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Comparison of long-term outcome of patients with ST-segment elevation myocardial infarction between pre-covid-19 and COVID-19 era

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Abstract

Aims: To compare major cardiovascular and cerebrovascular events (MACCE) rates between patients in the pre-COVID-19 era and COVID-19 era, and to assess the impact of the presence of COVID-19 (+) on long-term MACCE in ST-segment elevation myocardial infarction (STEMI) in Turkey.

Methods: Using the TURSER study (TURKISH ST-segment elevation myocardial infarction registry) data, the current study included 1748 STEMI patients from 15 centers in Turkey. Patients were stratified into COVID-19 era (March 11st–May 15st, 2020; n = 723) or pre-COVID-19 era (March 11st–May 15st, 2019; n = 1025) cohorts. Long-term MACCE rates were compared between groups. In addition, the effect of COVID-19 positivity on long-term outcomes was evaluated. The primary outcome was the occurrence of MACCE at long-term follow-up, and the secondary outcome was hospitalization with heart failure.

Results: The MACCE and hospitalization with heart failure rates between pre-COVID-19 era and COVID-19 era were 23% vs 22% (p = 0.841), and 12% vs %8 (p = 0.002), respectively. In the covid-19 era, the rates of MACCE and hospitalization with heart failure COVID-19 positive versus COVID-19 negative patients were 40% vs 20%, (p < 0.001), and 43% vs 11% (p < 0.001), respectively.

Conclusion: There was no difference between the pre-COVID-19 era and the COVID-19 era in terms of MACCE and heart failure hospitalization in STEMI patients in Turkey. In the Covid-19 era, STEMI patients positive for COVID-19 had a higher rate of MACCE and heart failure hospitalization at the long-term follow-up.

Keywords: COVID-19, ST-segment elevation myocardial infarction, mortality.

INTRODUCTION

The COVID-19 pandemic, caused by the new SARS-CoV-2, has killed more than 6 million people worldwide as of May 2022. ST-segment elevation myocardial infarction (STEMI) admissions decrease significantly due to the COVID-19 pandemic (1,2). Also, symptom to first medical contact time has been prolonged during this period. In addition to all this, lower left ventricular ejection fraction (LVEF) values, higher troponin levels, and high intracoronary thrombus burden were commonly seen in these patients in the COVID-19 era compared with the pre- COVID-19 era (3,4).

Although there was no difference between the pre- COVID-19 era and the COVID-19 era regarding in-hospital mortality, COVID-19 (+) STEMI patients had a higher risk of mortality than those without (1, 4). There is limited data with respect to the long-term outcomes of these patients (5,6). In the presented study, we aimed to assess the effects of both COVID-19 -era and the presence of COVID-19 (+) on long-term major cardiovascular and cerebrovascular events (MACCE) in STEMI patients in Turkey.

METHODS

Study design and patient population

We used data from the TURKISH ST-segment elevation myocardial infarction registry (TURSER), which is a multicenter, retrospective, observational study that enrolled 1788 patients between 18 and 90 years of age, who were diagnosed with STEMI in 15 centers (4). Forty patients who were lost, or whose data could not be reached in follow-up were not included in this study. The final study population consisted of 1748 STEMI patients (Figure 1). The patients were divided into two groups: COVID-19 era (March 11st– May 15 st, 2020; n = 723) and pre- COVID-19 era group (March 11st– May 15st, 2019; n = 1025). Moreover, the patients in COVID-19 era were grouped as COVID-19 positive (n = 62) or negative (n = 661). STEMI was defined according to the fourth universal definition of myocardial infarction (7). Evidence-

based optimal medical therapy and coronary revascularization were carried out according to current guidelines and recommendations (8). All interventional procedures and strategies such as balloon angioplasty, type of stent, aspiration thrombectomy, and the usage of intra-aortic balloon pumps were left to the discretion of interventional cardiologists. The thrombolysis in myocardial infarction (TIMI) thrombus grade (TG) was used for the thrombus burden classification (9). Patients with Grade 5 thrombus burden were reclassified to a thrombus category after flow achievement either with a guidewire or a small (1.5 mm) balloon (10). Procedural success was defined as post PCI TIMI-3 flow. The left ventricle ejection fraction (LVEF) was calculated after measuring the end-diastolic and end-systolic left ventricle (LV) volumes in the apical four-chamber and two-chamber views using the modified Simpson's method. Valve disease was considered as moderate or severe regurgitation in mitral or aortic valves, or severe stenosis for mitral or aortic valves.

The bleeding classification was performed according to the thrombolysis in myocardial infarction (TIMI) bleeding score. Major hemorrhage was defined as 5 gr/dl hemogram, a 15% or greater decline in hematocrit, or intracranial hemorrhage. Minor bleeding was defined as 3–5 gr/dl Hb, a 10–15% gr/dl hematocrit decline, or gastrointestinal bleeding. Cardiogenic shock was defined as systolic blood pressure <90 mmHg for at least 30 min with evidence of poor tissue perfusion after correction of non-myocardial factors.

After the STEMI diagnosis, the patients with no signs of COVID-19 infection were transferred to the routine cardiac catheterization laboratory, however, the patients with symptoms indicating possible COVID-19 were transferred to an allocated cardiac catheterization laboratory.

The COVID-19 diagnosis was made by detecting SARS-CoV-2 on a nasal/pharyngeal swab (11) or by evaluating the symptoms plus radiological imaging (12). All of these patients were treated as COVID-19 patients in these centers. The study was approved by the ethics

committee of the Dokuz Eylul University Faculty of Medicine (2020/10-35) and the Ministry of Health (2020-05-02T23_17_42).

Data collection

The patient's demographic, clinical, laboratory, interventional, and long-term outcomes data from each center were collected by the principial investigator of that center. Also, The National Death Registry System data was used to determine long-term mortality. Cineangiographic images of patients were retrospectively analyzed by two interventional cardiologists blinded to the patient's COVID-19 status. Data were finally checked for missing or contradictory entries.

Study outcomes

The primary end-point was the occurrence of MACCE which included all-cause mortality, hospitalization with heart failure, myocardial reinfarction defined as STEMI or non-non–ST-segment elevation myocardial infarction, target vessel revascularization defined as any repeat revascularization in the epicardial vessel of the prior stent (main branch or side branches), and cerebrovascular events. The secondary end-point of this study was hospitalization with heart failure in the follow-up.

Follow-up period

The patients in the COVID-19 period were followed until September 22, 2021, and the patients in the pre-COVID-19 period were followed until September 22, 2020.

Statistical analysis

Categorical variables are presented as absolute numbers, and percentages, and compared by the x^2 test. Continuous variables are shown as mean and Standard deviation (SD) and compared by the Student's t-test, or Mann-Whitney test as appropriate. Factors entered into the multivariate model comprised those with p-values <0.1 from the univariate analysis.

Multivariable Cox regression analysis with clinically relevant variables was made to detect independent predictors of long-term MACCE. The cumulative incidence of the primary and secondary endpoints was estimated by the Kaplan–Meier method. Two-sided p-values < 0.05 were considered statistically significant. All statistical analysis was performed with SPSS version 26 (SPSS Inc., Chicago, IL, USA).

Power Analysis

The study needed to recruit 490 participants for each group to have 80% power with 5% type 1 error level when assuming a primary endpoint rate of 18% at 1-year follow-up. The power of the study increased to 89.36 % with the selection of 954 patients in the pre-COVID-19 era and 662 patients during the COVID-19 era with a 5% type 1 error level.

Results

Patient characteristics

A total of 1748 STEMI patients were examined. The Median follow-up time was 524 days (507-541). Patients in pre- COVID-19 era were older than in COVID-19 era (61.9 ± 12.4 vs 60.6 ± 12.4, $p = 0.040$). As shown in Table 1, all groups were similar regarding the histories of diabetes mellitus, hypertension, coronary artery disease, and atrial fibrillation. Moreover, there was no significant difference between groups with respect to a pre-usage statin, and ACE-I angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ARB) (Table 1). The patients in the COVID-19 era had lower LVEF compared with those in the pre- COVID-19 era (46.7 ± 8.9 vs 47.8 ± 9.1, $p = 0.015$).

The time from symptom-to- FMC was significantly longer in COVID-19 group than in pre-COVID-19 group (120 [75-240] vs. 100 [60-180] minutes, $p < 0.001$). The laboratory values of the groups are illustrated in Table 1. There was no significant difference between groups concerning white blood cell counts (WBC), serum creatinine, and troponin levels (each $p > 0.05$).

62 STEMI patients were COVID-19 positive in COVID-19 era. These patients' characteristics are presented in Table 4. There was no significant difference between groups concerning the symptom onset to FMC time, histories of DM, HT, CAD, and COPD or asthma (Table 4). Valve disease was more frequent in COVID-19 positive STEMI patients than those without (25% vs 9%, $p < 0.001$). The levels of C-reactive protein (CRP), and troponin were higher in COVID-19 group (55.2 [21.4-147.4] vs 21.0 [2.8-51.3], $p < 0.001$; 19254 [6587-26477] vs 8170 [789-26477], $p = 0.005$, respectively, Table 4) than in non-COVID-19.

Procedural characteristics

The features of patients regarding procedures are provided in Table 2. Infarct-related artery, multivessel disease, glycoprotein IIb/IIIa inhibitors use, IABP, and thrombus aspiration device use, baseline TIMI 0/1 flow, modified thrombus grade > 3, and post-PCI TIMI -3 flow were similar in both groups.

The patients with covid -19 (+) had significantly lower rate of coronary intervention than those without (95% vs 100%, $p < 0.001$). Baseline modified thrombus grade > 3 was higher COVID-19 group than in non-COVID-19 group (59% vs 38%, $p = 0.001$). Glycoprotein IIb/IIIa inhibitors use was more common in patients with COVID-19 (34% vs 20%, $p = 0.032$). There was no difference between covid (+) and those without with respect to post-PCI TIMI 3 flow (Table 5). The COVID-19 positive patients had lower LVEF than COVID-19 negative patients (43.6 ± 9.0 vs 47.0 ± 8.8, $p = 0.004$). Complete revascularization during the index hospitalization was performed in 29% of COVID-19 (+) patients ($p = 0.012$).

In-hospital outcomes

Mortality, shock, and stent thrombosis rates was similar between pre-COVID-19 era and COVID-19 era (8% vs 7%, $p = 0.839$, Table 3) during in-hospital. However, patients who tested positive for COVID-19 among STEMI patients had higher percentage of mortality,

shock and stent thrombosis compared with non-COVID-19 patients (29% vs 7%, < 0.001; 21% vs 7%, < 0.001; 7% vs 1%, p = 0.002, recpectively, Table 6).

Long-term outcomes

We oberved similar MACCE rates between pre- COVID-19 era and COVID-19 era (23% vs 22%, p = 0.841, Table 3, Figure 2). However, hospitalization with HF was more common in the COVID-19 era compared with COVID-19 era (12% vs 8%, p = 0.002, Table 3, Figure 3).

The presence of COVID-19 (+) in STEMI patients was an independent predictor of MACCE at long-term follow-up (HR: 1.628, 95%CI: 1.042-2.542, p = 0.032, Table 7). The patients with COVID-19 (+) had higher MACCE rates, which were mainly driven by hospitalization with HF, than those with COVID-19 (-) (40% vs 20%, p < 0.001, Table 6, Figures 4, 5,6).

Discussion

To our best knowledge, this study may be the first study in terms of being a multicenter study involving a large number of STEMI patients and representing long-term follow-up of STEMI patients in both the COVID-19 era and pre- COVID-19 era. The current retrospective study found that STEMI patients with COVID-19 had a higher rate of MACCE compared with those without COVID-19 at long-term follow-up. Moreover, hospitalization with HF was more frequent during COVID-19 than pre-COVID-19.

Total ischemic time plays an important role in determining cardiovascular outcomes in STEMI patients. Mortality rates increase with increasing this time (13). Both symptom-to-FMC time and door-to-balloon time were prolonged in these patients in the COVID-19 era when compared with the pre- COVID-19 era (14-17). The presented study showed that symptom-to-FMC time during the COVID-19 era was longer than the pre-COVID-19 era in STEMI as found

in previous studies. Prolongation in this time may be due to patient-related delays as we did not have information regarding system-related delays in the presented study.

The data regarding long-term outcomes of STEMI patients in the COVID-19 era and the pre-COVID-19 era was limited. Different results have been reported on this in previous studies (5,18,19). Recently, a new study published by Phua et al., which included 321 STEMI patients, has shown that there were similar outcomes including all-cause mortality, recurrent coronary event, cardiac related readmission between the pre-COVID-19 period and COVID-19 period (5). Unlike that results, a higher mortality rate was seen in acute coronary syndrome patients during the COVID era compared with the pre-COVID-19 era in another study (19). In a prospective study by Rattka et al., survival was found to be significantly worse in STEMI patients during the COVID-19 pandemic (6). While the pre-COVID-19 period had a higher HF admission rate, there was no difference between groups in terms of MACCE in the presented study. The patients in the pre-COVID-19 era had higher troponin, and lower LVEF values than those in the pre-COVID-19 era as a reflection of the longer total ischemic time in our study. These may indicate larger myocardial damage in these patients. All of them may contribute to the development of HF and lead to a higher rate of hospitalization with HF in these patients.

The presence of COVID-19 in STEMI patients was found to be associated with short-term mortality in previous studies (4-18). The data concerning long-term mortality in these patients were limited. A recently published study showed that acute coronary syndromes patients who were infected with COVID-19 had higher mortality than those without (19). Contrary to that study, in our study, no difference was demonstrated between STEMI patients with COVID-19 (+) compared to those without in terms of long-term mortality, yet proportions of MACCE mainly driven by hospitalization with HF were higher in COVID-19 (+) patients.

The high MACCE rates in these patients may be due to many reasons. It has been shown that higher troponin levels were related to poor outcomes in COVID-19 patients (21). STEMI

patients infected with COVID-19 had higher troponin levels and lower LVEF values in the presented study. These may indicate the magnitude of cardiac damage. Furthermore, the presence of a high inflammatory process reflected by increased CRP might be a sign of myocardial destruction by virüs. The fact that these patients receiving invasive treatment were less, therefore this may be a reason for the high rate of MACCE in these patients. The presence of the multi-vessel disease may have contributed to the increased MACCE rates in our study.

There are several limitations of the current study. The nature of observational, retrospective study design might hinder causal inference. Since we did not have out-of-hospital mortality data, it was difficult to give information about the effect of this on total mortality. The follow-up time for both pre-COVID and post-COVID periods was relatively short, therefore to see the effect of COVID-19, these patients may need longer follow-up.

Conclusion

There was no difference between the pre-COVID-19 era and the COVID-19 era in terms of MACCE and heart failure hospitalization in STEMI patients in Turkey. In the Covid-19 era, STEMI patients positive for COVID-19 had a higher rate of MACCE and heart failure hospitalization at the long-term follow-up.

Author contributions

All authors contributed to the final manuscript.

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Declarations

Conflict of interest

The author(s) declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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Figure Legends

Figure 1. Flow diagram of patient recruitment.

Figure 2. Kaplan-Meier MACCE-free survival curves of STEMI patients according to two study periods.

Figure 3. Hospitalization with heart failure-free survival analysis of STEMI patients according to two study periods.

Figure 4. Kaplan-Meier MACCE-free survival curves of STEMI patients with COVID-19 (+) and those without during the COVID-19 era.

Figure 5. Hospitalization with heart failure-free survival analysis of STEMI patients with COVID-19 (+) and those without during COVID -19 era.

Figure 6. Kaplan-Meier MACCE-free survival curves of STEMI patients with COVID-19 (+) and those without in two study periods.

Table 1. Baseline characteristics of the study population.

Variables	Pre-COVID-19 era (n = 1025)	COVID-19 era (n = 723)	p-value
Age, years	61.9 ± 12.4	60.6 ± 12.4	0.040
Symptoms at admission n (%)			0.005
Chest pain	767 (75)	488 (68)	
Dyspnea	194 (19)	165 (23)	
Arrest	10 (1)	9 (1)	
Other	54 (5)	61 (8)	
Female gender (%)	257 (25)	166 (23)	0.310
Hypertension, n (%)	388 (38)	304 (42)	0.077
Diabetes mellitus, n (%)	302 (30)	207 (29)	0.461
Previous AF , n (%)	43 (4)	39 (5)	0.243
Smoking, n (%)	315 (31)	239 (33)	0.304
Astım or COPD, n (%)	105 (10)	71 (10)	0.772
Previous CAD, n (%)	125 (12)	93 (13)	0.677
COVID-19 positive n (%)	-	44 (7)	-
Echocardiographic findings			
LVEF (%)	47.8 ± 9.1	46.7 ± 8.9	0.015
LVWM abnormalities n (%)	645 (63)	484 (67)	0.084
Valve disease n (%)	104 (10)	66 (9)	0.630
Symptom-to-FMC, minutes (median [IQR])	100 (60-180)	120 (75-240)	< 0.001
Symptom-to- (FMC) time			< 0.001
Less than 2 hours, n (%)	542 (53)	312 (43)	
2 to 6 hours, n (%)	209 (20)	143 (20)	
6 to 12 hours, n (%)	232 (23)	203 (28)	
12 to 24 hours, n (%)	19 (2)	26 (4)	
More than 24 hours, n (%)	23 (2)	39 (5)	
Laboratory findings			

WBC ($\times 10^3/\mu L$)	11.9 ± 3.9	12.1 ± 4.6	0.205
Hemoglobin (mg/dl)	13.8 ± 2.1	13.9 ± 2.1	0.129
Creatinine* (mg/dl)	0.90 (0.74-1.03)	0.90 (0.76-1.10)	0.382
Platelet (x 10^9 /L)	256.5 ± 75.3	251.8 ± 73.3	0.185
C-reactive protein* (mg/L)	19.2 (2.0-47.6)	23.6 (3.0-53.8)	0.128
Troponin* (ng/L)	6259 (415-19176)	9739 (869-24810)	0.099

Abbreviations: AF: atrial fibrillation,CAD: coronary artery disease, COPD: chronic obstructive pulmonary disease, IQR: inter quartile range,LVEF; left ventricular ejection fraction, LVWM: left ventricular wall motion abnormalities, FMC: first medical contact , WBC; white blood cell.

*Comparison was made using Mann-Whitney *U* test at $P < 0.05$,and these values were described by median with inter-quartile range (25^{th} and 75^{th} percentile).

Table 2. Angiographic characteristics, interventions and medical treatment

Variables	Pre-COVID-19 era (n = 1025)	COVID-19 era (n = 723)	p-value
Coronary intervention n (%)	1024 (100)	719 (99)	0.079
Infarct related artery n (%)			0.175
LMCA	15 (2)	17 (2)	
LAD	388 (38)	303 (42)	
CX	195 (19)	133 (19)	
RCA	334 (33)	219 (31)	
Other	83 (8)	42 (6)	
Noncritical CAD	9 (1)	5 (1)	
Multi-vessel disease n (%)	412 (40)	292 (41)	0.874
Glycoprotein IIb/IIIa inhibitors n (%)	234 (23)	161 (22)	0.766
Thrombus aspiration device n (%)	60 (6)	55 (8)	0.148
IABP n (%)	29 (3)	12 (2)	0.112
Baseline TIMI flow n (%)			
TIMI flow 0-1	932 (91)	642 (89)	0.231
Baseline thrombus grade > 3	685 (67)	491 (68)	0.541
Modified thrombus grade > 3	415 (41)	287 (40)	0.673
Procedural success:			
Post-PCI TIMI 3 flow n (%)	878 (83)	594 (82)	0.319
Multi-vessel PCI during the index prodecure n (%)	96 (9)	70 (10)	0.824
Complete revascularization during the index hospitalization n (%)	187 (18)	126 (17)	0.661
Previous medication			
ACE-I/ARB, n (%)	251 (25)	199 (28)	0.153

Statin n (%)	175 (17)	112 (16)	0.379
In hospital or discharge ASA+P2Y12Y inhibitors			0.133
ASA plus Clopidogrel n (%)	754 (73)	498 (69)	
ASA plus Tigacrelor n (%)	176 (17)	146 (20)	
ASA plus Prasuqrel n (%)	94 (9)	75 (10)	
Pharmaco-invazive treatment n (%)	9 (1)	4 (1)	0.438
Patients treated with medical treatment n (%)	4 (0)	7 (1)	0.132

Abbreviations: LMCA: left main coronary artery, LAD: left descending artery, RCA: right coronary artery, CX: circumflex artery, ACE-I/ARB: angiotensin converting enzyme inhibitors/ angiotensin receptor blocker, ASA: acetylsalicylic acid, IABP: intra aortic baloon pump, IQR: inter quartile range, PCI: percutaneous coronary intervention.

Table 3. In-hospital and long-term outcomes of all patients.

Variables	Pre-COVID-19 era (n = 1025)	COVID-19 era (n = 723)	p-value
In-hospital outcomes			
Mortality n (%)	71(7)	61 (8)	0.239
Shock n (%)	91(9)	62 (9)	0.825
Stent thrombosis n (%)	15 (2)	12 (2)	0.742
Major bleeding n (%)	0 (0)	3 (0.4)	0.039
Minor bleeding n (%)	29 (3)	16 (2)	0.426
Long-term outcomes			
MACCE n (%)	231(23)	160 (22)	0.841
Mortality n (%)	74 (8)	40 (6)	0.186
Myocardial reinfarction n (%)	67 (7)	39 (6)	0.329
New revascularization n (%)	88 (9)	62 (9)	0.998
Stroke/TIA, n (%)	22 (2)	8 (1)	0.100
Hospitalization with HF , n (%)	78 (8)	87 (12)	0.002

Abbreviations: MACCE: major cardiovascular and serebrovascular events, TIA: transient ischemic attack, HF: heart failure.

Table 4. Baseline characteristics of the study population.

Variables	COVID-19 (-) (n = 661)	COVID-19 (+) (n = 62)	p-value
Age, years	60.0 ± 12.3	66.9 ± 12.2	< 0.001
Symptoms at admission n (%)			0.003
Chest pain	454 (69)	34 (55)	
Dyspnea	151 (23)	14 (23)	
Arrest	8 (1)	1 (2)	
Other	48 (7)	13 (21)	
Female gender (%)	146 (22)	20 (33)	0.069
Hypertension, n (%)	274 (42)	30 (49)	0.290
Diabetes mellitus, n (%)	190 (28)	17 (27)	0.930
Previous AF , n (%)	36 (5)	3 (5)	0.840
Smoking, n (%)	218 (33)	21 (34)	0.887
Astım or COPD, n (%)	60 (9)	11 (18)	0.028
Previous CAD, n (%)	81 (12)	12 (19)	0.110
Echocardiographic findings			
LVEF (%)	47.0 ± 8.8	43.6 ± 9.0	0.004
LVWM abnormalities n (%)	436 (66)	48 (77)	0.067
Valve disease n (%)	53 (9)	13 (25)	< 0.001
Symptom-to-FMC, minutes (median [IQR])	120 (75-245)	120 (84-240)	0.610
Symptom-to- (FMC) time			0.939
Less than 2 hours, n (%)	287 (43)	25 (40)	
2 to 6 hours, n (%)	129 (20)	14 (23)	
6 to 12 hours, n (%)	185 (28)	18 (29)	
12 to 24 hours, n (%)	24 (4)	2 (3)	
More than 24 hours, n (%)	36 (5)	3 (5)	
Laboratory findings			
WBC ($\times 10^3/\mu L$)	12.0 ± 4.5	13.5 ± 4.8	0.013

Hemoglobin (mg/dl)	14.0 ± 2.0	13.6 ± 2.4	0.246
Creatinine* (mg/dl)	0.90 (0.70-1.02)	0.91 (0.80-1.21)	0.940
Platelet(x 10^9 /L)	252 ± 72	252 ± 83	0.975
C-reactive protein* (mg/L)	21.0 (2.8-51.3)	55.2 (21.4-147.4)	< 0.001
Troponin* (ng/L)	8170 (789-23593)	19254 (6587-26477)	0.005

Abbreviations: AF: atrial fibrillation, CAD: coronary artery disease, COPD: chronic obstructive pulmonary disease, IQR: inter quartile range,LVEF; left ventricular ejection fraction, LVWM: left ventricular wall motion abnormalities, FMC: first medical contact, WBC; white blood cell.

*Comparison was made using Mann-Whitney *U* test at $P < 0.05$, and these values were described by median with inter-quartile range (25^{th} and 75^{th} percentile).

Table 5. Angiographic characteristics, interventions and medical treatment

Variables	COVID-19 (-) (n = 661)	COVID-19 (+) (n = 62)	p-value
Coronary intervention n (%)	660 (100)	59 (95)	< 0.001
Infarct related artery n (%)			0.285
LMCA	16 (2)	1 (2)	
LAD	278 (42)	25 (42)	
CX	119 (18)	14 (24)	
RCA	207 (31)	12 (20)	
Other	36 (6)	6 (10)	
Noncritical CAD	4 (1)	1 (2)	
Multi-vessel disease n (%)	265 (40)	27 (46)	0.400
Glycoprotein IIb/IIIa inhibitors n (%)	126 (20)	15 (34)	0.032
Thrombus aspiration device n (%)	46 (7)	9 (15)	0.032
IABP n (%)	10 (2)	2 (3)	0.313
Baseline TIMI flow n (%)			
TIMI flow 0-1	587 (89)	55 (93)	0.308
Baseline thrombus grade > 3	437 (66)	56 (95)	< 0.001
Modified thrombus grade > 3	252 (38)	35 (59)	0.001
Procedural success:			
Post-PCI TIMI 3 flow n (%)	538 (82)	48 (81)	0.976
Multi-vessel PCI during the index prodecure n (%)	65 (10)	5 (8)	0.652

Complete revascularization during the index hospitalization n (%)	108 (16)	18 (29)	0.012
Previous medication			
ACE-I/ARB, n (%)	181 (27)	18 (29)	0.781
Statin n (%)	98 (15)	14 (23)	0.107
In hospital or discharge ASA+P2Y12Y inhibitors			0.929
ASA plus Clopidogrel n (%)	458 (70)	40 (68)	
ASA plus Tigacrelor n (%)	134 (20)	12 (20)	
ASA plus Prasuqrel n (%)	68 (10)	7 (12)	
Pharmaco-invazive treatment n (%)	1 (0)	3 (5)	0.240
Patients treated with medical treatment n (%)	3 (1)	4 (7)	< 0.001

Abbreviations: LMCA: left main coronary artery, LAD: left descending artery, RCA: right coronary artery, CX: circumflex artery, ACE-I/ARB: angiotensin converting enzyme inhibitors/ angiotensin receptor blocker, ASA: acetylsalicylic acid, IABP: intra aortic baloon pump, IQR: inter quartile range, PCI: percutaneous coronary intervention,

Table 6. In-hospital and long-term outcomes of patients during COVID-19 era.

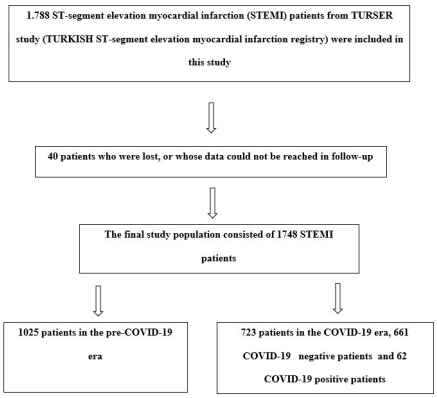
Variables	COVID-19 (-) (n = 661)	COVID-19 (+) (n = 62)	p-value
In-hospital outcomes			
Mortality n (%)	43 (7)	18 (29)	< 0.001
Shock n (%)	49 (7)	13 (21)	< 0.001
Stent thrombosis n (%)	8 (1)	4 (7)	0.002
Major bleeding n (%)	3 (1)	0 (0)	0.598
Minor bleeding n (%)	14 (2)	2 (3)	0.556
Long-term outcomes			
MACCE	135 (20)	25 (40)	< 0.001
Mortality n (%)	38 (6)	2 (5)	0.666
Myocardial reinfarction n (%)	34 (5)	5 (8)	0.326
New revascularization n (%)	56 (9)	6 (10)	0.738
Stroke/TIA, n (%)	7 (1)	1 (2)	0.687
Hospitalization with HF, n (%)	68 (11)	19 (43)	< 0.001

Abbreviations: MACCE: major cardiovascular and serebrovascular events, TIA: transient ischemic attack, HF: heart failure.

Table 7. Univariate and multivariate analysis for predictors of MACCE.

Variables	Univariate			Multivariate		
	HR	95%CI	p-value	HR	95%CI	p-value
Age	1.030	1.021-1.038	< 0.001	1.016	1.006-1.026	0.001
Male gender	0.657	0.529-0.817	< 0.001	0.750	0.589-0.955	0.020
Hypertension	1.736	1.423-2.177	< 0.001			
Diabetes mellitus	0.999	0.988-1.009	0.777			
Symptoms at admission	1.260	1.116-1.422	< 0.001			
Astım/COPD	1.683	1.253-2.260	0.001			
Muti-vessel disease	1.948	1.595-2.380	< 0.001	1.507	1.216-1.868	< 0.001
Multi-vessel PCI during index prodecure	1.993	1.513-2.626	< 0.001	1.561	1.167-2.088	0.003
IABP	2.320	1.273-4.226	0.006	2.657	1.436-4.918	0.002
Modified thrombus grade ≥ 4	1.467	1.202-1.792	< 0.001	1.413	1.149-1.736	0.001
Thrombus aspiration device usage	0.563	0.336-0.944	0.029			
In-hospital total bleeding	2.856	1.839-4.435	< 0.001			
COVID -19 (+)	2.588	1.725-3.882	< 0.001	1.628	1.042-2.542	0.032
Pre-COVID-19 era vs COVID-19 era	0.903	0.738-1.105	0.321			
ACE-I/ARB preusage	1.472	1.187-1.826	< 0.001			
LVEF	0.962	0.952-0.973	< 0.001	0.975	0.964-0.986	< 0.001
Hemoglobin	0.900	0.860-0.943	< 0.001			
Creatinine	1.312	1.197-1.437	< 0.001	1.206	1.079-1.349	0.001
CRP	1.002	1.000-1.003	0.060			

A **Abbreviations:** ACE-I/ARB: angiotensin converting enzyme inhibitors/ angiotensin receptor blocker, COPD: chronic obstructive pulmonary disease IABP: intra aortic baloon pump, LVEF; left ventricular ejection fraction, abnfraction, PCI: percutaneous coronary inteintervention, CRP: C -reactive protein.



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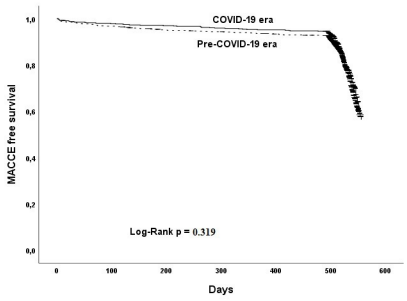

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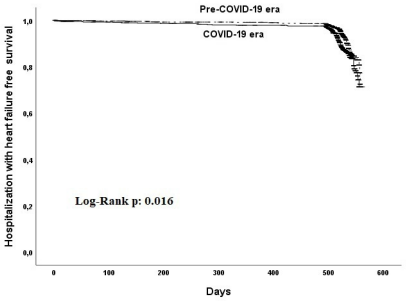

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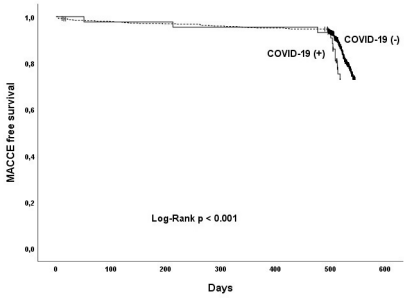

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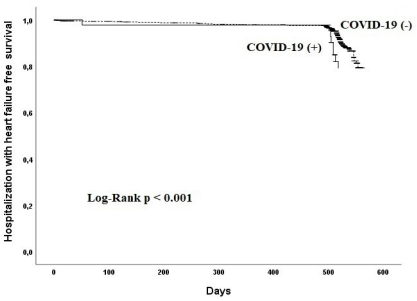

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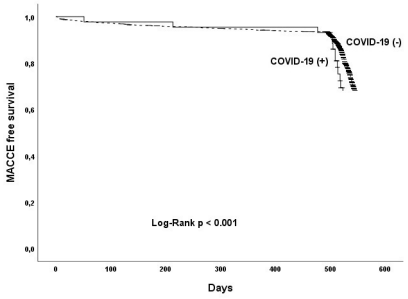

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