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Research Article

Clinical Characteristics and In-Hospital Outcomes of STEMI Patients Admitted during the SARS-CoV-2 Pandemic – an Observational Comparative Study

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Abstract

Background: During the ongoing SARS-CoV-2 pandemic, a significant decline in acute coronary syndromes (ACS) including ST segment elevation myocardial infarction (STEMI) has been reported from several countries. Studies on the effect of the pandemic itself and measures of social restriction on clinical presentation and outcome of STEMI patients are contradictive.

Methods: 103 consecutive STEMI patients admitted to our clinic between November 21st, 2019 and May 20th, 2020 were divided into a pre-pandemic cohort (62 patients, November 21st -March 20th, 2020), and a pandemic cohort (41 patients, March 21st -May 20th, 2020). Clinical presentation, in-hospital complications, outcome, laboratory data, and procedural characteristics of acute percutaneous coronary interventions (PCI) between the cohorts were compared.

Results: Compared to the pre-pandemic period patients in the pandemic cohort had higher peak high sensitivity troponin T (2903ng/l, interquartile range {IQR} 9->10000ng/l vs. 3967ng/l, IQR 289->10000ng/l, p=0.04), more often a TIMI flow <3 at the end of the revascularization procedure (8% vs. 34%, p<0.01), were more often treated with tirofiban (3% vs. 29%, p<0.01), stayed longer on ICU (1.06 vs. 2.39 days, p=0.02), and had more in-hospital complications (16% vs. 39%, p=0.01).

Conclusion: Presumably due to a delay in seeking acute medical care during the SARS-CoV-2 pandemic, patients with STEMI presented with higher troponin, worse restoration of coronary flow after acute PCI and suffered from more in-hospital complications compared to previous months. Public awareness for life-threatening diseases such as ACS has to be maintained to ensure adequate medical care for all patients during the SARS-CoV-2 pandemic.

Keywords: COVID-19; STEMI; Acute Coronary Syndrome; Angiography; Troponin; Thrombus

1. Introduction

During the SARS-CoV-2 pandemic and concomitant lockdown, reports from many countries described a significant decline of patients admitted by the emergency medical services with acute coronary syndrome to the hospital, reduced activity of cardiac catheterization laboratories and higher rates of out of hospital cardiac arrest [1-13]. Several studies demonstrated that patients with ST-segment elevation myocardial infarction (STEMI) had higher plasma concentrations of high-sensitivity troponin T (hs-TnT) at admission [1, 14-16]. This suggests delayed hospital admissions and thus delayed acute coronary revascularization, potentially increasing their risk of an adverse outcome. Time to revascularization and reperfusion is clearly associated with outcomes of acute coronary syndromes and medical services are enforced to follow recommendations to ensure timely care of these patients on a 24/7 basis [17]. As the SARS-CoV-2 coronavirus spread with vast regional differences, reports on time delays in STEMI management and care during the SARS-CoV-2 pandemic are heterogeneous [7, 9, 11, 12, 18, 19]. However, a recent report from Germany did not indicate substantial time delay in the management of acute coronary syndromes following first medical contact (FMC) during SARS-CoV-2 pandemic compared to the pre-pandemic period [11]. Despite increasing numbers of reports on deferred admissions of STEMI patients, data on in-hospital course and outcome of these patients are contradictive [1, 7, 11-14, 19-21]. This study sought to compare the clinical presentation, in-hospital complications, outcomes, biomarkers, and procedural characteristics of acute percutaneous coronary interventions (PCI) of patients with STEMI admitted to our hospital before and during the SARS-CoV-2 pandemic.

2. Methods

2.1 Study design and data collection

In this monocentric, retrospective observational study, we included all consecutive patients who were admitted to Ulm University Hospital tertiary care center with a diagnosis of STEMI between November 21st, 2019 and May 20th, 2020. STEMI treatment was performed according to current guidelines and procedures adapted for the SARS-CoV-2 pandemic [17, 22]. Patients admitted between November 21st, 2019 and March 20th, 2020 were assigned to the pre-pandemic cohort and those admitted after public

restrictions came into effect on March 21st 2020 were assigned to the pandemic cohort (March 21st to May 20th, 2020). To avoid allocation bias, only patients from the greater Ulm area were eligible and patients transferred from other hospitals were excluded from the study [1]. All collected data are part of standard patient assessment and routine medical care and extracted from electronic medical records and reviewed by two physicians (MB and MR) independently and adjudicated by a supervising physician (AI) in case of any difference. The study complies with the Declaration of Helsinki and was approved by the local ethics committee (Number of application and positive vote 130/20).

2.2 Laboratory samples

Blood samples were drawn at the time of hospital admission for measurements of hs-TnT (ElectroChemiLumineszenz ImmunoAssay "ECLIA" Roche, Cobas 8000) as part of the clinical routine. Furthermore, after acute PCI troponin was measured on a daily basis until concentrations began to decrease. Also, starting in late March, every patient was tested for SARS- CoV-2 by throat swab test (Sigma-Virocult® with 2 ml Virocult® medium, Check Diagnostics GmbH, Germany) and analyzed by RT-PCR at the local Institute for Virology.

2.3 Percutaneous coronary intervention

Using the clinical process management program angiographic findings, time of total radiation and procedure time of the PCI were assessed. Initial systolic function was assessed by ventriculogram. Thrombus formation and TIMI flow were assessed before and after PCI as described previously [23-25]. A thrombus burden ≥ TIMI thrombus grade 4 was defined a high thrombus burden [25, 26]. In case of high thrombus burden or reduced TIMI flow at the end of the PCI and at the discretion of the attending physician, tirofiban was administered as a bailout strategy [17]. Tirofiban was applicated weight-adapted following manufactures instructions.

2.4 Adverse events and patient outcomes

After acute PCI, all patients were monitored at our intensive care unit (ICU) for at least 12 hours until transfer to cardiology ward in stable condition following individual clinical judgement. In case of any severe complication, such as ventricular arrhythmia, cardiogenic shock, need for ventilatory or circulatory support, the stay at ICU was prolonged accordingly. We evaluated acute STEMI complications, including need for ventilatory support with non-invasive ventilation (NIV) or intubation (ITN), need for mechanical circulatory support with intra-aortic balloon pump counterpulsation (IABP) or extracorporeal membrane oxygenation (ECMO), ventricular arrhythmias (ventricular tachycardia or ventricular fibrillation), as well as the time-to-transfer from ICU to cardiology ward and in-hospital death rates. Left ventricular systolic function was re-assessed using transthoracic echocardiography before hospital discharge.

2.5 Statistical analysis

Continuous variables were listed as mean ± standard deviation or median together with interquartile range, as appropriate. Categorical variables were presented as absolute and relative frequencies, respectively. Group comparison of continuous variables was performed by two-sided independent samples student's t-test or Wilcoxon rank sum test as appropriate. The chi² test or Fisher's exact test was used for comparison of categorical values as appropriate. The daily incidence rate ratio incl. 95 %

confidence interval (CI) comparing the pre-pandemic cohort with the pandemic cohort were calculated by use of Poisson regression. Statistical analysis was performed using SAS version 9.4 under Windows. A two-sided p value of less than 0.05 was considered statistically significant. Due to the explorative nature of this study, all results from statistical tests have to be interpreted as hypothesis generating. An adjustment for multiple testing was not done.

3. Results

3.1 Study groups and patient characteristics

During the study period, a total of 103 STEMI patients were treated at Ulm University. Of those, 41 patients were admitted during the SARS-CoV-2 pandemic (pandemic cohort; March 21st to May 20th, 2020) and 62 patients in the months prior (pre-pandemic cohort; November 21st to March 20th, 2020). No patient was tested positive for SARS-CoV-2 infection by RT-PCR. The majority of included patients were male (78%) with a mean age of 64.5 ± 13.2 years. There were no significant differences between both groups at baseline (Table 1). However, following a sex-specific analysis, women in the pandemic cohort were significantly older (72.7 ± 10.9 vs. 62.2 ± 12.9 years; p<0.01), and were more often diagnosed with arterial hypertension (96% vs. 64%; p<0.01) and diabetes mellitus (43% vs. 20%; p=0.02) compared to women of the pre-pandemic cohort. For men, there were no significant differences between both study groups. As for the crude incidence rate per day (pandemic cohort: 0.548 vs. pre-pandemic cohort: 0.508) and daily incidence rate ratio for STEMI admissions there was no significant difference (IRR 1.08; 95% CI 0.63-1.85; p=0.78) (Table 4, Supplementary Appendix).

3.2 Clinical presentation and cardiac biomarkers

To assess the clinical condition of patients and severity of myocardial infarction, we compared vital parameters at admission and peak cardiac biomarkers of myocardial ischemia between both groups [27, 28]. Serum median peak concentrations of hs-troponin T were significantly higher in the pandemic cohort (Median 3967 [IQR, 289->10000] ng/l compared to the pre-pandemic cohort (Median 2903 IQR [9->10000] ng/l; p=0.04). No significant differences could be observed regarding the hemodynamic parameters (Table 1).

3.3 Angiographic findings and procedural characteristics

Next, we analyzed procedural data and findings in both groups as serum hs-TNT concentrations correlate with ischemic burden, size and location of myocardial infarction, coronary artery perfusion and systolic function in acute myocardial infarction [17, 28, 29]. In 75% of patients (N=77) of the total cohort LV-function as assessed by ventriculogram either was moderately or severely reduced. Most patients had diagnosis of a three-vessel disease (N=65, 63%), with the culprit lesion being located in the left anterior descending artery (N=49, 48%). Both, initial mean TIMI flow (pandemic cohort 1.2 vs. pre-pandemic cohort 1.6, p<0.01) and TIMI flow at the end of PCI (pandemic cohort 2.6 vs. 2.9 in the pre-pandemic cohort, p<0.01) were significantly more impaired in the pandemic cohort (Table 2). Moreover, overall thrombus burden was higher in the pandemic cohort and tirofiban was significantly more often administered in these patients (29% vs. 3%, p<0.01). Left ventricular systolic function by ventriculogram, extent of vessel disease, and location of the culprit lesion did not show any differences. Additionally, PCI duration and fluoroscopy time were similar in both groups (Table 2).

3.4 In-hospital complications and outcomes

Cardiogenic shock was significantly more often present in STEMI patients admitted to our tertiary care center after measures of social restriction had been initiated (pandemic cohort 12 patients [29%] vs. pre-pandemic cohort 6 patients [10%]; p=0.01). Moreover, significantly more patients in the pandemic cohort were in need for mechanical circulatory (n= 9 [22%] vs. n= 2 [3%]; p=0.01) and ventilation support (n= 12 [29%] vs. n=7 [11%]; p=0.02) (Table 3). Additionally, patients of the pandemic cohort stayed longer on the ICU compared to the pre-pandemic cohort (2.39 days vs. 1.06 days; p<0.02). In patients admitted during the pandemic period, analysis of left ventricular systolic function before discharge from hospital revealed a significantly lower ejection fraction, which was driven by a larger number of patients with severely reduced left ventricular function (n=12 [34%] vs. n=7 [13%]; p=0.02). Moreover, substantially more patients (n=7 [17%]) of the pandemic cohort died in hospital compared to the pre-pandemic cohort (n=4 [6%]), albeit it is not statistically significant (p=0.11).

	All Patients (n= 103)	**Pre-pandemic cohort (n= 62)**	**Pandemic cohort (n= 41)**	***p* value**
Female	23 (22%)	14 (23%)	9 (22%)	0.94
Age (years)	65 ± 13	64 ± 13	66 ± 13	0.42
Known CAD	17 (17 %)	12 (19%)	5 (12%)	0.34
Arterial hypertension	73 (71%)	41 (66%)	32 (78%)	0.19
Dyslipidemia	65 (63%)	39 (63%)	26 (63%)	0.96
Diabetes mellitus	26 (25%)	17 (27%)	9 (22%)	0.53
Family history	22 (21%)	16 (26%)	6 (15%)	0.18
Obesity	18 (17%)	8 (13%)	10 (24%)	0.13
Smoker	52 (50%)	31 (50%)	21 (51%)	0.90
OSAS	3 (3%)	1 (2%)	2 (5%)	0.56
COPD	6 (6%)	4 (6%)	2 (5%)	1.00
History of TIA/Stroke	5 (5%)	3 (5%)	2 (5%)	1.00
Heart rate (bpm)	83 ± 19	81 ± 19	85 ± 18	0.25
Systolic blood pressure (mmHg)	126 ± 27	128 ± 27	123 ± 27	0.42
Diastolic blood pressure (mmHg)	73 ± 18	72 ± 18	75 ± 19	0.33
Peak hs-TnT (ng/l)	3393 [9->10000]	2903 [9->10000]	3967 [289->10000]	0.04

CAD, coronary artery disease; OSAS, obstructive sleep apnea syndrome; COPD, chronic obstructive pulmonary disease; TIA, transient ischemic attack; bpm, beats per minute; hs-TnT, high sensitivity troponin T; The data are presented as mean ± standard deviation, absolute frequencies (percent) or median [interquartile range].

Table 1: Baseline characteristics, hemodynamic parameters, and myocardial biomarkers.

	All Patients (n= 103)	**Pre-pandemic cohort (n= 62)**	**Pandemic cohort (n= 41)**	***p* value**
LV-Function in Ventriculogram				0.32
Normal	6 (6%)	5 (8%)	1 (2%)	
Mildly reduced	19 (19%)	14 (23%)	5 (12%)	
Moderately reduced	37 (36%)	20 (33%)	17 (41%)	
Severely reduced	40 (39%)	22 (36%)	18 (44%)	
Initial TIMI flow				<0.01
0	37 (36%)	21 (34%)	16 (39%)	
1	12 (12%)	2 (3%)	10 (24%)	
2	21 (20%)	14 (23%)	7 (17%)	
3	33 (32%)	25 (40%)	8 (20%)	
TIMI flow at the end of PCI				<0.01
0	1 (1%)	1 (2%)	0 (0%)	
1	4 (4%)	0 (0%)	4 (10%)	
2	14 (14%)	4 (6%)	10 (24%)	
3	84 (82%)	57 (92%)	27 (66%)	
No. of coronary arteries affected				0.66
1	8 (8 %)	5 (8%)	3 (7%)	
2	30 (29%)	20 (32%)	10 (24%)	
3	65 (63%)	37 (60%)	28 (68%)	
Culprit lesion				0.67
Left main stem	7 (7%)	4 (6%)	3 (7%)	
Left anterior descending artery	49 (48%)	30 (48%)	19 (46%)	
Left circumflex artery	15 (15%)	7 (11%)	8 (20%)	
Right coronary artery	32 (31%)	21 (34%)	11 (27%)	
TIMI thrombus grade				0.04
Thrombus grade ≤ 3	47 (46%)	33 (52%)	14 (34%)	
Thrombus grade 4	19 (18%)	7 (11%)	12 (29%)	
Thrombus grade 5	38 (37%)	23 (37%)	15 (37%)	
Use of tirofiban	14 (14%)	2 (3%)	12 (29%)	<0.01
Antiplatelet therapy				0.14
Prasugrel	71 (70%)	47 (77%)	24 (59%)	
Ticagrelor	8 (8%)	4 (7%)	4 (10%)	
Clopidogrel	23 (23%)	10 (16%)	13 (32%)	
Duration of PCI (minutes)	60 ± 31	57 ± 26	64 ± 38	0.31
Fluoroscopy time (minutes)	16 ± 13	15 ± 13	16 ± 13	0.90

TIMI, thrombolysis in myocardial infarction; PCI, percutaneous coronary intervention, LV left ventricle. The data are presented as absolute frequencies (percent).

Table 2: Angiographic findings.

	All Patients (n= 103)	Pre-Pandemic cohort (n= 62)	Pandemic cohort (n= 41)	*p* value
Complications	26 (25%)	10 (16%)	16 (39%)	0.01
Cardiogenic shock	18 (17%)	6 (10%)	12 (29%)	0.01
Mechanical circulation support	11 (11%)	2 (3%)	9 (22%)	0.01
IABP	7 (7%)	1 (2%)	6 (15%)	0.02
ECMO	4 (4%)	1 (2%)	3 (7%)	0.30
Ventilatory support	19 (18%)	7 (11%)	12 (29%)	0.02
NIV	5 (5%)	0 (0%)	5 (12%)	0.01
Endotracheal intubation	14 (14%)	7 (11%)	7 (17%)	0.40
VT/VF	5 (5%)	3 (5%)	2 (5%)	1.00
LV-Function in TTE before discharge				0.03
Normal	14 (16%)	12 (22%)	2 (6%)	
Mildly reduced	30 (33%)	18 (33%)	12 (34%)	
Moderately reduced	27 (30%)	18 (33%)	9 (26%)	
Severely reduced	19 (21%)	7 (13%)	12 (34%)	0.02
ICU stay duration (days)	1.57 ± 2	1.06 ± 1	2.39 ± 3	0.02
In-Hospital death	11 (11%)	4 (6%)	7 (17%)	0.11

IABP, intra-aortic balloon pump; ECMO, extracoporeal membrane oxygenation; NIV, non-invasive ventilation; VT, Ventricular tachycardia; VF, ventricular fibrillation; TTE, transthoracic echocardiography; ICU, intensive care unit, LV left ventricle. The data are presented as absolute frequencies (percent)

Table 3: In-Hospital complications and outcome.

4. Discussion

In this observational study of a local sample of the german population, patients admitted with STEMI during the SARS-CoV-2 pandemic from March 21st until May 20th 2020 had (1) significantly elevated hs-troponin T plasma concentrations, (2) a higher intracoronary thrombotic burden, (3) were more often in need of ventilatory and circulatory mechanical support, (4) stayed longer at the ICU, and (5) showed more often severely impaired left ventricular systolic function compared to the control pre-pandemic cohort of patients admitted between November 21st 2019 and March 20th 2020. Over the last months, a growing number of reports from many countries and regions worldwide showed reduced admissions of patients with acute coronary syndromes including STEMI during the SARS-CoV-2 pandemic and the concomitant restrictions of public life [1, 7, 11-14, 21, 30]. As large regional differences in the extent of the drop of admission rates of STEMI patients were reported, an interdependency with the regional outbreak of the SARS-CoV-2 pandemic and its sequelae seems likely [1, 7, 11-14, 21, 30]. Therefore, countries hit hard by the pandemic such as Spain, England, Italy or China, report severely prolonged times from symptom to first medical

contact or door-to-ballon-times, in contrast to countries rather spared from the Covid-19 pandemic, like Belgium, Austria or Germany that reported only short delays [10-13, 15, 19, 21, 31].

Concerning regional data from Germany, only one study has been published. Contrary to our results, it analyzed potential impact of the SARS-CoV-2 pandemic on management of STEMI patients in a STEMI network and found no significant differences in pre-clinical, clinical and procedural parameters [11]. However, the authors were limited to data collected up to March 2020 and thus might underestimate the effect of general public restriction which did not come into effect until March 21st 2020. Moreover, the evolution of the COVID-19 pandemic in Germany was still quite uncertain and dynamic at the end of March. Several reasons have been proposed that potentially explain the decrease of admissions and time delay, including framing issues and iatrophobia [1, 14, 30]. In the study of Hammad et al. of the 11 STEMI patients with delayed admission, three stated fear of COVID-19 infection, two attributed their symptoms to be COVID-19 related and one did not want to burden the emergency department during COVID-19 crisis [14]. We presume that in our study patients might delay seeking medical advice for similar reasons but did not systematically assess this during the pandemic period.

Further studies are needed to address this issue. Despite increasing numbers of publications on reduced admissions of STEMI patients, data on in-hospital course and outcome of these patients are contradictive [7, 9, 11-15, 20, 21]. In our study, none of the patients with STEMI was tested positive for SARS-Cov-2 indicating other causes for the adverse clinical course of patients during the pandemic. Patients in our pandemic cohort were more often in need of ventilation and circulatory mechanical support, stayed longer at the ICU and showed more often severely impaired left ventricular systolic function compared to the pre-pandemic cohort admitted between November 21st 2019 and March 20th 2020. Other studies on intra-hospital complications report divergent findings. While some did not observe differences other stated a significant increase in overall complications potentially because of large local differences of COVID-19 spread [7, 9, 11-15, 20, 21]. Analysis of left ventricular ejection fraction before discharge revealed a significantly impaired systolic function in patients of the pandemic cohort, which is in line with other studies presumably leading to increased rates of future chronic heart failure in these patients [3, 32, 33].

Our study has some limitations. This single center retrospective observational study carries all the inherent limitations of retrospective research. The possibility to conduct a prospective study on the incidence of acute cardiovascular events has been and is still very limited. Nevertheless, the parameters analyzed in our study are all part of clinical routine and have been collected the same manner for years. Moreover, we closely assessed the patients admitted to our hospital with STEMI during the analyzed periods and similar routine procedures were applied in both groups. Thus, we believe that not a single event in the pre-pandemic as well as in the pandemic period has been missed.

5. Conclusion

In summary, these findings confirm and extend results from previous reports of delayed medical

consultation of patients with STEMI during the SARS-CoV-2 pandemic and concomitant public restrictions resulting in adverse effects on clinical course and outcome of these patients. Further studies should focus on causes of delayed medical treatment and their long-term effects in these patients. From a public health, perspective strategies are needed to maintain public awareness for life-threatening diseases such as acute coronary syndromes to ensure adequate and timely medical care for all patients in order to prevent additional excess morbidity and mortality not caused by COVID-19 itself.

Declarations

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Declaration of conflicting interests

None

Ethics approval

The study complies with the Declaration of Helsinki and was approved by the local ethics committee (number of application and positive vote 130/20).

Availability of data and material

The data underlying this article will be shared on reasonable request to the corresponding author.

Author contributions

Michael Baumhardt: Conceptualization, Methodology, Validation, Data Curation, Writing – Original Draft, Writing Review & Editing, Visualization Manuel Rattka: Conceptualization, Methodology, Validation, Data Curation, Writing Review & Editing Jens Dreyhaupt: Formal analysis, Validation, Writing – Review & Editing Kevin Thiessen: Writing – Review & Editing Sinisa Markovic: Data Curation, Investigation, Writing – Review & Editing Dominik Buckert: Data Curation, Investigation, Writing – Review & Editing Johannes Mörike: Data Curation, Investigation, Writing – Review & Editing Leonhard Schneider: Data Curation, Investigation, Writing – Review & Editing Birgid Gonska: Data Curation, Investigation, Writing – Review & Editing Dominik Scharnbeck: Data Curation, Investigation, Writing – Review & Editing Alexander Pott: Data Curation, Investigation, Writing – Review & Editing Mirjam Keßler: Data Curation, Investigation, Writing – Review & Editing Tillman Dahme: Data Curation, Investigation, Writing – Review & Editing Wolfgang Rottbauer: Conceptualization, Supervision, Funding acquisition Armin Imhof: Conceptualization, Methodology, Validation, Data Curation, Writing – Original Draft, Writing Review & Editing, Supervision, Funding acquisition

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Supplementary Appendix

	Pre-pandemic Cohort (21.11.2019 to 20.03.2020)	**First month of pandemic cohort (21.03.2020 to 20.04.2020)**
No. of daily STEMI admissions	0.508	0.548
Daily incidence rate ratio (95% CI)	1.08 (0.63 – 1.85)	
p-value	0.78	

STEMI, ST elevation myocardial infarction

Table 4: Poisson regression analysis of daily STEMI admissions in pre-pandemic versus first month of the pandemic period.