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Impact of COVID-19-related public containment measures on the ST elevation myocardial infarction epidemic in Belgium: a nationwide, serial, cross-sectional study

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ABSTRACT

Aims: The current study assessed the impact of COVID-19-related public containment measures (i.e. lockdown) on the ST elevation myocardial infarction (STEMI) epidemic in Belgium.

Methods and results: Clinical characteristics, reperfusion therapy modalities, COVID-19 status and in-hospital mortality of consecutive STEMI patients who were admitted to Belgian hospitals for percutaneous coronary intervention (PCI) were recorded during a three-week period starting at the beginning of the lockdown period on 13 March 2020. Similar data were collected for the same time period for 2017–2019. An evaluation of air quality revealed a 32% decrease in ambient NO₂ concentrations during lockdown (19.5 µg/m³ versus 13.2 µg/m³, $p < .001$). During the three-week period, there were 188 STEMI patients admitted for PCI during the lockdown versus an average 254 STEMI patients before the lockdown period (incidence rate ratio = 0.74, $p = .001$). Reperfusion strategy was predominantly primary PCI in both time periods (96% versus 95%). However, there was a significant delay in treatment during the lockdown period, with more late presentations (>12 h after onset of pain) (14% versus 7.6%, $p = .04$) and with longer door-to-balloon times (median of 45 versus 39 min, $p = .02$). Although the in-hospital mortality between the two periods was comparable (5.9% versus 6.7%), 5 of the 7 (71%) COVID-19-positive STEMI patients died.

Conclusion: The present study revealed a 26% reduction in STEMI admissions and a delay in treatment of STEMI patients. Less exposure to external STEMI triggers (such as ambient air pollution) and/or reluctance to seek medical care are possible explanations of this observation.

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STEMI; COVID-19; containment; pollution; PCI; mortality

Introduction

The rapidly evolving coronavirus disease 2019 (COVID-19) pandemic is placing an overwhelming burden on health care systems and authorities [1]. To mitigate the spread of the virus and gain control of the chains of transmission of the epidemic, governments are taking compulsory measures to restrict all kinds of congregation and ensuring the supply of living resources

[2]. In addition to social distancing interventions, such as closures of schools and banning of all socio-cultural events, an increasing number of businesses and companies have asked their employees to work remotely. People are forced to stay at home and restrict their movement to only essential activities. Simultaneous with these public measures, hospitals established effective systems for triage and essential care in

emergency units and wards, including patient separation and staff safety [3].

Since the installation of these containment measures, anecdotal reports have emerged from local hospitals in areas hit by the COVID-19 disease showing a marked reduction (up to 40%) in the admissions of patients with acute coronary syndromes [4]. Press and editorial reports suggest that patients with chest pain were more reluctant to seek medical help because of their fear of hospitalisation and viral contamination. Other sources linked the drop in STEMI admissions to a reduction in air pollution. Tam et al. mentioned delays in the reperfusion treatment of their STEMI patients [5]. All of these reports reflect experiences from a limited number of centres and/or describe STEMI epidemics during the COVID break out period without appropriate controlled populations, and many of these thoughts and opinions are not supported by real facts. To better understand the impact of COVID-related containment measures on STEMI epidemics, we established a nationwide serial cross-sectional study in Belgium. Following the first contaminated patients, the Belgian government launched a lockdown on 13 March 2020. The present study analysed the epidemics of STEMI patients who were admitted during a three week period between 13 March and 3 April 2020, versus STEMI patients who were admitted during the same three-week period in 2017–2019. We also compared baseline characteristics, reperfusion treatment modalities and outcomes of STEMI patients admitted to Belgian hospitals and the levels of air pollution before and during the studied lockdown period.

Methods

Study population and data collection

The data were collected from consecutive STEMI patients between March 13th and April 3rd for the years 2017, 2018, 2019, and 2020. STEMI patients were defined as patients with symptoms suggestive of acute coronary syndromes (ACS) and with a significant ST-T segment deviation (i.e. an ST elevation of more than 0.1 mV in 2 or more continuous electrocardiogram (ECG) leads, a new left bundle branch block, or an ST segment depression of 0.1 mV or greater in 2 of the precordial leads V1–V4). Patient data for the period before lockdown (2017, 2018, and 2019) were extracted from the Belgian Coronary Stent Registry and the Belgian STEMI Database. The Coronary Stent Registry is a compulsory government-directed database linked to stent reimbursement, containing primarily data on stent material and procedural characteristics, including

indications for coronary stenting (e.g. primary PCI, PCI after thrombolysis, late PCI) and in-hospital complications, including mortality.

The Belgian STEMI database is a prospective, observational voluntary database containing the demographics, practice patterns and health outcomes of unselected patients with STEMI [6]. This database includes approximately 60% of all STEMI patients, and it is managed by an independent electronic data capture provider (Lambda-plus, Gembloux, Belgium). An external commission audited the data validity of 5% of the patient files. For the period of 2017–2019, the average concordance rate between source documents and database files was 95%. The database was approved by the Belgian Data Protection Agency and was registered on clinicaltrials.gov (NCT00727623). Informed consent was obtained from all patients or their legal representatives.

For the data during the lockdown period (2020), all Belgian PCI hospitals were contacted to provide aggregated data of the number of STEMI patients admitted for PCI, COVID-19 status and in-hospital mortality. Data were acquired from 36 of the 49 PCI-capable hospitals in Belgium. To allow accurate comparisons between study periods, data analyses of the pre-COVID period was restricted to these 36 PCI networks. Nineteen of the 36 PCI hospitals also provided data on baseline characteristics and treatment modalities at the patient level. These hospitals also participated in the Belgian STEMI database.

The following baseline characteristics were included in the STEMI database for each patient (15): age; gender; cardiac risk factors; history of coronary artery disease (CAD) or peripheral artery disease (PAD); presence of chronic kidney disease, defined as eGFR < 60 ml/min/1.73 m²; location of the infarction; Killip class and cardiac arrest at admission. The reperfusion strategy (primary PCI, PCI after thrombolysis, urgent coronary artery bypass grafting or no reperfusion therapy) were recorded as well as the time delay between the onset of pain and diagnosis, and the time delay between diagnosis and treatment, which was subdivided into diagnosis-to-balloon time (time between first ECG with STEMI diagnosis and balloon inflation) and door-to-balloon time (time between admission in the PCI centre and balloon inflation).

COVID-19 epidemics

Official data of COVID-19-related hospitalisations in Belgium were retrieved from the National Scientific Institution in the Epidemiology of Infectious Diseases

(Sciensano). Aggregated data of the COVID status of patients were available from 36 PCI networks. SARS-CoV-2 detection in respiratory specimens was performed using real-time reverse transcriptase–polymerase chain reaction assay (RT-PCR).

Environmental exposures

The pollutant concentration data used in this study were based on air quality measurements from three Belgian regions and compiled into a database from the Belgian Interregional Environment Agency (CELINE-IRCEL, <http://www.irceline.be>). Sixty-five automatic stations located across Belgium in urbanised and rural areas assessed PM10 concentrations, 38 stations assessed PM2.5, 41 stations measured O₃, and 93 stations assessed NO₂. Based on these air pollutant measurements and an interpolation method, a national daily 24-hour average was obtained for each pollutant after adjustment for population density [7]. Details of the interpolation method used in the present study were published previously [8]. Daily mean atmospheric temperature (in degrees Celsius) was obtained from the Royal Meteorological Institute of Belgium (RMIB).

Statistics

Continuous variables are presented as means with the corresponding standard deviation (SD) or as medians with interquartile range (IR). Comparisons between periods before and during the lockdown were made using Student's t-test or the Mann-Whitney test for variables with a skewed distribution (cf. time delays). Differences between proportions were assessed using chi-squared analyses. Comparison of environmental exposures across the different years were carried out with ANOVA. The incidence rate of STEMI was calculated from the number of STEMI patients admitted to the hospitals and the official population statistics of Belgium for the year 2018 (for the pre-COVID period) and 2020 (for the COVID period). The 36 PCI hospitals received 86% of all STEMI patients in Belgium in 2018. Therefore, a correction factor of 0.86 was used to determine the number of inhabitants in Belgium.

To describe the short-term effect of air pollution on STEMI, the odds ratio (OR)=1.051 per 10 µg/m³ increase of NO₂ was used as the exposure-response relationship [7].

The following equation was used to transform the odds ratio from 10 µg/m³ to the specific exposure OR (Equation (1)):

$$OR = e \times (\ln(OR_{10}/10 * \Delta NO_2))$$

where OR₁₀ is the OR per 10 µg/m³ increase and ΔNO_2 the decrease in the pollutant concentration. The population attributable fraction (PAF) was then calculated (Equation (2)) with the assumption of 100% exposure

$$((Pe = 1) : PAF = (Pe (OR - 1)) / (Pe (OR - 1) + 1))$$

For all analyses, a *p* value <.05 was considered statistically significant. All statistical analyses were performed using MedCalc Statistical Software version 13.0.6 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2014).

Results

COVID-19 epidemics in Belgium

Figure 1 shows the cumulative event rate of COVID-19-related hospitalisation (blue line) and COVID-related mortality (orange line) from 13 March 2020 until 3 April 2020 in Belgium. The hospitalisation rate due to infection outbreak followed the expected exponential trend and started to flatten 20 days later as a result of containment measures. By the end of the study period, a total of 7760 COVID-19-affected patients were hospitalised, and there were 1518 deaths related to COVID-19 disease.

STEMI epidemics, treatment modalities, COVID status and outcome

From March 13th until April 3rd, there were 188 STEMI patients admitted for PCI during the lockdown period versus an average of 254 patients before the lockdown period (see also Figure 2). These numbers correspond with incidence rates 19/100,000 inhabitants and 26/100,000 inhabitants, respectively, and a incidence rate ratio of 0.74 (*p* value = .001).

The baseline characteristics of STEMI patients before and during the lockdown period are detailed in Table 1. There were no significant differences, except for a higher prevalence of diabetes and chronic kidney disease, during the lockdown period.

Reperfusion strategy was predominantly primary PCI in both groups (96% versus 95%). PCI after thrombolysis was 2% in both study groups, and the proportion of patients without reperfusion therapy was comparable for both study groups.

The time delay between onset of pain and diagnosis was longer during the lockdown period compared to before lockdown (median 138 min (IQR 67-331) versus 114 min (IQR 50-240), *p* = .02). Late presentation (>12 h after onset) was observed in 14% during

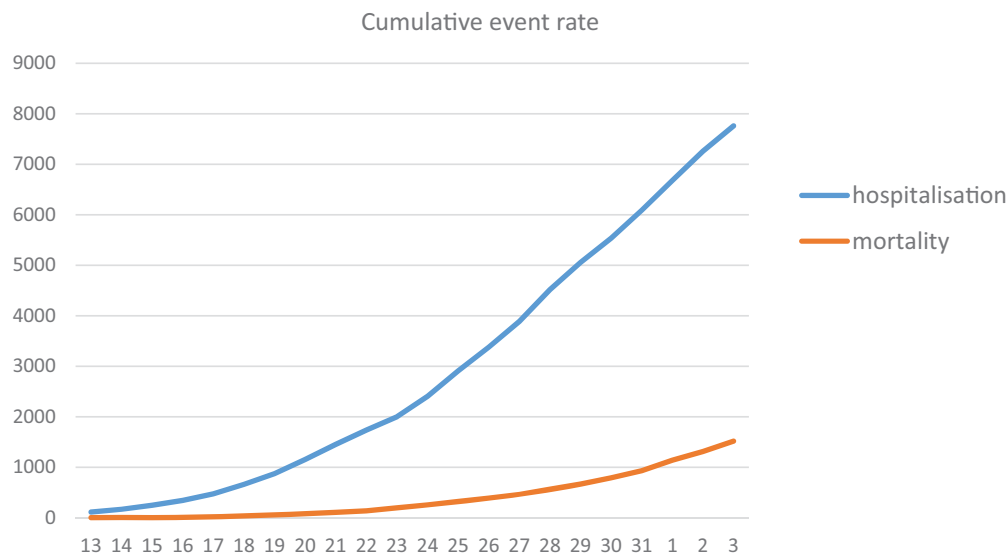


Figure 1. Figure showing the cumulative event rates of COVID-19-related hospitalisation (blue line) and COVID-related mortality (orange line) from 13 March 2020, until 3 April 2020.

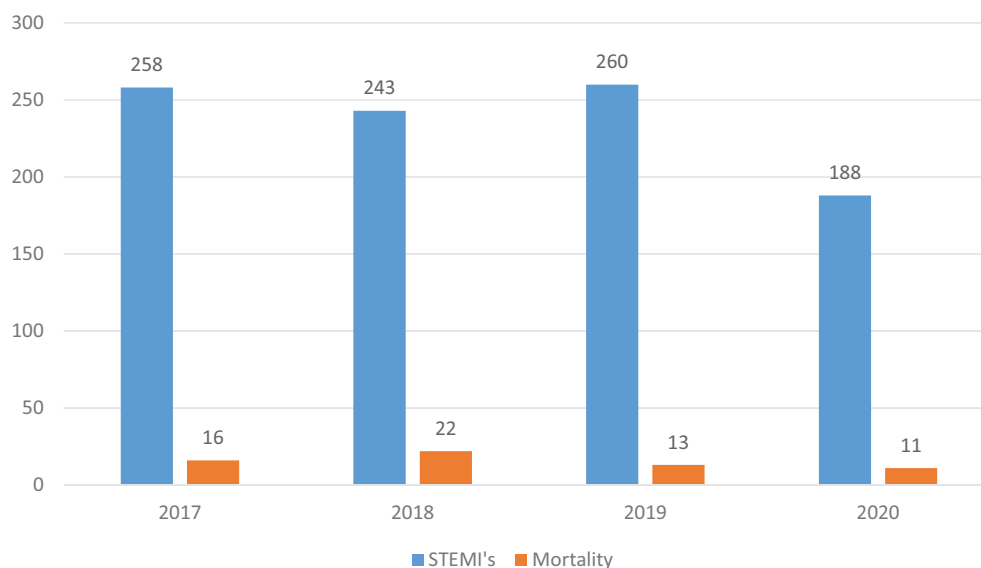


Figure 2. Bar graph showing the number of STEMI hospital admissions treated with PCI (blue bar) and the number of STEMI patients who died during the index hospitalisation from 13th March until 3rd April for the years 2017, 2018, 2019, and 2020.

lockdown versus 7.6% before lockdown ($p = .04$). The time delay between diagnosis and treatment was comparable between both study groups, but the door-to-balloon time was longer during the lockdown period (median of 45 min (IQR 30-83) versus 39 min (IQR 22-69), p value = .02).

Data from the 36 PCI networks revealed that 7 (3.7%) patients had proven positive COVID-19 status, 73 (39%) patients had proven negative COVID-19 status, and 108 (57%) patients did not undergo COVID-19 testing because of no clinical evidence of COVID 19 disease.

The average in-hospital mortality during lockdown was 5.8% (11/188) versus 6.7% (51/761) before lockdown ($p = .6$) (see also Figure 2).

During the lockdown period, the mortality of COVID-19-positive STEMI patients was 71%, (5/7) versus 3.3% (6/181) for the patients without evidence of COVID-19 infection ($p < .0001$).

Environmental exposures

Average data of ambient particle concentrations, NO₂ and O₃ and temperature during the study period for the different years are shown in Table 2. The average temperature was lower during the lockdown compared to before lockdown: 6.1 °C versus 7.6 °C ($p = .04$). No significant differences were noted across the different years for a particular matter, but there

Table 1. Clinical and procedural characteristics of the study populations.

	13/3-3/4 2017-18-19	13/3-3/4 2020	p Value
Number	479 (2017: 150, 2018: 152 2019: 177)	116	
Age	63 ± 15	63 ± 12	.7
Male, %	74	80	.2
Previous CAD, %	12	10	.4
Previous PAD, %	4	5	.7
Diabetes, %	15	27	.004
Arterial Hypertension, %	47	48	.8
Renal failure, %	6.5	12	.04
Killip class > 1, %	20	18	.7
Cardiac arrest, %	12	13	.7
Infarct location, %			
Anterior	45	47	.3
Non-anterior	54	51	
LiBB	1	3	
Reperfusion therapy:			.7
Primary PCI, %	95	96	
PCI after TT, %	2	2	
Urgent CABG, %	1	0	
no reperf. T, %	2	2	
Time onset to diagnosis, min	114 (IQR 50-240)	138 (IQR 67-331)	.02
Number with time >720 min, %	7.6	14	.04
Time diagnosis to balloon, min	72 (IQR 48-110)	76 (IQR 48-119)	.5
Time door-to-balloon, min	39 (IQR 22-69)	45 (30-83)	.02

Data are presented as means ± SD or medians (IQR: interquartile range).

Table 2. Temperature and air pollution levels from 13th March to 3rd April.

	2017	2018	2019	2020	p Value
Temp., °C	9.7 ± 2.2	5.2 ± 3.2	8.0 ± 1.7	6.2 ± 2.0	<.001
PM 2.5, µg/m ³	14.1 ± 6.6	13.1 ± 6.5	14.5 ± 9.4	12.5 ± 8.0	.8
PM 10, µg/m ³	21.7 ± 8.6	18.1 ± 6.9	21.6 ± 10.7	20.0 ± 11.0	.5
O ₃ , µg/m ³	48.9 ± 11.1	51.6 ± 9.8	54.0 ± 13.6	57.9 ± 10.7	.07
NO ₂ , µg/m ³	21.1 ± 7.4	18.6 ± 5.4	18.9 ± 7.5	13.2 ± 5.2	.001

Data are presented as means ± SD.

PM₁₀: particulate matter with aerodynamic diameter <10 µm; PM_{2.5}: particulate matter with aerodynamic diameter <2.5 µm; NO₂: nitrogen dioxide; O₃: ozone; Temp: temperature.

was a 32% decrease in ambient NO₂ concentrations during lockdown (19.5 µg/m³ versus 13.2 µg/m³, $p < .001$) and a mild increase of O₃ (51.5 µg/m³ versus 57.9 µg/m³, $p = .02$). Figure 3 illustrates the drop in ambient NO₂ concentrations during the lockdown, which was more pronounced during the week than during the week-end (p value <.001).

For a change in NO₂ concentration of 6.3 µg/m³, the expected calculated reduction of STEMI admission is 3.1% (or 8 patients).

Discussion

The present study described, for the first time at a national level, the impact of COVID-19-related containment measures on STEMI epidemics. We observed a 26% reduction in STEMI admissions and a delay in the

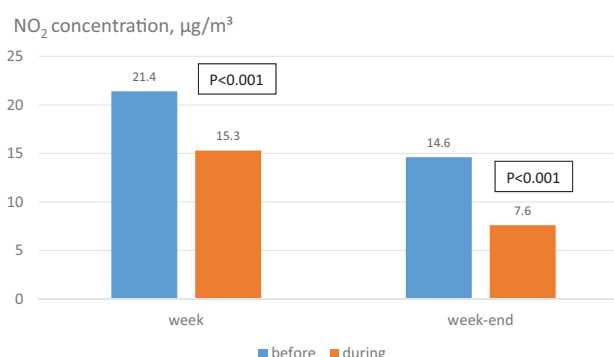


Figure 3. Bar graphs showing the average daily concentration of nitrogen dioxide (NO₂ µg/m³) during the week and week-ends from 13th March until 3rd April. The blue bars describe the level of air pollution before lockdown (average of 2017-2018-2019), and the orange bars represent the level of air pollution during lockdown (2020).

treatment of STEMI patients along with a reduction in air pollution (particularly NO₂) during the lockdown period compared to before the lockdown.

Acute myocardial infarctions (AMIs) are a leading cause of cardiovascular mortality and are usually precipitated by acute thrombosis induced by a ruptured or eroded atherosclerotic coronary plaque, which causes a sudden and critical reduction in blood flow [9,10].

Although the exact trigger is not always evident, previous epidemiological studies identified several factors associated with the onset of AMI, including heavy

exercise or physical exertion, diet, sexual activity, emotional stress, and environmental conditions [11–13]. Among the environmental conditions, air pollution (primarily particulate matter and NO₂), influenza epidemics, and temperature changes were the most frequently reported environmental triggers for AMI, with an effect occurring within days after the changing conditions [14–18]. Although the magnitude of the effect is relatively small at the individual level (e.g. 5–10% increase in AMI risk for 10°C temperature decrease and 1–5% increase in AMI risk for 10 µg/m³ particulate matter increase), the public health relevance is considerable because environmental triggers expose the entire population. During the lockdown period, exposure to environmental triggers was reduced because people had to stay at home, and travel was limited to essential activities. The lower levels of NO₂ most likely reflect the dramatic reduction of traffic in Belgium with a disappearance of traffic jams. Recent studies demonstrated that in areas with high use of diesel-fuelled cars, such as Belgium, short-term AMI risk exhibited a particularly tight correlation with NO₂ concentration (OR = 1.051 for 10 µg/m³ increase in NO₂) [7]. We have calculated that for the observed change in NO₂ concentration of 6.3 µg/m³, a 3% reduction of STEMI can be expected. So, reduced exposure to air pollution and ambient cold temperature may have resulted in less STEMI's and less STEMI admissions. The effect of stress was not measured in the present study, but positive stress factors (e.g. more leisure time, no traffic stress) may prevail in this early phase of the lockdown over negative stress factors (e.g. anxiety driven by job or health uncertainties) and may have prevented some new AMI's. Although difficult to estimate, it is reasonable to consider that less exposure to AMI triggers could explain up to one third of the observed reduction.

The reduction of STEMI admissions may also have been caused by fear of hospitalisation and viral contamination. The longer delay between onset of pain and diagnosis during the lockdown period may reflect the reluctance of patients to seek urgent medical help when they experienced chest pain. More restricted healthcare access may have caused an additional delay in the diagnosis. Although we did not show major differences in the patient profiles of the STEMI patients who were admitted before and during the COVID-19 crisis, more patients with heart failure due to late or untreated transmural infarctions may appear in the upcoming months. Primary PCI remained the most frequently used reperfusion treatment strategy, and its use was comparable with the period before

the lockdown. The high density of PCI-capable hospitals, the high capacity of hospital beds in Belgium and the cancellation of most elective cardiac programme, guaranteed sufficient capacity and resources to offer the best evidence-based care to our STEMI patients and obviated the need to switch to thrombolytic strategies, which was proposed by some organisations [18]. Despite the additional workload related to safety measures, the delay in treatment in the PCI hospital was only slightly longer during the lockdown period.

The overall reduction in STEMI's in the present study was lower than in most recent reports where an estimated reduction of 30–40% was observed [4,19,20,21]. The lower temperature during lockdown period compared to the control time periods may have attenuated the reduction of STEMI in our study. Differences in STEMI reduction may also be related to regional differences in public health systems and/or differences in population behaviour.

Only a minority (<5%) of the STEMI patients had a positive COVID test, which reflects the contamination level in Belgium at that time. No direct link has been established between COVID-19 infection and STEMI, but influenza-like illness are a well-known trigger for acute myocardial infarction [16,17]. Our study highlighted the infaust prognosis of STEMI patients with COVID-9 disease, but the numbers were small.

The results of the present study should be considered in the light of following limitations. No audit of the data could be performed during the lockdown period. However, in view of the positive audit reports in the period before COVID-19 crisis, the 2020 data are likely reliable moreover because we directly contacted the hospitals with an explanation of the project.

The observation period was short, and behavioural processes and quarantine measures will change with prolongation of the lockdown period. Therefore, a prolonged evaluation over many months is needed to fully understand the impact of the virus itself and subsequent behavioural changes on STEMI care and outcomes.

In conclusion, the dramatic containment measures used to reduce the transmission rate of the virus are associated with a 26% reduction of STEMI admissions. This observation is most likely but not exclusively the result of less exposure to external AMI triggers (e.g. ambient air pollution and cold weather) and/or avoidance and denial behaviour with fear of seeking urgent medical help when experiencing chest pain. Therefore, appropriate public campaigns are warranted to counterbalance the hospital avoidance behaviour of people during the COVID-19 pandemic and to mitigate collateral damage.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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