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The effect of COVID-19 pandemic on myocardial infarction care and on its prognosis – Experience at a high volume Hungarian cardiovascular center

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ABSTRACT

Introduction: The COVID-19 pandemic has impacted many aspects of acute myocardial infarction. Based on literature data, the prognosis of COVID+, STEMI patients is significantly worse than that of COVID-STEMI patients. On the other hand, physicians report fewer acute coronary syndrome (ACS) patients presenting to hospitals in countries severely affected by the pandemic. It is concerning that patients with life-threatening illness can suffer more complications or die due to their myocardial infarction.We *aimed* to investigate the changes in myocardial infarction care in the country's biggest PCI-center and to compare total 30-day mortality in COVID+ and COVID-patients with acute myocardial infarction treated at the Semmelweis University Heart and Vascular Center, and to investigate risk factors and complications in these two groups. *Methods:* Between 8 October 2020 and 30 April 2021, 43 COVID+, in 2018–2019, 397 COVID-patients with acute myocardial infarction were admitted. Total admission rates pre- and during the pandemic were compared. *Results:* Within 30 days, 8 of 43 patients in the COVID+ group (18.60%), and 40 of the 397 patients in the control group (10.07%) died ($P = 0.01$). Regarding the comorbidities, more than half of COVID+ patients had a significantly reduced ejection fraction (EF$\leq$ 40%), and the prevalence of heart failure was significantly higher in this group (51.16% vs. 27.84%, $P = 0.0329$). There was no significant difference between the two patient groups in the incidence of STEMI and NSTEMI. Although there was no significant difference, VF (11.63% vs. 6.82%), resuscitation (23.26% vs. 10.08%), and ECMO implantation (2.38% vs. 1.26%) were more common in the COVID+ group. The mean age was 68.8 years in the COVID+ group and 67.6 years in the control group. The max. Troponin also did not differ significantly between the two groups (1,620 vs. 1,470 ng/L). There was a significant

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decline in admission rates in the first as well as in the second wave of the pandemic. *Conclusions:* The 30-day total mortality of COVID+ patients was significantly higher, and a more severe proceeding of acute myocardial infarction and a higher incidence of complications can be observed. As the secondary negative effect of the pandemic serious decline in admission rates can be detected.

KEYWORDS

acute cardiovascular care, COVID-19 pandemic, secondary negative effect

INTRODUCTION

The SARS-COVID-19 pandemic has impacted many aspects of acute myocardial infarction care. Two main negative effects have to be highlighted. The prognosis of COVID positive acute myocardial infarction (AMI) patients is significantly worse than that of COVID negative patients [1]. On the other hand, the pandemic had a secondary effect on the acute cardiovascular care. The large number of COVID cases burdened the health care system. Physicians reported that there were fewer acute coronary syndrome (ACS) patients presenting to hospitals during the pandemic.

Severe cardiovascular complications are one of the most common causes leading to death. That is why patients suffering from chronic cardiovascular diseases are at higher risk.

Although it's known that SARS-CoV-2 rises the risk of thrombosis, there is a STEMI-paradox during the pandemic. A Spanish study involving 73 cardiac centers reports 40% decrease in STEMI patients [2]. Americans report 38% reduction in catheterization due to STEMI [3]. A multicenter, nationwide, observational study in Italy states a reduction in both STEMI by 26.5% and NSTEMI by 65.1% [4].

There are some possible reasons for the decrease in ACS cases. During the pandemic patients are less likely to seek medical attention, they fear being admitted to a hospital. Besides patient's anxiety there was a significant delay on the part of the care providers. During the pandemic the safety measures can slow down the usual process [5].

We aimed to examine the direct effect of the COVID infection on the prognosis of patients suffering acute myocardial infarction as well as the secondary effect of the pandemic on acute cardiovascular care.

METHODS

A single-center, retrospective analysis was performed based on data of COVID positive and COVID negative patients with acute myocardial infarction treated at the Semmelweis University Heart and Vascular Center.

Patients have been sorted in 3 groups. To the 1st group 43 COVID positive patients with acute myocardial infarction, admitted between 8th October 2020 and 30th April 2021, were enrolled. The second groups consisted of 397 patients suffering acute myocardial infarction in the same time period in 2018 and 2019. Into the third group 466 COVID negative myocardial infarction patients were enrolled, admitted between 8th October 2020 and 30th April 2021.

Inclusion and exclusion criteria. Only patients with PCR-confirmed COVID infection within 1 month were included in group 1. Patients with a history of COVID infection, fever of unknown origin, COVID contact, and COVID treatment within 1 month of enrollment were excluded from group 3.

Acute myocardial infarction was diagnosed on the basis of clinical symptoms, ECG, and elevated hs-Troponin T levels. The primary endpoint was 30-days all-cause mortality.

Demographic and clinical patient data of these consecutive patients have been collected from the medical database of our institution and from the database of the Hungarian Central Statistical Office. Results are expressed as mean ± standard deviation of mean (SD.) and sample size (n) for each treatment group of normal distribution. Continuous variables were compared with Mann-Whitney U test, categorical variables with Chi-square test. The level of significance was $\alpha = 0.05$.

To investigate the secondary effect of the pandemic on acute myocardial infarction care we compared the total number of patients admitted due to acute myocardial infarction pre-COVID, so in 2018 and 2019 vs in then COVID-era, so in 2020 throughout the pandemic waves.

RESULTS

We compared clinical characteristics of patients in the first and second group, so COVID positive AMI patients to AMI patients in the pre-COVID era (Table 1). There was no significant

Table 1. Demography and clinical characteristics of COVID positive myocardial infarction patients compared to the pre-pandemic controls

	COVID + AMI patients (n = 43)	Pre-COVID-era AMI patients (n = 397)	p
Age (years, mean (SD))	68.8 (±11.2)	67.6 (±12.8)	0.55
Gender (male, n, %)	31 (72.1%)	275 (69.3%)	0.75
Weight (kg, mean (SD))	83.6 (±16.7)	81.1 (±18.2)	0.42
Height (cm, mean (SD))	170.2 (±7.2)	169.8 (±9.5)	0.80
BMI (kg/m2, mean (SD))	28.7 (±5.2)	28 (±5.4)	0.42
STEMI (n, %)	20 (47.6%)	173 (43.9%)	0.75
NSTEMI (n, %)	22 (52.4%)	222 (56.1%)	0.74
Ventricular fibrillation (n, %)	5 (11.6%)	27 (6.8%)	0.71
Resuscitation (n, %)	10 (23.3%)	40 (10.1%)	0.27
Respiratory treatment (n, %)	14 (32.6%)	56 (14.1%)	0.11
ECMO (n, %)	1 (2.4%)	5 (1.3%)	0.94
Max. hs-Troponin T (ng L^{-1}, mean (SD))	1620 (±1890.1)	1470 (±2392)	0.70
Se Creatinine (μm L^{-1}, mean (SD))	118 (±73.5)	99.7 (±63)	0.12
eGFR (mlmin^{-1}1,73 m^2, mean (SD))	61.5 (±25.4)	69.0 (±21.9)	**0.04**
Se Glucose (mmol L^{-1}, mean (SD))	9.3 (±4.7)	8.7 (±4.4)	0.36
AMI in medical history (n, %)	10 (23.8%)	114 (29.0%)	0.73
Chronic kidney failure (eGFR<40, n, %)	11 (26.2%)	54 (13.9%)	0.31
Diabetes mellitus (n, %)	19 (44.2%)	134 (34.1%)	0.39
Atrial fibrillation (n, %)	10 (23.4%)	51 (12.9%)	0.40
Heart failure (n, %)	22 (51.2%)	108 (27.8%)	**0.03**
LV-EF (%, mean (SD))	43 (±14.6)	47 (±11.1)	0.07

Abbreviations: AMI = Acute myocardial infarction, BMI = Body Mass Index, STEMI = ST-segment elevation myocardial infarction, NSTEMI = Non-ST-segment elevation myocardial infarction, ECMO = Extra Corporal Membrane Oxygenator, LV-EF = Left Ventricle Ejection Fraction.

difference in gender distribution between the two groups, and more than half of COVID + patients had a significantly reduced ejection fraction for comorbidities (EF≤ 40%), and heart failure was significantly more common in this group (51.16% vs. 27.84%, $P = 0.0329$). There was no significant difference in the distribution of STEMI and NSTEMI between the two groups. Although there was no significant difference, the COVID + group had a higher incidence of VF (11.63% vs. 6.82%), resuscitation (23.26% vs. 10.08%), and ECMO implantation (2.38% vs. 1.26%). The mean age was 68.8 years in the COVID + group and 67.6 years in the control group. Maximal Troponin levels did not differ significantly between groups (1,620 vs. 1,470 ng/L), however, there was a significant difference between GFR values (61.51 vs. 68.96 mL/min/1.73m^2, $P = 0.04$).

After that, we wanted to compare the COVID positive and negative patients who were admitted in the same period (Table 2). There was no significant difference in age, gender, type of infarction. The difference in the occurrence of ventricular fibrillation and the need for resuscitation and ECMO implantation was also not significant, but mechanical ventilation was significantly more needed by COVID positive patients. Heart failure was also more common and patients had a significantly worse ejection fraction. More COVID positive patients received low molecular weight heparin (LMWH), but we were able to initiate beta-blocker in significantly fewer patients (Table 3).

Table 2. Demography and clinical characteristics of COVID positive myocardial infarction patients compared to COVID negative myocardial infarction patients

	COVID + AMI patients (*n* = 43)	COVID - AMI patients (*n* = 466)	*p*
Age (years, mean (SD))	68.8 (±11.2)	67.3 (±12.8)	0.46
Gender (male, *n*, %)	31 (72.1%)	312 (67%)	0.56
Weight (kg, mean (SD))	83.6 (±16.7)	82.9 (±17.5)	0.81
Height (cm, mean (SD))	170.2 (±7.2)	169.4 (±9.3)	0.61
BMI (kg/m2, mean (SD))	28.7 (±5.2)	28.8 (±5.4)	0.91
STEMI (*n*, %)	20 (47.6%)	228 (48.9%)	0.91
NSTEMI (*n*, %)	22 (52.4%)	235 (50.4%)	0.86
Ventricular fibrillation (n, %)	5 (11.6%)	25 (5.4%)	0.62
Resuscitation (*n*, %)	10 (23.3%)	41 (8.8%)	0.20
Respiratory treatment (n, %)	14 (32.6%)	36 (7.7%)	**0.03**
ECMO (*n*, %)	1 (2.4%)	3 (0.6%)	0.89
Hypertension (*n*, %)	28 (65.1%)	355 (76.2%)	0.19
Anaemia (*n*, %)	15 (34.9%)	109 (23.4%)	0.34
AV-block (*n*, %)	1 (0.2%)	20 (4.3%)	0.84
AMI in medical history (*n*, %)	10 (23.8%)	102 (21.9%)	0.89
Chronic kidney failure (eGFR<40, *n*, %)	11 (26.2%)	44 (9.4%)	0.14
Diabetes mellitus (n, %)	19 (44.2%)	135 (29%)	0.18
Atrial fibrillation (n, %)	10 (23.4%)	75 (16.1%)	0.57
Heart failure (n, %)	22 (51.2%)	96 (20.6%)	**0.01**
LV-EF (%, mean (SD))	43 (±14.6)	48.7 (±9.7)	**0.01**

Abbreviations: AMI = Acute myocardial infarction, BMI = Body Mass Index, STEMI = ST-segment elevation myocardial infarction, NSTEMI = Non-ST-segment elevation myocardial infarction, ECMO = Extra Corporal Membrane Oxygenator, LV-EF = Left Ventricle Ejection Fraction.

Table 3. Laboratory parameters and treatment characteristics of COVID positive and COVID negative AMI patients

	COVID + AMI patients (n = 43)	COVID - AMI patients (n = 466)	p
Max. Creatine-kinase (U/L, mean (SD))	1251.7 (±1920.5)	886.5 (±1371.8)	0.14
Max. CRP (mg L^{-1}, mean (SD))	54.4 (±85.3)	43.8 (±66.1)	0.35
NT pro-BNP (pg mL^{-1}, mean (SD))	3360.1 (±2827.5)	4008.8 (±6895.8)	0.81
Lymphocytes (Giga/L, mean (SD))	2 (±3.1)	2.9 (±3.4)	0.15
Lymphocytes (%, mean (SD))	15.5 (±10.4)	18.5 (±9.5)	0.10
Se Natrium (mmol L^{-1}, mean (SD))	136.9 (±4.6)	137.9 (±4)	0.13
Se potassium (mmol L^{-1}, mean (SD))	4.3 (±0.8)	4.3 (±0.6)	1.00
GOT (U/L, mean (SD))	177.4 (±398.4)	106.1 (±354)	0.28
GPT (U/L, mean (SD))	92.4 (±254.1)	46.3 (±126.3)	**0.05**
ALP (U/L, mean (SD))	91.8 (±43.1)	82 (±47.9)	0.29
OAC (n, %)	10 (23.3%)	71 (15.2%)	0.52
LMWH (n, %)	22 (51.2%)	26 (5.6%)	**<0.01**
ASA (n, %)	40 (93%)	424 (91%)	0.67
Clopidogrel (n, %)	23 (53.5%)	222 (47.6%)	0.59
Prasugrel (n, %)	14 (32.6%)	176 (37.8%)	0.70
Ticagrelor (n, %)	4 (9.3%)	24 (5.2%)	0.75
ACEi/ARB (n, %)	32 (74.4%)	364 (78.1%)	0.63
Betablockers (n, %)	27 (62.8%)	390 (83.7%)	**<0.01**
Steroids (n, %)	20 (46.5%)	1 (0.2%)	0.37

Abbreviations: OAC = Oral anticoagulant, LMWH = Low molecular weight heparin, ASA = Aspirin, ACEi = Angiotensin convertase inhibitor, ARB = Angiotensin receptor blocker.

Considering the primary endpoint 8 (18.60%) of 43 patients in the COVID group died within 30-days and 40 (10.07%) of 397 patients in the control group (P = 0.01) (Fig. 1).

We compared the MI admission rates in 2020 to the mean of 2018s and 2019s totals.

A 41.4% decrease in ACS cases (116/298) can be noticed in 2020 compared to 2018-2019. Similar tendency can be seen examining the two different infarction types separately. ST-elevation myocardial infarction (STEMI) cases reduced by 29% (61/87). The decline in

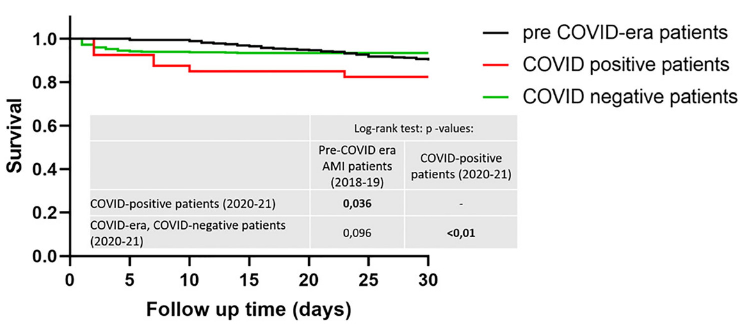

Fig. 1. Kaplan-Meier Analysis of 30-day survival of patients pre-COVID and during the pandemic

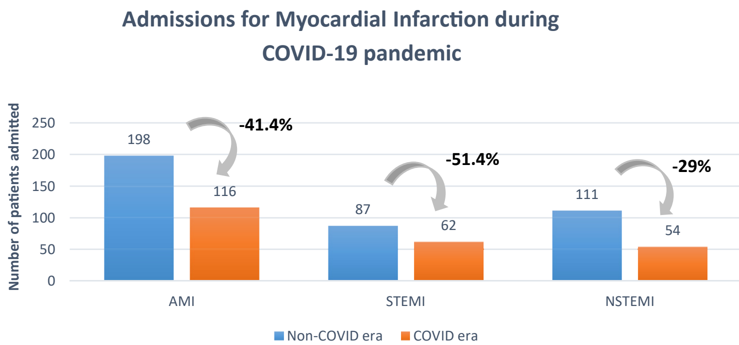

Fig. 2. Dropping number of admissions during the first wave of the COVID-19 pandemic
Abbreviations: AMI = Acute myocardial infarction, STEMI = ST-segment elevation myocardial infarction, NSTEMI = Non ST-segment elevation myocardial infarction

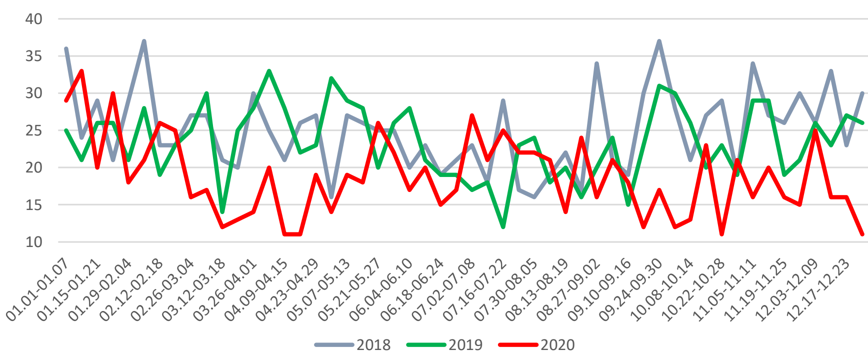

Fig. 3. Weekly distribution of acute coronary syndrome cases before and during of the COVID-19 pandemic

NSTE-ACS patients is more alarming, it is by 51.4% (54/111). The admission rates for myocardial infarction during the COVID-19 pandemic are presented in Fig. 2.

Significant decline in the admission rates can be detected in the first as well as in the second wave of the pandemic. However, in the first wave the peak positive case number was around 200 patients, in the second wave this number was close to 10,000 (Fig. 3).

DISCUSSION

A North American COVID-19 study compared COVID positive patients, individuals with suspected COVID infection and pre-COVID controls [1]. COVID positive patients were more likely to present with cardiogenic shock but less likely to receive invasive treatment compared to controls. From those who were treated invasively, 71% received primary percutaneous coronary angiography. They found that COVID positive STEMI patients are at high risk, therefore they should be treated invasively. We also found that COVID positive patients were at higher risk. 30-days all-cause mortality was significantly higher. Moreover, the course of the disease was more severe: VF, resuscitation were more frequent, ECMO implantation and invasive ventilation were required more, and cardiac necroenzymes also reached higher levels. Significantly more patients had reduced EF after AMI, more than half of COVID + patients remained with heart failure. Examining drug therapy, only LMWH administration was significantly higher in the COVID-positive group compared to the COVID-negative group, which may be logically explained by the thrombogenic effect of SARS-CoV-2.

Similar to the numbers seen in Spain, Italy or in the USA [2–4] we saw a serious decline in admission rates due to myocardial infarction. A systematic meta-analysis found similar results [5]. In these countries one of the main reasons for the delay was the overwhelmed healthcare system due to the daily raising numbers of new coronavirus cases. There are some possible reasons for the decrease in ACS cases. During the pandemic patients are less likely to seek medical attention, they fear being admitted to a hospital. Besides patient's anxiety there was a significant delay on the part of the care providers. During the pandemic the safety measures can slow down the usual process [6]. Compared to the countries mentioned above, in Hungary the virus had a slower spread in the first wave, the number of the confirmed cases and the mortality rates lags behind those in Italy or Spain. The moderate number of COVID cases did not lean much burden on the healthcare system in the first wave of the pandemic, patients with life-threatening illness could have been treated as usual protocols recommend. However, we noticed 41% decrease in ACS cases, 29 decline in STEMI, 51% decline in NSTEMI. Interestingly, after the first wave of the pandemic, in the summer of 2020, we experienced similar admission rates as pre-pandemic. However, during the second wave admission rates declined again.

The data suggests that high number of MI patients remained untreated. We saw the decline in case numbers a week before the first COVID-19 positive case was confirmed in Hungary. Which supports that the mental impact of the pandemic precedes its actual clinical effect.

CONCLUSION

The 30-day total mortality of COVID+ patients was significantly higher, and a more severe proceeding of acute myocardial infarction and a higher incidence of complications can be observed. That's why it would be necessary to investigate the thrombogenic effect of the virus and it's increasing inflammatory activity at both molecular and at disease level. Investigation of additional thrombogenic complications would be also important (eg. deep vein thrombosis, pulmonary embolism, ischemic stroke). Examining the temporality of all these processes, analyzing the complications in the long run and incorporating experience into clinical care is also needed.

Because of the possibly high number of untreated myocardial infarction patients' mortality rates, in the next few months-, years more complicated cases, more patients with heart failure, malignant arrhythmias can be expected due to their untreated infarction.

The pandemic has a serious secondary effect which will have an emphasized importance in the future. The hazards of the delayed care due to anxiety and other mental reasons should be stated among healthcare providers as well as population wise.

Statement of competing interest: None declared.

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Ethical statement: The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

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