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Article

STEMI Patients in the First and Second Wave of Covid-19 Pandemic in Northeast Slovenia – A Retrospective, Single Center Observational Study

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Abstract: Covid-19 pandemic affected outcome in ST-elevation myocardial infarction (STEMI) patients in majority of countries. We aimed to assess retrospectively admissions, treatments, complications and mortality of STEMI patients in the northeast of Slovenia in the first (March-May 2020) and the second wave (October-December 2020) of Covid-19 pandemic and compare them with the data from 2019 (March-October). Comparing 2019 and both waves of Covid-19 pandemic we observed nonsignificant differences in the number of STEMI admissions, in baseline characteristics, in the use of primary percutaneous coronary intervention (PCI), either within the first 3 (40.5%* vs 30.2% vs 25%*, *p = 0.074) and 6 hours, nonsignificant differences in TIMI III flow after primary PCI and in hospital complications, except for significant increase in hospital heart failure (23.3% vs 42%, p = 0.015) and mitral regurgitation in the second wave (10% vs 26.9%, p = 0.008) of the pandemic with nonsignificant increase in hospital mortality (8.9% vs 9.4% vs 13.6%) in both waves of the pandemic. We conclude, that with increased severity of Covid-19 pandemic in the second wave there was a longer delay to primary PCI in STEMI patients, resulting in significantly increased hospital heart failure and nonsignificantly increased hospital mortality.

Keywords: ST-elevation myocardial infarction; Covid-19 pandemic; time delay; primary percutaneous coronary intervention; heart failure; mortality

1. Introduction

In early March 2020 WHO proclaimed Covid-19 pandemic due to the rapid, worldwide spread of highly contagious SARS-CoV-2 virus. Until today more than 500 million people were infected and more than 6 million people died of new corona virus disease (Covid-19). In more than 80% of cases Covid-19 is an asymptomatic or mild-moderate respiratory disorder. In approximately 14% Covid-19 is more severe respiratory disease with dyspnea and the need of ICU admission and in 5% a critical illness with ARDS and multiorgan failure syndrome, responsible for increased mortality of Covid-19 patients. To limit the spread of Covid-19, majority of countries, including Slovenia, implemented strict social containment measures, including lockdown of social life [1]. In the peak of the pandemics, in every country hospitals and in particular intensive care units were overcrowded and at the same time, there was an excess mortality from respiratory failure in critically ill Covid-19 patients [1]. To accommodate to the increased workload in intensive care units, hospitals and emergency rooms (ER), the health care facilities were reorganized [1, 2]. There was a rapid mobilization of substantial healthcare resources worldwide only for Covid-19 cases, care for other noncommunicable disorders was reduced The consequence was reduced patients' visits to ER, to family physicians, outpatient clinics and hospitals for other medical conditions except for Covid-19 [1, 2]. Elective surgery, elective

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diagnostic and therapeutic procedures were canceled, only emergency and urgent procedures and treatments were performed. At the same time the patients were anxious and avoided medical facilities to prevent infection.

In majority of countries cardiologists reported a significant decrease in admission of ST-segment elevation myocardial infarction (STEMI) patients, a decrease in the number of primary percutaneous coronary interventions (PCI) and substantial delays in the start of treatment [2-7]. Most important causes were fear, prolonged transport to the ER due to the use of personal protective equipment of the medical staff, testing for Covid-19, waiting for the results with prolonged triage in the ER, prolonged transport to the catheterization laboratory and prolonged time of coronary interventions [8-10]. Studies reported mainly worse outcome in STEMI patients with hospital mortality exceeding 10%, in particular in Covid-19 epicenters in Italy and China [4, 7, 10, 11].

In the first months (March to May 2020) of the pandemic in Slovenia among 2.000.000 inhabitants only 1398 Covid-19 cases were registered, but the number of Covid-19 cases increased to 117.853 from October to December 2020 with the parallel increase of their mortality [12]. To overcome the pandemic, social restrictions continued, as well as mobilization of healthcare resources for Covid-19 patients. Reduction in care of other noncommunicable disorders, except for Covid-19, escalated even further in autumn 2020 [1, 12].

Our aim was to assess STEMI admissions, the delay in treatment, in-hospital complications and mortality of STEMI patients in the first and second wave of SARS-CoV19 pandemic and compare the data to the pre-pandemic period in 2019.

2. Materials and Methods

This was a retrospective monocenter observational study of STEMI patients in the first and the second wave of the Covid-19 pandemic in 2020, compared to STEMI patients in 2019. The study was conducted in the University clinical centre Maribor, a tertiary clinical institution in the north-east of Slovenia. It is the referral 24/7 regional center for primary PCI in STEMI patients, covering the area with population of 850.000.

2.1. Data collection.

In this study we retrospectively included all consecutive patients referred with the diagnosis of STEMI from March to May 2020 (first wave of the Covid-19 pandemic) and from October to December 2020 (second wave of Covid-19 pandemic) and STEMI patients from March to May 2019. We extracted standard patients' data from the electronic medical records, according to ICD-10 codes and supervising physician carefully reviewed them. Well-known criteria established the diagnosis of STEMI [13]. We registered demographic, clinical, and mortality data of STEMI patients.

2.2. Methods

Primary PCI was the main reperfusion strategy. The treatment of STEMI patients in 2019 was in accordance with the guidelines. In 2020 treatment procedures were adapted to the Covid-19 pandemic, in particular regarding prior, time-consuming testing for SARS-CoV-2 infection until obtaining the results, as well as the use of protective equipment [13, 14].

We registered gender, age, prior myocardial infarction, diabetes, arterial hypertension, resuscitation before admission, time to primary PCI. Among laboratory data, we registered measurements of cardiac hisg-sensitivity troponin I and of serum creatinine on admission and peak levels during in-hospital stay. Among treatment data, we registered the use of primary PCI, TIMI III flow after primary PCI, radial or femoral access.

After primary PCI, we monitored the patients in the medical ICU or coronary care unit for approximately 24 hours or longer in case of complications until we transferred them to the cardiology ward or local hospitals in stable condition [13, 14].

During hospital stay we registered acute complications such as in-hospital acute heart failure, arrhythmias, acute bleeding, acute kidney dysfunction, in-stent thrombosis,

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non-SARS-CoV-2 infection and mortality. Acute heart failure was classified as either pulmonary congestion (Killip class II), pulmonary edema (Killip class III) or cardiogenic shock or any hypotension necessitating a vasopressor infusion (Killip class IV) [13 - 15]. We registered arrhythmias as ventricular and/or atrial. We registered acute kidney dysfunction as an increase in serum creatinine for at least 50% from the baseline within the first 72 hours [13]. We registered all the standard pharmacological treatments (the use of acetylsalicylic acid – ASA with clopidogrel or ticagrelor or prasugrel, the use of heparins, noradrenalin, dobutamin, levosimendan, loop diuretic, glycoprotein receptor antagonist IIb/IIIa) and treatment of complications (insertion of intra-aortic balloon pump (IABP), mechanical ventilation). Left ventricular systolic function was assessed using transthoracic echocardiography during in-hospital stay [13, 14].

2.3. Data Analysis and endpoints

We compared baseline and treatment data, complications and mortality data between STEMI patients in 2019 and STEMI patients in the first and the second wave of Covid-19 pandemics with the emphasisi on:

- The number of STEMI admissions in the both waves of Covid-19 pandemic
- Time delay to primary PCI in the both waves of the pandemic
- The prevalence of complications in STEMI patients in the both waves of the pandemic
- Mortality data of STEMI patients in the both waves of the pandemic.

2.3. Ethical approval

Institutional Medical Ethics Committee (University clinical center Maribor – Medical Ethics Committee (KME) approved the retrospective observational study (approval UKC-MB-KME-62/19). The informed consent of included patients was waived due to the retrospective nature of the study. The study was in accordance with the 1964 Declaration of Helsinki and its subsequent amendments. We protected personal data of the patients according to the Law on Personal Data Protection.

2.4. Statistical analysis

Statistical analysis was performed using the SPPS Statistical package, version 19 (IBM Corp., Armonk, N.Y., USA) for Windows. We presented the data as means ± standard deviations or percentages. We used the two-sided Student's t-test to test the differences between the groups for means ± standard deviation and Fisher's exact test for percentages. A p value <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

We present the baseline characteristics of all included patients in Table 1. Between STEMI patients in 2019 and STEMI patients in both waves of Covid-19 pandemic there were nonsignificant differences in the number of STEMI admissions (90 patients vs 96 patients vs 81 patients), nonsignificant differences in gender, mean age, age over 65 years, comorbidities, resuscitation before admission, anterior STEMI location and increased admission troponin I levels.

Between STEMI patients in 2019 and STEMI patients in both waves of Covid-19 pandemic, we observed a nonsignificant increase in admission acute heart failure (30% vs 34.4% vs 40.5%) and an increase in prior resuscitation in the second wave of the pandemic (10% vs 10.4% vs 16%). Between STEMI patients in 2019 and STEMI patients in both wave of Covid-19 pandemic, we observed nonsignificant decline of primary PCI within the first six hours and within the first 3 hours (40.5% vs 38.7% vs 25, $p = 0.075$).

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Table 1. Comparison of baseline characteristics between STEMI patients in March - May 2019 and STEMI patients in March-May 2020 (first wave of Covid-19 pandemic) and October-December 2020 (second wave of Covid-19 pandemic).

Baseline characteristics	**March-May 2019 (n = 90)**	**March-May 2020 (n = 96)**	**P** (March-May 2019 vs March-May 2020)	**October-December 2020 (n = 81)**	**P** (March-May 2019 vs October-December 2020)
Men (%)	75.6	69.8	0.414	69,1	0.393
Mean age ± SD (years)	65.6 ± 11.2	63.9 ± 13.4	0.341	65.8 ± 12.1	0.915
Age ≥ 65 years (%)	53.3	49	0.561	51.9	0.879
Arterial hypertension (%)	51.1	52.1	0.999	58.8	0.356
Diabetes (%)	28.9	18.8	0.122	18.8	0.151
Prior MI (%)	12.2	8.3	0.470	17.5	0.389
< 6 hours to primary PCI (%)	51.9	52	0.999	45.3	0.502
< 3 hours to PPCI (%)	40.5	38.7	0.870	25	0.074
Anterior STEMI (%)	42.7	49	0.461	45.6	0.757
Admission Killip II-IV (%)	30	34.4	0.535	40.5	0.196
Prior resuscitation (%)	10	10.4	0.999	16.5	0.255
Troponin ≥ 5μg/L (%)	42	33.7	0.286	30.4	0.148

Legend:

SD; standard deviation, PCI; percutaneous coronary intervention, STEMI; ST-elevation myocardial infarction, MI; myocardial infarction

3.1. Treatment data

We present hospital treatments in Table 2. We observed similar rate of primary PCI (94.4% vs 94.8% vs 91.4%), TIMI III flow after primary PCI and radial access in all three time periods. The use of mechanical ventilation was similar in 2019 and in the first wave of Covid-19 pandemic, but it was nonsignificantly increased in the second wave (Table2).

There were nonsignificant differences in the use of pharmacological therapy between 2019 and the first and the second wave of Covid-19 pandemic (Table 2).

3.2. Hospital complications and mortality data

Hospital complications and mortality data are presented in Table 3. We observed similar increase in peak troponin I levels ≥ 50ug/L, a similar decrease of EF levels < 45%, similar prevalence of in-stent thrombosis and reinfarctions in all three time periods. Between STEMI patients in 2019 and STEMI patients in the first wave of Covid-19 pandemic, we observed similar prevalence of acute kidney injury (6.6% vs 5.2% vs 9.8%), and arrhythmias, but nonsignificant increase in the second wave of the pandemic. In comparison to 2019 we observed a nonsignificant increase in non-Covid-19 hospital infection (15.6% vs 20.8% vs 27.2%) and in bleeding (8.9% vs 12.5% vs 11.1%) in both waves of Covid-19 pandemic.

According to 2019 we observed a nonsignificant increase in hospital heart failure (23.3%* vs 27.1% vs 42%*, p = 0.015) and mitral regurgitation (10%* vs 18.8% vs 26.9%*, p = 0.008) in the first wave and a significant increase of both complications in the second one. We observed increased hospital mortality of STEMI patients in both waves of Covid-19 pandemic, in particular in the second one, but the difference did not meet statistical significance (8.9% vs 9.4% vs 13.6%).

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Table 2. Comparison of treatments in STEMI patients between March - May 2019 and STEMI patients in March-May 2020 (first wave of Covid-19 pandemic) and October-December 2020 (second wave of Covid-19 pandemic).

Treatments (%)	**March-May 2019 (n = 90)**	**March-May 2020 (n = 96)**	**P** (March-May 2019 vs March-May2020)	**October-December 2020 (n = 81)**	**P** (March-May 2019 vs October-December 2020)
Primary PCI	94.4	94.8	0.999	91.4	0.552
TIMI III flow after primary PCI	78.4	87.8	0.111	83.3	0.439
Radial access	50	53.3	0.761	55.4	0.524
ASA	96.7	97.9	0.674	100	0.248
Ticagrelor	74.2	74	0.999	68.8	0.492
Prasugrel	6.7	11.5	0.315	15.6	0.082
Klopidogrel	19.1	14.6	0.437	15.6	0.682
Unfractionated heparin	62.2	67.7	0.446	75.4	0.117
LMWH	16.7	25	0.207	30.3	0.053
GP IIb/IIIa inhibitor	41.6	45.6	0.657	50.7	0.270
Diuretic	20.2	17.7	0.710	19.8	0.999
Noradrenalin	15.6	18.8	0.698	18.5	0.685
Dobutamin	5.6	4.2	0.741	8.6	0.552
Levosimendan	4.4	5.2	0.999	1.2	0.371
Mechanical ventilation	8.9	9.4	0.999	14.8	0.241

Legend: PCI; primary percutaneous coronary intervention, TIMI; thrombolysis in myocardial infarction, ASA; acetylsalycilic acid, LMWH; low-molecular weight heparin, GP; glycoprotein

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Table 3. Comparison of hospital complications in STEMI patients between March - May 2019 and STEMI patients in March-May 2020 (first wave of Covid-19 pandemic) and October-December 2020 (second wave of Covid-19 pandemic).

Complications (%)	**March-May 2019 (n = 90)**	**March-May 2020 (n = 96)**	**P** (March-May 2019 vs March-May 2020)	**October-December 2020 (n = 81)**	**P** (March-May 2019 vs October-December 2020)
Peak Troponin ≥ 50 μg/L	40.2	41.9	0.878	36.8	0.744
EF < 45%	46.3	31	0.143	39.6	0.668
Hospital Killip classes II-IV	23.3	27.1	0.614	42	0.014
Hospital shock	15.6	20.8	0.448	27.2	0.090
Arrhythmias	34.4	31.3	0.755	38.8	0.633
Non-Covid-19 infection	17.8	18.8	0.999	29.6	0.073
Bleeding	8.9	12.5	0.484	11.1	0.799
Mitral regurgitation	10	18.8	0.100	26.9	0.005
Reinfarction	0	2.1	0.498	0	/
Acute kidney injury	6.8	5.2	0.760	10.7	0.413
In-stent thrombosis	1.1	2.1	0.999	1.2	0.999
Hospital mortality	8.9	9.4	0.999	13.6	0.343
30-day mortality	8.9	9.4	0.999	13.6	0.343
6-month mortality	11.1	14.6	0.519	13.6	0.648

Legend: EF; ejection fraction

4. Discussion

Our results show that during the first and the second wave of Covid-19 pandemics in 2020 the number of STEMI patients as well as primary PCI procedures did not change significantly in comparison to 2019. In comparison to 2019 there was a nonsignificant decrease in the primary PCI procedures within the first 3 and 6 hours of chest pain in the first and in particular in the second wave of the pandemic. However, in the first wave of the pandemic there was a nonsignificant increase in hospital heart failure and mitral regurgitation, but a significant increase of both complications in the second wave. There was nonsignificant difference in other hospital complications, including mortality data between 2019 and both waves of the pandemic.

Similar numbers of admitted STEMI patients in all three time-periods – in both waves of Covid-19 pandemic and in 2019 - differ from some other studies, reporting significant decrease in admissions of STEMI patients in the pandemic in comparison to the pre-pandemic period [2-7]. Epidemiological studies also pointed out that European regions were not equally hit by Covid-19 pandemic. Strong differences existed between the areas with limited Covid-19 cases and epicenters of Covid-19 [16]. The regional and local impact of Covid-19 had significant consequences for crisis management and policy responses, including STEMI management [16].

Gender and age in our STEMI patients in both waves of Covid-19 pandemic were similar to the pre-pandemic period. This observation was similar to some other studies [17, 18]. However, some studies even reported prevailing admissions of younger STEMI patients.

We observed nonsignificant differences in comorbidities among STEMI patients in all studied periods, what was similar to other studies. However, regarding the nonsignificant increase in arterial hypertension and prior myocardial infarction in the second wave of the pandemic in our patients, we can speculate that patients with comorbidities were more aware of the importance of chest pain in the time of the pandemic than patients without any prior comorbidity.

In parallel to reduced admission of STEMI patients in the epicenters of Covid-19, studies reported also of the significant decline of primary PCI procedures. However, in

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areas with better healthcare resources and limited number of Covid-19 the same use of primary PCI procedures was reported in the pandemics as in the pre-pandemic period [7, 9, 10, 17, 18]. In our STEMI patients primary PCI remained the leading reperfusion strategy in the pandemics, performed in more than 90% of patients with the similar TIMI III flow after primary PCI, reaching even 80% in the second wave of Covid-19 pandemic.

In spite of more than 90% of primary PCI procedures in our STEMI patients in the pandemics, only 25% of primary PCIs were performed within the first 3 hours in the second wave of the pandemic in comparison to 40% in 2019 and 38% in the first wave. However, this difference was nonsignificant. Several factors were associated with more pronounced time delay to primary PCI in the secod wave of the pandemic. In the first place there was an increased number of Covid-19 cases in the ER. On the other hand, several STEMI patients avoided hospitals because of the fear to get infected and in addition to the general recommendation to stay at home. There was time-consuming use of personnel protection equipment of the medical staff during transport, in ER and in the catheterization laboratory, as well as time-consuming nasopharyngeal swab sampling and waiting for the results before entering the catheterization laboratory [1]. Other studies report similar reasons for time delay to primary PCI [8-10].

In our patients, we observed an increased incidence of hospital heart failure, assessed by Killip classification, in particular in the second wave of Covid-19 pandemic. The prevalence of cardiogenic shock in the second wave of the pandemic was even 27%, but the difference in comparison to 2019 was not significant. Longer delays to primary PCI and to appropriate pharmacological treatment represented the most important contributors of heart failure, which in turn was most important cause of death after STEMI as well.

In spite a significant difference in heart failure was assessed at bedside by Killip classification between 2019 and the second wave of the pandemic (23.3% vs 42%, $p = 0.014$), we observed only a nonsignificant difference in decreased EF < 45% (21.1% vs 23.5%, $p = 0.66$), reflecting the predominant congestive nature of heart failure. This observation was similar to the multicenter registry of STEMI patients by Fardman et al, demonstrating that longer total ischemia time in STEMI patients in the Covid-19 pandemic resulted in an increase of congestive heart failure [19].

Hospital mortality of our STEMI patients in 2019 was 8.9% and increased to 9.4% in the first wave and to 13.5% in the second wave of the pandemic. However, the differences were nonsignificant. One of the meta-analysis reported significant increase in mortality of STEMI patients in the pandemic in comparison to the pre-pandemic period in 2020. However, another one demostrated a significant increase in hospital mortality only in Covid-19 epicenters in Italy and China, but globally only nonsignificant changes in STEMI mortality during the pandemic [4, 7, 10, 11]. Rapid optimization of pre-hospital and in-hospital procedures by the medical community and cardiology professionals could be most probable reasons for better outcome in STEMI patients in some centers during Covid-19 pandemic [7, 20].

Limitations of our study are several. The study is retrospective, observational, performed in a single tertiary medical center in northeastern part of Slovenia. Therefore, limited number of patients were included in a limited time-interval. However, the data give an important insight in STEMI admissions, percentage of early treatment by primary PCI and hospital outcome of STEMI patients. Our data suggest, that in future more effort should be put to educate the population to be aware of oppressive chest pain and call emergency services for help as soon as possible in spite of the epidemic. We also learned that faster and more accurate microbiological testing, better organization of medical facilities and vaccination of population could improve the prognosis in non-communicable diseases such as acute STEMI in future pandemics.

5. Conclusions

In parallel to the increased severity and number of Covid-19 patients in the second wave of the pandemic in 2020 we observed more delays to primary PCI in STEMI patients,

resulting in a significant increase of hospital heart failure and a nonsignificant increase of hospital mortality from October-December 2020 in comparison to the pre-pandemic period.

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Informed Consent Statement: "Patient consent was waived due to due to the retrospective nature of the study."

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