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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



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Summarv

Background The COVID-19 pandemic has had a profound effect on general health care. We aimed to evaluate the effect of a nationwide lockdown in France on admissions to hospital for acute myocardial infarction, by patient characteristics and regional prevalence of the pandemic.

Methods In this registry study, we collected data from 21 centres participating in the ongoing French Cohort of Myocardial Infarction Evaluation (FRENCHIE) registry, which collects data from all patients admitted for ST segment elevation myocardial infarction (STEMI) or non-ST segment elevation myocardial infarction (NSTEMI) within 48 h of symptom onset. We analysed weekly hospital admissions over 8 weeks: the 4 weeks preceding the institution of the lockdown and the 4 weeks following lockdown. The primary outcome was the change in the number of hospital admissions for all types of acute myocardial infarction, NSTEMI, and STEMI between the 4 weeks before lockdown and the 4 weeks after lockdown. Comparisons between categorical variables were made using χ^2 tests or Fisher's exact tests. Comparisons of continuous variables were made using Student's t tests or Mann-Whitney tests. Poisson regression was used to determine the significance of change in hospital admissions over the two periods, after verifying the absence of overdispersion. Age category, region, and type of acute myocardial infarction (STEMI or NSTEMI) were used as covariables. The FRENCHIE cohort is registered with ClinicalTrials.gov, NCT04050956.

Findings Between Feb 17 and April 12, 2020, 1167 patients were consecutively admitted within 48 h of acute myocardial infarction (583 with STEMI, 584 with NSTEMI) and were included in the study. Admissions for acute myocardial infarction decreased between the periods before and after lockdown was instituted, from 686 before to 481 after lockdown (30% decrease; incidence rate ratio 0.69 [95% CI 0.51-0.70]). Admissions for STEMI decreased from 331 to 252 (24%; 0.72 [0.62-0.85]), and admissions for NSTEMI decreased from 355 to 229 (35%; 0.64 [0.55-0.76]) following institution of the lockdown, with similar trends according to sex, risk factors, and regional prevalence of hospital admissions for COVID-19.

Interpretation A marked decrease in hospital admissions was observed following the lockdown, irrespective of patient characteristics and regional prevalence of COVID-19. Health authorities should be aware of these findings, in order to adapt their message if the COVID-19 pandemic persists or recurs, or in case of future major epidemics.

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Introduction

The COVID-19 pandemic has required profound changes in the organisation of care for patients without COVID-19; it has also generated anxiety in the general population, in particular regarding going out during lockdown, and might have affected the way patients have used healthcare facilities.

Worldwide, it has been observed that admissions for acute myocardial infarction during the pandemic have markedly declined. This decline has been quantified in several countries, such as the USA and France, with the decrease in ST segment elevation myocardial

infarction (STEMI) admissions ranging from 18% to 48%,²⁻⁵ and estimates in some regions in Spain and Italy being as high as 80%.⁶ Little information is available as to non-ST segment elevation myocardial infarction (NSTEMI) admissions,⁴⁻⁷ and the association between hospital admissions, profile and therapeutic management of patients with acute myocardial infarction, and nationwide lockdown policies has not been precisely investigated. France has been affected by COVID-19, but with large regional variations. A general and nationwide lockdown was imposed on March 16, 2020.

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Research in context

Evidence before this study

The COVID-19 pandemic has had a profound effect on the organisation of care worldwide. It has also profoundly affected the general population, possibly explaining the decrease in admissions for acute conditions such as acute myocardial infarction. We searched PubMed, medRxiv, and Google for data on the incidence of hospital admissions for acute myocardial infarction in relation to the COVID-19 pandemic from April 20 to July 6, 2020, using the keywords "COVID-19", "SARS-CoV-2", "myocardial infarction", "incidence", "hospital admissions", and "lockdown". We did not use any language restrictions. Data from the USA, Italy, and Spain documented gradual decreases ranging from 20% to more than 50% in hospital admissions for acute myocardial infarction, comparing periods in the preceding years with the same months or weeks in 2020.

Added value of this study

France set up a general nationwide lockdown policy in response to the COVID-19 pandemic, irrespective of the regional prevalence of the disease. We used a different approach from previous studies to compare the number of hospital admissions for acute myocardial infarction in the 4 weeks preceding institution of the general lockdown in France with those in the following 4 weeks in a network of 21 large hospitals throughout the French metropolitan territory. We found a 30% reduction in hospital admissions for acute myocardial infarction, which began in the week after lockdown and

Our aim was to quantify changes in hospital admissions for acute myocardial infarction according to type of myocardial infarction and regional prevalence of COVID-19, comparing the 4 weeks preceding the lockdown with the following 4 weeks, and to identify potential changes in management of patients with STEMI or NSTEMI.

Methods

Study design and population

This registry study used data from the ongoing, permanent, prospective French Cohort of Myocardial Infarction Evaluation (FRENCHIE) registry. We included data collected on all patients admitted to intensive cardiac care units for a recent acute myocardial infarction in 21 large centres that were taking part in FRENCHIE, had begun recruitment, and were able to ensure consecutive recruitment during the lockdown period. All included centres had catheterisation facilities available 24 h per day. 7 days per week, and most centres are members of the French Alliance for Cardiovascular Trials network. For an acute myocardial infarction to be defined as recent, symptom onset must have occurred fewer than 48 h before hospital admission. Acute myocardial infarction was defined as being characterised by dynamic changes of cardiac markers (troponins or creatine kinase myocardial

remained constant over the following 4 weeks. The decrease was more marked for patients with non-ST segment elevation myocardial infarction than for patients with ST segment elevation myocardial infarction, and was larger in patients older than 80 years, but was similar whatever the regional prevalence of COVID-19. Patients admitted to hospital before and after lockdown had similar characteristics and were managed similarly. In-hospital mortality was numerically higher following the lockdown, but the increase was not statistically significant.

Implications of all the available evidence

The reasons for the decrease in hospital admissions observed in all countries studied, however analysed, are conjectural. Both our findings and those of previous studies suggest that patients confronted with extended chest pain or symptoms suggestive of myocardial infarction were reluctant to call emergency services and go to hospital during the COVID-19 pandemic. However, in our study, the marked decrease in hospital admissions immediately after lockdown, irrespective of the regional prevalence of the disease, could also reflect a truly reduced incidence of myocardial infarction, possibly linked to reduced triggers such as physical activity or air pollution. Health authorities should be fully aware of the risk of patients avoiding health services, irrespective of disease prevalence, and provide appropriate public health messages in the case of a continued COVID-19 pandemic, or if a second wave or similar epidemics occur in the future.

band), and associated with at least one of the following elements: symptoms compatible with myocardial ischaemia; appearance of pathological Q waves; and ST-T wave changes compatible with myocardial ischaemia (ST segment elevation or depression, T-wave inversion). Patients included in FRENCHIE gave written informed consent for their participation and had to be covered by the French medical insurance system (Sécurité Sociale). Patients were excluded from FRENCHIE in case of iatrogenic myocardial infarction (eg, myocardial infarction occurring within 48 h of a therapeutic procedure), or if the acute myocardial infarction diagnosis was invalidated in favour of another diagnosis (eg, myocarditis).

FRENCHIE has been approved by the Comité de Protection des Personnes and by the French data regulatory authority (Commission Nationale de l'Informatique et des Libertés).

Procedures

Data were collected for an 8-week period, covering the 4 weeks before and 4 weeks after the lockdown on March 16, 2020. Because the aim was to describe external admissions to intensive cardiac care units for acute myocardial infarction, patients who developed acute myocardial infarction while initially admitted to hospital for COVID-19 were not included. By contrast, patients

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who were admitted to hospital primarily for acute myocardial infarction in whom COVID-19 was also diagnosed were included.

We collected the following data: patient age; patient sex; risk factors; date of admission; type of acute myocardial infarction (STEMI or NSTEMI); use of emergency medical services; time from symptom onset to first call to the emergency services; time from symptom onset to hospital admission; use of primary percutaneous coronary intervention; intravenous fibrinolysis or absence of reperfusion therapy in patients with STEMI; coronary angiography within 24 h from admission and from 24 to 72 h from admission in patients with NSTEMI; the use of percutaneous coronary intervention during hospital stay for all patients; maximal Killip class during hospital stay; in-hospital death; duration of stay in intensive cardiac care units; suspected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection; and confirmed SARS-CoV-2 infection. Testing for SARS-CoV-2 infection was done using CE-marked RT-PCR techniques.

The primary outcome was the change in the number of hospital admissions for all types of acute myocardial infarction, NSTEMI, and STEMI between the 4 weeks before lockdown and the 4 weeks after lockdown. Other objectives were subgroup analyses of the number of admissions for acute myocardial infarction before and after the institution of lockdown, according to regional prevalence of hospital admissions for COVID-19, age, sex, diabetic status, history of hypertension, smoking status, obesity, and maximal Killip class. We also analysed the change in mortality and the change in patient treatment and management during the hospital stay between the two periods.

Statistical analysis

The results are shown as absolute values and percentages for discrete variables and mean (SD) or median (IQR) for continuous variables. Comparisons between categorical variables were made using χ^2 tests or Fisher's exact tests. Comparisons of continuous variables were made using Student's t tests or Mann-Whitney tests. Poisson regression was used to determine the significance of change in hospital admissions over the two periods, after verifying the absence of overdispersion (Pearson χ^2 value on degree of freedom ratio close to 1). Age category, region, and type of acute myocardial infarction (STEMI or NSTEMI) were used as covariables. Regional analyses were based on the reported ratios of hospital admissions for COVID-19 per 100000 inhabitants, using the following thresholds: 30 or more hospital admissions for COVID-19 per 100 000 inhabitants, 15-29 hospital admissions for COVID-19 per 100 000 inhabitants, and fewer than 15 hospital admissions for COVID-19 per 100 000 inhabitants.85

Detailed information on time from onset to admission was missing in some patients, for whom the only information was that they were admitted fewer than 48 h

from symptom onset. The corresponding information was handled as a missing data category. We nevertheless reported p values for patient characteristics and complications before and after the lockdown, in order to illustrate potentially important changes. All superiority tests were two-sided and p values less than 0.05 were considered significant. SPSS (version 25.0) was used for statistical analyses.

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline (appendix pp 5, 6). The FRENCHIE cohort is registered with Clinical Trials.gov, NCT04050956.

Role of the funding source

There was no funding source for this specific study. The funder of the FRENCHIE registry had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between Feb 17 and April 12, 2020 (ie, 4 weeks before and 4 weeks after the March 16, 2020, lockdown in France) 1167 patients were consecutively admitted within 48 h of acute myocardial infarction (583 with STEMI, 584 with NSTEMI) and were included in the study (appendix p 3). 686 patients (331 with STEMI, 355 with NSTEMI) were admitted in the 4 weeks before national lockdown, and 481 patients (252 with STEMI, 229 with NSTEMI) were admitted in the 4 weeks after lockdown. This represented a decrease in admissions for acute myocardial infarction of 30% (incidence rate ratio [IRR] 0.69 [95% CI 0.61-0.77]), a decrease in admissions for STEMI of 24% (IRR 0.72 [0.62-0.85]), and a decrease in admissions for NSTEMI of 35% (IRR 0.64 [0.55-0.76]; figure 1). Weekly admissions for STEMI and NSTEMI during the 4 weeks preceding the lockdown showed no evidence of a progressive decrease; likewise, weekly admissions after the lockdown were also uniform, although at a lower level, with no evidence of a progressive decrease or increase over the 4 weeks (figure 2).

The decrease in admissions for acute myocardial infarction between the two periods was independent of the

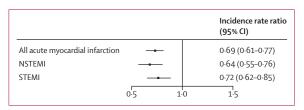


Figure 1: Incidence rate ratios for weekly number of admissions for all types of acute myocardial infarction, and for STEMI or NSTEMI, in the whole population before versus after lockdown

 $\label{thm:normalized} NSTEMI = non-ST\ segment\ elevation\ myocardial\ infarction.\ STEMI = ST\ segment\ elevation\ myocardial\ infarction.$

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See Online for appendix

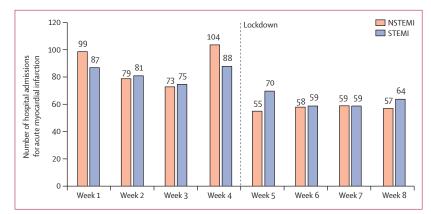


Figure 2: Weekly numbers of admissions for STEMI or NSTEMI at participating institutions before and after lockdown

NSTEMI=non-ST segment elevation myocardial infarction. STEMI=ST segment elevation myocardial infarction.

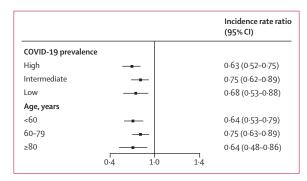


Figure 3: Incidence rate ratios for weekly number of hospital admissions for all types of acute myocardial infarction before versus after lockdown, according to local prevalence of hospital admissions for COVID-19 and age group

High COVID-19 prevalence=30 or more hospital admissions for COVID-19 per 100 000 inhabitants. Intermediate COVID-19 prevalence=15-29 hospital admissions for COVID-19 per 100 000 inhabitants. Low COVID-19 prevalence=fewer than 15 hospital admissions for COVID-19 per 100 000 inhabitants.

local prevalence of hospital admissions for COVID-19 (figure 3; appendix p 4). By contrast, the decrease was more profound in the 205 patients who were aged 80 years or older than in all patients younger than 80 years (figure 3). There was no interaction of decrease in hospital admissions with gender (30% decrease in hospital admissions in both men [from 509 to 357; IRR 0.70, 95% CI 0.61-0.80] and women [from 177 to 124; 0.70, 0.56-0.88] between the two periods), history of diabetes (36% decrease in patients with diabetes [from 149 to 96; IRR 0.64, 95% CI 0.50-0.83] vs 29% decrease in patients without diabetes [from 536 to 382; 0.71, 0.62-0.81), history of hypertension (29% decrease in patients with hypertension [from 350 to 247; IRR 0.72, 95% CI 0.61–0.85] vs 31% decrease in patients without hypertension [from 334 to 230; 0.68, 0.57-0.80]), or current and past smoking (34% decrease in patients who currently smoke or formerly smoked [from 393 to 260; IRR 0.63, 95% CI 0.53-0.73] vs 26% decrease in patients who have never smoked [from 292 to 215; 0.70, 0.59 - 0.83]).

Patient profile did not differ in terms of age, gender distribution, or prevalence of risk factors between the two periods (table). In patients with STEMI, time from symptom onset to hospital admission was similar in the two periods. Revascularisation procedures were used as often in the two periods. 288 (87%) of 331 patients with STEMI before lockdown had primary percutaneous coronary intervention versus 223 (89%) of 252 patients after lockdown (p=0.59). 224 (63%) of 355 patients with NSTEMI before lockdown had coronary angiography within 24 h of admission versus 143 (62%) of 229 patients after lockdown (p=0.87); 102 (29%) patients with NSTEMI before lockdown had coronary angiography within 24-72 h of admission versus 57 (25%) patients after lockdown (p=0·31). Neither maximal Killip class during the hospital stay nor mean duration of stay in the intensive cardiac care unit differed between the two periods (table). Consistent results were found when STEMI and NSTEMI populations were analysed separately (appendix pp 1, 2). In-hospital death occurred in 23 (3%) of 686 patients before lockdown, and in 25 (5%) of 481 patients after lockdown (p=0·12). Inhospital death occurred in 14 (4%) of 331 patients with STEMI before lockdown versus 16 (6%) of 252 patients with STEMI after lockdown (p=0.26), and in nine (3%) of 355 patients with NSTEMI before lockdown versus nine (4%) of 229 patients with NSTEMI after lockdown (p=0.34). 16 (2%) of 743 patients (434 before lockdown, 309 after lockdown) who were tested for SARS-CoV-2 were positive, all during period two, and four (25%) of them died.

Discussion

We found a 24% reduction in hospital admissions for STEMI and a 35% reduction in hospital admissions for NSTEMI between the periods directly before and after the lockdown in France. No catch-up phenomenon was observed over the 4 weeks following the lockdown, and the decrease in hospital admissions appeared to be independent of the regional prevalence of COVID-19, but more marked for older patients. Time from symptom onset to admission in patients with STEMI, and the invasive management of both patients with STEMI and patients with NSTEMI were not affected. However, in-hospital mortality was numerically higher after the lockdown than before the lockdown.

Our results are consistent with those from the Kaiser Permanente in Northern California⁴ and from a multicentre Italian registry,⁷ showing a marked decrease of admissions for acute myocardial infarction during the COVID-19 pandemic, compared with the previous year. The decrease after lockdown that we observed in France seemed to be sudden, whereas it was more gradual in the Kaiser Permanente data.⁴ In the Californian data, the decrease was of a similar magnitude for admissions for STEMI and NSTEMI,⁴ whereas the decrease shown in the Italian registry was much larger for admissions

	Before lockdown (n=686)	After lockdown (n=481)	p value
Age, years			
Mean	65-8 (13-6)	65-2 (12-7)	0.49
Median	66 (55-76)	65 (55-75)	0.44
<60	250 (36%)	178 (37%)	0.24*
60–79	305 (45%)	229 (48%)	
≥80	131 (19%)	74 (15%)	
Sex			
Women	177 (26%)	124 (26%)	0.99
Men	509 (74%)	357 (74%)	
Regional prevalence of COVID inhabitants	-19 hospital adm	issions per 100 0	00
>30	279 (41%)	180 (37%)	0.44†
15-29	267 (39%)	204 (42%)	
<15	140 (20%)	97 (20%)	
Hypertension	350 (51%)	247 (52%)	0.84
Diabetes	149 (22%)	96 (20%)	0.49
Obesity	151 (22%)	105 (23%)	0.96
Smoking status			
No smoking	292 (43%)	215 (45%)	0.50‡
Past smoking	163 (24%)	100 (21%)	
Current smoking	230 (34%)	160 (34%)	
STEMI	331 (48%)	252 (52%)	0.16
Precise time from onset to admission not available	17 (5%)	24 (10%)	0.049
Time from symptom onset to admission, min	180 (108–390)	180 (115–363)	0.70
Primary percutaneous coronary intervention	288 (87%)	223 (89%)	0.59
Fibrinolysis	6 (2%)	6 (3%)	0.58
NSTEMI	355 (52%)	229 (48%)	0.16
Coronary angiography within 24 h of admission	224 (63%)	143 (62%)	0.87
Coronary angiography 24–72 h after admission	102 (29%)	57 (25%)	0.31
Any percutaneous coronary intervention during hospital stay	567 (83%)	401 (85%)	0.38
	(Table	continues in nex	t column)

for NSTEMI (65% decrease) than for STEMI (26·5% decrease). As in the Italian registry, we found a larger decrease for admissions for NSTEMI, although the difference from STEMI was less pronounced in our study. Although we cannot exclude that the lesser decrease in admissions for STEMI might have been partly explained by misdiagnosis (inclusion of acute myocarditis and not true STEMI), as has been observed in Italy, this could be at best a marginal reason, because 94% of the patients who were admitted for STEMI had percutaneous coronary intervention. In the Kaiser Permanente population, demographics, risk factors, and baseline characteristics did not differ during the pandemic compared with the reference periods, whereas history of coronary artery disease was less frequent in

	Before lockdown (n=686)	After lockdown (n=481)	p value
(Continued from previous	column)		
Maximal Killip class§			
1	543 (85%)	344 (82%)	0.61¶
II	49 (8%)	37 (9%)	
III	19 (3%)	17 (4%)	
IV	29 (5%)	22 (5%)	
Duration of ICCU stay, days	II		
Mean	3.18 (2.9)	3.37 (2.41)	0.25
Median	3 (2-4)	3 (2-4)	0.046
In-hospital death	23 (3%)	25 (5%)	0.12
Data are mean (SD), median (I NSTEMI=non-ST segment elev elevation myocardial infarction ranges. †p value is for the com for the comparison across all t	vation myocardial in n. *p value is for the parison across all thr hree smoking status	farction. STEMI=ST comparison across ree prevalence level	segment all three age s. ‡p value is s had data

patients admitted during the pandemic period.⁴ In the Italian registry, patients who were admitted during the pandemic were older than those who were admitted 1 year before.⁷ As in the Kaiser Permanente data,⁴ the decrease in admissions among the population in our study was of a similar magnitude in all subgroups according to gender, presence of diabetes, hypertension, and smoking. In Italy, De Rosa and colleagues⁷ found larger reductions in hospital admission rates in women than in men. In our study, the decrease was also numerically larger in patients aged 80 years or older than in younger patients. The difference between age groups might be explained by a fear of worse clinical course in case of contagion in older patients, or an absence of support from the family during lockdown.

The reasons for the decrease in admissions for acute myocardial infarction are conjectural. The most likely explanation is that patients feared being taken to hospitals that are likely to receive patients with COVID-19, or that they feared adding to the pressure on doctors and nurses in these difficult times. These concerns might have been amplified by the general message that people should stay at home. Interestingly, the decrease in admissions for acute myocardial infarction was unrelated to the local prevalence of COVID-19; the lockdown was applied irrespective of the local magnitude of the pandemic, and the whole hospitalisation structure was affected, with elective procedures postponed and a possible effect on health workers, including the emergency services, as has been previously observed in other countries.11 Both the fact that the decrease was more marked for patients with NSTEMI, a condition in which chest pain is usually less intense than in STEMI, and the fact that an increase in out-of-hospital cardiac arrests has been observed during the COVID-19 pandemic, 12,13 support this hypothesis, as does the fact that the decrease was more marked in older patients. However, it is noteworthy that in the Paris cardiac arrest survey the increase in out-of-hospital cardiac arrests was limited to the first 2 weeks after lockdown.13 whereas the decrease in admissions for acute myocardial infarctions in the FRENCHIE registry remained constant over 4 weeks in all regions, including the Paris area. Other explanations might have coexisted with patient concerns about attending hospital. Air pollution is a known trigger of acute myocardial infarction.14 and a decrease in air pollution could have contributed to the decrease in hospital admissions between the two periods: indeed, a 30% reduction in nitrogen dioxide was observed as soon as the first week after lockdown in Paris, although no change in PM₁₀ was documented.¹⁵ However, other climate changes are unlikely to explain changes in acute myocardial infarction incidence because February and March, 2020, were characterised by mild temperatures in most French regions. Finally, decreased physical activity and professional stress subsequent to the lockdown might also have contributed to a genuine decrease in the number of acute myocardial infarctions.16 The fact that we observed no catch-up phenomenon during the first 4 weeks after the lockdown might also suggest a true decrease in the occurrence of acute myocardial infarction.

The French system of acute cardiac care relies in large part on the Service d'Aide Médicale Urgente (SAMU), which receives initial calls from patients and dispatches mobile intensive care units on site to bring the patients to hospitals capable of percutaneous coronary intervention. During the COVID-19 pandemic, SAMU call centres were sometimes saturated, with longer than usual delays in the time to answering calls. In Hong Kong, times from symptom onset to first emergency call in patients with STEMI were considerably longer during the pandemic than at other times.17 Unexpectedly, however, we found that in patients with STEMI, delays from symptom onset to hospital admission were unchanged after lockdown started, as was acute management, with as many patients having myocardial reperfusion with either primary percutaneous coronary intervention or intravenous fibrinolysis as during the period before lockdown.

In-hospital mortality remained low after lockdown, but in spite of similar patient management before and after lockdown, we observed a numerically increased inhospital death rate during the lockdown (5%) compared with before the lockdown (3%); the increase was less than what was found in the Iranian registry (from 2.8% to 9.7%). Although the increase in mortality might be a chance finding, prolonged in-hospital delays before primary percutaneous coronary intervention, related to the implementation of COVID-19 prevention protocols, as well as high mortality in the few patients positive for SARS-CoV-2 who were admitted for acute myocardial

infarction, might have contributed to the mortality increase we observed.

This study has limitations. It was done in the context of the general lockdown, which meant that we could not collect extensive data on the population; precise time delays in the admission of patients with STEMI were missing in a greater number of patients during lockdown (10%) versus before lockdown (5%). Also, time from hospital admission to primary percutaneous coronary intervention was not recorded; because of the specific inhospital infection prevention protocols set up during the pandemic, it is likely that time from admission to percutaneous coronary intervention was longer in the second period than in the first period. Finally, the registry included only patients covered by the national health coverage system (Sécurité Sociale), and de facto excluded undocumented and immigrant workers living in France, who are likely to have many diverse health problems, but who are usually young and less likely to develop myocardial infarction than older populations.

A marked decrease in hospital admissions for acute myocardial infarction was observed following the lockdown, irrespective of patient characteristics and local prevalence of COVID-19. A longer survey period will be needed to determine whether some catch-up phenomena will be observed beyond the first month, and after the end of lockdown. Meanwhile, health authorities should be fully aware of the current situation in order to deliver appropriate public health messages. This is crucial in countries still fighting COVID-19, but also in the case of a second wave in countries that are past the first wave of the pandemic, or in case another pandemic occurs in the future.

Contributors

ND and JM drafted the manuscript. ND, MC, and AR did the statistical analyses. All other authors collected the data and made critical revisions to the manuscript.

Declaration of interests

JM has received personal fees from Owkin, outside of the submitted work. YC has received personal fees and research grants to their institution from Novartis, Amgen, and Sanofi-Aventis; and has received personal fees from AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, and Pfizer, outside of the submitted work. PC has received personal fees from Amgen, Sanofi, Servier, AstraZeneca, and Abiomed, outside of the submitted work, FS has received personal fees from Amgen, Sanofi, AstraZeneca, Merck Sharp & Dohme, Bayer, Servier Mylan, and Novo Nordisk, outside of the submitted work. GL has received personal fees from Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Merck Sharp & Dohme, Daiichi Sankyo, Lilly, Mylan, Novartis, Novo Nordisk, Pfizer, Sanofi Aventis, and Servier, outside of the submitted work. DA has received personal fees from AstraZeneca, Bayer, Bristol-Myers-Squibb, Pfizer, Sanofi, Amgen, Novartis, Novo Nordisk, Servier, and Merck Sharp & Dohme, outside of the submitted work. GC has received personal fees from Amgen, AstraZeneca, Bayer, Biotronik, Bristol-Myers Squibb, MSD, Pfizer, and Sanofi; and grants and personal fees from Medtronic, outside of the submitted work. PG has received grants and personal fees from Sanofi and Amgen; personal fees from Boehringer Ingelheim; and grants from AstraZeneca and Abbot, outside of the submitted work, TL has received personal fees and non-financial support from Abbott Vascular; and grants and non-financial support from Boston Scientific, outside of the submitted work. J-GD has received grants and personal fees from Bayer and Bristol-Myers Squibb; and personal fees from AstraZeneca,

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Data sharing

We are prepared to share our data in accordance with the French law on health data upon specific request to ND (nicolasdanchin@yahoo.fr), TS (tabassome.simon@aphp.fr), or PGS (gabriel.steg@aphp.fr).

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