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CLINICAL RESEARCH

ST-segment elevation myocardial infarction: Management and association with prognosis during the COVID-19 pandemic in France[☆]

Infarctus du myocarde avec sus-décalage du segment ST : prise en charge et association au pronostic lors de la pandémie de COVID-19 en France

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Abbreviations: BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; FMC, first medical contact; IQR, interquartile range; LVEF, left ventricular ejection fraction; MODIF, myocardial infarction rates overview during COVID-19 pandemic in France; OR, odds ratio; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction.

[☆] Tweet: During the first peak of the COVID-19 pandemic in France, there was a decrease in STEMI admissions, associated with longer ischemic time, exclusively driven by an increase in patient-related delays and an increase in mechanical complications.

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² A complete list of the MODIF registry investigators is provided in the online [Appendix B](#).

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KEYWORDS

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Summary

Background. – Systems of care have been challenged to control progression of the COVID-19 pandemic. Whether this has been associated with delayed reperfusion and worse outcomes in French patients with ST-segment elevation myocardial infarction (STEMI) is unknown.

Aim. – To compare the rate of STEMI admissions, treatment delays, and outcomes between the first peak of the COVID-19 pandemic in France and the equivalent period in 2019.

Methods. – In this nationwide French survey, data from consecutive STEMI patients from 65 centres referred for urgent revascularization between 1 March and 31 May 2020, and between 1 March and 31 May 2019, were analysed. The primary outcome was a composite of in-hospital death or non-fatal mechanical complications of acute myocardial infarction.

Results. – A total of 6306 patients were included. During the pandemic peak, a $13.9 \pm 6.6\%$ ($P=0.003$) decrease in STEMI admissions per week was observed. Delays between symptom onset and percutaneous coronary intervention were longer in 2020 versus 2019 (270 [interquartile range 150–705] vs 245 [140–646] min; $P=0.013$), driven by the increase in time from symptom onset to first medical contact (121 [60–360] vs 150 [62–420] min; $P=0.002$). During 2020, a greater number of mechanical complications was observed (0.9% vs 1.7%; $P=0.029$) leading to a significant difference in the primary outcome (112 patients [5.6%] in 2019 vs 129 [7.6%] in 2020; $P=0.018$). No significant difference was observed in rates of orotracheal intubation, in-hospital cardiac arrest, ventricular arrhythmias and cardiogenic shock.

Conclusions. – During the first peak of the COVID-19 pandemic in France, there was a decrease in STEMI admissions, associated with longer ischaemic time, exclusively driven by an increase in patient-related delays and an increase in mechanical complications. These findings suggest the need to encourage the population to seek medical help in case of symptoms.

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MOTS CLÉS

SCA ST+ ;
COVID-19 ;
Complications
mécaniques ;
Confinement

Résumé

Contexte. – Les systèmes de santé à travers le monde ont été fortement mis à l'épreuve afin de contrôler la progression de l'épidémie de la COVID-19. L'éventualité que la réorganisation des soins ait pu influencer les délais de rereperfusion ou le devenir des patients présentant des syndromes coronaires aigus avec sus-décalage du segment ST (SCA ST+) n'a pas été explorée en France.

Objectif. – Comparer le taux d'admissions pour SCA ST+, les délais de traitement et enfin le devenir de ces patients entre la première vague épidémique de la COVID-19 et pendant la période similaire en 2019.

Méthodes. – Dans ce registre national multicentrique, les patients avec SCA ST+ provenant de 65 centres français admis en urgence pour revascularisation entre le 1^{er} mars et le 31 mai 2020 et entre le 1^{er} mars et le 31 mai 2019 ont été analysés. Le critère de jugement principal était un critère composite regroupant la mortalité intrahospitalière toute cause confondue et les complications mécaniques en lien avec l'infarctus.

Résultats. – Un total de 6306 patients ont été inclus. Pendant le pic de la pandémie une réduction de $13,9 \pm 6,6$ % ($P=0,003$) des admissions pour SCA ST+ a été observée par semaine. Les délais entre l'apparition des symptômes et l'angioplastie percutanée était significativement augmentés 270 (150–705) versus 245 (140–646) minutes ($P=0,013$). Cette augmentation était exclusivement liée à une augmentation du temps entre l'apparition des symptômes et le premier contact médical 121 (60–360) en 2019 versus 150 (62–420) minutes en 2020 ($P=0,002$). Durant cette période a été constaté un plus grand nombre de complications mécaniques (0,9 % vs 1,7 % ($P=0,029$)) conduisant à une augmentation significative de notre critère de jugement principal 112 patients (5,6) en 2019 vs 129 (7,6 %) en 2020 ($P=0,018$).

Conclusions. – Pendant le premier pic de la pandémie il a été constaté : une diminution du taux de SCA ST+ associé à un temps d'ischémie prolongé, poussé par l'augmentation du temps entre l'apparition des symptômes et le premier contact médical et enfin un plus grand nombre de complications mécaniques. Ces observations suggèrent la nécessité d'encourager la population à consulter au moindre symptôme inquiétant.

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Background

The COVID-19 pandemic remains active worldwide. The number of new cases continues to rise in many countries, none of which have yet managed to definitely restrain its circulation. At the early phase of the pandemic, during the first peak, the French government imposed a strict and complete lockdown on the country's entire population from 17 March to 10 May 2020 to control the spread. People were required to stay at home and any unjustified outings were forbidden. These rules were applied uniformly to all regions of France, regardless of their respective pandemic levels. During the lockdown period, systems of care were reorganized in an effort to preserve hospital bed capacity for COVID-19 patients, and to prevent exposure of others to the hospital environment.

Several publications have demonstrated a reduction in admissions for myocardial infarction during this critical period in a few centres in France [1] and worldwide [2–6].

Alteration of the healthcare network and conflicting messages to the population from the authorities and media have been proposed as potential explanations [7]. On another note, an increase in treatment delay was described in a preliminary study from Hong Kong, which raises concerns about potential implications of delayed treatment of myocardial infarction [8] and risk of mechanical complications [9]. This increase in treatment delay may have modified the presentation of infarct during this period, and might lead to the reappearance of mechanical complications that have become increasingly rare in recent decades [10]. Moreover, some clinical cases suggested a worse prognosis in STEMI patients with COVID-19 [11]. However, studies investigating outcomes in STEMI patients during this period and the evolution of admission following the lockdown period are scarce [12,13]. The aim of this study was to evaluate the rate of STEMI, delays to treatment, and in-hospital outcomes during the period encompassing the lockdown in French regions variously affected by the outbreak.

Methods

Study design

The Myocardial Infarction Rate Overview during the COVID-19 Pandemic in France (MODIF) survey is a nationwide, retrospective, observational study involving 65 public and private interventional cardiology centres across 12 contiguous regions in France and a French island in the Indian Ocean, La Réunion (Table A.1). The registry was initiated by the French Society of Cardiology and endorsed by the Coronary Atheroma and Interventional Cardiology Group (*Groupe Atherome Coronaire et Cardiologie*). Despite hospital reorganization, all catheterization centres have been able to continue their activity, contrary to other countries that had to designate regional hub-and-spoke centres [14]. This survey included all consecutive patients with ST-segment elevation myocardial infarction (STEMI), defined according to the European Society of Cardiology [15], referred for urgent revascularization to the heart catheterization laboratory in two periods: 1 March to 31 May 2019 and 1 March to 31 May 2020. Patients with delayed presentation with criteria for revascularization were included in the analysis.

The MODIF survey was declared to the French data protection committee (Commission Nationale Informatique et Liberté, MR0617050520), was registered on the clinical trial website ClinicalTrials.Gov (NCT04357314) and was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The authors had full access to and take full responsibility for the integrity of the data.

Data collection

All data were collected by local investigators in an electronic case report form via REDCap software (Research Electronic Data Capture, Vanderbilt University) hosted by a secured server from the French Institute of Health and Medical Research at the Paris Cardiovascular Research Center. Patient demographics including age, body mass index (BMI) and sex were obtained. Underlying cardiovascular risk factors or previous coronary disease present in patients' electronic health records were collected. Additional data included delays to percutaneous coronary intervention (PCI) and infarction complications during hospitalization.

Collection of information on the number of COVID-19 hospitalizations was done using the government's official public website to analyse our results in relation to the number of hospitalizations in France [16].

Comparisons between periods

This study aimed to describe two years, divided into three periods: the pre-lockdown period from 1 to 16 March 2020, the lockdown period from 17 March to 10 May 2020, and the post-lockdown period from 11 to 31 May 2020. Each period was compared with the equivalent periods in 2019.

Comparisons between regions

Public data published by the French government and *Santé Publique France* have defined the regions highly affected by the COVID-19 pandemic in relation to the number of cases diagnosed, the number of patients hospitalized, and the number of deaths in relation to the population density and the healthcare structures [17]. For information, these regions had more than 200,000 cumulative patient-days of hospitalization due to COVID-19 over the 3 months.

Study outcomes

The primary composite outcome was in-hospital death from all causes or mechanical complications of acute myocardial infarction. In-hospital mechanical complications were defined as any of the following events:

- post-myocardial infarction spontaneous rupture of the myocardium, defined by echocardiography supplemented by a cardiac computed tomography scan in the event of diagnostic suspicion, according to the area of the myocardial rupture [15];
- free wall rupture;
- acute ischaemic mitral regurgitation due to papillary muscle rupture;
- ventricular septal rupture. Secondary outcomes included STEMI admission rates, delay from symptom onset to STEMI diagnosis, delay from symptom onset to primary PCI, and in-hospital outcomes, including orotracheal intubation, cardiogenic shock, arrhythmias (ventricular tachycardia or ventricular fibrillation) and in-hospital cardiac arrest.

Statistical analysis

Categorical data are reported as counts and percentages. Continuous data are reported as mean \pm standard deviation (SD) for normally distributed data and as median (interquartile range [IQR]) for non-normally distributed data. Comparisons used the chi-squared test or Fisher's exact test for categorical variables and Student's *t* test or the Mann–Whitney–Wilcoxon test, as appropriate, for continuous variables.

We analysed rates of STEMI between 2019 and 2020 and measured SD rates per week, and compared them, stratifying by periods, using the Mann-Whitney-Wilcoxon test. Temporal trend of rates was assessed using the chi-squared test for trend in proportion, also known as the Cochran-Armitage trend test.

Logistic regression analysis was applied to identify parameters associated with the primary composite outcome during the lockdown period in 2020 and the same period in 2019.

In univariate analysis, parameters were selected from the results of bivariate analyses (variables with $P < 0.1$). The final multivariable model was selected using a stepwise backward selection, with final selection based on the most favourable goodness-of-fit measures (Akaike information criterion).

A 2-tailed $P < 0.05$ was considered statistically significant. All data were analysed using R software, version 3.6.3 (R Project for Statistical Computing, Vienna, Austria).

Results

Study population

The study population comprised 6306 patients admitted for STEMI during 2019 and 2020. Mean age was 64.2 ± 13.5 years and 75.7% were male (Table 1). There was a high rate of high-risk cardiovascular risk factors including hypertension (45.2%), active smoking (40.5%), dyslipidaemia (34.1%) and diabetes (19.3%). Initial presentation was cardiac arrest for 459 (7.3%) patients. The majority of patients were admitted to the catheterization laboratory through the French prehospital emergency medical assistance service (*Service d'aide médicale urgente*) network (62.7%) or via the emergency ward (34.2%). Median duration of hospitalization was 5 days (interquartile range 3–7). Regarding reperfusion therapy, 249 (4.0%) patients received fibrinolysis, and coronary angioplasty with stent implantation was performed in 84.0% of patients. Ultimately, the overall death rate during hospitalization was 5.9% (370 deaths).

Among the 606 patients initially suspected of having COVID-19 before catheterization laboratory admission and requiring specific precautions during the intervention, 58 cases were confirmed with a positive test result on reverse transcriptase polymerase chain reaction (1.97% of the study population). In this subgroup, mortality was 27.6% (16 deaths) and mechanical complications were reported in 5.2% (3 patients), leading to a 27.6% primary outcome rate.

Evolution of STEMI admission rate

During the months of March, April and May, 3055 patients were admitted in 2020 versus 3251 in 2019. Baseline characteristics are roughly balanced between the 2 years, except for the sex category, with fewer men in 2019 compared with 2020 (74.3% vs 77.1%; $P=0.012$). As illustrated in Fig. 1, a drop in STEMI admissions per week during the lockdown period was observed in 2020 compared with 2019 ($n=1706$ vs $n=2005$, respectively; $-13.9 \pm 6.6\%$; $P=0.003$) paralleling the increase in the number of hospitalized COVID-19 patients. This decrease in STEMI admission rates was balanced by a trend for an augmentation in STEMI admission rates during the pre- and post-lockdown period (pre-lockdown 2020 $n=591$ vs 2019 $n=556$, $+7.5 \pm 4.0\%$, $P=0.41$; and post-lockdown 2020 $n=758$ vs 2019 $n=690$, $+6.6 \pm 5.8\%$ respectively, $P=0.20$).

Disparity during pre-lockdown and post-lockdown periods

During the pre-lockdown period, no differences concerning delays, infarction complications or outcomes were found between 2019 and 2020 (Table A.2). During the lockdown period, a significant increase in total ischaemic time, defined as the delay between symptom onset and reperfusion therapy, was observed: 270 min (IQR 150–705) in 2020 versus 245 min (IQR 140–646) in 2019 ($P=0.013$) (Table 2). This was driven exclusively by the observed increase in median patient-related time, defined as the delay between symptom onset and first medical contact (FMC): 150 min (IQR 62–420) in 2020 versus 121 min (IQR 60–360) in 2019 ($P=0.002$) (Fig. 2). Median physician-related time, defined

as the time between FMC and primary PCI, did not differ between the two periods: 87 min (IQR 55–169) versus 87 min (IQR 53–165) in 2019 ($P=0.78$).

During the post-lockdown period, there was no difference in total ischaemic delay between 2020 and 2019: 260 min (IQR 148–683) in 2020 versus 244 min (IQR 137–579) in 2019. Only an increase in delays between symptom onset and FMC was observed: 120 min in 2019 (IQR 60–330) versus 150 min in 2020 (IQR 60–420) ($P=0.034$) (Table A.3).

In an analysis comparing regions with high and low levels of the epidemic during the lockdown period (Table 3), patient-related delays between symptom onset and FMC were significantly increased in both regions; physician-related delays between FMC and primary PCI were not significantly increased in either region. During the same period, the length of hospitalization was shorter in highly affected regions (6.4 vs 5.7 days; $P=0.010$), while there was no difference in slightly affected regions (6.3 vs 6.0 days; $P=0.35$) (Table A.4).

Outcomes during the lockdown period

During the lockdown period, a significant increase was observed in the primary outcome of in-hospital death or mechanical complications ($P=0.018$), with a significant increase in the rate of mechanical complications (0.9% in 2019 vs 1.7% in 2020; $P=0.029$) and a numerical increase in in-hospital death (5.3% vs 6.5%, respectively; $P=0.15$) (Table 2). Compared to non-complicated patients, patients with mechanical complications had a longer median delay between symptom onset and primary PCI (390 min in 2020 vs 150 min in 2019; $P<0.001$) and a higher death rate (34.5 vs 6.0% respectively; $P<0.001$) (Table A.5). Patients with a mechanical complication had a significantly increased risk of death (odds ratio [OR] 15.8, 95% confidence interval [CI] 10.2–24.5; $P<0.001$). No difference was observed in the rates of orotracheal intubation, in-hospital cardiac arrest, ventricular arrhythmias and cardiogenic shock (Table 3).

Univariate and multivariable analysis of the primary outcome

In the univariate analysis (Table A.6), during the lockdown period from 17 March to 10 May 2020 and the same period in 2019, we identified several significant variables related to the primary outcome: female sex, age, active smoking, hypertension, diabetes, cardiovascular heredity, peripheral artery disease, stroke, ischaemic cardiopathy, initial cardiac arrest, mode of arrival, delay between symptom onset and FMC, total ischaemic time, primary PCI, haemoglobin concentration, impaired renal function, higher C-reactive protein concentration, impaired ejection fraction, left ventricular aneurysm, medical treatment and balloon coronary angioplasty with no stent implantation ($P<0.05$ for all).

In multivariable analysis, independent factors associated with the primary outcome were age ($P<0.001$), female sex ($P=0.037$), diabetes ($P=0.045$), previous coronary artery disease ($P=0.009$), cardiac arrest as initial presentation ($P<0.001$), time between symptom onset and primary PCI ($P=0.001$) and the lockdown period ($P=0.008$), with adjustment for previous peripheral artery disease (Fig. 3).

Table 1 Comparison of the patient characteristics, delays to treatment, management and outcomes of patients with STEMI referred for urgent revascularization between 1 March and 31 May in 2019 and in 2020 (*n* = 6306).

Variable	<i>N</i>	Overall population (<i>n</i> = 6306)	2019 (<i>n</i> = 3251)	2020 (<i>n</i> = 3055)	<i>P</i>
Demographics					
Male sex	6306	4775 (75.7)	2505 (77.1)	2270 (74.3)	0.012
Age, years	6303	64.2 (13.5)	64.0 (13.6)	64.4 (13.5)	0.34
Body mass index, kg/m ²	5951	26.9 (6.03)	26.9 (6.59)	26.8 (5.37)	0.33
Cardiovascular risk factors					
Active smoking	6053	2450 (40.5)	1270 (41.1)	1180 (39.8)	0.30
Diabetes	6297	1217 (19.3)	626 (19.3)	591 (19.4)	0.98
Hypertension	6296	2848 (45.2)	1476 (45.5)	1372 (44.9)	0.67
Dyslipidaemia	6286	2142 (34.1)	1108 (34.2)	1034 (33.9)	0.83
Family history of CAD	6290	1162 (18.5)	608 (18.8)	554 (18.2)	0.55
Comorbidities					
Peripheral artery disease	6294	267 (4.2)	135 (4.2)	132 (4.3)	0.80
Stroke	6295	268 (4.3)	130 (4.0)	138 (4.5)	0.34
Previous CAD	6295	890 (14.1)	464 (14.3)	426 (14.0)	0.73
Presentation					
Initial cardiac arrest	6296	459 (7.3)	243 (7.5)	216 (7.1)	0.58
Mode of arrival	6304				0.035
SAMU network		3950 (62.7)	2022 (62.2)	1928 (63.1)	
Emergency ward		2159 (34.2)	1142 (35.1)	1017 (33.3)	
In-hospital transfer		195 (3.1)	85 (2.6)	110 (3.6)	
Delays, min					
Symptom onset to first medical contact	5908	136 (60.0–387)	125 (60.0–360)	150 (60.0–420)	0.001
First medical contact to primary PCI	5969	85.0 (54.0–164)	85.0 (53.0–168)	85.0 (55.0–160)	0.73
Symptom onset to primary PCI	6185	254 (145–660)	245 (140–650)	260 (150–684)	0.04
Duration of hospitalization, days					
	5903	5 (3–7)	5 (3–7)	4 (3–6)	<0.001
Thrombolytic therapy					
Successful thrombolysis ^a	6299	249 (4.0)	133 (4.1)	116 (3.8)	0.59
Treatment during angiography	243	150 (61.7)	73 (55.7)	77 (68.8)	0.051
Treatment during angiography					
Angioplasty with stent	6306	5295 (84.0)	2744 (84.4)	2551 (83.5)	0.11
No PCI		653 (10.4)	323 (10.0)	330 (10.8)	
Balloon angioplasty alone		132 (2.1)	58 (1.8)	74 (2.4)	
Initial laboratory tests					
Leucocytes (g/L)	5971	13.9 (168)	16.0 (234)	11.6 (4.49)	0.30
Haemoglobin (g/dL)	5990	14.1 (2.5)	14.1 (1.8)	14.1 (3.0)	0.75
GFR (mL/min/m ²)	6005	87.9 (69.6–105)	87.3 (69.8–105)	88.6 (69.5–105)	0.56
C-reactive protein (mg/L)	5174	4.00 (2.00–12.0)	4.10 (2.00–12.0)	4.00 (1.80–12.0)	0.06
Troponin elevation × URL median	5890	40.1 (4.84–248)	42.5 (4.64–267)	38.7 (5.07–231)	0.77
Echocardiographic characteristics					
LVEF (%)	5931	49.1 (11.1)	49.1 (11.2)	49.0 (11.1)	0.66
Impaired LVEF	5931	2391 (40.3)	1240 (40.5)	1151 (40.1)	0.82
Left ventricular aneurysm	6306	30 (0.5)	11 (0.3)	19 (0.6)	0.15
Intraventricular thrombus	6306	82 (1.3)	36 (1.1)	46 (1.5)	0.20

Variable	N	Overall population (n = 6306)	2019 (n = 3251)	2020 (n = 3055)	P
Table 1 (Continued)					
Mechanical complications					
Free wall rupture	6306	48 (0.8)	17 (0.5)	31 (1.0)	0.036
Acute ischaemic mitral regurgitation	6306	17 (0.3)	9 (0.3)	8 (0.3)	0.91
Ventricular septal rupture	6306	24 (0.4)	8 (0.3)	16 (0.5)	0.113
Composite primary outcome	6306	415 (6.6)	194 (6.0)	221 (7.2)	0.048
All-cause in-hospital death	6306	370 (5.9)	184 (5.7)	186 (6.1)	0.50
Mechanical complications	6306	86 (1.4)	31 (1.0)	55 (1.8)	0.005
Complications during hospitalization					
Orotracheal intubation	6157	567 (9.2)	293 (9.1)	274 (9.3)	0.85
Cardiac arrest	6306	362 (5.7)	190 (5.8)	172 (5.6)	0.76
Ventricular tachycardia/fibrillation	6306	276 (4.4)	139 (4.3)	137 (4.5)	0.73
Cardiogenic shock	6306	434 (6.9)	221 (6.8)	213 (7.0)	0.82

Data are expressed as absolute number (%), median (IQR), or mean (SD). CAD: coronary artery disease; GFR: glomerular filtration rate; LVEF: left ventricular ejection fraction; IU: international unit; SAMU: service d'aide médicale urgente (emergency medical assistance service); SD: standard deviation; STEMI: ST-elevation myocardial infarction; URL: upper reference limit.

^a Defined as the presence of at least two of the following criteria 2 hours after thrombolytic treatment: (1) significant relief of pain (a 5-point reduction on a 1–10 subjective scale); (2) $\geq 50\%$ reduction of sum of ST-segment elevation; and (3) abrupt initial increase in creatine kinase concentration (more than twofold over the upper-normal or baseline elevated values).

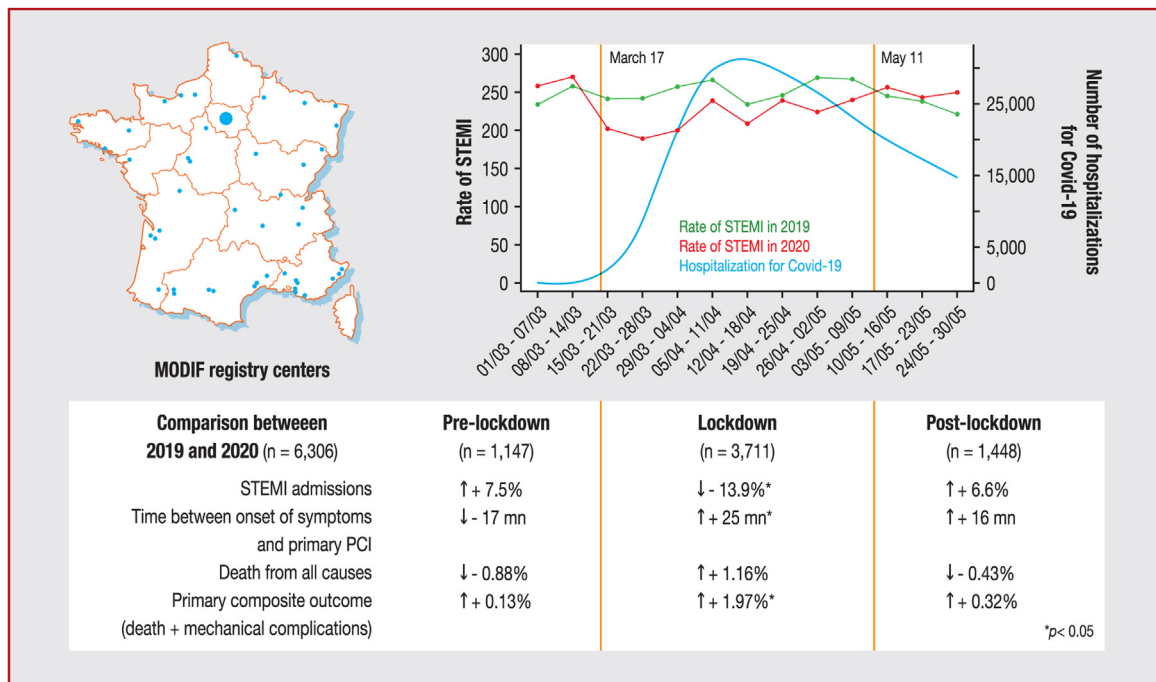


Figure 1. Admission rates for STEMI before, during and after the lockdown period in French centres in 2020 and during the same period in 2019, in relation to the rate of hospitalizations for COVID-19. The blue and red curves represent the weekly admission rates for STEMI from 1 March to 31 May in 2019 and 2020, respectively. The green curve represents the number of hospitalizations with the diagnosis of COVID-19 in France, based on public data given by the French government and "Santé Publique France". The blue vertical bars define the lockdown period from 17 March to 10 May 2020. PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.

Table 2 Delays in care between regions slightly and highly affected by the epidemic, between 17 March and 10 May (the lockdown period in 2020) in 2019 and in 2020.

Variable	Slightly affected regions (n = 2158)			Highly affected regions ^a (n = 1553)		
	2019 (n = 1179)	2020 (n = 979)	P	2019 (n = 826)	2020 (n = 727)	P
Delays, min						
Symptom onset to first medical contact	122 (60–60)	144 (65–410)	0.042	120 (60–360)	172 (60–450)	0.013
First medical contact to primary PCI	96 (60–181)	95 (60–190)	0.98	75 (45–148)	75 (50–145)	0.49
Symptom onset to primary PCI	252 (146–669)	266 (151–715)	0.21	240 (133–611)	276 (150–702)	0.019
Duration of hospitalization, days	6.3 (5.5)	6.0 (5.5)	0.35	6.4 (5.7)	5.7 (5.4)	0.010

Values are mean ± SD, or median (interquartile range). PCI: percutaneous coronary intervention, STEMI: ST-elevation myocardial infarction.

^a Regions with a median threshold of >200,000 patient-days of cumulative hospitalization caused by COVID-19 over the 3-month period were considered to be highly affected by the COVID-19 epidemic.

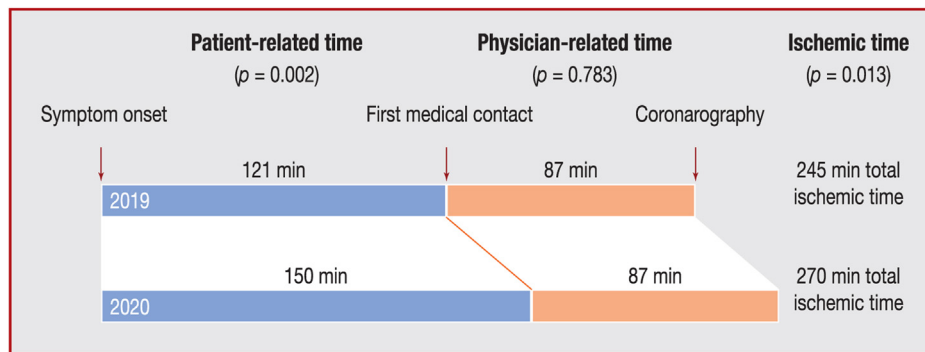


Figure 2. Treatment delays according to time of admission from 17 March to 10 May 2020 in 2020 and in 2019. The different medians of delay are represented over the same period from 17 March to 10 May, comparing 2019 and 2020. The orange bars represent patient-related times and the blue bars physician-related times.

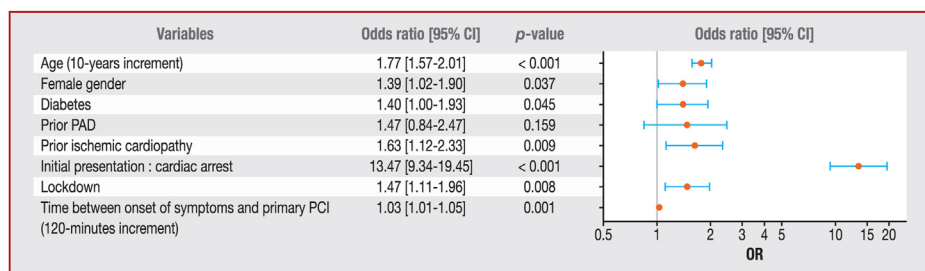


Figure 3. Forest plot of factors associated with the primary outcome in multivariable analysis (n = 3610). Multivariable analysis performed on data from the period March 17 to May 10 2019 (1965 patients) and in 2020 (lockdown period) (1645 patients).

Discussion

The key findings of this nationwide observational study, supported by the French Society of Cardiology and including 6306 patients with STEMI across 65 French centres are,

first, during the lockdown period corresponding to the first peak of the COVID-19 pandemic in France, STEMI admission rates decreased by 13.9% compared with the same period in 2019. Second, total ischaemic times between symptom onset and primary PCI during the lockdown period 2020

Table 3 Comparison of the presentation, delays to treatment, management and outcomes of patients with STEMI referred for urgent revascularization between 17 March and 10 May, in 2019 and in 2020 (the period of lockdown in 2020).

Variable	2019 (n = 2005)	2020 (n = 1706)	P
Initial cardiac arrest	141 (7.0)	106 (6.2)	0.36
Mode of arrival			0.47
SAMU network	1226 (61.2)	1054 (61.8)	
Emergency ward	724 (36.1)	596 (34.9)	
In-hospital transfer	54 (2.7)	56 (3.3)	
Delays			
Time between symptom onset and first medical contact, min	121 (60–360)	150 (62–420)	0.002
Time between first medical contact and primary PCI, min	87 (53–165)	87 (55–169)	0.78
Time between onset of symptoms and primary PCI, min	245 (140–646)	270 (150–705)	0.013
Duration of hospitalization, days	5.0 (3.0;7.0)	4.0 (3.0;6.0)	<0.001
Thrombolytic therapy	80 (4.0)	64 (3.8)	0.77
Successful thrombolysis	44 (55.7)	39 (66.1)	0.29
Echocardiographic characteristics			
LVEF (%)	49.3 (11.3)	49.1 (11.2)	0.61
Impaired LVEF	767 (40.7)	636 (39.6)	0.54
Left ventricular aneurysm	9 (0.5)	8 (0.5)	0.93
Intraventricular thrombus	24 (1.2)	25 (1.5)	0.57
Mechanical complications			
Free wall rupture	8 (0.4)	17 (1.0)	0.04
Acute ischaemic mitral regurgitation	6 (0.3)	5 (0.3)	0.97
Ventricular septal rupture	3 (0.2)	7 (0.4)	0.20
Composite primary outcome	112 (5.6)	129 (7.6)	0.018
All-cause in-hospital death	106 (5.3)	110 (6.5)	0.15
Mechanical complications	17 (0.9)	29 (1.7)	0.029
Complications during hospitalization			
Orotracheal intubation	171 (8.7)	151 (9.2)	0.63
Cardiac arrest	111 (5.5)	99 (5.8)	0.78
Ventricular tachycardia/fibrillation	77 (3.8)	82 (4.8)	0.17
Cardiogenic shock	135 (6.7)	111 (6.5)	0.83

Data are expressed as absolute number (%), median (IQR), or mean (SD). GFR: glomerular filtration rate; LVEF: left ventricular ejection fraction; IU: international unit; PCI: percutaneous coronary intervention, SAMU: *Service d'aide médicale urgente* (emergency medical assistance service); SD: standard deviation; STEMI: ST-elevation myocardial infarction; URL: upper reference limit.

were significantly longer compared to the same period in 2019, driven exclusively by an increase in patient-related delays between symptom onset and FMC. Third, during the same period, an increase in all-cause death and mechanical complications was observed. Fourth, our observations were consistent, irrespective of the level of the pandemic. Indeed, we performed an analysis between regions that were slightly or highly affected by the spread of the first pandemic wave. The lack of differences between suggests that these delays were unlikely to be due to saturation of health-care services. Fifth, the lockdown period in 2020 compared with 2019 was independently associated with the primary outcome of in-hospital death or mechanical complications when adjusted for age, sex, diabetes, previous peripheral artery disease, previous ischaemic cardiopathy, cardiac arrest as an initial presentation and delays. Sixth, during this same period, there was no difference in terms of physician-related delay (between FMC and primary PCI) and reperfusion strategies (thrombolytic therapy, angioplasty with stent) compared with 2019. These elements

illustrate the particular complexity of this period and the outstanding questions on the characteristics of STEMI during the first wave, which can be further investigated in our analysis.

Our study parallels previous observations demonstrating a reduction in STEMI admissions during the period of lockdown compared with the same period in 2019 [2–6]. Nevertheless, it seemed important to us to bring further elements from the largest French cohort on this subject, with a good granularity of data allowing a better description of the phenomena already described. We evidenced a lower STEMI decrease than the 38% decrease observed in large US centres during the initial phase of the epidemic [2]. This survey focused only on STEMI admissions because they seemed less subject to selection bias. It is interesting to note that in an Italian registry, the decrease in STEMI admissions was less (26.5%) than the decrease in NSTEMI admissions (65.1%) [5]. This difference could be related to a more brutal and painful clinical presentation in STEMI, pushing patients to seek medical assistance. This difference

supports the theory that the public's fear of hospitalization during the lockdown period is the reason for some of the decline in patients admitted for myocardial infarction [18]. Although the scope of the present work was not to identify potential mechanisms leading to this reduction, some assumptions may be made. Inability of the healthcare system to adequately deal with the cases can probably be excluded, as there was no difference in this study between time from FMC to primary PCI compared with the same period in regions affected to a lesser or greater extent by the outbreak. This result is interesting to put into perspective with data reported from China, where STEMI patients' access to care was restricted, increasing the rate of thrombolysis and decreasing the rate of angioplasty [19]. The observed decrease in STEMI admissions was global and independent of the scale of the epidemic in the French regions, making it unlikely that the saturation of healthcare services, including emergency services, could explain the observed difference. Unwillingness to present to the emergency department or doctor's office because of fear of infection with severe acute respiratory syndrome coronavirus 2 seems more likely. The observed increase in the incidence of out-of-hospital cardiac arrest in France and Italy during the lockdown period provides further insights into the potential consequences of delayed management of ischaemic cardiac emergencies [20,21]. The decrease in admissions from other non-cardiac emergencies has also been described in the literature, which reinforces the idea that the population may have experienced a fear of going to hospital [22]. This apprehension could also have been promoted by the general message that people should stay home in an effort to preserve hospital bed capacity and avoid exposure to the hospital environment. Interestingly, the effect of lockdown was shown to be reversible, as a rapid return to normal number of STEMI admissions during the post-lockdown period was observed.

Moreover, an increase in the delay between symptom onset and primary PCI, and an increase in the rate of mechanical complications, which have not been previously described in Europe, was also found in this study. The 1.0% rate of mechanical complications observed during 2019 is similar to previously reported data [23]. In this cohort, mechanical complications were associated with longer delays and resulted in higher mortality rates. We speculate that the observed increase in delays from symptom onset of primary PCI led to an increase in mechanical complications, explaining the increased mortality during 2020. However, other potential factors could have accounted for this rise in mortality. First, some deaths are probably related to complications of COVID-19 (with a death rate between 26.9% and 27.6%) as previously reported [24,25]. Second, the acute management of STEMI patients could have been different during this critical period. However, there was no significant difference regarding fibrinolysis use, reperfusion therapy during primary PCI and time of hospitalization.

These results highlight the importance of carefully educating the public on when and how to react to the warning signs of STEMI, without instilling fear. It seems important to reinforce the message to seek medical care urgently, without delay, in the presence of symptoms suggestive of STEMI, even during lockdowns. This fear of going to the hospital has probably increased total ischaemic time, leading

to mechanical complications with a poor prognosis in terms of intra-hospital death. In preparation for further waves of the epidemic, this communication from health professionals could be particularly important to avoid the same pitfalls. Our results also raise the question of a non-centralized lockdown, adapting to the situation more locally, which could also prevent patients from exposing themselves to these types of potential complications in areas less affected by the epidemic.

Limitations

Our study has some limitations. First, the design was retrospective, and the collection of information came from medical records, which explains the rate of missing data. Second, patients with late presentation of STEMI and no indication for urgent primary PCI were not included, leading to a potential selection bias. Third, our study did not include all STEMI admissions in France, although we were able to establish national coverage of 58% of STEMI cases over the two periods [26]. Fourth, we compared patients from 2020 with patients only from 2019 and the follow-up was limited to the length of hospitalization. Finally, the findings are from the French medical system and our results may not be applicable to other health systems.

Conclusions

This study shows a decrease in STEMI admissions during the first pandemic peak period in France compared with the same period in 2019, associated with an increase in the total ischaemic time, driven exclusively by the patient-related delays between symptom onset and FMC and an increase in in-hospital deaths and mechanical complications. The absence of an increase in physician-related delays from the FMC to PCI, and the absence of a change in reperfusion strategies, reflect the preservation of access to urgent cardiac care during the first wave of the COVID-19 pandemic in France.

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Christian Spaulding declare that he has no competing interest. Other COI:consultant for Medtronic, Edwards, Techwald, Stentys, honorarium from Astra Zeneca, Boehringer Ingelheim, BMS, Abbott.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.acvd.2021.01.005>.

References

- [1] Rangé G, Hakim R, Motreff P. Where have the ST-segment elevation myocardial infarctions gone during COVID-19 lockdown? *Eur Heart J Qual Care Clin Outcomes* 2020;6, <http://dx.doi.org/10.1093/EHJQCCO/QCAA034>.
- [2] Garcia S, Albaghdadi MS, Meraj PM, Schmidt C, Garberich R, Jaffer FA, et al. Reduction in ST-segment elevation cardiac catheterization laboratory activations in the United States during COVID-19 pandemic. *J Am Coll Cardiol* 2020;75:2871–2, <http://dx.doi.org/10.1016/j.jacc.2020.04.011>.
- [3] Roffi M, Guagliumi G, Ibanez B, Ibanez B, Ibanez B. The obstacle course of reperfusion for ST-segment-elevation myocardial infarction in the COVID-19 pandemic. *Circulation* 2020;195:1–3, <http://dx.doi.org/10.1161/CIRCULATIONAHA.120.047523>.
- [4] Solomon MD, McNulty EJ, Rana JS, Leong TK, Lee C, Sung S-H, et al. The Covid-19 pandemic and the incidence of acute myocardial infarction. *N Engl J Med* 2020;383, <http://dx.doi.org/10.1056/nejmc2015630>.
- [5] De Rosa S, Spaccarotella C, Basso C, Calabrò MP, Curcio A, Filardi PP, et al. Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era. *Eur Heart J* 2020;41:2083–8, <http://dx.doi.org/10.1093/eurheartj/ehaa409>.
- [6] Mafham MM, Spata E, Goldacre R, Gair D, Curnow P, Bray M, et al. COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. *The Lancet* 2020;396:381–9, [http://dx.doi.org/10.1016/S0140-6736\(20\)31356-8](http://dx.doi.org/10.1016/S0140-6736(20)31356-8).
- [7] Lantelme P, Couray Targe S, Metral P, Bochaton T, Ranc S, Le Bourhis Zaimi M, et al. Worrying decrease in hospital admissions for myocardial infarction during the COVID-19 pandemic. *Arch Cardiovasc Dis* 2020;113:443–7, <http://dx.doi.org/10.1016/j.acvd.2020.06.001>.
- [8] Tam CCF, Cheung KS, Lam S, Wong A, Yung A, Sze M, et al. Impact of Coronavirus Disease 2019 (COVID-19) outbreak on ST-segment-elevation myocardial infarction care in Hong Kong, China. *Circ Cardiovasc Qual Outcomes* 2020;2019:2019–21, <http://dx.doi.org/10.1161/CIRCOUTCOMES.120.006631>.
- [9] Tam CF, Cheung K, Lam S, Wong A, Yung A, Sze M, et al. Impact of coronavirus disease 2019 (COVID-19) outbreak on outcome of myocardial infarction in Hong Kong, China. *Catheter Cardiovasc Interv* 2020, <http://dx.doi.org/10.1002/ccd.28943>, ccd.28943.
- [10] Honda S, Asaumi Y, Yamane T, Nagai T, Miyagi T, Noguchi T, et al. Trends in the clinical and pathological characteristics of cardiac rupture in patients with acute myocardial infarction over 35 years. *J Am Heart Assoc* 2014;3:1–11, <http://dx.doi.org/10.1161/JAHA.114.000984>.
- [11] Bangalore S, Sharma A, Slotwiner A, Yatskar L, Harari R, Shah B, et al. ST-segment elevation in patients with Covid-19 — A case series. *N Engl J Med* 2020;382:10–2, <http://dx.doi.org/10.1056/NEJMc2009020>.
- [12] De Luca G, Verdoia M, Cercek M, Jensen LO, Vavlukis M, Calmac L, et al. Impact of COVID-19 pandemic on mechanical reperfusion for patients with STEMI. *J Am Coll Cardiol* 2020;76:2321–30, <http://dx.doi.org/10.1016/j.jacc.2020.09.546>.
- [13] Mesnier J, Cottin Y, Coste P, Ferrari E, Schiele F, Lemesle G, et al. Hospital admissions for acute myocardial infarction before and after lockdown according to regional prevalence of COVID-19 and patient profile in France: a registry study. *Lancet Public Health* 2020;5:e536–42, [http://dx.doi.org/10.1016/S2468-2667\(20\)30188-2](http://dx.doi.org/10.1016/S2468-2667(20)30188-2).
- [14] Ferlini M, Andreassi A, Carugo S, Cuccia C, Bianchini B, Castiglioni B, et al. Centralization of the ST elevation myocardial infarction care network in the Lombardy region during the COVID-19 outbreak. *Int J Cardiol* 2020;312:24–6, <http://dx.doi.org/10.1016/j.ijcard.2020.04.062>.
- [15] Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2018;39:119–77, <http://dx.doi.org/10.1093/eurheartj/ehx393>.
- [16] Santé Publique France - Suivi de l'épidémie de COVID-19 en France n.d. <https://dashboard.covid19.data.gouv.fr/vue-d-ensemble?location=FRA> (accessed August 19, 2020).
- [17] COVID-19 : point épidémiologique du 4 juin 2020 n.d. <https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/infection-a-coronavirus/documents/bulletin-national/covid-19-point-epidemiologique-du-4-juin-2020> (accessed August 19, 2020).
- [18] Mahmud E, Dauerman HL, Welt FGP, Messenger JC, Rao SV, Grines C, et al. Management of acute myocardial infarction during the COVID-19 pandemic. *J Am Coll Cardiol* 2020, <http://dx.doi.org/10.1016/j.jacc.2020.04.039>.
- [19] Xiang D, Xiang X, Zhang W, Yi S, Zhang J, Gu X, et al. Management and outcomes of patients with STEMI during the COVID-19 pandemic in China. *J Am Coll Cardiol* 2020, <http://dx.doi.org/10.1016/j.jacc.2020.06.039>.
- [20] Marijon E, Karam N, Jost D, Perrot D, Frattini B, Derkenne C, et al. Out-of-hospital cardiac arrest during the COVID-19 pandemic in Paris, France: a population-based, observational study. *Lancet Public Health* 2020;5:e437–43, [http://dx.doi.org/10.1016/S2468-2667\(20\)30117-1](http://dx.doi.org/10.1016/S2468-2667(20)30117-1).
- [21] Baldi E, Sechi GM, Mare C, Canevari F, Brancaglione A, Primi R, et al. Out-of-hospital cardiac arrest during the Covid-19 outbreak in Italy. *N Engl J Med* 2020;383:496–8, <http://dx.doi.org/10.1056/NEJMc2010418>.
- [22] Kansagra AP, Goyal MS, Hamilton S, Albers GW. Collateral effect of covid-19 on stroke evaluation in the United States. *N Engl J Med* 2020;383:400–1, <http://dx.doi.org/10.1056/NEJMc2014816>.
- [23] Puerto E, Viana-Tejedor A, Martínez-Sellés M, Domínguez-Pérez L, Moreno G, Martín-Asenjo R, et al. Temporal trends in mechanical complications of acute myocardial

- infarction in the elderly. *J Am Coll Cardiol* 2018;72:959–66, <http://dx.doi.org/10.1016/j.jacc.2018.06.031>.
- [24] Cammann VL, Szawan KA, D’Ascenzo F, Gili S, Dreiding S, Würdinger M, et al. Outcomes of acute coronary syndromes in coronavirus disease 2019. *Clin Res Cardiol* 2020, <http://dx.doi.org/10.1007/s00392-020-01742-6>.
- [25] Koutsoukis A, Delmas C, Roubille F, Bonello L, Schurtz G, Manzo-Silberman S, et al. Acute coronary syndromes in the era of SARS-CoV-2 infection: a registry of the French Group of Acute Cardiac Care. *CJC Open* 2020, <http://dx.doi.org/10.1016/j.cjco.2020.11.003>.
- [26] Barbato E, Noc M, Baumbach A, Dudek D, Bunc M, Skolidis E, et al. Mapping interventional cardiology in Europe: the European Association of Percutaneous Cardiovascular Interventions (EAPCI) Atlas Project. *Eur Heart J* 2020;41:2579–88, <http://dx.doi.org/10.1093/eurheartj/ehaa475>.