.1.3 | Exposure

From March 16 to May 10, 2020, the French government ordered a large-scale lockdown to counter the wave of COVID-19 infections in the country. The lockdown halted non-essential economic, educational, and entertainment activities, mandated people to remain at home and venture out only for essential reasons. Food retailers and health care institutions remained operational.

During the COVID 19 outbreak and according to current guidelines,^{4,5,7} any STEMI patient was considered a carrier of COVID-19. Accordingly, additional measures were introduced for the care of this population, including systematic protection of health care personnel and careful questioning of the patient. In order not to lengthen delays, PPCI was carried out with all the precautions considering the patient as a suspect at COVID-19; testing for the virus and possibly chest computed tomography were performed only after the revascularization procedure. Patients were tested for the virus only if there was a clinical suspicion of COVID-19 infection. This approach was taken by all interventional centers in France.

2.2 | Outcome measures

The following outcomes were analyzed: (1) mean monthly number of patients undergoing PPCI for STEMI; (2) delays in the care pathway: patient delay, defined as the overall time from symptom onset to FMC; system delay, defined as the overall time from FMC to PPCI;

and total ischemic time, defined as time from symptom onset to PPCI. In-hospital outcomes were analyzed on a composite of death, definite stent thrombosis (Academic Research Consortium), myocardial infarction, unplanned coronary revascularization, stroke, and major bleeding (Bleeding Academic Research Consortium ≥ 3). FMC was defined as the time point for the qualifying electrocardiogram.⁸

2.3 | Statistical analysis

A descriptive method was used for the data analysis. The comparisons between periods for categorical data were performed using chi-square or Fisher's exact tests. A mixed model with random intercepts corrected for time as a continuous variable was used to estimate the percent change between periods. All tests were 2-sided, with a type I error set at 5%. All analyses were performed using Stata 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

3 | RESULTS

From January 15, 2019 to April 14, 2020, 2064 STEMI patients undergoing PPCI were included: 1942 in the prelockdown group and 122 in the lockdown group (Figure 2). There were no significant differences in baseline characteristics between the 2 groups (Table 1). Only 2 patients in the lockdown group had a COVID-19 infection, confirmed by a positive reverse transcription polymerase chain reaction test. Cardiogenic shock was almost twice as common in the lockdown group (2.9% vs 5.7%; $P = 0.07$).

There was a significant difference between the mean numbers of STEMI patients undergoing PPCI per month in the prelockdown and

TABLE 1 Characteristics of STEMI patients undergoing PPCI according to lockdown period January 15, 2019 to April 14, 2020

	Overall population (N = 2064)		Pre-lockdown group (N = 1942)		Lockdown group (N = 122)		P value
	N	%	N	%	N	%	
Risk factors							
Age ≥75 years	489	23.8	463	23.8	26	21.3	0.52
Age median [SD]	63.56 [54–73]		63.60 [54–73]		62.93 [54–72]		0.59
Women	501	24.3	465	23.9	36	29.5	0.16
BMI ≥25 kg/m ²	1297	63.8	1226	64.1	71	58.2	0.18
Diabetes mellitus	308	15.2	285	14.9	23	19	0.23
Hypercholesterolemia	629	33.4	596	33.8	33	28.2	0.21
Hypertension	857	42.4	802	42.2	55	45.8	0.43
Current smoker	780	38.4	732	38.3	48	39.7	0.26
Medical history							
Family history of CAD	409	20.8	387	20.8	25	20.8	0.98
Prior myocardial infarction	140	6.8	135	7	5	4.1	0.22
Prior PCI	247	12	236	12.1	11	9	0.29
Prior CABG	35	1.7	35	1.8	0	0	0.13
History of CAD ^a	271	13.1	259	13.3	12	9.8	0.26
History of PAD	77	3.8	73	3.8	4	3.3	0.75
History of stroke	63	3	60	3.1	3	2.5	0.69
History of CKD	61	3.3	55	3.1	6	5.4	0.20
Clinical presentation							
COVID-19 status	2	0.1	0	0	2	1.6	/
Ischemia localization							
Anterior	859	42.5	802	42.3	57	46.7	0.33
Inferior or lateral	1161	57.5	1096	57.7	65	53.3	0.33
LVEF < 40%	220	22	204	21.9	16	23.9	0.70
Cardiogenic shock	63	3	56	2.9	7	5.7	0.07
Cardiac arrest	65	3.1	60	3.08	5	4.1	/
Prehospital pathway							
EMS call	1333	64.6	1258	64.8	75	61.5	0.45
FMC							0.21
EMS	1345	65.3	1270	65.5	75	61.5	
ED	535	26	504	26	31	25.4	
Others	181	8.8	165	8.5	16	13.1	
Optimal care pathway ^b	813	39.4	764	39.3	49	40.2	0.85
Preprocedure medication							
Antiplatelet therapy							
Aspirin	1985	96.3	1868	96.2	117	96.7	0.79
P2Y12 inhibitor	1919	93	1803	92.8	116	95.1	0.34
Heparin	1813	87.9	1700	87.6	113	93.4	0.05
Procedural characteristics							
Radial access	1913	92.7	1803	92.9	110	90.2	0.26
Number of diseased vessels							
0	5	0.2	5	0.3	0	0	0.84
1	861	41.7	809	41.7	52	42.6	

(Continues)

TABLE 1 (Continued)

	Overall population (N = 2064)		Pre-lockdown group (N = 1942)		Lockdown group (N = 122)		P value
	N	%	N	%	N	%	
≥2	1198	58	1128	58.1	70	57.38	
Left main	76	3.7	69	3.5	7	5.7	0.21
N PCI site, mean	2064	1.30	1942	1.29	122	1.37	0.24
Drug eluting stent	1817	88	1704	87.7	113	92.6	0.10
N stents per procedure, mean	2064	1.27	1942	1.26	122	1.37	0.18
AGP2b3a	469	22.8	444	22.9	25	20.7	0.32
Thromboaspiration	455	22	432	22.2	23	18.8	0.38
PCI success	2015	98.1	1898	98.2	117	96	0.06

AGP2b3, antglycoprotein 2b3a; BMI, body mass index; CABG, coronary arterial bypass graft; CAD, coronary artery disease; CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; EMS, emergency medical system; ED, emergency department; FMC, first medical contact; LVEF, left ventricular ejection fraction; m [SD], mean (standard deviation); N, number; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PPCI, primary percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

^a Combination of the 3 previous variables.

^b Pathway with only 1 medical practitioner before PCI.

TABLE 2 Incidence and pathway delays of STEMI patients undergoing PPCI according to lockdown period, from January 15, 2019 to April 14, 2020

	Overall population (N = 2064)		Prelockdown group (N = 1942)		Lockdown group (N = 122)		P value
	N	Median or Mean	N	Median or Mean	N	Median or Mean	
Number of PPCI/month, mean	2064	138 [131;146]	1942	139	122	122	0.04
Patient delay, median							
Symptom onset to FMC (min)							
Overall population	2059	186 [51;100]	1937	181 [51;100]	122	263 [57;121]	0.09
According to FMC							
EMS	1343	155 [50;164]	1268	154 [50;164]	75	175 [51–176]	0.65
ED	532	251 [77;328]	501	238 [77;305]	31	450 [95;761]	0.04
Others	181	226 [15;281]	165	218 [12;280]	16	310 [72;329]	0.23
System delay, median							
FMC to PPCI (min)	2061	119 [69;137]	1939	119 [69;136]	122	125 [72;144]	0.14
Symptom onset to PPCI (min), median	2040	296 [146;340]	1923	294 [145;340]	117	337 [160;360]	0.16

EMS, emergency medical system; ED, emergency department; FMC, first medical contact; min, minutes; N, number; PPCI, primary percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

the lockdown groups (139 vs 122; $P < 0.04$) (Table 2). The “symptom onset-FMC” delay in patients who presented directly to the ED was significantly longer in the lockdown group (450 minutes vs 238 minutes; $P = 0.04$). For the overall population, non-significant increases in symptom onset-to-FMC (181 minutes vs 263 minutes; $P = 0.09$), FMC-to-PPCI (119 minutes vs 125 minutes; $P = 0.14$), and symptom onset-to-PPCI delays (294 minutes vs 337 minutes; $P = 0.16$) were observed in the lockdown group. The median duration of hospitalization was similar in both groups: 5 days (range 3–7) versus 4 days (range 3–6), $P = 0.30$. Rates of in-hospital composite outcomes were higher in the lockdown

group (7.7% vs 12.3% v; $P = 0.06$) and mortality almost doubled (4.9% vs 8.2%; $P = 0.10$) (Table 3) but the differences for these comparisons were not statistically significant.

3.1 | Limitations

The main limitation of this study is the modest sample size and duration of follow-up in the postlockdown data that reduced the statistical power of the analysis. Several differences did not reach statistical

TABLE 3 In-hospital outcomes of STEMI patients undergoing PPCI according to lockdown period, from January 15, 2019 to April 14, 2020

	Overall population (N = 2064)		Prelockdown group (N = 1942)		Lockdown group (N = 122)		P value
	N	%	N	%	N	%	
Outcomes							
Composite outcomes	164	7.9	149	7.7	15	12.3	0.06
Death	105	5.1	95	4.9	10	8.2	0.10
Definite stent thrombosis (ARC)	5	0.2	5	0.3	0	0	0.58
Urgent revascularization	20	1	18	0.9	2	1.8	0.37
Recurrent MI	21	1	20	1	1	0.9	0.88
Stroke	10	0.5	9	0.5	1	0.9	0.56
Severe bleeding \geq BARC 3)	41	2	38	2	3	2.6	0.60

ARC, Academic Research Consortium; BARC, Bleeding Academic Research Consortium; MI, myocardial infarction; PPCI, primary percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

significance. The location of centers in French regions less affected by the outbreak may have minimized the impact of lockdown on STEMI care. A longer study period may confirm the trends. Exclusion of fibrinolysis patients from the analysis may limit the overview of revascularization modalities during the COVID-19 period. However, the rate of fibrinolysis in our practice was very low (5.1% before lockdown and 2.4% during lockdown) and not likely to influence the results of the study. There is a possibility for bias if French patients became averse to seeking care prior to lockdown, as news spread about the pandemic. However, we did not find a decline in STEMI in the months prior to lockdown, which indicates that this did not happen. A final limitation is that only STEMI patients undergoing PPCI are included in the France PCI registry. Therefore, conservatively treated patients were not analyzed. However, patients who were suspected or positive for COVID-19 also received unrestricted PPCI.

4 | DISCUSSION

This is to the best of our knowledge the largest multicenter study to date to report data on pathway delays and in-hospital outcomes for STEMI patients during the COVID-19 outbreak. In addition to a significant 12% drop in the number of STEMI patients treated by PPCI in France, the "symptom onset-FMC" delay in patients who presented directly to the ED almost doubled after the national lockdown.

Reductions in STEMI admissions as a result of the COVID-19 pandemic have been reported from Austria (25.5%), Italy (26.5%), Spain (40%), and the United States (48%).⁹⁻¹² The centers in the France PCI registry are located in the western part of France, which was less affected than other parts by the COVID-19 outbreak, which probably explains the smaller reduction in admissions observed in our data.

The decrease in admissions may be related either to a reduction in the incidence of STEMI or to fewer cases arriving at the hospital. A reduced incidence in acute coronary syndromes may be owing to reduced air pollution, less work-related stress, and less physical activity such as sport during the lockdown. The correlation between

urban air pollution and myocardial infarction is controversial.^{13,14} The rural location of the centers participating in this study and the drop in STEMI immediately after the imposition of lockdown do not support an effect from air quality improvement. Stress may increase the risk of myocardial infarction^{15,16} but the impact of lockdown on mental or physical stress has been difficult to assess.¹⁷ In a recent French study, the population stress index doubled during the COVID-19 lockdown,¹⁸ which indicates that overall stress cannot explain the reduction in STEMIs. Reduced physical activity during lockdown might have contributed to a decrease in the incidence of STEMI, but the size of the reduced incidence and the steep fall in cases very soon after lockdown make such an explanation unlikely.

Another potential explanation for our observations is under-detection of STEMIs in the community during lockdown. Patients may have feared infection at hospitals, postponing STEMI admissions. The trend toward increased symptom onset-FMC time observed in our study supports a change in patient behavior during the lockdown period. A reluctance of patients to present to hospital has been described for other medical emergencies such as stroke or transient ischemic attack.¹⁹ The tendency toward more presentations with greater hemodynamic instability in the lockdown group in our study may indicate that lower-risk or mildly symptomatic patients represent the greatest part of the "missing" STEMIs.

We observed the greatest "symptom onset-FMC" delay in patients presenting directly to emergency departments, which doubled during the lockdown period. A recent Asian small study²⁰ warned about a significant increase in out-of-hospital and door-to-device delays for acute STEMI patients during the COVID-19 period. EMS are generally well equipped to minimize delays in transferring STEMI patients to the cath lab,³ but during an epidemic, these systems can be overwhelmed. For STEMI patients this would impose a double penalty: patients react later and the transfer time within the EMS is extended. Bespoke pathways in EDs for patients suspected of infection and for other emergencies may improve workflows during an epidemic.

Delayed reperfusion is a powerful predictor of adverse outcomes in STEMI patients.^{21,22} A recent publication reported mortality rate of

73% in STEMI patients with COVID-19 in the United States²³ and an Italian survey likewise report significantly higher mortality in patients admitted for myocardial infarction during the COVID-19 outbreak compared with the same period in 2019.¹⁰ In our cohort, the doubling of mortality in the lockdown group was not statistically significant, but this was possibly because of a modest sample size.

In conclusion, these data from the large multicenter France PCI registry show that the COVID-19 outbreak in France was associated with a significant decline in STEMI undergoing PPCI and longer transfer times for patients who presented directly to the ED. Mortality doubled but the difference was not statistically significant. With an ongoing second wave of COVID-19 infections, the reasons for this adverse situation need to be clearer identified in order to target appropriate actions to reduce inefficiencies in care delivery, as well as promote changes in patient awareness and behavior.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

GR, PM, RK, and GM obtained research funding. GR, RH, and PM conceived and designed the study. GR, RH, and PM drafted the manuscript and all authors contributed substantially to its revision. All authors were involved in the execution of the study. GR takes responsibility for the paper as a whole.

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