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LETTER TO THE EDITOR
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The impact of being in the COVID-19 pandemic on in-hospital mortality of non-infected patients aged 80 years and older with ST-elevation myocardial ınfarction

Mustafa Ebik[1], Muhammet Gürdoğan[2,✉], Uğur Özkan[2]

1. Department of Cardiology, Edirne Sultan 1. Murat State Hospital, Edirne, Turkey; 2. Department of Cardiology, School of Medicine, Trakya University, Edirne, Turkey

✉ Correspondence to: drmgurdogan@gmail.com

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The COVID-19 outbreak in late 2019 was declared a pandemic by the World Health Organization (WHO) on March 12, 2020.[1] As of the latest WHO data, COVID-19 has caused over 770 million cases and nearly 7 million deaths worldwide.[2] Hospitalizations due to COVID-19 are correlated with advanced age.[3,4] According to reports, individuals over the age of 65 account for 80% of COVID-19-related deaths.[3,4] This is primarily due to the increased burden of comorbidity with age. It has been noted that patients aged 80 years and over had a mortality rate five times higher than the worldwide average during the pandemic.[4] Atherosclerotic cardiovascular diseases are the primary cause of mortality in the elderly population worldwide.[5,6] ST-segment elevation myocardial infarction (STEMI) is a significant complication of atherosclerotic heart disease.[6–10] Studies have shown that mortality rates were higher during the COVID-19 pandemic compared to the pre-pandemic or post-pandemic period, despite management algorithms recommended by current guidelines for elderly patients hospitalized with STEMI.[6–10] The reason for the high mortality rates reported in non-COVID-19-infected elderly patients remains unclear, although this could be explained by COVID-19-infected elderly patients with STEMI.[11]

The objective of this study is to investigate the impact of being in the COVID-19 period on the development of in-hospital mortality in ST-Elevation Myocardial Infarction (STEMI) patients aged 80 and over who are not infected with COVID-19. A total of 188 patients aged 80 years and over who underwent percutaneous coronary intervention for STEMI between April 1, 2020, and May 1, 2023, were included in this single-center retrospective study. Patients were divided into two groups according to the date of admission: COVID-19 period (CP) and post-COVID-19 period (P-CP). The dates of March 11, 2020, when the first COVID-19 case was seen in Turkey, and March 22, 2022, when the transition to the normalization process in society was completed, were taken as the reference for this grouping.[12,13] Patients aged 80 years and over who were admitted to the hospital with a diagnosis of STEMI between April 1, 2020, and March 22, 2022, were defined as CP (99 patients in this group). Patients aged 80 years and over hospitalized with a diagnosis of STEMI between March 23, 2022, and May 1, 2023, were defined as P-CP (88 patients in this group). The diagnosis of STEMI in all patients was based on the Universal 4th Myocardial Infarction Definition criteria.[14] COVID-19 polymerase chain reaction (PCR) testing was performed on the first day of admission in all patients with or without symptoms. However, COVID-19 PCR was repeated in all patients who developed COVID-19 symptoms and signs during hospitalization, despite a negative initial test. Four patients with CP and one patient with P-CP were excluded from the study due to a positive COVID-19 PCR test. In the end, 95 patients with CP and 88 patients with P-CP were included in the study. Figure 1 shows the flow chart of the patients included in the study.

Sociodemographic, clinical, laboratory, echocardi-

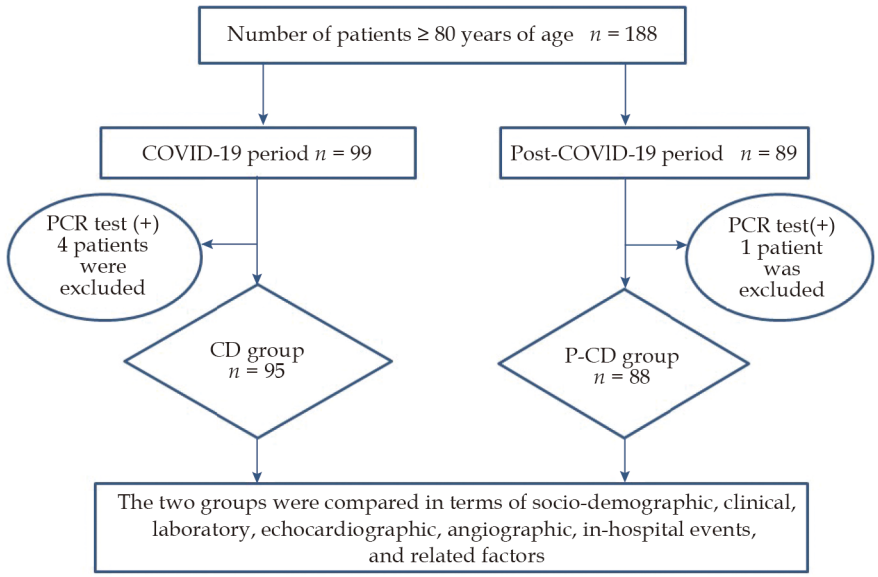

Figure 1 Flow chart for inclusion and exclusion criteria in the study.

ographic, and angiographic data of the 183 patients included in the study were recorded. Symptom Onset to Emergency Admission (SOEA) was defined as the time from the onset of the first STEMI-related symptom (chest pain or other angina exacerbation) to admission to the emergency department and was recorded in hours. Door-to-balloon time (DBT) was defined as the time from the patient's admission to the emergency department until the guidewire passed through the coronary lesion responsible for the STEMI to TIMI-3 (Thrombolysis in Myocardial Infarction) flow or the best available coronary flow.[15] Total ischemic time (TIT) was defined as the sum of SOEA and DBT. LV ejection fraction (EF) values obtained by volumetric assessment with the modified Simpson method, pulse wave Doppler of the mitral valve, and E/E' ratio from tissue Doppler analysis were calculated from echocardiographic examinations of the patients according to international guidelines (Vivid7; GE Medical Systems, Horten, Norway).[16] Coronary angiography (CAG) and percutaneous coronary intervention (PCI) procedures were performed by experienced cardiologists using standard femoral and radial routes.[17] Successful percutaneous coronary intervention was defined as the presence of TIMI-3 flow in the infarct-related responsible artery after percutaneous transluminal coronary angioplasty (PTCA) and/or coronary stent implantation.[18]

Data analysis was performed with the Statistical Package for the Social Sciences (SPSS) software, version 26.0 (SPSS Inc., Chicago, Illinois, USA).The normality of the data distribution was assessed by the Kolmogorov-Smirnov test. Descriptive statistics are presented as mean, standard deviation, or median (minimum-maximum) based on the normality of the distribution. An independent sample *t*-test was used to compare normally distributed continuous variables, whereas non-normally distributed continuous variables were compared using the Mann-Whitney *U* test. Categorical data were compared using the chi-squared test. Binary logistic regression analysis was used for univariate and multivariate analyses. All statistical tests were performed at a predetermined significance level of $P < 0.05$.

The study was conducted on a total of 183 patients aged 80 years and over admitted to the coronary intensive care unit with a diagnosis of STEMI. There were 95 patients in CP and 88 patients in P-CP. The mean age of both groups was 82 years. The males were 61.4% in P-CP and 37.9% in CP. There was a statistically significant difference between both groups in terms of gender ($P < 0.001$). Comparative results of sociodemographic characteristics, cardiovascular risk factors, admission clinical features, PCI, echocardiography, and laboratory data are given in Table 1 and Table 2. Acute inferior myocardial infarction (50.5%) was more common in CP and acute anterior myocardial infarction (48.9%) in P-CP. SOEA duration was 4 h in the CP group and 3 h

Table 1 Patient characteristics regarding socio-demographic, clinical, echocardiographic, laboratory and coronary intervention data.

	COVID-19 Period (*n* = 95)	Post COVID-19 period (*n* = 88)	*P*-value
Age, yrs	82 (80-95)	82 (80-96)	0.2
Gender (male)	36 (37.9%)	54 (61.4%)	**0.001**
BMI, kg/m²	23.2 (18-40.4)	23.8 (18-40.4)	0.42
Smoking			
Never used	71 (74.7%)	67 (76.1%)	
Quit	20 (21.1%)	18 (20.5%)	0.95
Active user	4 (4.2%)	3 (3.4%)	
Hypertension	69 (72.6%)	65 (73.9%)	0.49
Hyperlipidemia	4 (4.2%)	4 (4.5%)	0.91
Diabetes mellitus	26 (27.4%)	26 (29.5%)	0.43
Heart failure	3 (3.2%)	2 (2.3%)	0.71
Atrial fibrillation	7 (7.4%)	7 (8%)	0.88
Chronic renal failure	7 (7.4%)	7 (8%)	0.88
Peripheral artery disease	3 (3.2%)	4 (4.5%)	0.62
Stroke	10 (10.5%)	11 (12.5%)	0.67
Chronic obstructive pulmonary disease	13 (13.7%)	7 (8%)	0.21
Dementia-Alzheimer's	8 (8.4%)	8 (9.1%)	0.87
Family history of CAD	8 (8.4%)	5 (5.7%)	0.66
History of MI	19 (20%)	18 (20.5%)	0.94
History of PCI	15 (15.8%)	16 (18.2%)	0.66
History of CABG	5 (5.3%)	4 (4.5%)	0.82
Admission during MI localization			
Anterior MI	39 (41.1%)	43 (48.9%)	
Inferior MI	48 (50.5%)	38 (43.2%)	
Lateral MI	6 (6.3%)	5 (5.7%)	0.75
Posterior MI	2 (2.1%)	2 (2.3%)	
Systolic blood pressure, mmHg	122.8 ± 33.8	123.1 ± 22.3	0.94
Diastolic blood pressure, mmHg	75 (40-120)	78.5 (40-100)	**0.05**
Heart rate	87 (30-132)	88 (39-128)	0.9
Admission during Killip classification			
1	54 (56.8%)	63 (71.6%)	
2	17 (17.9%)	14 (15.9%)	
3	7 (7.4%)	6 (6.8%)	**0.05**
4	17 (17.9%)	5 (5.7%)	
SOEA, h	4 (1-72)	3 (0.5-72)	**0.05**
Door-to-balloon time, min	88 (45-160)	82.5 (45-120)	0.08
Total ischemic time, h	5.41 (1.85-74.42)	4.54 (1.5-73.5)	**0.035**
EF	43 (20-61)	42 (20-65)	0.42
E/E'	8 (5-13)	7 (5.4-12.1)	**< 0.001**
CRP, mg/dL	1 (0.2-20)	0.7 (0.1-19.4)	0.17
Admission troponin, ng/L	5700 (19-40000)	2117 (1.5 -40000)	**< 0.001**
Successful PCI	89 (93.7%)	86 (97.7%)	0.18

Data are presented as mean ± SD or *n* (%) unleass other indicated. BMI: body mass index; CABG: coronary artery bypass grafting; CAD: coronary artery disease; CRP: C-reactive protein; EF: ejection fraction; MI: myocardial ınfarction; PCI: percutaneous coronary ınterven-tion; SOEA: symptom onset-emergency admission (Hours).

in the P-CP group, and this difference was statistically significant (P = 0.05). Although the difference between the two groups was not statistically significant, the mean duration of DBT was 88 minutes in the CP group and 82.5 min in the P-CP group (P = 0.08). When the two groups were compared in terms of TIT, the mean duration was 5.41 h in the CP group and 4.54 h in the P-CP group, and this difference was statistically significant (P = 0.035). The Troponin-I value at admission was 5700 ng/L in the CP group and 2117 ng/L in the P-CP group, and this difference was statistically significant (P < 0.001). In-hospital mortality rates were 30.5% in the CP group and 17% in the P-CP group, and this difference was statistically significant (P = 0.02) (Table 3). According to the results of logistic regression analysis indicated that being in CP increased in-hospital mortality approximately 2.2-fold [OR = 2.199 (1.027–4.71), P = 0.043] in patients aged 80 years and over, while other parameters were not significant (Table 4).

The most important data obtained as a result of this study can be listed as follows: (1) In STEMI patients aged ≥ 80 years, being in CP is an important predictor of in-hospital mortality by 2.1-fold; (2) Despite successful reperfusion therapy in STEMI patients aged ≥ 80 years, mortality in CP was approximately 2-fold higher than in P-CP (30.5% *vs.* 17%); (3) In STEMI patients aged ≥ 80 years, TIT before PCI is significantly longer in CP than in P-CP (mean 5.41 hours *vs.* 4.54 h); and (4) this increase in TIT is not due to a longer DBT, but to a longer interval between SOEA.

In parallel with the increase in the proportion of elderly people worldwide, the frequency of elderly and very elderly patients diagnosed with STEMI has also increased in clinical practice.[19] The basic principles of STEMI diagnosis and treatment in the elderly population aged 80 years and over are not different from the general population. However, the frailty and increased burden of comorbidities in this patient group make STEMI treatment more challenging in this group compared to the younger patient population.[20] Comorbidities such as hypertension, diabetes mellitus, chronic kidney disease, heart failure, chronic lung disease, peripheral arterial disease, stroke, increased susceptibility to multivessel coronary artery disease, and the presence of coronary calcification and tortuosity affecting the success of PCI procedures increase in-hospital mortality rates due to STEMI in the elderly population.[21] In our study, the burden of comorbidities and coronary anatomical difficulties was similar in both CP and P-CP patients admitted to the hospital with STEMI.

In a study investigating the relationship between mortality and age in patients with STEMI during the pandemic, in-hospital mortality was 17.6% in patients aged 75–84 and 30% in those aged ≥ 85 years.[22] In our study, similarly, in-hospital mortality in CP was 30.5%. In our study, similar to that, the in-hospital mortality in CP was found to be 30.5%. Again, this study reported that the predictors associated with in-hospital mortality were low EF and a positive COVID-19 PCR test (in this study, positive test rates were seen as 8% in those aged 75–84 and 5% in those aged ≥ 85 years).[22] As in this study, patients infected with COVID-19 are generally included in other studies of STEMI during the pandemic.[23,24] However, the cardiac manifestations of COVID-19 and its direct impact on mortality are well known.[24] In our study, patients with a positive COVID-19 PCR test were excluded from the study. In addition to what is known, we found that CP was an important predictor of STEMI mortality in patients aged 80 years and over. The possible reasons why mortality in patients aged 80 years and over with STEMI treated by PCI was found to be two times higher in P-CP than in CP may be related to many factors. It has been reported in the literature that elderly STEMI patients are admitted to the hospital later, regardless of the COVID-19 period, which directly means an increase in TIT.[20,21] The delay in the hospitalization of elderly patients may be related to the atypical nature of STEMI-related symptoms compared with younger patients and the fact that communication with this patient group is more difficult due to neurocognitive disorders.[7,20,21,25] In addition, the increased underlying co-morbidity burden of elderly patients, several restrictions imposed by countries to protect the elderly population from the devastating effects of infection during the pandemic, healthcare organizations modifying clinical units to care for more COVID-19 patients during the pandemic, and the increased incidence of COVID-19 in the elderly during the pandemic have all contributed to the increased incidence of COVID-19 in the elderly.[10,26] All of these problems may be related to the high mortality of CP in eld-

Table 2 Results of patients' clinical, echocardiographic, laboratory and coronary intervention data at admission.

	COVID-19 period (*n* = 95)	Post COVID-19 period (*n* = 88)	*P* value
Admission during MI localization			
Anterior MI	39 (41.1%)	43 (48.9%)	0.75
Inferior MI	48 (50.5%)	38 (43.2%)	
Lateral MI	6 (6.3%)	5 (5.7%)	
Posterior MI	2 (2.1%)	2 (2.3%)	
Systolic blood pressure, mmHg	122.8 ± 33.8	123.1 ± 22.3	0,94
Diastolic blood pressure, mmHg	75 (40-120)	78.5 (40-100)	**0,05**
Heart rate	87 (30-132)	88 (39-128)	0,9
Admission during Killip classification			
1	54 (56.8%)	63 (71.6%)	**0.05**
2	17 (17.9%)	14 (15.9%)	
3	7 (7.4%)	6 (6.8%)	
4	17 (17.9%)	5 (5.7%)	
Symptom onset-emergency admission, h	4 (1-72)	3 (0,5-72)	**0.05**
Door-balloon time, min	88 (45-160)	82,5 (45-120)	0,08
Total ischemic time, h	5.41 (1.85-74.42)	4.54 (1.5-73.5)	**0.035**
EF	43 (20-61)	42 (20-65)	0.42
E/E'	8 (5-13)	7 (5.4-12.1)	**< 0.001**
CRP, mg/dL	1 (0.2-20)	0.7 (0.1-19.4)	0,17
Admission troponin, ng/L	5700 (19-40000)	2117 (1.5-40000)	**< 0.001**
Successful PCI	89 (93.7%)	86 (97.7%)	0.18

Data are presented as mean ± SD or *n* (%) unleass other indicated. CRP: C-reactive protein; EF: ejection fraction; MI: miyocardial infarction.

Table 3 In-hospital adverse clinical events.

	Covid-19 Period (*n* = 95)	Post Covid-19 period (*n* = 88)	*P*-value
Emergency CABG	1 (1.1%)	0	0.51
Recurrent MI	4 (4.2%)	0	**0.05**
Acute stent thrombosis	5 (5.3%)	1 (1.1%)	0.11
VT,VF	24 (25.3%)	15 (17%)	0.17
Newly developing AF	15 (15.8%)	8 (9.1%)	0.16
Need for temporary pacemaker	15 (15.8%)	9 (10.2%)	0.26
Need for inotropes	36 (37.9%)	25 (28.4%)	0.11
Use of intraaortic balloon pump	1 (1.1%)	0	0.51
Mechanical complication	2 (2.1%)	0	0,39
Acute renal failure	35 (36.8%)	25 (28.4%)	0.14
Non-COVID infection	16 (16.8%)	8 (9.1%)	0.11
Bleeding requiring blood transfusion	2 (2.1%)	1 (1.1%)	0.6
New stroke	3 (3.2%)	3 (3.4%)	0.92
Delirium	36 (37.9%)	16 (18.2%)	**0.002**
Death	29 (30.5%)	15 (17%)	**0.02**

Data are presented as *n* (%). AF: atrial fibrillation; CABG: coronary artery bypass grafting; MI: miyocardial infarction; VF: ventricular fibrillation; VT: ventricular tachycardia.

Table 4 Univariate and multivariate regression analysis results of parameters associated with the development of in-hospital mortality.

	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age	1.126 (1.034-1.227)	**0.007**	-	-
COVID-19 period	2.138 (1.055-4.335)	**0.035**	2.199 (1.027-4.71)	**0.043**
Gender (male)	0.502 (0.25-1.010)	**0.053**	0.797 (0.355-1.788)	0.581
No smoker	0.33 (0.13-0.841)	**0.02**	0.36 (0.127-1.015)	0.053
Hypertension	1.883 (0.806-4.398)	0.144	1.703 (0.688-4.216)	0.250
Hyperlipidemia	1.056 (0.205-5.428)	0.948	0.975 (0.162-5.875)	0.978
Diabetes mellitus	1.426 (0.689-2.953)	0.339	1.38 (0.627-3.037)	0.423
Heart failure	2.099 (0.225-12.103)	0.303	2.384 (0.352 -16.141)	0.373
Atrial fibrillation	0.851 (0.227-3.201)	0.812	0.822 (0.203-3.333)	0.783
Chronic renal failure	0.504 (0.108-2.344)	0.382	0.513 (0.106-2.494)	0.408
Stroke	2.154 (0.828-5.600)	0.116	-	-

erly STEMI patients, who are difficult to diagnose, treat, and follow.

In our study, in addition to the high mortality rates, Killip ≥2 acute heart failure class, admission troponin T levels, and E/E' values were found to be significantly higher in patients aged ≥80 with CP compared with patients with P-CP. It has been observed in the literature that Killip ≥2 class, troponin T/I levels, and E/E' are generally high in STEMI patients admitted with CP.[7,22,25–27] Although our results overlap with these studies, the difference in our study is that our patient group is homogeneous, and patients with a positive PCR test were excluded from the study. When these parameters are evaluated as a whole, they can be explained by the long total ischemic time, which is the most important parameter associated with mortality in patients hospitalized with a diagnosis of STEMI in CP. It is a fact that the world was caught unprepared for the pandemic, despite the great developments in industry, technology, science, and medicine. Reasons such as logistical problems, lack of medical equipment, specialized healthcare facilities, and healthcare workers are the most important factors affecting the provision of quality healthcare services during the pandemic.[26–30] Although the fight against infection is the priority during a pandemic, the necessary health measures should be taken to monitor the chronic diseases of the frail elderly population and to facilitate access to health care in acute situations. Literature data show that cardiovascular mortality remained the leading cause of death worldwide during COVID-19.[7,22,24] Our study has shown that measures should be taken to reduce total ischemic time, which is one of the major problems affecting access to reperfusion therapy, especially in elderly patients with acute coronary syndrome, during a pandemic.

Conflicts of Interests

None.

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