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Original article

Impact of COVID-19 on ST-segment elevation myocardial infarction care. The Spanish experience

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ABSTRACT

Introduction and objectives: The COVID-19 outbreak has had an unclear impact on the treatment and outcomes of patients with ST-segment elevation myocardial infarction (STEMI). The aim of this study was to assess changes in STEMI management during the COVID-19 outbreak.

Methods: Using a multicenter, nationwide, retrospective, observational registry of consecutive patients who were managed in 75 specific STEMI care centers in Spain, we compared patient and procedural characteristics and in-hospital outcomes in 2 different cohorts with 30-day follow-up according to whether the patients had been treated before or after COVID-19.

Results: Suspected STEMI patients treated in STEMI networks decreased by 27.6% and patients with confirmed STEMI fell from 1305 to 1009 (22.7%). There were no differences in reperfusion strategy (> 94% treated with primary percutaneous coronary intervention in both cohorts). Patients treated with primary percutaneous coronary intervention during the COVID-19 outbreak had a longer ischemic time (233 [150-375] vs 200 [140-332] minutes, $P < .001$) but showed no differences in the time from first medical contact to reperfusion. In-hospital mortality was higher during COVID-19 (7.5% vs 5.1%; unadjusted OR, 1.50; 95%CI, 1.07-2.11; $P < .001$); this association remained after adjustment for confounders (risk-adjusted OR, 1.88; 95%CI, 1.12-3.14; $P = .017$). In the 2020 cohort, there was a 6.3% incidence of confirmed SARS-CoV-2 infection during hospitalization.

Conclusions: The number of STEMI patients treated during the current COVID-19 outbreak fell vs the previous year and there was an increase in the median time from symptom onset to reperfusion and a significant 2-fold increase in the rate of in-hospital mortality. No changes in reperfusion strategy were detected, with primary percutaneous coronary intervention performed for the vast majority of patients. The co-existence of STEMI and SARS-CoV-2 infection was relatively infrequent.

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◇ The investigators, institutions, and organizations participating in the Working Group on the Infarct Code of the Interventional Cardiology Association of the Spanish Society of Cardiology are listed in the Appendix.

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Impacto de la COVID-19 en el tratamiento del infarto agudo de miocardio con elevación del segmento ST. La experiencia española

Palabras clave:
IAMCEST
COVID-19
Angioplastia primaria
Red de atención al infarto

RESUMEN

Introducción y objetivos: El impacto del brote de COVID-19 en el tratamiento del infarto agudo de miocardio con elevación del segmento ST (IAMCEST) no está claro. El objetivo de este estudio es evaluar los cambios en el tratamiento del IAMCEST durante el brote de COVID-19.

Métodos: Se utilizó un registro multicéntrico, nacional, retrospectivo y observacional de pacientes consecutivos atendidos en 75 centros, se compararon las características de los pacientes y de los procedimientos y los resultados hospitalarios en 2 cohortes según se los hubiera tratado antes o durante la COVID-19.

Resultados: Los casos con sospecha de IAMCEST disminuyeron el 27,6% y los pacientes con IAMCEST confirmado se redujeron de 1.305 a 1.009 (22,7%). No hubo diferencias en la estrategia de reperfusión (más del 94% tratados con angioplastia primaria). El tiempo de isquemia fue más largo durante la COVID-19 (233 [150-375] frente a 200 [140-332] min; $p < 0,001$), sin diferencias en el tiempo primer contacto médico-reperfusión. La mortalidad hospitalaria fue mayor durante la COVID-19 (el 7,5 frente al 5,1%; OR bruta = 1,50; IC95%, 1,07-2,11; $p < 0,001$); esta asociación se mantuvo tras ajustar por factores de confusión (OR ajustada = 1,88; IC95%, 1,12-3,14; p = 0,017). La incidencia de infección confirmada por SARS-CoV-2 fue del 6,3%.

Conclusiones: El brote de COVID-19 ha implicado una disminución en el número de pacientes con IAMCEST, un aumento del tiempo entre el inicio de los síntomas y la reperfusión y un aumento en la mortalidad hospitalaria. No se han detectado cambios en la estrategia de reperfusión. La combinación de infección por SARS-CoV-2 e IAMCEST fue relativamente infrecuente.

Abbreviations

COVID-19: coronavirus disease 2019
PCI: percutaneous coronary intervention
PCR: polymerase chain reaction
pPCI: primary percutaneous coronary intervention
STEMI: ST-segment elevation acute myocardial infarction

INTRODUCTION

On December 31, 2019, a cluster of pneumonia cases of unknown etiology was reported in Wuhan, Hubei Province, China. On January 9, 2020, a new coronavirus, SARS-CoV-2, was identified as the causative agent of this outbreak, and its associated disease was named coronavirus disease 2019 (COVID-19). The infection spread rapidly, and the World Health Organization characterized COVID-19 as a pandemic on March 11.[1] By May 1, 2020, more than 1.6 million cases had been diagnosed in 179 countries on 5 continents, with nearly 100 000 confirmed deaths.[1] The Spanish Government activated a State of Emergency on March 14, which restricted the movement of all citizens, except those going to work, to hospitals or health centers, and to financial institutions and those shopping for groceries, pharmaceutics, and basic necessities.[2]

The impact of this new disease on societal behavior and on health care system performance is unprecedented in recent history. During the current COVID-19 outbreak, some preliminary reports have highlighted a decrease in the number of ST-segment elevation myocardial infarction (STEMI) patients attending hospitals in Europe and North America,[3–5] but we have limited information on how the outbreak has affected STEMI networks in terms of delays to reperfusion, revascularization strategies, and clinical outcomes.[6,7]

The objective of this study was to compare clinical characteristics, management, and hospital outcomes in a nationwide cohort between STEMI patients who attended in the first 30 days after the Spanish lockdown during the current COVID-19 outbreak and those who attended in a period prior to COVID-19.

METHODS

Spanish STEMI registry

There are 17 regional public service STEMI care networks in Spain, which comprise 83 hospitals capable of performing primary percutaneous coronary interventions (pPCIs) in year-round 24-hour, 7-day a week programs. In 2018, 21 261 interventions were performed for STEMI (91.6% pPCIs, 3.2% rescue percutaneous coronary interventions, and 5.1% routine early percutaneous coronary interventions strategies after fibrinolysis), representing 417 pPCIs per million population.[8]

In 2019, the Interventional Cardiology Association of the Spanish Society of Cardiology sponsored a prospective registry of consecutive STEMI patients who were treated within these specific STEMI care networks. The aim of this Spanish Infarct Code Registry was to detect interregional differences in the management of STEMI. Information was collected on number of cases, clinical characteristics, clinical management, and outcomes of STEMI patients. This registry enrolled 5240 consecutive patients treated between April and June 2019.

During the current COVID-19 outbreak, the Spanish Interventional Cardiology Association established a twin registry involving the retrospective collection of information on all consecutive STEMI patients by the same centers that participated in the 2019 registry. Information was retrospectively recorded on number of cases, clinical characteristics, clinical management, and outcomes from March 16, which was immediately after the activation of the Spanish State of Emergency and the countrywide lockdown.

The research protocol was approved by the Working Group on STEMI Code of the Spanish Interventional Cardiology Association and by a central ethics committee from León and Bierzo Health Areas.

Study design

This multicenter, retrospective, observational cohort study evaluated procedures recorded in the Spanish Infarct Code Registry database to assess whether the current COVID-19 outbreak has had a relevant impact on STEMI treatment in terms of number of cases, clinical characteristics, reperfusion delays, in-hospital management, and in-hospital clinical outcomes. Two different cohorts of patients were established according to whether they had been treated between April 1 and April 30, 2019 (prior to COVID-19 cohort) or between March 16 and April 14, 2020 (during COVID-19 cohort). The analysis included data from 75 hospitals that enrolled patients in both periods. Delay times were defined according to the relevant European guidelines.[9] Patients with a final diagnosis other than STEMI were not included in the final analysis. Data were collected through medical record review. The main outcome measure was in-hospital mortality.

Statistical analysis

Continuous variables are summarized as mean ± standard deviation, whereas categorical variables are presented as frequency and percentage. Baseline comparisons between cohorts were performed using *t* tests or chi-square tests, as appropriate. Variables with highly skewed distributions (ie, times for first medical contact, symptom onset, catheterization laboratory arrival, and reperfusion) are presented as median and interquartile range and were compared using the nonparametric Mann-Whitney *U* test. Univariate logistic regression models were created to evaluate the association between the cohort group and in-hospital mortality. Multivariate logistic regression modeling was performed to eliminate potential confounders and to assess the consistency of our findings. The covariates included in the multivariate models (symptom onset to reperfusion time, age, sex, Killip class, and a positive polymerase chain reaction [PCR] test for COVID-19) were selected based on medical knowledge and the results of the univariate analysis. Adjusted odds ratios (ORs) and their 95% confidence intervals (95%CIs) were therefore used to estimate the association between cohort and outcomes.

The robustness of our findings was tested through 2 sensitivity analyses by *a)* removing COVID-19 individuals from the main analyses to account for their potential contribution to the increase in outcomes; and *b)* using a mixed regression model including hospital as a random variable, which allowed some heterogeneity in order to take into account the expected variation between hospitals (between-hospital variation), weighting each hospital accordingly to obtain an overall estimate. Two-tailed *P* values < .05 were considered statistically significant. All analyses were performed using STATA software version 15.1 (Stata Corp, College Station, United States).

RESULTS

Patients

STEMI networks from 75 hospitals attended a total of 1113 patients during the COVID-19 outbreak, whereas 1538 individuals were treated in the same period the previous year, representing a drop of 27.6%. A flowchart of patients treated in the STEMI networks in the 2 time periods is shown in figure 1. Patients with confirmed STEMI diagnosis comprised 1009 and 1305, respectively (a fall of 22.7%). The trend was consistent among centers (65 of the 75 centers [87%] reported fewer STEMI events). There were also significant differences in the number of patients who required STEMI network assistance but were ultimately diagnosed with a non-ST-segment elevation acute myocardial infarction: 232 individuals (15.1%) in 2019 but 104 individuals (9.3%) in 2020 ($P < .001$).

Figure 2 shows the absolute number of pPCIs per day during both time periods and the official number of confirmed cases according to Spanish government data.[7]

During the COVID-19 outbreak, only 33 patients (3.3%) had confirmed COVID-19 diagnosis at admission; during admission, COVID-19 was diagnosed in 30 additional patients (3.0%), giving a total of 63 patients (6.3%) diagnosed with COVID-19. The COVID-19 diagnostic path in the 2020 cohort is shown in figure 3.

Patients' baseline clinical characteristics are shown in table 1. With the exception of previous coronary artery disease (more frequent in the COVID-19 cohort), the clinical characteristics were not different between the groups. The mode of presentation significantly differed between groups: during COVID-19, patients more frequently arrived at the hospital via the out-of-hospital emergency medical service and, once at the pPCI hospital, were more frequently admitted directly to the catheterization laboratory.

Angiographic and procedural characteristics

Angiographic characteristics and the treatment performed are shown in table 2. Radial access was more frequent during COVID-19 and, although there were no differences in the initial and final TIMI flows, there was an increase in mechanical thrombectomy and IIb/IIIa inhibitor administration. There was no difference in the reperfusion strategy after coronary angiography, with up to 94% of

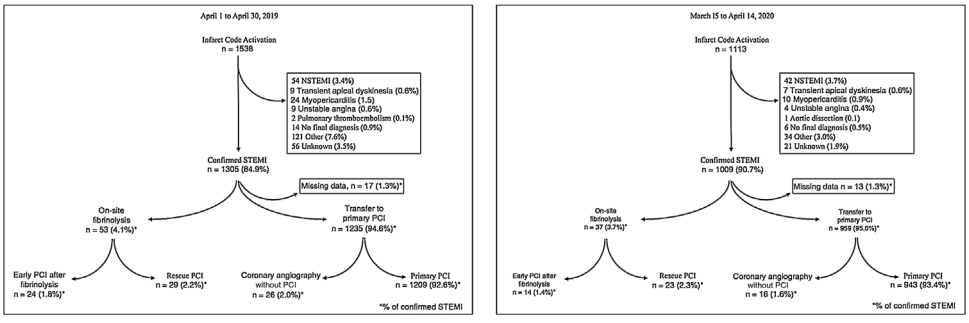

Figure 1. Patient flowchart. NSTEMI, non-ST-segment elevation acute myocardial infarction, PCI, percutaneous coronary intervention; STEMI, non-ST-segment elevation acute myocardial infarction.

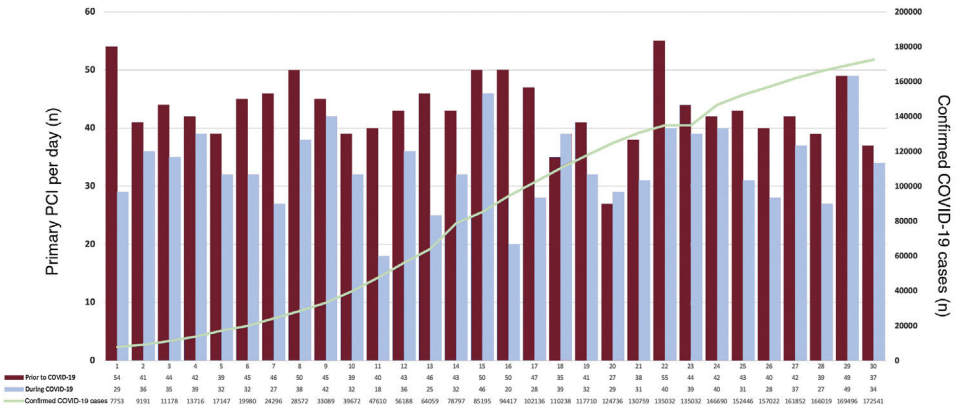

Figure 2. Absolute number of primary percutaneous coronary interventions per day during both time periods and the official number of confirmed COVID-19 cases. Numbers of confirmed COVID-19 cases are according to official Spanish government data.[7] PCI, percutaneous coronary intervention.

COVID-19 diagnostic status on admission		COVID-19 diagnostic status during hospitalization			
Unknown	**111 (11%)**	Not available	1 (0.9%)		
		PCR test not performed	79 (71.2%)		
		PCR performed	**31 (27.9%)**	Negative	30 (27%)
				Positive	**1 (0.9%)**
No symptoms compatible with COVID-19 / No previous PCR test	**803 (79.5%)**	Not available	9 (1.1%)		
		PCR test not performed	575 (71.6%)		
		PCR performed	**219 (27.3%)**	Negative	212 (26.4%)
				Positive	**7 (0.9%)**
Symptoms compatible with COVID-19 / No previous PCR test	**63 (6.2%)**	Not available	2 (3.2%)		
		PCR test not performed	4 (6.3%)		
		PCR performed	**57 (90.5%)**	Negative	35 (55.6%)
				Positive	**22 (34.9%)**
Previous positive PCR test	**33 (3.3%)**	Not available	0 (0%)		
		PCR test not performed	10 (30.3%)		
		PCR performed	**23 (69.7%)**	Negative	3 (9.1%)
				Positive	**20 (60.6%)**

Figure 3. COVID-19 diagnostic path. Patients were categorized on admission according to their COVID-19 status into 4 groups: unknown; no symptoms compatible with COVID-19 and no previous polymerase chain reaction (PCR) test; symptoms compatible with COVID-19 but no previous PCR test; and previous positive PCR test. Although a PCR assay needs to be performed at admission in all patients, it should be noted that PCR was not available in many facilities at the beginning of the pandemic, when this study was carried out.

patients treated with pPCI in both cohorts and with less than 2% of patients not undergoing any percutaneous coronary intervention.

Time intervals between symptom onset and reperfusion

During the COVID-19 outbreak, there was an increase in both time from symptom onset to first medical contact (105 [45-222] vs 71 [30-180] minutes, $P < .001$) and time from symptom onset to reperfusion (233 [150-375] vs 200 [140-332] minutes, $P < .001$). In contrast, no differences were observed in the time from first medical contact to reperfusion (110 [80-155] minutes vs 110 [81-151] minutes, $P = .54$). Five different time intervals between symptom onset and reperfusion are shown in table 3 and figure 4.

In-hospital outcomes

Differences in in-hospital outcomes between the 2 cohorts are shown in table 4. All-cause mortality during COVID-19 was 7.5% vs 5.1% in the prior to COVID-19 group (unadjusted OR, 1.50; 95%CI, 1.07-2.11; $P < .001$). This association remained consistent after adjustment for age, sex, Killip class, and time from symptom onset to reperfusion (OR, 1.88; 95%CI, 1.12-3.14; $P = .017$), but it was attenuated after additional adjustment for confirmed COVID-19 diagnosis (OR, 1.56; 95%CI, 0.91-2.67; $P = .108$).

Sensitivity analyses

The robustness of our findings was tested through 2 sensitivity analyses. By excluding COVID-19 patients from the main analyses, we removed their potential contribution to the increase in outcomes and confirmed that the excess mortality was partly explained by COVID-19 itself: the unadjusted OR (95%CI) for patients in 2020 was 1.28 (0.77-1.83) ($P = .173$), which remained nonsignificant after adjustment for confounding: 1.56 (0.90-2.68) ($P = .11$). By using random effects models, we allowed for some random heterogeneity across hospitals and obtained similar statistical significance ($P = .044$) for the association between in-hospital mortality and patients recruited during the COVID-19

Table 1
Baseline clinical characteristics of patients with confirmed diagnosis of STEMI

	Prior to COVID-19 N = 1305	During COVID-19 N = 1009	*P*
Age, y	63.7 ± 13.2	63.1 ± 12.5	.24
Male sex	1023 (78.4)	786 (78.4)	.99
Clinical history			
Hypertension	647 (50.0)	520 (51.9)	.36
Diabetes	324 (25.2)	226 (22.6)	.15
Hyperlipidemia	592 (45.8)	466 (46.7)	.67
Current smoker	581 (45.7)	442 (44.6)	.60
Previous coronary artery disease	131 (10.2)	139 (13.9)	.006
First medical contact			
Out-of-hospital emergency medical service	463 (35.8)	424 (42.3)	.017
Primary care centers	319 (24.6)	219 (21.8)	.017
Non-PCI hospitals	266 (20.6)	192 (19.1)	.017
PCI hospitals	246 (19.1)	168 (16.7)	.017
Reperfusion strategy at first medical contact			
pPCI	1113 (87.7)	881 (87.8)	.86
Fibrinolysis	51 (4.0)	34 (3.3)	.86
Diagnostic doubt: transfer to pPCI hospital for decision	85 (6.7)	71 (7.1)	.86
Diagnostic doubt: transfer to non-pPCI hospital for decision	20 (1.6)	17 (1.7)	.86
Complications before PCI			
Ventricular fibrillation	84 (6.4)	63 (6.2)	.85
Asystole	15 (1.1)	5 (0.5)	.092
Cardiogenic shock	53 (4.1)	42 (4.1)	.90
Mechanical ventilation	42 (3.2)	37 (3.7)	.56

PCI, percutaneous coronary intervention; pPCI, primary percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.
Values are reported as No. (%) or mean ± standard deviation.

outbreak vs those recruited 1 year before: patients with STEMI during the COVID-19 outbreak were at higher risk of in-hospital mortality after adjustment for confounding ($P = .033$), but this significant association disappeared when COVID-19 status was introduced into the model ($P = .203$), suggesting that COVID-19 was the driver of the increase in in-hospital mortality between cohorts.

DISCUSSION

In our study, we evaluated the influence of the COVID-19 outbreak on the management of STEMI patients attended in specific care networks nationwide in Spain, one of the countries most affected by the current pandemic. We compared data from a national registry establishing 2 different 30-day cohorts of patients: prior to the COVID-19 outbreak (from April 1 to April 30, 2019) and during the outbreak (from March 16 to April 14, 2020).

Fewer STEMI patients and longer delays to reperfusion

A previous report from our group revealed a 40% decrease in patients treated for STEMI during the first week of the current outbreak.[3] Similarly, an American study revealed an estimated 38% reduction in STEMI-related catheterization laboratory activations in 9 high-volume centers during the early phase of the COVID-19 pandemic.[4] Our results confirm a consistent decrease in the number of STEMI patients treated (in up to 87% of centers), albeit of a lower magnitude (22.7%) than initially believed.[3] In addition, there was a significant decrease in the number of patients managed in STEMI networks who ultimately received a diagnosis other than STEMI, reinforcing the belief that patients avoided hospitals. Furthermore, patients had longer delays to reperfusion, largely due to later consultation of the health system because we found no differences in the time from first medical contact to reperfusion. Ischemic time duration is a major determinant of infarct size in patients with STEMI, and prompt recognition and early management of acute STEMI is critical in reducing morbidity and mortality.[10–12] Interestingly, the COVID-19 cohort showed a higher prevalence of previous coronary artery disease and more multivessel disease, suggesting that patients with a history of ischemic heart disease may have been less reluctant to go to the hospital. Despite the logistical difficulties caused by the COVID-19 outbreak, we did not detect an increase in the time from first medical contact to reperfusion, which indicates a good adaptation of STEMI networks to the current crisis. On the contrary, there was a longer time from catheterization laboratory arrival to reperfusion, probably due to time spent on the protective measures required for the procedures.[13]

Potential behavioral explanations for these results would be a combination of avoidance of medical care due to social distancing and concerns about contracting COVID-19 in hospitals. The ongoing outbreak has received massive news coverage, with particular emphasis on the most common forms of infection and places where SARS-CoV-2 spreads more easily. Fear is a well-known determinant of medical care avoidance[14] and hospital avoidance behaviors have been linked to pandemics.[15]

Table 2
Angiographic and procedural characteristics of patients with confirmed diagnosis of STEMI

	Prior to COVID-19 N = 1305	During COVID-19 N = 1009	*P*
Site of patient reception at pPCI hospital			
Direct to catheterization laboratory	679 (57.3)	658 (66.0)	< .001
Emergency department	398 (33.6)	258 (25.9)	< .001
Critical care unit	49 (4.1)	40 (4.0)	< .001
Coronary critical care unit	45 (3.8)	25 (2.5)	< .001
Previously admitted to hospital	14 (1.2)	14 (1.4)	< .001
Other	1 (0.1)	2 (0.2)	< .001
Killip class at catheterization laboratory arrival			
I	1024 (81.0)	821 (82.4)	.86
II	115 (9.1)	83 (8.3)	.86
III	34 (2.7)	25 (2.5)	.86
IV	91 (7.2)	67 (6.7)	.86
Coronary artery disease extent			
1-vessel disease	789 (63.1)	597 (60.1)	.003
2-vessel disease	301 (24.1)	296 (29.8)	.003
3-vessel disease	161 (12.9)	100 (10.1)	.003
Radial access	1087 (88.7)	910 (91.4)	.036
Location of culprit vessel			
Left main coronary artery	16 (1.2)	15 (1.5)	.59
Left anterior descending	542 (41.5)	454 (45.0)	.095
Left circumflex	198 (15.1)	150 (14.9)	.84
Right coronary artery	476 (36.5)	388 (38.5)	.33
Bypass graft	9 (0.7)	5 (0.5)	.55
Initial TIMI flow			
0	847 (68.9)	724 (72.2)	.18
1	114 (9.3)	75 (7.5)	.18
2	116 (9.4)	99 (9.9)	.18
3	153 (12.4)	105 (10.5)	.18
Final TIMI flow			
0	22 (1.8)	17 (1.7)	.95
1	15 (1.2)	11 (1.1)	.95
2	48 (3.9)	43 (4.3)	.95
3	1152 (93.1)	925 (92.9)	.95
PCI characteristics			
IIb/IIIa inhibitor administration	112 (8.6)	150 (14.9)	< .001
Mechanical thrombectomy	337 (25.8)	356 (35.3)	< .001
Balloon angioplasty	428 (32.8)	361 (35.8)	.13
Bare-metal stent implantation	97 (7.4)	24 (2.4)	< .001
Drug-eluting stent implantation	1066 (81.7)	887 (87.9)	< .001
Decision after coronary angiography			
pPCI	1209 (93.9)	943 (94.7)	.74
Rescue PCI	29 (2.3)	23 (2.3)	.74
Routine early PCI after fibrinolysis	24 (1.9)	14 (1.4)	.74
Coronary angiography without PCI	26 (2.0)	16 (1.6)	.74

PCI, percutaneous coronary intervention; pPCI, primary percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.
Values are reported as No. (%).

Reperfusion strategies and angiographic findings in STEMI during the COVID-19 outbreak

Various scientific societies have developed recommendations on the reperfusion strategy during the COVID-19 outbreak, with advice that may be conflicting, depending on the conditions in each country. In China, the Peking Union Medical College Hospital recommend thrombolysis as first-line treatment and only recommend coronary intervention after COVID-19 is ruled out, even in patients with a thrombolytic contraindication.[16] The American

Table 3
Time intervals between symptom onset and reperfusion

	Median [interquartile range]	*P*
Symptom onset to first medical contact, min		
Prior to COVID-19 (n = 1160)	71 [30-180]	< .001
During COVID-19 (n = 901)	105 [45-222]	< .001
Symptom onset to reperfusion, min		
Prior to COVID-19 (n = 895)	200 [140-332]	< .001
During COVID-19 (n = 895)	233 [150-375]	< .001
First medical contact to reperfusion, min		
Prior to COVID-19 (n = 892)	110 [81-151]	.54
During COVID-19 (n = 892)	110 [80-155]	.54
First medical contact to catheterization laboratory arrival, min		
Prior to COVID-19 (n = 1174)	86 [59-125]	.089
During COVID-19 (n = 904)	83 [55-125]	.089
Catheterization laboratory arrival to reperfusion, min		
Prior to COVID-19 (n = 898)	20 [15-30]	< .001
During COVID-19 (n = 906)	24 [17-31]	< .001

College of Cardiology Interventional Council and the Society for Cardiovascular Angiography & Interventions state that fibrinolysis can be considered for relatively stable STEMI patients with active COVID-19 to prevent staff exposure.[17] In Spain, there have been no changes to the reperfusion strategy, with more than 98% of STEMIs treated with pPCI and no increase in the use of thrombolysis, in accordance with Spanish Interventional Cardiology Association recommendations on STEMI management during the COVID-19 outbreak.[18]

Two recently published short series of patients with COVID-19 who had ST-segment elevation showed a high prevalence of nonobstructive disease.[19,20] Overall, we did not find an increase in the number of patients without obstructive lesions. This could be *a)* because we analyzed only patients with confirmed STEMI diagnosis and thus excluded other causes of myocardial infarction with nonobstructive coronary arteries, such as myocarditis, takotsubo syndrome, non-STEMI, and pulmonary embolism, which represented about 10% of patients in our series; or *b)* because previously published data probably concerned nonconsecutive and highly selected patients.

Impact of the COVID-19 outbreak on STEMI-related mortality

A particularly relevant finding of our study is a disturbing elevation in in-hospital mortality during the COVID-19 outbreak. This increase remained consistent after adjustment for age, sex, Killip class, and time from symptom onset to reperfusion.

Recent epidemiologic data suggest a significant increase in mortality during this period that cannot be fully explained by COVID-19 patients alone.[21] In the current situation, patients avoid going to the emergency services, or defer going, which could explain the increase in out-of-hospital cardiac arrest, as recently described in Italy.[22] Although it is difficult to determine the real

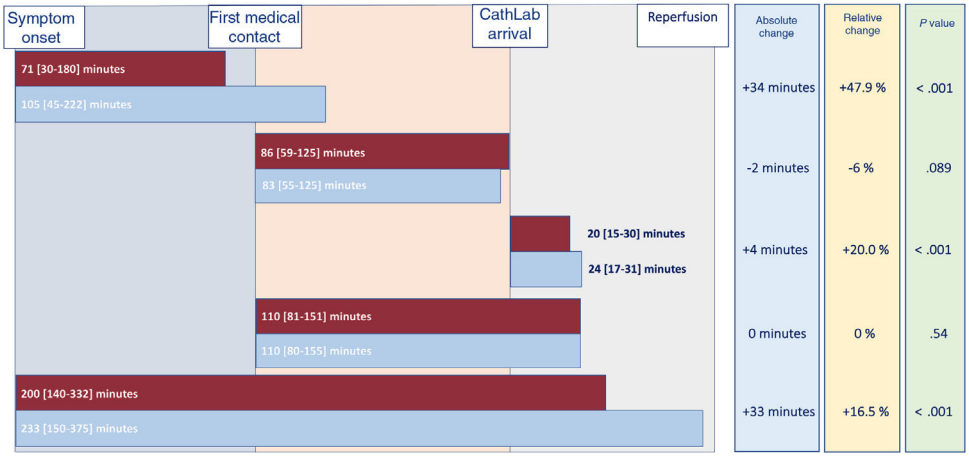

Figure 4. Time intervals between symptom onset and reperfusion.

Table 4
In-hospital outcomes of patients with confirmed diagnosis of STEMI

	Prior to COVID-19 N = 1305	During COVID-19 N = 1009	*P*
Mortality	67 (5.1)	75 (7.5)	.019
Acute stent thrombosis	11 (0.8)	11 (1.1)	.54
Major bleeding	8 (0.6)	11 (1.1)	.21
Cardiogenic shock after PCI	75 (5.7)	48 (4.8)	.29
Pulmonary edema after PCI	30 (2.3)	17 (1.7)	.30
Mechanical ventilation after PCI	31 (2.4)	19 (1.9)	.42
Mechanical complication	5 (0.4)	9 (0.9)	.12

PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.
Values are reported as No. (%).

prevalence of out-of-hospital cardiac arrest in the setting of STEMI, we did not observe an increase in cases of ventricular fibrillation or asystole or in a need for mechanical ventilation prior to the catheterization laboratory in patients with confirmed STEMI. Up to 75% of deaths are estimated to occur before contact with the health system[23] and the main way to prevent out-of-hospital cardiac arrest is for patients to seek hospital treatment as soon as symptoms of STEMI appear.[24] Therefore, it is possible that an increase in out-of-hospital cardiac arrest may not be reflected in our study.

Lack of access to reperfusion treatment would also increase subacute STEMI complications, such as heart failure and/or cardiogenic shock, intraventricular thrombus formation and peripheral embolism, and mechanical complications.[25] These patients were not included in the present registry because they were not candidates for pPCI but they undoubtedly contribute to STEMI-related excess mortality.

Finally, in the long term, suboptimal revascularization and a larger infarct size will increase complications related to worse ventricular remodeling, such as chronic heart failure and ventricular arrhythmias.[26]

Limitations

This study has limitations inherent to the analysis of multicentric observational data. Baseline and follow-up data were assessed at the center-level by each clinician-investigator, without central confirmation, potentially resulting in inaccuracies and misclassifications. Nevertheless, data on interventional cardiology are quite standardized worldwide and the electronic case report form was designed to be intuitively and universally completed by all clinicians. Moreover, we applied a mixed regression model including hospital as a random variable, which considered within- and between-hospital variations over time. In any case, the potential variability among clinicians approximates our findings to those of clinical practice and improves their generalizability. Any potential selection bias was addressed by adjustment of logistic regressions for potential confounders with prognostic implications, although some residual confounding (either measured or unmeasured) might remain after multivariate modeling.

CONCLUSIONS

In conclusion, this nationwide, observational study has revealed a decrease in the number of patients with STEMI managed during the current COVID-19 outbreak, with an increase in time from symptom onset to reperfusion and a significant 2-fold increase in in-hospital mortality. No changes in reperfusion strategy were detected. Concomitant SARS-CoV-2 infection in STEMI patients was infrequent but had an impact on in-hospital mortality.

CONFLICTS OF INTEREST

A. Pérez de Prado has received personal fees from iVascular, Boston Scientific, Terumo, B. Braun, and Abbott Laboratories. Á. Cequier has received personal fees from Ferrer International, Terumo, AstraZeneca, and Biotronik. All other authors have reported that they have no relationship relevant to the contents of this paper to disclose.

WHAT IS KNOWN ABOUT THE TOPIC?

- Some preliminary reports have highlighted a decrease in the number of STEMI patients attending hospitals during the current COVID-19 outbreak.
- There is little information on the influence of the COVID-19 outbreak on STEMI care and outcomes.

WHAT DOES THIS STUDY ADD?

- We found a significant decrease in the number of patients with STEMI managed in specific care networks in Spain during COVID-19.
- When compared with a cohort from the previous year, patients managed during the COVID-19 outbreak had a longer ischemia time and increased mortality, although there were no differences in the reperfusion strategy.

APPENDIX. WORKING GROUP ON THE INFARCT CODE OF THE SPANISH INTERVENTIONAL CARDIOLOGY ASSOCIATION INVESTIGATORS

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