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BRIEF COMMUNICATION

Who Has Seen Patients With ST-Segment–Elevation Myocardial Infarction? First Results From Italian Real-World Coronavirus Disease 2019

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BACKGROUND: After the coronavirus disease 2019 outbreak, social isolation measures were introduced to contain infection. Although there is currently a slowing down of the infection, a reduction of hospitalizations, especially for myocardial infarction, was observed. The aim of our study is to evaluate the impact of the infectious disease on ST-segment–elevation myocardial infarction (STEMI) care during the coronavirus disease 2019 pandemic, through the analysis of recent cases of patients who underwent percutaneous coronary intervention.

METHODS AND RESULTS: Consecutive patients affected by STEMI from March 1 to 31, 2020, during social restrictions of Italian government, were collected and compared with patients with STEMI treated during March 2019. During March 2020, we observed a 63% reduction of patients with STEMI who were admitted to our catheterization laboratory, when compared with the same period of 2019 (13 versus 35 patients). Changes in all time components of STEMI care were notably observed, particularly for longer median time in symptom-to-first medical contact, spoke-to-hub, and the cumulative symptom-to-wire delay. Procedural data and in-hospital outcomes were similar between the 2 groups, whereas the length of hospitalization was longer in patients of 2020. In this group, we also observed higher levels of cardiac biomarkers and a worse left ventricular ejection fraction at baseline and discharge.

CONCLUSIONS: The coronavirus disease 2019 outbreak induced a reduction of hospital access for STEMI with an increase in treatment delay, longer hospitalization, higher levels of cardiac biomarkers, and worse left ventricular function.

Key Words: acute coronary syndrome ■ complications ■ coronavirus ■ interstitial pneumonia ■ percutaneous coronary intervention

Coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus-2, was first identified in China and evolved into a global pandemic.[1,2] Patients displayed various clinical presentations, from asymptomatic to severe acute respiratory syndrome needing oral intubation and intensive care assistance.

Such condition reaches an extremely high mortality, especially in frail subjects experiencing cardiovascular diseases.[3–5] On February 21, 2020, the first Italian case of severe acute respiratory syndrome coronavirus-2 infection was diagnosed in northern Italy, and later huge number of people were infected. On March 9, 2020, the Italian government declared a state of emergency, issuing severe restrictions. Hospitals started to institute infection emergency protocols, and imposed widespread restrictions on nonurgent hospital admissions

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and hospital-based ambulatory care.[6,7] Adoption of these limitations has led to a gradual containment of epidemic, but on the other hand, a reduction of all admissions to the emergency departments (EDs), including acute coronary heart diseases, was observed.[8–10]

The aim of our study is to evaluate the impact of the severe acute respiratory syndrome coronavirus-2 infection on ST-segment–elevation myocardial infarction (STEMI) care during the COVID-19 pandemic, through the analysis of recent cases of patients who underwent percutaneous coronary intervention (PCI) at our department.

METHODS

Patient Population

In this observational study, we included patients admitted for STEMI to the catheterization laboratory of Cardiology Department of "Policlinico Tor Vergata" of Rome, and in whom PCI was performed. We analyzed the period between March 1, 2020, when hospitals in our city started to institute protocols to contain COVID-19, to March 31, 2020. Thirteen consecutive patients with STEMI arrived in our ED and were treated in our catheterization laboratory in March 2020. They were compared with 35 consecutive patients with STEMI who arrived in our catheterization laboratory in March of the previous year. None of the patients included in the study experienced COVID-19 infection. No patient was excluded from the study.

When feasible, a complete revascularization has been achieved during index procedure or before discharge (staged PCI). All patients were informed about the procedure and provided written consent. Institutional review board approval was obtained.

Data Collection

The data that support the findings of this study are available from the corresponding author on reasonable request. Time intervals (minutes) until the reperfusion have been recorded as follows: symptom-to-first medical contact, obtained by interviewing each patient about the time from the onset of symptoms to call an ambulance or go to our ED (hub center) or ED of other hospital (spoke center); spoke-to-hub, defined as the time between admission to the ED of another center (spoke) to the ED of our center (hub); the ambulance transportation time was included in the spoke-to-hub delay; ED-to-catheterization laboratory, defined as the time from access to our ED to the entrance in the catheterization laboratory; catheterization laboratory-to-wire, defined as the time from patient arrival at the catheterization laboratory to the time of a successful wire crossing. In addition, we calculated the following cumulative times: symptom-to-wire and first medical contact-to-wire from patient-reported symptom onset and first medical contact time to successful wire crossing time during PCI. Procedural data were systematically collected and reported. The final coronary flow was defined according to TIMI (Thrombolysis in Myocardial Infarction) flow grading system. In case of slow/no flow after stent implantation, an intracoronary glycoprotein IIb/IIIa inhibitor (eptifibatide) was administered.

Standard color Doppler transthoracic echocardiography was performed, at the moment of hospital admission and discharge, recording left ventricle ejection fraction (LVEF) and possible mechanical complications of STEMI, as free wall rupture, ventricular septal rupture, infarct expansion with left ventricular aneurysm formation, intraventricular thrombus, and acute/ischemic mitral regurgitation.

The duration of in-hospital stay and adverse events were reported as follows: cardiac death, cardiogenic shock, prolonged orotracheal intubation (>24 hours), use of mechanical circulatory support, acute pulmonary edema, acute renal failure, cerebral ischemic events, ventricular fibrillation/sustained ventricular tachycardia, nonsustained and ventricular tachycardia, new onset of atrial fibrillation, implantation of temporary or permanent pacemaker, acute stent thrombosis, and pericardial effusion.

Laboratory tests, including hemoglobin, fibrinogen, creatinine, creatine kinase–myocardial band, myoglobin, and ultrasensitive troponin I, were obtained before the PCI and during the hospitalization.

Statistical Analysis

Descriptive statistic was used to summarize the data; results are reported as means and SDs or medians and interquartile ranges (IQRs), as appropriate. They were compared using Student *t* test or the Mann-Whitney rank sum test. Categorical variables are presented as counts and percentage values and were compared with the χ^2 or Fisher exact test. Logistic and linear regressions were used to examine the relationship between demographic data and variables of outcomes. Results are reported as point estimates and 95% CIs. Both CI and *P* value are not adjusted for multiple testing. A 2-sided $P<0.05$ was considered of statistical significance. Statistical analyses were performed using the Statistical Package for Social Sciences, version 26 (SPSS, Chicago, IL).

RESULTS

In the period between March 1 and 31, 2020, we observed a 63% reduction of patients with STEMI who were admitted to our catheterization laboratory, when compared with the same period of 2019. Particularly,

Table 1. Clinical Characteristics of Patients and Procedural Data

Characteristic	March 2019 (n=35)	March 2020 (n=13)	Difference (95% CI)	*P* Value
Population				
Age, y	62±10	65±12	−2.1 (−9.2 to 5.0)	0.559
Male sex, n (%)	31 (87)	11 (85)		0.713
Dyslipidemia, n (%)	11 (31)	8 (61.5)		0.058
Smoke, n (%)	19 (54)	10 (77)		0.180
Diabetes mellitus, n (%)	8 (23)	3 (23)		0.571
Hypertension, n (%)	23 (66)	7 (54)		0.450
Familiarity, n (%)	14 (40)	3 (23)		0.276
Chronic renal failure, n (%)	3 (9)	2 (14)		0.492
Chronic obstructive pulmonary disease, n (%)	2 (6)	2 (15)		0.281
Previous acute myocardial infarction, n (%)	2 (6)	1 (8)		0.801
Previous percutaneous coronary intervention, n (%)	3 (9)	0 (0)		0.276
Previous coronary artery bypass graft, n (%)	0 (0)	0 (0)		…
STEMI localization, n (%)				
Anterior	12 (34)	6 (46)		0.675
Inferoposterior	16 (46)	5 (38.5)		0.902
Lateral	7 (20)	2 (15)		0.958
Source, n (%)				
Our hospital	12 (34)	2 (15)		0.356
Emergency ambulance	8 (23)	3 (23)		0.711
Other hospital (spoke)	15 (43)	8 (61.5)		0.409
Time components of STEMI care, median (IQR), min				
Symptom-to-FMC	80 (60–207)	120 (52.5–3600)	−60 (−738 to 23)	0.284
Spoke-to-hub*	60 (37–122)	132 (43–173)	−23 (−102 to 6)	0.084
ED-to-cathlab	18 (10–42)	10 (5–26)	6 (−1 to 16)	0.081
Cathlab-to-wire	24 (20–30)	18 (8.5–40.5)	4 (−8 to 13)	0.472
Symptom-to-wire	200 (131–319)	388 (177–3746)	−149 (−990 to −16)	0.038
FMC-to-wire	89 (70–159)	141 (65–196)	−22 (−81 to 18)	0.251
Procedure				
Primary percutaneous coronary intervention, n (%)	34 (97)	13 (100)		0.538
Rescue percutaneous coronary intervention, n (%)	1 (3)	0 (0)		0.538
Percutaneous coronary intervention duration, min	44.2±19.1	49.6±28.6	−5.4 (−19.8 to 8.9)	0.450
Contrast medium, mL	142±58.8	172±136.9	−30 (−87 to 27)	0.295
Staged percutaneous coronary intervention, n (%)	15 (43)	6 (46)		0.838
No. of vessels, n (%)				
Single vessels	14 (40)	3 (23)		0.546
Double vessels	12 (34)	6 (46)		0.546
Triple vessels	9 (26)	4 (31)		0.546
Culprit lesion, n (%)				
Left anterior descending artery	12 (34)	6 (46)		0.759
Diagonal branch	2 (6)	0 (0)		0.759
Left circumflex artery	4 (11)	1 (8)		0.759
Left obtuse marginal artery	1 (3)	1 (8)		0.759
Right coronary artery	16 (46)	5 (38.5)		0.759
Outcome, n (%)				
TIMI grade flow ≤2	1 (3)	4 (31)		0.022
Eptifibatide	1 (3)	4 (31)		0.022

(*Continued*)

Table 1. Continued

Characteristic	March 2019 (n=35)	March 2020 (n=13)	Difference (95% CI)	*P* Value
Complete revascularization after PPCI	19 (54)	7 (54)		0.978
Complete revascularization at discharge	32 (91)	9 (69)		0.053

Results presented as mean±SD, unless otherwise indicated. Percentages may not total 100 because of rounding. A 2-sided $P<0.05$ was considered of statistical significance. Cathlab indicates catheterization laboratory; ED, emergency department; FMC, first medical contact; IQR, interquartile range; PPCI, primary percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; and TIMI, Thrombolysis in Myocardial Infarction.

*Patients who arrived directly to our ED were excluded. Spoke-to-hub time was calculated in 23 and 11 patients of 2019 and 2020, respectively.

in March 2019, 35 consecutive patients with STEMI arrived in our catheterization laboratory, whereas 13 consecutive patients arrived in March 2020, during the first period of the COVID-19 emergency in Italy. Demographic data are reported in Table 1. Changes in every time component of STEMI care were observed when compared with historical data from the prior year. Particularly, longer median times were observed in patients of 2020 (Table 1). All patients underwent primary PCI, except for one patient who underwent a rescue PCI in March 2019. Higher prevalence of patients with TIMI flow ≤2 at the end of the procedure and a greater use of intracoronary glycoprotein IIb/IIIa inhibitors were reported in patients of March 2020 (31% versus 3%; *P*=0.022). Complete procedural data are presented in Table 1.

Patients of March 2019 had higher values of LVEF at baseline when compared with patients of 2020 (42% [IQR, 37%–47%] versus 35% [IQR, 32.5%–42.5%]; difference, 5 [95% CI, 0–10]; *P*=0.014); this difference was also maintained at discharge, when patients of March 2019 improved significantly the LVEF to a median of 48% (IQR, 42%–55%), whereas patients of March 2020 did not show any significant variation (35% [IQR, 35%–40%]) (Figure). No mechanical complications were observed in the overall population, but functional mitral regurgitation grade more than moderate was 6% in 2019 and 15% in 2020 (*P*=0.03) (Table 2).

Longer duration of in-hospital stay was observed in patients of March 2020. Nevertheless, no differences were observed in adverse events (Table 2). Blood test values showed numerically higher values of

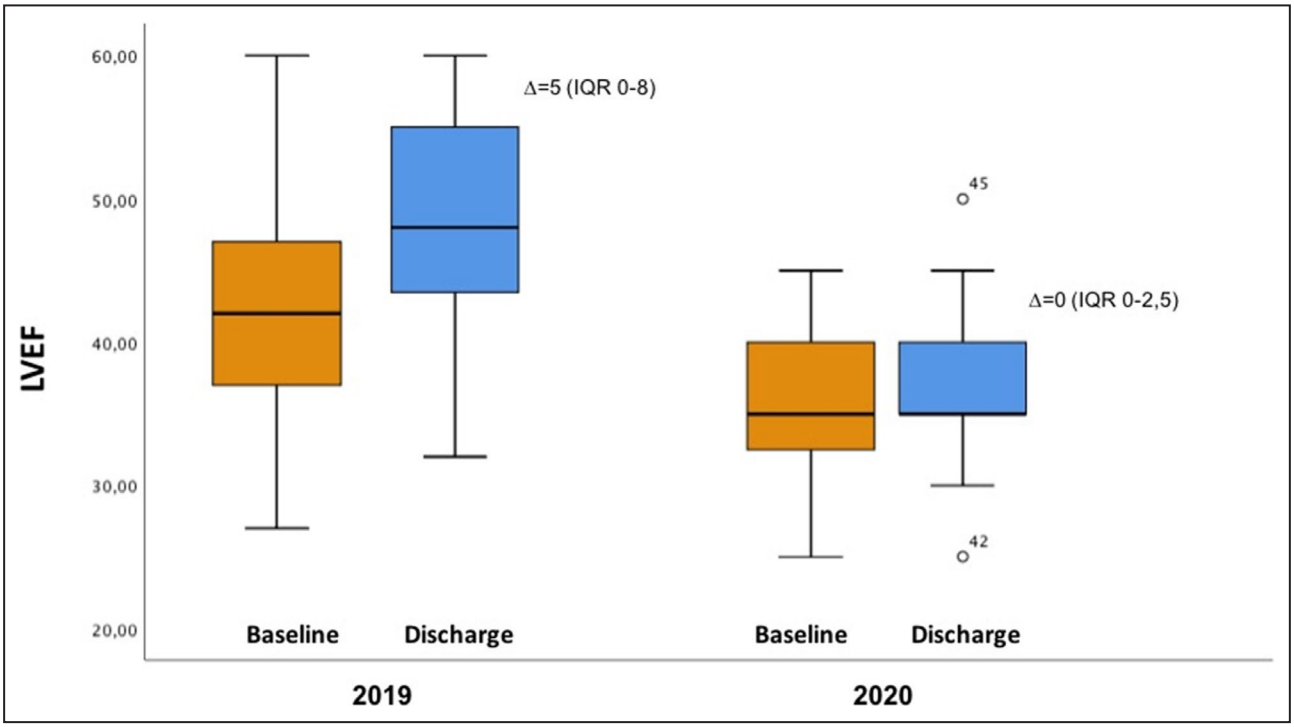

Figure. Left ventricular ejection fraction (LVEF) at baseline and discharge of patients with ST-segment–elevation myocardial infarction of March 2019 and March 2020.

Data are expressed as median and interquartile range (IQR). The baseline and discharge median and IQR of LVEF in March 2019 was 42% (IQR, 37%–47%) and 48% (IQR, 42%–55%), respectively. The baseline and discharge median and IQR of LVEF in March 2020 was 35% (IQR, 32.5%–42.5%) and 35% (IQR, 35%–40%), respectively. The median of delta (Δ) between baseline and discharge LVEF in patients of 2019 is 5 (IQR, 0–8); and in patients of 2020, 0 (IQR, 0–2.5). The difference was 3 (95% CI, 0–5; *P*=0.011).

Table 2. In-Hospital Data and Laboratory Blood Tests

Characteristic	March 2019 (n=35)	March 2020 (n=13)	Difference (95% CI)	*P* Value
Complications, n (%)				
Cardiac death	0 (0)	0 (0)		…
Cardiogenic shock	0 (0)	0 (0)		…
Prolonged orotracheal intubation	0 (0)	0 (0)		…
Mechanical circulation support	0 (0)	0 (0)		…
Acute pulmonary edema	3 (9)	3 (23)		0.390
Acute renal failure	3 (9)	1 (8)		0.922
Cerebral ischemic events	1 (3)	0 (0)		0.538
Ventricular fibrillation/sustained ventricular tachycardia	1 (3)	0 (0)		0.538
Nonsustained ventricular tachycardia	13 (37)	2 (15)		0.148
Atrial fibrillation (new onset)	3 (9)	2 (15)		0.492
Temporary pacing	2 (6)	0 (0)		0.379
Permanent pacemaker	1 (3)	0 (0)		0.538
Acute stent thrombosis	1 (3)	0 (0)		0.538
Free wall rupture	0 (0)	0 (0)		…
Ventricular septal rupture	0 (0)	0 (0)		…
Ventricular aneurysm	0 (0)	0 (0)		…
Intraventricular thrombus	0 (0)	1 (8)		0.097
Pericardial effusion	1 (3)	2 (15)		0.111
Acute mitral regurgitation	0 (0)	0 (0)		…
Ischemic MR >2+	2 (6)	2 (15)		0.03
Time of hospitalization, median (IQR), d				
CCU	3.0 (2–4)	5 (2.5–6)	−2 (−3 to 0)	0.018
Total	6 (5–7)	7 (6–10)	−2 (−4 to −1)	0.008
Laboratory blood tests				
Hemoglobin, g/dL				
Admission	14.7±1.6	14.3±1.9	0.3 (−0.9 to 1.4)	0.702
24 h	13.9±1.6	13.2±2.2	0.4 (−1 to 2)	0.608
Discharge	13.6±1.7	13.0±2.2	0.5 (−8 to 2.4)	0.583
Fibrinogen, median (IQR), mg/dL				
Admission	354.5 (313–427.8)	436 (403.5–626.5)	−101 (−197 to −30)	0.007
Serum creatinine, median (IQR), mg/dL				
Admission	1.0 (0.8–1.2)	1.0 (0.8–1.2)	−0.04 (−0.2 to 0.2)	0.625
24 h	0.9 (0.7–1.2)	1.0 (0.8–1.6)	−0.09 (−0.4 to 0.1)	0.272
Discharge	1.0 (0.8–1.1)	1.1 (0.9–1.9)	−0.2 (−0.5 to 0.3)	0.144
Ultrasensitive troponin, median (IQR), ng/mL				
Admission	317.6 (25–5675.7)	1310 (58.4–18 394)	−668 (−3430 to 234)	0.27
Peak	35 507 (14 462.8–86 726.0)	57 098 (28 047.5–146 626.0)	−18 530 (−52 038 to 10 867)	0.27
Creatine kinase–myocardial band, median (IQR), ng/mL				
Admission	6.7 (2.4–75.3)	71.8 (11.6–83.5)	−31 (−70.7 to 6)	0.128
Peak	119.0 (50.6–197.8)	97.0 (53.3–323.0)	−16.6 (−89.4 to 55.9)	0.617
Myoglobin, median (IQR), ng/mL				
Admission	134.5 (43–445.5)	1710 (124.7–3409.2)	−127 (−3212 to 206)	0.198
Peak	334 (111–1091)	463 (250–3389.5)	−147 (−1615 to 147)	0.270

Results presented as mean±SD, unless otherwise indicated. Percentages may not total 100 because of rounding. A 2-sided $P<0.05$ was considered of statistical significance. CCU indicates cardiology care unit; IQR, interquartile range; and MR, mitral regurgitation.

cardiac biomarkers and fibrinogen in patients of March 2020, as reported in Table 2. The regression analyses did not show any relationship between demographic characteristics and the following variables: number of patients experiencing STEMI, LVEF at baseline and discharge, length of hospitalization, and symptom-to-wire (Table S1).

DISCUSSION

Similar to recent published studies in diverse geographic areas, we observed a reduction of 63% of STEMI-related hospitalizations in our high-volume center in Rome during the first month of COVID-19 epidemic in Italy, when compared with the same period of 2019.[8–10] Also, relevant changes in time components of STEMI care were recorded. Our results confirmed numerically longer median times in most of components when compared with historical data from the prior year. The largest time difference was in the time from symptom onset to first medical contact and in the cumulative symptom onset to wire crossing during PCI. Most visibly, the huge delay was in the small number of patients with STEMI seeking medical help after institution of the control measures. Surely, the fear of patients to hospitalize and contract COVID-19 plays an important role; this may also suggest why some patients with STEMI did not seek care at all. In addition, our results showed longer delays from the spoke center to the ED of our hub department. This could be explained by the implementation of precautionary measures with the aim of an early identification of the infection and its containment. Detailed medical and contact history, assessment of symptoms, and execution of radiological examinations, made before transferring patients to our catheterization laboratory, could be responsible for the longer spoke-to-hub time observed in patients with STEMI during the COVID-19 outbreak. These are essential measures for containing infection, but this could significantly increase delays in diagnosis, staff activation, and transfer of patients with STEMI if healthcare systems are not prepared. Another aspect that has been highlighted is the numerical reduction of the patient transit time inside our hospital, from ED to the catheterization laboratory. This may have been influenced by the presence of an interventional cardiologist on site and the fact that most patients arrived from other hospitals and were directly transported inside the catheterization laboratory to avoid severe acute respiratory syndrome coronavirus-2 intrahospital infection.

Once in catheterization laboratory, we observed shorter time in patients of 2020 for the catheterization laboratory-to-wire time. Nevertheless, we documented a higher prevalence of patients with TIMI flow ≤2 at the end of the procedures for the patients of March 2020, and greater use of glycoprotein IIb/IIIa inhibitor. These data are probably correlated with the late presentation after symptom onset and more complex lesions, despite the experience of the operators.

In addition, we observed that patients who arrived in March 2020 had higher values of serum fibrinogen and cardiac biomarkers at moment of hospital admission and as peak value. This suggests that a longer precoronary time induced greater myocardial damage, which depends on the interruption of the coronary flow during acute myocardial infarction. It is well known and widely demonstrated that ischemic time duration is the major determinant of infarct size; therefore, a prompt recognition and early management of STEMI is critical to reduce morbidity and mortality.[11,12] Coronary occlusion persisting for >90 minutes determines a degree of cell death involving 40% to 50% of myocardium at risk and, after 6 hours of continuous ischemia, myocardial recovery will be minimal, despite the fact that the collateral flow is good.[13,14] Many individuals who survive an acute myocardial infarction have residual infarct pathological features that predispose them to the subsequent development of left ventricular dysfunction and heart failure, which remain the major causes of death after myocardial infarction.[15] To confirm this, in our population of patients with STEMI who arrived later in March 2020, a worse left ventricular dysfunction at the echocardiography was assessed at baseline, when compared with patients of 2019. In this group, LVEF remains lower also at discharge, with an increased risk to develop heart failure.

As evidence of an early worse outcome, in March 2020, there was an extension of hospitalization time in the whole hospital stay, particularly influenced by cardiology care unit stay. This is related to the late presentation of these patients in the hospital, who have a greater reduction of ventricular function, requiring more intensive and targeted treatments.

Finally, we want to underline that the delay in treatment of STEMI during the COVID-19 pandemic not only may entail a prognostic worsening of these patients, but also can weigh the economic burden of national healthcare system, because there is a threatening potential risk of evolving into heart failure.

Study Limitations

This is a preliminary observation report, and our study should be considered in the context of these limits. We present the experience of a single hospital in

the treatment of STEMI, after the implementation of COVID-19 pandemic protection protocols in a small cohort of patients. It is possible that the results obtained will improve over time as the experience of the medical staff and patients becomes more mature. In consideration of the small sample size and the study design, we cannot make meaningful statistical conclusions. In addition, the modest sample size of the study and its single-center nature may not reflect the experience of other centers.

CONCLUSIONS

During the first phase of the COVID-19 outbreak in Italy, a suggestive reduction in patients with STEMI who were admitted to our PCI center was observed, as was a longer time from symptom onset to first medical contact and to wire cross, influencing negatively the duration of hospitalization, cardiac biomarkers, and left ventricular function. Hospitals should not only consider the methods of containing and treating this infection, but also how the outbreaks of infection can affect the care systems of other conditions that endanger the lives of patients.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. Logistic and Linear Regression analysis of 2020 group.

Variable	2020 Group		ΔLVEF		In Hospital stay (days)		Symptoms to Wire (min)	
	P value	**CI (95%)**	**P value**	**CI (95%)**	**P value**	**CI (95%)**	**P value**	**CI (95%)**
Age	0,296	-7,255 - 24,814	0,536	-0,242 – 0,085	0,130	0,089 – 0,400	0,644	-109,109 – 42,756
Male	0,216	-172,639 - 583,851	0,169	-7,531 – 1,192	0,337	-1,512 – 4,605	0,206	-596,371 – 5109,518
Dyslipidemia	0,112	-19,367 - -1,497	0,248	-1,077 – 5,332	0,807	-1,715 – 2,848	0,310	-2244,592 – 600,401
Smoke	0,898	-39,777 – -20,102	0,991	-3,450 – 4,172	0,045	-6,809 – 1,099	0,723	-1491,716 – 840,331
Diabetes	0,171	-39,077 - -0,794	0,297	-1,916 – 5,940	0,918	-3,066 – 2,804	0,158	-2538,391 – 106,635
Hypertension	0,112	-21,333 – -1,102	0,107	-0,501 – 6,645	0,322	-3,279 – 0,806	0,257	-2142,810 – 380,797
Family history of CVD	0,144	-7,876 - 1,161	0,477	-2,733 – 5,792	0,883	-2,363 – 3,707	0,508	-1945,491 – 731,024

Previous ACS	0,332	-22,969 – 103,846	0,358	-8,336 – 5,156	0,085	-10,216 – 0,496	0,788	1790,782 – 1242,872

Δ left ventricular ejection fraction, in hospital stay (days) and symptoms to wire (minutes).

2-sided p value <0.05 were considered of statistical significance. CI indicates confidence interval; LVEF, left ventricular ejection fraction; CVD, cardiovascular disease; ACS, acute coronary syndrome.