

## Indirect Effect of the COVID-19 Outbreak in Germany North Rhine Westfalia: Fewer Patients with Acute Coronary Syndrome?

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### Abstract

**Background:** After carnival North-Rhine Westphalia (NRW) developed into a hot spot for COVID-19 in Germany. To increase hospital capacities for treatment of COVID-19 patients the federal ministry of health issued a decree to postpone all elective interventions in German hospitals on the 16<sup>th</sup> of March. This study evaluates the impact of the COVID-19 outbreak on acute coronary syndrome (ACS) admissions and presentation in a tertiary care center in NRW.

**Methods:** Consecutive patients with ACS were assessed during the COVID-19 outbreak from January 2020 to the 30<sup>th</sup> of April 2020. The data were compared to ACS patients treated during the same time period in 2018 and 2019.

**Results:** In the respective first 4 months of 2020 (n=86), 2019 (n=130) and 2018 (n=101) fewer ACS patients were treated in our hospital. More ACS patients had a total ischemic time of > 6 hours in 2020 than in 2019 and 2018 (44% versus 31% and 29%; p= 0.04). Patient demographics and procedural characteristics did not differ for the respective groups. In-hospital mortality was not different for the respective time periods (3%, 6% and 10%; p=0.22).

**Conclusions:** The COVID-19 outbreak in NRW resulted in a decrease in admissions of ACS as compared to the years 2018 and 2019. Furthermore, the number of ACS patients with a total ischemic time of > 6 hours was significantly higher during the COVID-19 outbreak than in the previous years. Health care providers and physicians should be aware of the indirect effects of the COVID-19 pandemic on ACS.

**Abbreviations:** ACS: Acute coronary syndrome; COVID-19: Coronavirus disease 2019; NRW: North Rhine Westphalia; STEMI: ST-segment-elevation myocardial infarction

**Keywords:** COVID 19; SARS-COV-2; Acute coronary syndrome

## Introduction

Acute coronary syndrome (ACS) is a serious disease with high morbidity and mortality if not treated rapidly and adequately. Previous studies have shown that guideline-directed treatment with early invasive therapy improves outcomes in patients with ACS [1]. In December 2019 SARS-COV-2 emerged in China, Wuhan, spreading quickly over the world causing a pandemic within a few months. As a consequence, health governments were obliged to establish strict measures to control further spreading of the disease.

On the 22nd of February, the first European dies of Coronavirus disease 2019 (COVID-19). At the end of February, COVID-19 infections increase significantly in North-Rhine Westphalia (NRW) after a carnival session in Heinsberg. NRW develops into a hot spot of COVID-19 in Germany. On the 29<sup>th</sup> of February, an elementary school in Bonn is closed due to two known COVID-19 infections of teachers. On the 9<sup>th</sup> of March, the first two Germans die in NRW. Exit restrictions are issued by the government of NRW on the 15<sup>th</sup> of March. The federal ministry of a health issue a decree to postpone all elective interventions or surgery in German hospitals on the 16<sup>th</sup> of March.

Recently, Tam et al. reported the impact of the COVID-19 outbreak in Hongkong in 7 patients with ST-segment-elevation myocardial infarction (STEMI) and compared the results to data from 2018 and 2019. The authors of that study found that the time from symptom onset to first medical contact increased sharply from 83 minutes to 318 minutes in 2019 [2]. Another study from Austria reported the number of ACS admissions between the 2<sup>nd</sup> and 29<sup>th</sup> of March during the COVID-19 outbreak in Austria. The authors found both a decrease of STEMI as well as non-STEMI admissions during this time period [3].

The aims of our study were to evaluate the impact of the COVID-19 outbreak in the Rhein-Sieg area with respect to the rate of ACS admissions, outcome, and procedural characteristics of patients with ACS.

## Methods

### Patients

The 'GFO Kliniken Bonn' is a tertiary care center and is part of a network of clinics treating ACS patients in the Rhein-Sieg area of NRW. The clinic has a certified chest pain unit and treats ACS patients in a regional network of 6 hospitals belonging to a group of hospitals since 2009. The cardiac catheter laboratory is operational for 24 hours / 7 days. During the COVID-19

outbreak, the chest pain unit remained continuously open. Night and weekend shifts were doubled to provide sufficient staff for potentially treating COVID-19 patients.

To enhance the quality of care, consecutive patient data are documented in a central data bank. The data include demographics of the patients, physical findings, risk factors, laboratory values, procedural characteristics, and outcome data. Patients gave written informed consent to provide data for quality control and publications.

Criteria for myocardial infarction were derived from the fourth universal definition of myocardial infarction [4].

High sensitivity cardiac troponin I levels were measured at admission to the hospital. If the patient was directly transferred to the cardiac catheterization laboratory, blood samples were taken at the beginning of the study.

The total ischemic time (time from symptom onset to first coronary artery balloon inflation) was documented according to ACCF/AHA task force on clinical data standards using a structured interview with the patient after the index event. The ACCF/AHA defines the time of symptom onset as the time when the patient first notes ischemic symptoms lasting 10 minutes or longer. These symptoms may include chest pain or pressure, shortness of breath, jaw or arm pain, nausea/vomiting, fatigue/malaise, or other symptoms of discomfort. If the patient has intermittent symptoms, the time of the most recent symptoms before hospital presentation is used. If symptoms are initially varying in quality or intensity (stuttering), the time of symptom onset is defined as the time when symptoms become constant [5].

An echocardiogram was obtained within 2 days of admission and the ejection fraction (EF) measured using a Vivid E9™ or Vivid S70 GE™ machine (Milwaukee, USA) using either the auto EF function of the machine or biplane determination of the EF.

The primary endpoint of this study was the number of ACS admission and the total ischemic time.

### Statistics

Statistics of continuous variables are presented as means  $\pm$  standard deviation, categorical variables are shown as absolute numbers and percentages. Student t-tests were used for testing of continuous variables. For more than two groups simple linear models (ANOVA) or the Kruskal-Wallis-test were used. Fisher exact test was used to assess differences in categorical variables. Statistical significance was considered as a 2-tailed probability

value <0.05. Statistical analyses were performed with SPSS version 26 and STATA version 14.2.

## Results

### Patient demographics

Table 1 provides the demographics of the ACS patients treated in 2018, 2019, and 2020 during the first four months of the respective year. There was no difference with respect to age, heart rate, blood pressure, BMI, risk factors, type of myocardial infarction (STEMI and NSTEMI), anterior or posterior wall myocardial infarction between groups.

However, the number of patients presenting with ACS was lower in 2020 as compared to both 2019 and 2018. The respective rates of daily admissions for patients with ACS were 0.84 for 2018, 1.08 for 2019, and 0.71 for 2020 ( $p < 0.05$ ). Importantly, the number of ACS patients increased from 2018 to 2019, before falling in 2020.

There were only two patients with known COVID-19 infection during the observation period. One patient had a STEMI and the other patient NSTEMI.

Furthermore, the number of patients with a total ischemic time > 6 hours was significantly longer in ACS patients during the COVID-19 outbreak in 2020 as compared to the years 2018 and 2019.

### Procedural characteristics

Table 2 provides the procedural characteristics of the patients. All patients underwent successful cardiac catheterization. Mortality, GRACE score, duration of the procedure, fluoroscopy time, and amount of contrast agent were not different between groups.

## Discussion

The major finding of our study is that during the COVID-19 outbreak in NRW, Germany, the rate of admission of patients with ACS was significantly lower than in 2018 (-15%) and 2019 (-34%). Our findings are in concordance with a report from Austria, which showed a 39% decrease of ACS admission from the first to the last week in March 2020 [3]. A French study compared the daily rate of admissions of ACS patients to intensive care units between the period before and after containment measures. They found a decrease from 4.8 to 2.6 patients per day (minus 46%) during the containment period [6].

Similarly, we observed a decrease in the daily rate of admissions of ACS patients from 2019 to 2020 of 37%.

Importantly, the total ischemic time, i.e. time of symptom onset to first coronary artery balloon inflation, was significantly longer during the COVID-19 outbreak in our hospital. Tam et al. reported of 7 consecutive patients with STEMI treated during the COVID-19 outbreak in Hong Kong, China. The authors of that study also found numerically longer median times in symptom onset to first medical contact [2].

There are several potential explanations for the findings of our study. Symptoms may be ignored or trivialized by the patient because of anxiety to achieve medical treatment risking a SARS-COV-2 infection. General practitioners may be more difficult to contact due to the high workload during the outbreak of COVID-19. Furthermore, the emergency number may be more difficult to reach.

Another potential explanation is the prolongation of the ischemic time due to delayed referral of ACS patients from referring hospitals. However, referring hospitals had increased capacities during the COVID-19 outbreak because of the government decree to reduce elective surgery and interventions. Nevertheless, physicians in referring hospitals may have dedicated more time to treating COVID-19 patients than other patients and, potentially, may have misinterpreted symptoms of the patients and hence delayed diagnosis and referral.

A reduced capacity of our chest pain units for treating ACS patients could be another explanation for our findings. However, the capacity of our chest pain unit was unchanged during the COVID-19 outbreak. Furthermore, the chest pain unit of our hospital was intentionally not signed off or used as an additional COVID-19 unit during the COVID-19 outbreak in order to ensure the treatment of ACS patients.

The mortality of untreated ACS is high, therefore the reduction in ACS admissions could result in increased mortality of untreated ACS during the COVID-19 outbreak [7].

Our study found no difference in-hospital mortality for ACS patients between 2018, 2019, and during the COVID-19 outbreak. However, the numbers are too low to detect statistically relevant findings. The results of our study are in concordance with another study in Hong Kong, who did not find a difference in-hospital mortality during the COVID-19 outbreak [8]. However, the latter study found an increase in the compound endpoint of cardiogenic shock, mechanical circulatory support, ventricular arrhythmia and in-hospital death during the COVID-19

Baseline Characteristic of patients with acute coronary syndrome				
	2018 n=101	2019 n=130	2020 n=86	P value
Age	66.4±12.8	66.4±12.2	68.1±12.1	0.57
Age > 75 years, n (%)	28 (27.7)	37 (28.4)	30 (34.9)	0.52
Male sex, n (%)	73 (72.3)	95 (73.1)	59 (68.6)	0.77
BMI	29.2±5.7	28.0±4.5	28.0±4.6	0.26
Current Smoking, n (%)	50 (49.5)	65 (50.0)	44 (51.2)	0.98
Hypertension, n (%)	73 (72.3)	90 (69.2)	61 (70.9)	0.93
Hypercholesterolemia, n (%)	45 (44.6)	57 (43.8)	20 (23.3)	0.002
Diabetes mellitus, n (%)	21 (21.0)	31 (23.8)	19 (22.1)	0.85
Peripheral artery disease, n (%)	13 (12.9)	5 (3.8)	7 (8.1)	0.04
Chronic renal insufficiency				
Previous myocardial infarction, n (%)	12 (11.9)	18 (13.8)	10 (11.6)	0.85
Previous PCI, n (%)	16 (15.8)	29 (22.3)	14 (16.3)	0.37
Previous coronary artery bypass grafting, n (%)	3 (3.0)	5 (3.8)	6 (6.7)	0.42
Troponin I	557 (62 - 7050)	423 (54 - 4150)	325 (75 - 1497)	0.21
Creatinine	1.0±0.5	1.0±0.3	1.0±0.4	0.65
Creatinine clearance	77±24	78±23	77±24	0.93
Low-density lipoprotein cholesterol	133±44	131±48	183±53	0.63
Hemoglobin	13.6±1.9	13.6±1.9	13.9±1.8	0.41
Hematocrit	41±5.4	40.0±5.5	41.5±5.2	0.10
ST-segment elevation myocardial infarction, n (%)	58 (57.4)	66 (50.8)	42 (48.8)	0.50
Non-ST- segment elevation myocardial infarction, n (%)	43 (42.6)	63 (48.5)	43 (50.0)	0.50
GRACE-Score	151±46	147±40	142±44	0.37
GRACE-score < 109	20 (19.8)	13 (10.0)	14 (16.3)	0.11
GRACE-score 109 - 149	31 (30.7)	64 (49.2)	43 (50.0)	0.06
GRACE-score >149	50 (49.5)	52 (40.0)	29 (33.7)	0.09
Number of affected Vessels, n (%)				
1	33 (32.7)	46 (35.4)	27 (31.4)	0.73
2	38 (37.6)	48 (36.9)	30 (34.9)	0.89
3	30 (29.7)	32 (24.6)	29 (33.7)	0.42
Left ventricular ejection fraction	50±11	51±12	48±11	0.17
Time from Symptom onset to index PCI, N (%)				
≤6	70 (69.3)	93 (71.5)	48 (55.8)	0.04
>6	31 (30.7)	35 (28.5)	37 (44.2)	0.04

**Table. 1** Baseline Characteristics

<b>Tab. 2 Procedural characteristic of patients with acute coronary syndrome</b>				
	<b>2018</b>	<b>2019</b>	<b>2020</b>	<b>P-value</b>
	<b>n=101</b>	<b>n=130</b>	<b>n=86</b>	
Arterial Access, n (%)				
femoral	99 (98.0)	81 (62.3)	39 (45.3)	<0.001
radial	2 (2.0)	46 (35.4)	47 (54.7)	<0.001
Stent in culprit lesion	98	127	85	0.93
Length of procedure	63±30	56±25	63±29	0.14
The total dose of contrast material	190±67	1778±67	191±67	0.16
The total duration of fluoroscopy	11.3±8.6	11.0±8.4	11.9±6.9	0.74
Mortality				
In-hospital mortality, n (%)	10 (9.9)	8 (6.2)	3 (3.5)	0.22
Medication at discharge, n (%)				
Aspirin	97 (96.0)	124 (95.4)	84 (97.7)	0.92
Ticagrelor	83 (82.2)	103 (79.3)	74 (86.0)	0.50
Prasugrel	1 (1.0)	4 (3.1)	2 (2.3)	0.56
Clopidogrel	12 (11.9)	19 (14.6)	8 (9.3)	0.52
Beta-blocker	88 (87.1)	104 (80.0)	70 (81.4)	0.21
Angiotensin-converting enzyme inhibitor	68 (67.3)	88 (67.7)	57 (66.3)	0.94
Angiotensin-receptor blocker	68 (67.3)	88 (67.7)	57 (66.3)	0.94
Statin	93 (92.1)	119 (91.5)	82 (95.3)	0.65

**Table. 2** Procedural characteristics

outbreak.

During the Covid-19 outbreak, only two patients with known SARS-COV-2 infections were treated in our center. One patient had STEMI and the other patient had NSTEMI. Our hospital did not decline patients with SARS-COV-2 infections. After two documented cases of SARS-COV-2 infection in Bonn, infection control measures were implemented in our hospital and in the catheter laboratory with full protective equipment for our staff as recommended by the Robert-Koch-Institute of Germany. Shifts for the emergency service in the cardiac catheterization laboratory were doubled to allow the optimal treatment of potentially infected patients. Our plan of action for treating ACS patients was communicated with referring centers, therefore, we do not believe that referring centers changed their collaboration with our center. Furthermore, regular training sessions for treating COVID-19 patients were performed in our center in conjunction with the emergency department.

Interestingly, the duration of the procedure, fluoroscopy time, and amount of contrast agent did not differ between the investigated periods in 2018, 2019, and 2020, indicating unchanged treatment standards during the COVID-19 outbreak.

Another interesting finding of our study is that neither gender nor age differed between the investigated periods. This is of importance since a previous study showed a sex difference in mortality following STEMI and stated that this phenomenon may be driven by prehospital delays in hospital presentation leaving women more vulnerable to prolonged untreated ischemia [9].

**Impact on daily practice:** During the COVID-19 outbreak in NRW the rate of ACS, admissions were significantly reduced as compared to previous years. Furthermore, the number of patients with a total ischemic time > 6 hours increased during the COVID-19 outbreak. Health care providers, physicians, and patients should be aware of those indirect effects of the COVID-19 outbreak on ACS patients.

## Limitations

Our study is a single-center study and hence may not reflect the findings in other centers. However, the number of patients included in the study is relatively large. Furthermore, increasing knowledge about the SARS-COV-2 virus and its treatment may change treatment options and may influence the treat-

ment of ACS patients. Rapid testing for SARS-COV-2 infections in cardiac catheterization and / or referring centers may also change treatment strategies and patient behavior. Hence, our data reflect current information in a rapidly changing situation.

### Contributorship statement

Guarantor of integrity of the entire study: HO and LB. Study concepts and design: HO, LB, and SS. Literature research: All authors. Clinical studies: all authors. Statistical analysis: HO. Manuscript preparation: HO, LB, AV. Manuscript editing: HO.

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