Original research

COVID-19 pandemic, mechanical reperfusion and 30-day mortality in ST elevation myocardial infarction

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ABSTRACT

Objective The initial data of the International Study on Acute Coronary Syndromes - ST Elevation Myocardial Infarction COVID-19 showed in Europe a remarkable reduction in primary percutaneous coronary intervention procedures and higher in-hospital mortality during the initial phase of the pandemic as compared with the prepandemic period. The aim of the current study was to provide the final results of the registry, subsequently extended outside Europe with a larger inclusion period (up to June 2020) and longer follow-up (up to 30 days).

Methods This is a retrospective multicentre registry in 109 high-volume primary percutaneous coronary intervention (PPCI) centres from Europe, Latin America, South-East Asia and North Africa, enrolling 16 674 patients with ST segment elevation myocardial infarction (STEMI) undergoing PPPCI in March/June 2019 and 2020. The main study outcomes were the incidence of PPCI, delayed treatment (ischaemia time >12 hours and door-to-balloon >30 min), in-hospital and 30-day mortality.

Results In 2020, during the pandemic, there was a significant reduction in PPCI as compared with 2019 (incidence rate ratio 0.843, 95% CI 0.825 to 0.861, p<0.0001). This reduction was significantly associated with age, being higher in older adults (>75 years) (p=0.015), and was not related to the peak of cases or deaths due to COVID-19. The heterogeneity among centres was high (p<0.001). Furthermore, the pandemic was associated with a significant increase in door-to-balloon time (40 (25–70) min vs 40 (25–64) min, p=0.01) and total ischaemia time (225 (135–410) min vs 196 (120–355) min, p<0.001), which may have contributed to the higher in-hospital (6.5% vs 5.3%, p<0.001) and 30-day (8% vs 6.5%, p=0.001) mortality observed during the pandemic.

Conclusion Percutaneous revascularisation for STEMI was significantly affected by the COVID-19 pandemic,

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with a 16% reduction in PPCI procedures, especially among older patients (about 20%), and longer delays to treatment, which may have contributed to the increased in-hospital and 30-day mortality during the pandemic.

Trial registration number NCT04412655.

BACKGROUND

Our healthcare system has strongly been impacted by the COVID-19 pandemic, with most of the resources being diverted to face this disease.[1] Many clinical units have been converted to treat patients with COVID-19, limiting the access for patients with chronic conditions while maintaining acute services for the treatment of acute coronary syndromes (ACS), particularly ST segment elevation myocardial infarction (STEMI). The International Study on Acute Coronary Syndromes - ST Elevation Myocardial Infarction (ISACS-STEMI) COVID-19 was established in response to the emerging outbreak of COVID-19 and provides a snapshot that aims at estimating the true impact of the COVID-19 pandemic on the treatment and outcome of patients with STEMI treated by primary angioplasty. Our initial data,[2 3] in step with other reports,[4–10] showed a reduction in primary percutaneous coronary intervention (PPCI) procedures, presumably due to a public fear of coronavirus contagion, which impacted on patient willingness to present to hospital. Further observation was the prolonged time from symptom onset to treatment,[11–13] which contributed to explaining the higher in-hospital mortality in this population during the pandemic. The aim of the current study was to provide the final results of the ISACS-STEMI COVID-19 registry, subsequently extended outside Europe with a larger inclusion period (up to June 2020) and longer follow-up (up to 30 days).

METHODS

Study design and population

This is a large-scale retrospective multicentre registry promoted by the Eastern Piedmont University, Novara, Italy, initially planned to include European primary PCI centres[2] but subsequently extended to several other regions (Latin America, South-East Asia and North Africa). Detailed data have previously been reported.[2] The initial inclusion period was of 2 months (from 1 March until April 30) but was subsequently prolonged to 30 June 2020. Data were compared with those retrospectively collected during the same months of 2019 (from 1 March until June 30).

Inclusion criteria

The inclusion criteria were patients with STEMI treated by PPCI (including mechanical reperfusion for failed thrombolysis).

Data collection

Anonymised data were collected through a dedicated clinical record 'form (CRF). Each centre identified a local principal investigator. We collected demographic, clinical and procedural data including total ischaemia time (defined as the time from symptom onset to first balloon inflation) and door-to-balloon time (defined as the time from arrival at the PCI hospital and first balloon inflation), referral to primary PCI facility, COVID-19 positivity, PCI procedural data and in-hospital mortality. After collection, each participating centre submitted the CRF to the coordinating unit at Eastern Piedmont University, in charge of reporting all data onto the central electronic database. Data were finally checked for missing or contradictory entries.

Study outcomes

The study outcomes were (1) the number of patients with STEMI undergoing percutaneous revascularisation; (2) the proportion of patients with ischaemia time >12 hours; (3) the proportion of patients with a door-to-balloon time >30 min; and (4) in-hospital and 30-day mortality.

Patient and public involvement

It was not possible to involve patients or the public in the design, or conduct, or reporting or dissemination plans of our research.

Statistics

Data were analysed using SPSS Statistics Software V.23.0 and R V.3.6.2 software by an independent statistician (GC). Quantitative variables were described using median and IQR. Mean and CI were obtained assuming Poisson distributions for count data. Incidence rate ratio (IRR) was defined as the ratio between count data in 2020 and count data in 2019. Data were normalised for the different size of the populations and for the possibly different time period of observation, and we considered the number of STEMI per million of local residents in the corresponding population in a year. Poisson regression models (with log link function) were applied to compare the incidence rate of primary PCI per million of residents per year in 2020 with the same rate in 2019, correcting for possible impact of major risk factors.[14] The heterogeneity between centres was explored by a random effect Poisson model. Details are described in the online supplemental materials. Analyses were also conducted according to major European geographical areas (see online supplemental materials) and subgroups of patients, such as according to age, gender, diabetes and hypertension.

A subsequent analysis was based on individual patient data, which were grouped according to the year of the intervention (2019 vs 2020). Absolute frequencies and percentages were used for qualitative variables. Analysis of variance (ANOVA) or Mann-Whitney and χ^2 test were used for continuous and categorical variables, respectively. Normal distribution of continuous variables was tested by the Kolmogorov-Smirnov test.

Multivariable logistic regression analyses were performed to identify the impact of the year of intervention on time delays and in-hospital mortality after adjustment for baseline confounding factors between the two groups. All significant variables (set at $p<0.1$) were entered in block into the model. Kaplan-Meier survival curves were to compare 30-day survival between the two groups, whereas multivariable Cox regression analysis was performed to identify the impact of the year of intervention on 30-day mortality after adjustment for baseline confounding factors between the two groups. All significant variables (set at $p<0.1$) were entered in block into the model. Model adequacy and goodness of fit were performed via a residual analysis for the Poisson and regression models. $P<0.05$ was considered statistically significant. The data coordinating centre was established at the Eastern Piedmont University.

Sample size calculation

In view of the observational nature of this registry, no sample size calculations or statistical power analyses were performed.

RESULTS

We included 109 centres that enrolled a total of 16 674 patients with STEMI undergoing mechanical reperfusion: 9044 patients in 2019 and 7630 patients in 2020. Online supplemental table 1 shows the characteristics of the included study

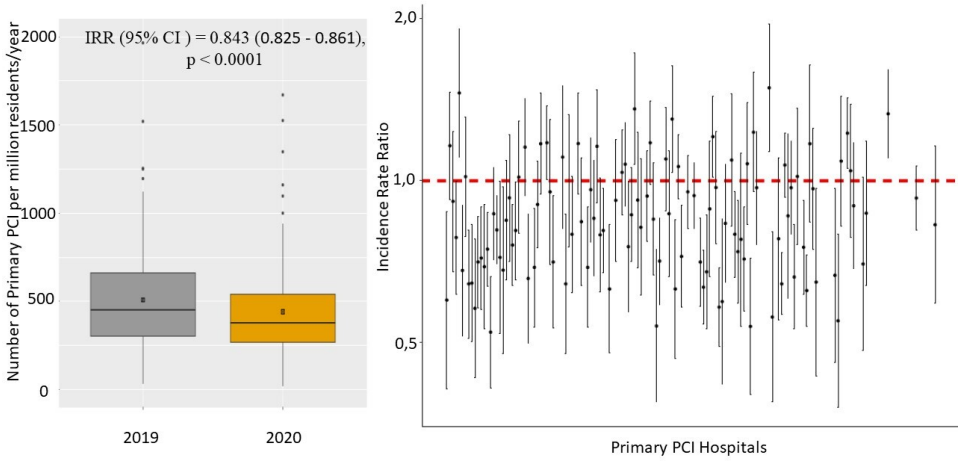

Figure 1 Box-and-whisker plot (left) showing the number of patients with STEMI treated by mechanical reperfusion per million of inhabitants per year in 2019 and 2020. The right graph shows the IRR with 95% CI across each centre. IRR, incidence rate ratio; PCI, percutaneous coronary intervention; STEMI, ST segment elevation myocardial infarction.

centres (Europe=90, Latin America=10, South-East Asia=7, North Africa=2). A total of 22 European centres provided data restricted only to March and April.

The number of STEMI treated percutaneously per million residents showed a consistent reduction, on average, from 559 (95% CI 514 to 607) in 2019 to 477 (95% CI 435 to 522) in 2020 (figure 1 and online supplemental figures 1–3). The IRR was 0.843 (95% CI 0.825 to 0.861, p<0.0001), showing a significant reduction of 15.7% in the number of STEMI cases from 2019 to 2020. Applying a mixed effect Poisson model (with centre as random effect), a high variability of IRR was observed among centres, measured by an SD of 0.207 of the random coefficient of centre (figure 1). This high heterogeneity was found to be significant (p<0.001) when performing an ANOVA χ^2 test between Poisson models with random effect and without such effect. The IRR was not related to the national incidence of cases or deaths due to COVID-19 (online supplemental figures 4 and 5). Moreover, the reduction in STEMI procedures was not associated with the type of institutional centre (private, academic or non-academic hospitals) (online supplemental table 2). Almost all participating geographical areas had a significant reduction in STEMI (figure 2 and online supplemental figures 6 and 7). While a more marked reduction of PPCI procedures was observed in Europe during March to April as compared with May to June 2020, opposite findings were observed in South-East Asia and North Africa (online supplemental table 2).

Poisson regression was used to evaluate the reduction in patients with STEMI in subgroups of subjects, according to age (≤75, >75), gender, diabetes and hypertension. We found a significant age-related reduction (7%, p=0.015), with a larger effect in older adults (IRR=0.800, 95% CI 0.761 to 0.838, p<0.0001) than in younger patients (IRR=0.854, 95% CI 0.834 to 0.875, p<0.001) (figure 3 and online supplemental figure 8). No significant difference was found for the other risk factors (figure 3 and online supplemental figure 9).

Baseline demographic and clinical characteristics

Individual data analysis was restricted to 16 083 patients with complete demographic, clinical procedural and outcome data (complete cases: 96.4%), 8698 in 2019 and 7385 in 2020. Table 1 shows the baseline characteristics of the two groups of patients according to the year of intervention. No difference was observed in baseline characteristics, except for smoking (55.5% vs 53.6%, p=0.014) and family history of coronary artery disease (21.1% vs 19.8%, p=0.044), which were more frequently observed in 2019. Detailed data according to the period of inclusion are reported in online supplemental tables 3 and 5.

As shown in table 1, a significantly longer total ischaemia and door-to-balloon time was observed in 2020 as compared with 2019 (table 1 and figure 4). The association between the COVID-19 pandemic and ischaemia time longer than 12 hours was confirmed after correction for baseline clinical confounders (geographical area, door-to-balloon, radial access, additional in-hospital revascularisation, use of drug-eluting stent (DES) and in-hospital renin-angiotensin system inhibitors (RASI)) (adjusted OR=1.32, 95% CI 1.19 to 1.47, p<0.001). No significant

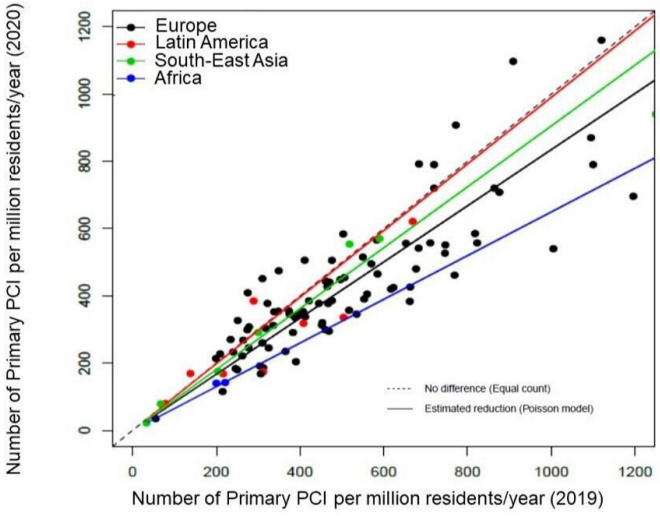

Figure 2 Results of Poisson regression analysis on the relationship between the number of primary PCI per million of residents per year in 2020 versus the number in 2019, according to continent. PCI, percutaneous coronary intervention.

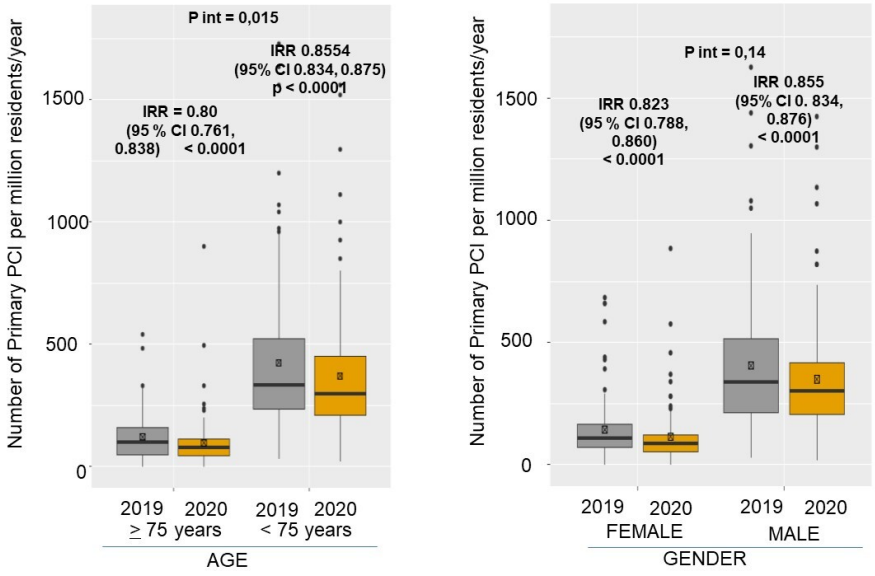

Figure 3 Box-and-whisker plot showing the number of patients with STEMI treated by mechanical reperfusion per million of residents per year in 2019 and 2020 according to age (left graph) and gender (right graph). A significant association was observed with age (p=0.015). IRR, incidence rate ratio; PCI, percutaneous coronary intervention; STEMI, ST segment elevation myocardial infarction.

interaction was observed for major risk factors (age, p=0.64; gender, p=0.091; diabetes, p=0.78; hypertension, p=0.74).

The association between the COVID-19 pandemic and door-to-balloon longer than 30 min was confirmed after correction for baseline clinical confounders (geographical area, ischaemia time, radial access, use of DES, additional in-hospital revascularisation and in-hospital RASI) (adjusted OR=1.1, 95% CI 1.03 to 1.17, p=0.005). No significant interaction was observed for most risk factors (age, p=0.9; gender, p=0.45; diabetes, p=0.21), except for hypertension (p=0.044). In 2019, patients with hypertension had a shorter door-to-balloon time (p<0.001) as compared with patients without hypertension, but not in 2020.

The rate of cardiogenic shock at presentation, infarct location, out-of-hospital cardiac arrest or rescue procedures after failed thrombolysis did not differ between the two groups.

Procedural characteristics

As shown in table 2, radial approach (77.8% vs 75.0, p<0.001), use of DES (89.3% vs 88.0%, p=0.008) and additional in-hospital revascularisation (20.5% vs 19.2%, p<0.001) were more frequent in 2020, whereas no significant difference was observed in culprit vessel, lesion location, preprocedural and postprocedural thrombolysis in myocardial infarction flow, use of intravenous antiplatelet therapies, thrombectomy, and multivessel disease. Further detailed data according to the period of treatment are reported in online supplemental tables 4 and 6.

In-hospital and 30-day mortality

Patients treated in 2020 had a slightly shorter duration of hospitalisation as compared with 2019 (median (mean) (IQR)=5 (5.8) (3–7) days vs 5 (6.1) (3–7) days, p<0.001). A significantly higher in-hospital mortality was observed in 2020 as compared with 2019 (481 deaths (6.5%) vs 457 deaths (5.3%); OR=1.26, 95% CI 1.10 to 1.44, p<0.001) (figure 4). The mortality rate was extremely high among COVID-19-positive patients. In fact, a total of 28 out of 109 COVID-19-positive patients died (25.7% vs 5.7%; OR=5.7, 95% CI 3.7 to 8.8, p<0.001).

The significantly poorer outcomes observed in patients with STEMI treated in 2020 persisted after correction for all potential confounding factors (geographical area, ischaemia time, door-to-balloon time, radial access, use of DES, additional in-hospital revascularisation and in-hospital RASI, duration of hospitalisation) (adjusted OR=1.38, 95% CI 1.19 to 1.59, p<0.001), and even after exclusion of COVID-19-positive patients (adjusted OR=1.23, 95% CI 1.07 to 1.41, p=0.003).

Data on 30-day mortality were available in 14 321 (89.0%). Patients treated in 2020 had a significantly higher mortality (8% vs 6.5%; HR=1.25, 95% CI 1.09 to 1.4, p=0.001) (figures 4 and 5), confirmed after adjustment for all potential confounders (geographical area, ischaemia time, door-to-balloon time, radial access, use of DES, additional in-hospital revascularisation and in-hospital RASI, duration of hospitalisation) (adjusted HR=1.29, 95% CI 1.14 to 1.45, p<0.001).

DISCUSSION

To date, the ISACS-STEMI COVID-19 represents the largest worldwide registry of patients with STEMI undergoing mechanical reperfusion during the COVID-19 pandemic, including more than 16 000 patients treated from March to June 2019 and 2020, and the first to provide data on 30-day mortality. We found a significant reduction in the number of primary PCI procedures during the pandemic (in 2020) as compared with 2019, especially in older patients. Yet there was a significant heterogeneity among centres which was explained neither by the local nor national deaths due to COVID-19. Furthermore, we observed a significantly higher in-hospital and 30-day mortality during the pandemic period, which may have been determined by the longer ischaemia time associated with logistics and treatment during this time.

Since the end of January 2020, when the pandemic was declared, SARS-CoV-2 has rapidly spread across the world, with quite 200 million of people infected and more than 4 million deaths. The real impact of COVID-19 on cardiovascular disease

Table 1 Baseline demographic and clinical characteristics

	2019 (n=8698)	2020 (n=7385)	P value
Age, median (IQR)	63 (54–72)	62 (54–71)	0.098*
Age >75 years, n (%)	1682 (19.3)	1365 (18.5)	0.17
Male gender, n (%)	6571 (75.5)	5593 (75.7)	0.78
Medical history, n (%)			
Diabetes mellitus	2038 (23.4)	1774 (24.0)	0.38
Hypertension	4745 (54.6)	4067 (55.1)	0.41
Hypercholesterolaemia	3445 (39.6)	2908 (39.4)	0.77
Active smoker	4805 (55.5)	3936 (53.5)	0.013
Family history of CAD	1835 (21.1)	1463 (19.8)	0.044
Previous STEMI	832 (9.6)	711 (9.6)	0.89
Previous PCI	1038 (11.9)	955 (12.9)	0.056
Previous CABG	144 (1.7)	127 (1.7)	0.703
Geographical area, n (%)			<0.001
Europe	6983 (80.3)	5831 (79.0)	
Latin America	630 (7.2)	720 (9.7)	
South-East Asia	706 (8.1)	587 (7.9)	
North Africa	379 (4.4)	247 (3.3)	
Referral to primary PCI hospital, n (%)			
Type			0.704
Direct access to hub	2449 (28.2)	2064 (27.9)	
Ambulance (from community)	4162 (47.8)	3576 (48.4)	
Transfer from spoke	2087 (24.0)	1745 (23.6)	
Time delays			
Total ischaemia (min), median (IQR)	196 (120–355)	225 (135–410)	<0.001*
Total ischaemia time, n (%)			<0.001
<6 hours	6622 (76.1)	5300 (71.8)	
6–12 hours	12 841 (14.8)	1215 (16.5)	
12–24 hours	537 (6.2)	551 (7.5)	
>24 hours	255 (2.9)	319 (4.3)	
Total ischaemia time >12 hours	792 (9.1)	870 (11.8)	<0.001
Door-to-balloon time (min), median (IQR)	40 (25–64)	40 (25–70)	0.01*
Door-to-balloon time, n (%)			<0.001
<30 min	3579 (41.1)	2854 (38.6)	
30–60 min	2845 (32.7)	2414 (32.7)	
>60 min	2274 (26.1)	2117 (28.7)	
Door-to-balloon time >30 min	5111 (58.9)	4531 (61.4)	0.001
Clinical presentation, n (%)			
Anterior STEMI	3986 (45.8)	3460 (46.9)	0.19
Out-of-hospital cardiac arrest	515 (5.9)	441 (6.0)	0.92
Cardiogenic shock	625 (7.2)	543 (7.4)	0.6
Rescue PCI for failed thrombolysis	605 (7.0)	494 (6.7)	0.51

*Mann-Whitney test.
CABG, coronary artery bypass graft; CAD, coronary artery disease; PCI, percutaneous coronary intervention; STEMI, ST segment elevation myocardial infarction.

and mortality, by both direct and indirect effects, remains the object of debate.[15]

Initial concerns emerged about an increased number of patients presenting with ACS during the COVID-19 pandemic supported by the presence of inflammatory pathophysiological mechanisms, triggering plaque disruption and generating a prothrombotic milieu.[16–18] Conversely, initial small reports from small-sized registries showed relevant reductions in the number of patients with ACS. These data have been confirmed in a large Chinese registry[10] and in our previous reports restricted to Europe, including patients treated in March and April 2019–2020.[2 3]

Several factors may have led to these findings, with large regional and national variations, ranging from −20% to −70% as compared with the prepandemic times.[2–10] It has been hypothesised that during the lockdown patients may have been discouraged to access the healthcare system even for acute treatments for fear of COVID-19 infection or overloading an already engulfed clinical service. Patient behaviour may have contributed to an increased morbidity and mortality, especially in patients with STEMI in whom a prolonged time to treatment remarkably affects myocardial salvage, left ventricular function, and both short-term and long-term mortality.[11–13] Logistic challenges for the ambulance system and emergency departments may have contributed to the overall delay in treating patients with STEMI during the pandemic.

The ISACS-STEMI COVID-19 represents the largest worldwide international multicentre registry among patients with

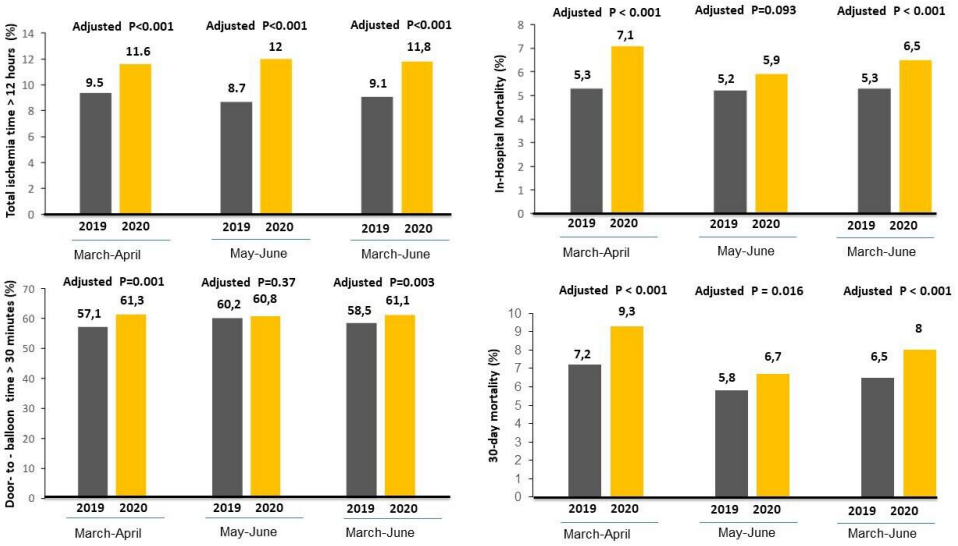

Figure 4 Bar graphs show the association between year of intervention and time delays (ischaemia time longer than 12 hours, upper left graph; door-to-balloon time longer than 30 min, lower left graph) and mortality (in-hospital, upper right graph; 30-day, lower right graph).

STEMI who underwent mechanical revascularisation, conducted in high-volume primary PCI centres on several continents (Europe, Latin America, South-East Asia and North Africa). Therefore, it provides important and reliable information to this controversy. In step with other small-sized registries and our previous report,[2] we observed a remarkable reduction in the number of patients with STEMI undergoing mechanical reperfusion. We found that this reduction was not consistent across all centres and not related to the local or national incidence of COVID-19 or rates of death due to COVID-19.

In our previous report we found a significant interaction with decline in procedures in patients with hypertension and only a trend in older patients, whereas no interaction was observed for gender and diabetes.

We may speculate that these public campaigns may have positively impacted on the fear of patients suffering from hypertension. In fact, in the present study, extended to May and June, we did not find an interaction with hypertension anymore, but only with age, as older adults presented with STEMI less often than in 2019. This more marked reduction in older adults may certainly reflect the fear of contagion in this population of mostly fragile patients.

In addition, older patients represent a higher risk subset of patients, with more atypical symptoms and longer ischaemia time, where an adequate management and organisation of the STEMI network have emerged as critical factors in conditioning their outcomes.[19] Furthermore, increased thrombotic burden has been previously associated with advanced age, even in patients with ACS treated with dual antiplatelet therapy,[20] which could have been even more pronounced in concomitance to the COVID-19 infection, which has been shown to enhance per se the thrombotic risk.

Table 2 Angiographic and procedural characteristics

	2019 (n=8698)	2020 (n=7385)	P value
Radial access, n (%)	6523 (75.0)	5745 (77.8)	<0.001
Culprit vessel, n (%)			0.45
Left main	141 (1.6)	111 (1.5)	
Left anterior descending artery	3989 (45.8)	3371 (45.6)	
Circumflex	1246 (14.3)	1104 (14.9)	
Right coronary artery	3260 (37.5)	2741 (37.1)	
Anterolateral branch	25 (0.3)	16 (0.2)	
SVG	37 (0.4)	42 (0.6)	
In-stent thrombosis, n (%)	339 (3.9)	293 (4.0)	0.82
Multivessel disease, n (%)	4236 (48.7)	3660 (49.4)	0.12
Preprocedural TIMI 0 flow, n (%)	5766 (66.3)	4965 (67.2)	0.21
Thrombectomy, n (%)	1402 (16.1)	1161 (15.7)	0.49
Stenting, n (%)	7998 (92.0)	6769 (91.6)	0.443
Drug-eluting stent, n (%)	7656 (88.0)	6598 (89.3)	0.008
Postprocedural TIMI 3 flow, n (%)	8030 (92.3)	6791 (92.0)	0.43
Gp IIb-IIIa inhibitors/cangrelor, n (%)	1753 (20.2)	1514 (20.5)	0.59
Bivalirudin, n (%)	34 (0.4)	18 (0.2)	0.101
Mechanical support, n (%)	246 (2.8)	251 (3.4)	0.037
Additional PCI, n (%)			0.001
During the index procedure	787 (9.0)	789 (10.7)	
Staged	886 (10.2)	800 (10.8)	
DAPT, n (%)	8552 (98.9)	7278 (99)	0.186
In-hospital RASI, n (%)	4626 (53.2)	4271 (57.8)	<0.001

DAPT, dual antiplatelet therapy; GP, glycoprotein; PCI, percutaneous coronary intervention; RASI, renin-angiotensin system inhibitors; SVG, saphenous vein graft; TIMI, thrombolysis in myocardial infarction.

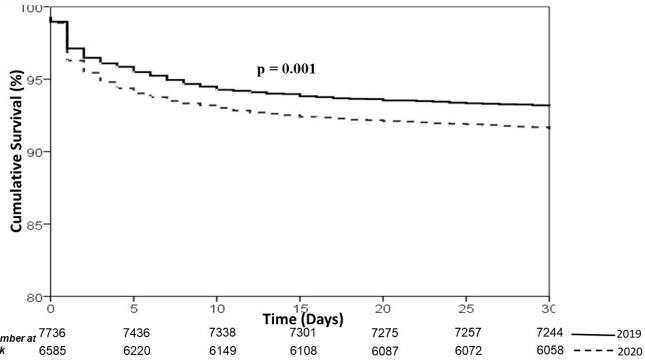

Figure 5 Kaplan-Meier survival curves of patients with STEMI treated in 2019 and 2020. STEMI, ST segment elevation myocardial infarction.

Confirming our previous report,[2] a significant reduction in patients with STEMI was observed in most of the centres under investigation and was neither related to the incidence of COVID-19 disease nor to COVID-19 mortality. Moreover, the reduction in primary PCI was not associated with the type of institutional centre and a similar reduction in primary PCI was seen in all geographical areas. A larger reduction in mechanical treatment of patients with STEMI was observed in Europe in March to April (the timing of the first wave on this continent), whereas in other continents a larger reduction was observed in May to June due to differences in the spread of the virus.

We cannot exclude local disparities among healthcare organisations and management of cardiovascular emergencies during the COVID-19 pandemic, which may have impacted on both the fear of contagion and the risk of out-of-hospital sudden death. Both factors may have contributed to the observed heterogeneity among centres.

The significantly longer ischaemia time observed in our registry may be a consequence of longer delayed time from symptoms to first medical contact, as a consequence of both direct patient or emergency system-related delay, as recently described,[18] and longer in-hospital delay, due to the specific COVID-19 protocols for screening patients and preparing equipment and personnel in the catheterisation laboratory.

Nevertheless, the use of DES and guidelines-recommended strategies were more frequent in 2020, suggesting that the suboptimal performance and inadequacy of protocols mainly affected the network of transportation and emergency, while when patients accessed primary PCI the standard of care was even improved.

We observed a significantly higher in-hospital and 30-day mortality during this pandemic, as compared with 2019, which may have been influenced by the longer delay to treatment. This association persisted after correction for major differences and, additionally, for COVID-19 positivity. Importantly, in step with previous small-sized studies and our previous report,[2 21] we observed a remarkable high mortality among the COVID-19-positive population, exceeding 25%.

We found a slightly significant shorter hospitalisation in 2020 as compared with 2019, probably dictated by constraints in hospital ward facilities during the pandemic. However, while hypothetically affecting survival, we do not believe that such a shorter reduction in hospitalisation observed during the pandemic may be clinically relevant with a significant impact on mortality. In fact, the difference in mortality between the pandemic and prepandemic period was confirmed after adjustment for the duration of hospitalisation.

Due to the prolonged emergency, large public campaigns, led by scientific societies and healthcare authorities, have to be repeatedly conducted in order to highlight the importance of recognition and response to characteristic symptoms of acute myocardial infarction, especially among older patients.

Limitations

A major limitation of the current study is represented by its retrospective design. It was conducted during a challenging pandemic emergency. Therefore, we expected missing data and potential limited quality in data collection. Nevertheless, our main data analysis and conclusions are based on absolute counts and therefore the overall cohort of patients was included. Furthermore, even in the analysis based on full individual patient data, this limitation and the potential risk of type II error were largely overcome by the high rate of complete cases (>95%) and the high statistical power due to the size of the study population. Furthermore, we cannot exclude that the observed reduction in patients with STEMI may partly have resulted from higher prehospital mortality due to longer delays to first medical contact, as described during the COVID-19 pandemic.[22]

The number of PPCI for STEMI was standardised per million of local residents (referral population) in order to avoid any potential bias related to the higher numerical impact of centres with larger case load. Furthermore, we selected centres where the strategy of STEMI treatment did not change during the pandemic, and therefore we do not expect a significant impact of a larger administration of thrombolysis observed in some regions during the pandemic. Finally, most of the centres were located in Europe, whereas only two centres were from Africa. Therefore, caution should be exercised in the extension of our conclusion to all the continents.

CONCLUSIONS

Our study showed that the COVID-19 pandemic relevantly impacted on the treatment of patients with STEMI, with a significant reduction in primary PCI procedures, especially among older adults patients, and on longer delay to treatment, which may have contributed to the higher in-hospital and 30-day mortality during the pandemic. Due to the persistent pandemic, health authorities, with the support of scientific societies, should conduct large and repeated public campaigns to exhort patients in paying large attention to characteristic symptoms of an acute myocardial infarction and rapidly activate the emergency system, especially among older patients.

Key messages

What is already known on this subject?

- The diversion of resources, lockdown rules, guidance on social distancing and a public fear of coronavirus contagion appear to have impacted on patient willingness to present to hospital during the COVID-19 pandemic.
- Initial reports have described a reduction in the number of cases of ST segment elevation myocardial infarction and increased mortality during the COVID-19 pandemic.

What might this study add?

- We found that the number of primary percutaneous coronary intervention procedures is significantly reduced during the pandemic (in 2020) as compared with 2019, especially in older adults.
- We observed heterogeneity among centres which may be due to local disparities among healthcare organisations and management of COVID-19 cardiovascular emergencies, which may have impacted on both the fear of contagion and the risk of out-of-hospital sudden death.
- The COVID-19 pandemic period was independently associated with higher in-hospital and 30-day mortality, and this is likely to reflect the significantly longer ischaemia time associated with treatment during this challenging time.

How might this impact on clinical practice?

- Our data suggest that health authorities, supported by scientific societies, should take vigorous action to prevent patients from neglecting characteristic symptoms of an acute myocardial infarction, especially among older adults.

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