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Impact of the COVID-19 pandemic on acute coronary syndromes

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Summary

AIM: To assess the impact of the first wave of the COVID-19 pandemic on acute coronary syndromes and on the delay from symptom onset to first medical contact among patients presenting with ST-segment elevation myocardial infarction (STEMI), as well as to investigate whether there were patient-related reasons related to COVID-19 for delaying first medical contact.

METHODS AND RESULTS: All patients undergoing percutaneous coronary intervention (PCI) at the Geneva University Hospitals for acute coronary syndromes (ACS) during the first COVID-19 wave were compared with a control group consisting of all ACS patients who underwent PCI during the same period in 2019 and those treated in the period immediately preceding the pandemic. The primary outcome measure was the difference in the delay from symptom onset to first medical contact in the setting of STEMI between the COVID-19 period and the control period. Secondary outcome measures were the difference in ACS incidence and the impact of the COVID-19 pandemic on patients' decisions to call the emergency services, assessed using a questionnaire. Delay from symptom onset to first medical contact was longer among patients suffering from STEMI in the COVID-19 period compared with the control period (112 min vs 60 min, p = 0.049). The incidence rate of ACS was lower during the COVID-19 period (incidence rate ratio 0.6, 95% confidence interval [CI] 0.449–0.905). ACS patients delayed their call to the emergency services mainly because of fear of contracting or spreading COVID-19 following hospital admission, as well as of adding burden to the healthcare system.

CONCLUSION: We observed prolonged delays from symptom onset to first medical contact and a decline in overall ACS incidence during the first wave of the COVID-19 pandemic, with a higher threshold to call for help among ACS patients.

Keywords: *COVID-19, SARS-COV-2, acute coronary syndromes, STEMI, NSTEMI, delay*

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Introduction

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has been the cause of an unprecedented worldwide healthcare challenge. In early March 2020, the World Health Organization classified the disease as a pandemic [1] and strict social containment measures were implemented in most European countries to limit its spread [1]. On 13 March 2020, the Swiss Federal Council imposed nationwide measures to reduce the risk of COVID-19 transmission [2], including the cancellation of all non-urgent medical and surgical interventions [2]. Within Switzerland, the Geneva canton was among the most impacted by the disease [3].

The management of medical emergencies, such as ST-segment elevation myocardial infarction (STEMI), may have been affected at multiple levels by the COVID-19 pandemic, including an increase in patients' threshold to calling emergency medical services, decreased availability of ambulances, increased waiting time in the emergency departments, and time delay in percutaneous coronary intervention (PCI) due to the implementation of personal protective measures [4]. In addition, a decrease in hospital admissions for acute coronary syndromes (ACS) in regions highly affected by COVID-19 has been reported[5].

Therefore, we hypothesised that changes in the perception of urgent care during the COVID-19 pandemic increased the delay between symptom onset and first medical contact in patients with STEMI. Moreover, we wanted to investigate whether people's fear of getting infected or to inappropriately overloading the emergency departments would affect the decision to call emergency medical services during the first wave of the pandemic. Thus, we planned to assess whether the delay from symptom onset to first medical contact increased among patients treated for STEMI at the Geneva University Hospitals during the peak of the COVID-19 pandemic. In addition, we investigated whether there were COVID-19-related reasons for delaying first medical contact. Finally, we assessed whether there was a change in the incidence of ACS patients undergoing PCI during the first wave of the COVID pandemic.

Methods

Study design and patient population

The study was investigator-initiated and divided into two parts (fig. 1). The first part consisted of a retrospective analysis of inpatient data and the second part was an observational analysis using a questionnaire. The protocol was submitted and accepted by the local ethics committee.

All patients treated at the Geneva University Hospitals with PCI for ACS, as defined by European Society of Cardiology [6, 7], during one of the three periods of interest were included in the retrospective analysis (fig. 1). For the purpose of this study, the first wave of the COVID-19 pandemic, described hereafter as the COVID-19 period, was defined as the time from 13 March 2020 (the day on which the Swiss Federal Council imposed nationwide measures to be implemented to reduce the risk of transmission of this disease) to 30 April 2020, which corresponded to the end of the acute phase of COVID-19 hospitalisations. During this period, the prevalence of COVID-19 was at its highest, as were the social restrictive measures dictated by the Swiss Federal Council. As a consequence, all non-urgent medical and surgical interventions at Geneva University Hospitals were cancelled or postponed. The control periods were defined as the same period in 2019 (13 March to 30 April 2019) and a same length period immediately preceding the first diagnosed case of COVID-19 in Switzerland (7 January to 24 February 2020). Acute myocardial infarction incidence during these two time periods should not have been significantly impacted by seasonal variation as only a slight non-significant reduction in incidence between winter and spring is reported [8–10]. According to their clinical presentation, patients were divided into STEMI and non-ST-elevation ACS (NSTE-ACS).

Only patients included in the COVID-19 period who signed and returned the written informed consent form were included in the second observational part of the study (fig. 1).

Data collection

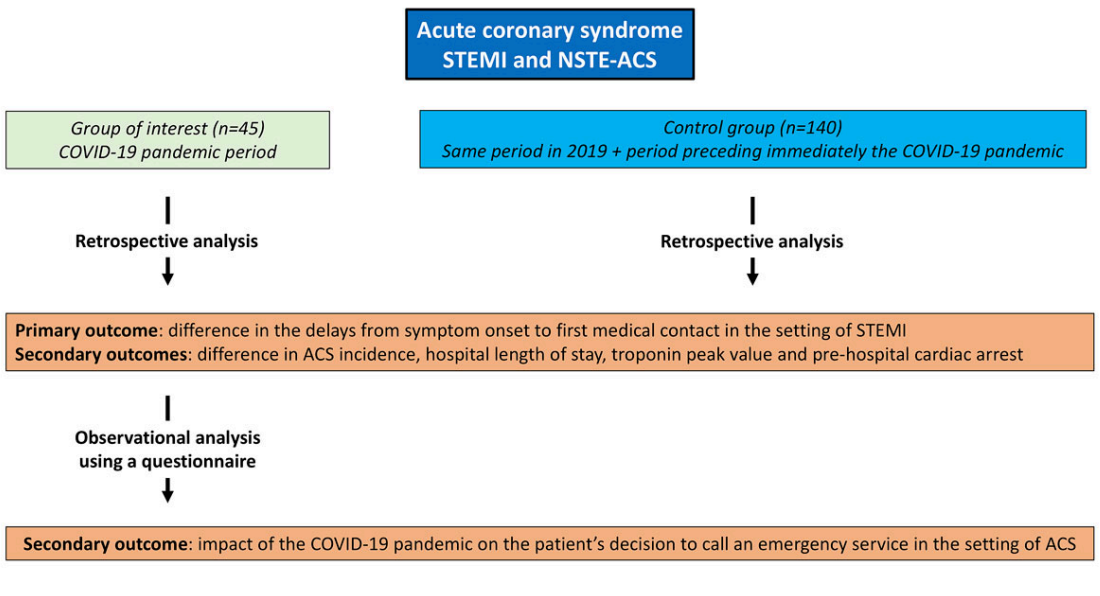
Baseline and study-related characteristics were retrospectively collected from the patients' hospital electronic medical records. Delays from symptom onset to first medical contact were derived either from the pre-hospital intervention forms or the emergency department medical records.

In order to assess the impact of the COVID-19 pandemic on the patient's decision to call an emergency service, we used a questionnaire (appendix 1) completed directly by the patient and addressing three main points:

- Did the patient suspect that symptoms were related to an acute myocardial infarction?
- Was the patient afraid that their hospital admission would increase the risk of a SARS-COV-2 infection or their spreading the disease to a relative?
- Did the patient experience symptoms of anxiety or depression during the seven days preceding the cardiac event that impacted the decision to call the emergency services?

Answers to the questions were rated according to the Likert scale to measure the degree to which patients agreed or disagreed with the statement. To quantify anxiety and depression, we used the validated Hospital Anxiety and Depression Scale (HADS) [11], referring to the seven days preceding the start of the ACS symptoms. Briefly, this score is composed of 14 questions separated into 7 questions related to anxiety symptoms and 7 questions to depression. For each of the two parts, patients with a score of less or equal to 7 points are considered as asymptomatic, between 8 and 10 points as borderline, and more or equal than 11 points as symptomatic. Patients who did not return the completed questionnaire after a delay of 4 weeks were

Figure 1: Study flowchart



ACS: acute coronary syndrome; COVID-19: coronavirus disease 2019; NSTE: non ST segment elevation myocardial infarction; STEMI: ST segment elevation myocardial infarction

contacted by telephone and encouraged to do so. Questions were not asked by telephone because the score has not been validated in that setting.

Outcome measures

The primary outcome measure was delay from symptom onset to first medical contact in the setting of STEMI during the COVID-19 period as compared with the control period. This delay was not assessed for NSTE-ACS patients because of the difficulty in determining symptom onset as well as the lack of impact of this parameter on outcomes in this patient population. Time from symptom onset to first medical contact was defined as the time of onset of chest discomfort or other ACS-related symptoms, as reported by the patient, to first medical contact. Based on this measure, STEMI patients were divided into early (<6 hours), delayed (between 6–12 hours) and late (>12 hours) presenters.

Secondary outcome measures included the difference in ACS incidence between the COVID-19 period and the control period, and the impact of the COVID-19 pandemic on the patient's decision to call emergency services, evaluated using the questionnaire described above. After excluding the patients who were transferred to another hospital following revascularisation or those presenting their highest troponin value in the initial blood sample, we also analysed the hospital length of stay and troponin peak value. Peak troponin value was defined as the maximum troponin value when this value was preceded and followed by a lower value. High sensitive cardiac troponin assays were used.

Statistical analysis

Normally distributed variables are presented as means ± standard deviations and differences compared using the Student's t-test. Non-normally distributed variables are presented as medians (interquartile ranges [IQRs]) and differences are compared using the Wilcoxon rank-sum test, as appropriate. Categorical data are expressed as numbers and frequencies (%) and compared using the Fisher's exact test or Pearson's chi-square test as appropriate. The incidence of ACS is presented as daily new admissions during the COVID-19 and control period and was calculated by dividing the number of ACS patients by the number of days in each period of interest. Incidence rates are expressed per 1000 person-years assuming a population of 500,000 inhabitants for Geneva. Incidence rate ratios were calculated between the active and the control period.

Results

Baseline characteristics

Of the 45 patients admitted for an ACS at the Geneva University Hospitals during the COVID-19 period, 20% were females; the mean age was 63.8 ± 9.2 years. Two thirds of the patients presented typical chest pain. Baseline characteristics are presented in table 1. There was no statistically significant difference in terms of baseline characteristics of ACS patients between the COVID-19 period (n = 45) and the control period (n = 140). The supplementary tables S1–S3 in appendix 2 present the control group divided into two periods comprising the same period in 2019 and the period immediately preceding the first case of COVID-19 in Switzerland.

Outcome measures

Results are for the entire ACS population as well as stratified according to STEMI or NSTE-ACS presentation (tables 2, 3 and 4). The median delay from symptom onset to first medical contact was significantly longer among patients suffering from a STEMI in the COVID-19 period than the control period (112 min vs 60 min, p = 0.049), with data available in 94.0% and 83.3% of the patients, respectively. Delayed (between 6 and 12 hours) or late (>12 hours) presentations were reported in 18.2% and 9% of patients in the COVID-19 and control periods, respectively (p = 0.3) (fig. 2). The incidence rate of ACS was lower during the COVID-19 period than the control period (0.7 vs 1.1 per 1000 person-years, p <0.01) with an incidence rate ratio of 0.6 (95% confidence interval [CI] 0.449–0.905). This difference was driven by lower incidence rates among NSTE-ACS patients (incidence rate ratio 0.324, 95% CI 0.160–0.601) during the COVID-19 period, with no difference in incidence rates among STEMI patients (incidence rate ratio 1, 95% CI 0.638–1.541).

We observed significantly more patients presenting with out-of-hospital cardiac arrest during the COVID-19 period compared with the control period (22.2% vs 7.1%, p <0.01). The median peak value of troponins in the overall ACS population was higher among patients in the COVID-19 period (data available for 73% of patients) than those in the control period (data available for 98% of the

Table 1: Baseline characteristics of all acute coronary syndrome patients. Values are presented as mean (± standard deviation) or number (percentage).

	COVID-19 n = 45	Pre-COVID-19 n = 140	p-value
Age	63.8 ± 11.6	68.0 ± 13.9	0.07
Female	9 (20.0)	35 (25.0)	0.5
BMI	26.9 ± 3.8	26.4 ± 4.6	0.6
Smoking (past or active)	17 (37.8)	50 (35.7)	0.8
Diabetes	10 (22.2)	44 (31.4)	0.2
Hypertension	18 (40.0)	76 (54.3)	0.08
Dyslipidaemia	12 (26.7)	58 (41.4)	0.08
Prior PCI	8 (17.8)	11 (7.9)	0.06
Prior CABG	1 (2.3)	1 (0.7)	0.4
Typical chest pain	29 (65.9)	105 (75.0)	0.2
SARS-CoV-2 tested/positive	32 (71.1)/4 (8.9)	-	-

BMI = body mass index; CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

patients) (2247 ng/l, IQR 975–5200 vs 1076 ng/l, IQR 402–3799, p = 0.02), mostly driven by a significant difference in the NSTEMI patients (1137 ng/l, IQR 764–2090 vs 502 ng/l, IQR 213–1059, respectively, p = 0.02).

Among surviving ACS patients of the COVID-19 period, 18 (43%) returned the questionnaire and signed the written informed consent form. Eleven (61% of the respondents) did not recognise their symptoms as those of an acute myocardial infarction. None of the patients reported difficulty in reaching their family doctor as a cause of delaying their medical care. Six patients (33%) delayed their call to the emergency services because of fear of contracting or spreading the COVID-19 or fear of adding additional work to the healthcare system. Among them, four patients (22%) were afraid of contracting the SARS-COV-2 and four (22%) were afraid of spreading the disease to a relative in the event of hospital admission. Five patients (28%) delayed their call to the emergency services because of fear of adding additional work to a healthcare system already burdened by the pandemic (fig. 3). The median HADS score was 3.5 (IQR 2.0–7.5) for anxiety and 3 (IQR 1.0–5.5) for depression. Among the respondents, 27.8% and 22.2% presented at the least borderline features of anxiety or depression, respectively (fig. 4). There was no difference between respondents and non-respondents in baseline characteristics (with the exception of significantly more diabetes in the non-respondent group) or in terms of time delays in STEMI patients, left ventricular ejection fraction, troponin peak value or hospital length of stay (tables S4 and S5 in appendix 2).

Among patients who spent the entire acute hospitalisation in our centre (78% and 95% in the COVID-19 period vs control period, respectively), hospital length of stay was statistically significantly shorter for the COVID-19 period as compared to the control period (6 vs 7 days, p = 0.03).

Discussion

The main findings of the present study are:

- The median time from symptom onset to first medical contact among patients with STEMI was almost two-fold longer during the COVID-19 period as compared with the control period
- The overall incidence rate of ACS undergoing PCI during the COVID-19 period was significantly lower, driven by three-fold lower incidence among NSTE-ACS patients in comparison with the control period whereas the STEMI incidence did not differ significantly.
- Approximately one third of the patients delayed their call to the emergency services because of fear of contracting or spreading the COVID-19 in the event of hospital admission, or fear of adding additional work to the healthcare system.
- ACS patients presented higher cardiac enzymes during the COVID-19 period as compared with the control period.

Table 2: Outcome measures in all acute coronary syndromes patients. Values are presented as medians (interquartile ranges), numbers (percentage) and ratios.

	COVID-19 n = 45	Pre-COVID-19 n = 140	p-value
LVEF (%)	55 (43–60)	50 (40–60)	0.70
Peak hs-cTn (ng/l)	2247 (975–5200)	1076 (402–3799)	0.02
Hospital LoS (days)	6 (5–7)	7 (5–11)	0.03
Out-of-hospital cardiac arrest	10 (22.2)	10 (7.1)	<0.01
Number of daily admissions	0.9	1.5	–
Incidence rate for 1000 person-years	0.7	1.1	<0.01

hs-cTn= highly sensitive cardiac troponin; LoS = length of stay; LVEF left ventricular ejection fraction

Table 3: Outcome measures in ST-segment elevation myocardial infarction patients. Values are presented as medians (interquartile ranges), numbers (percentage) and ratios.

	COVID-19 n = 33	Pre-COVID-19 n = 66	p-value
Symptom onset to first medical contact (minutes)	112 (16–211)	60 (20–165)	0.049
LVEF (%)	53 (37–59)	48 (40–58)	0.68
Peak hs-cTn (ng/l)	4102 (1684–6108)	3753 (1509–8960)	0.84
Hospital LoS (days)	6.5 (5–7)	7 (6–12)	0.02
Out-of-hospital cardiac arrest	9 (27.2)	9 (13.6)	0.10
Number of daily admissions	0.7	0.7	–
Incidence rate for 1000 person-years	0.5	0.5	1.0

hs-cTn = highly sensitive cardiac troponin; LoS = length of stay; LVEF = left ventricular ejection fraction

Table 4: Outcome measures in non-ST-segment elevation-acute coronary syndrome patients. Values are presented as medians (interquartile ranges), numbers (percentage) and ratios.

	COVID-19 n = 12	Pre-COVID-19 n = 74	p-value
LVEF (%)	58 (52–62)	55 (45–63)	0.42
Peak hs-cTn (ng/l)	1137 (764–2090)	502 (213–1059)	0.02
Hospital LoS (days)	5.5 (5–8)	7 (4–10)	0.42
Out-of-hospital cardiac arrest	1 (8.3)	1 (1.4)	0.11
Number of daily admissions	0.3	0.8	–
Incidence rate for 1000 person-year	0.2	0.6	<0.01

hs-cTn = highly sensitive cardiac troponin; LoS = length of stay; LVEF = left ventricular ejection fraction

– Significantly more patients presented with out-of-hospital cardiac arrest during the COVID-19 period as compared with the control period.

– The hospital length of stay was shorter during the COVID-19 period as compared with the control period.

Figure 2: Delay from symptom onset to first medical contact.

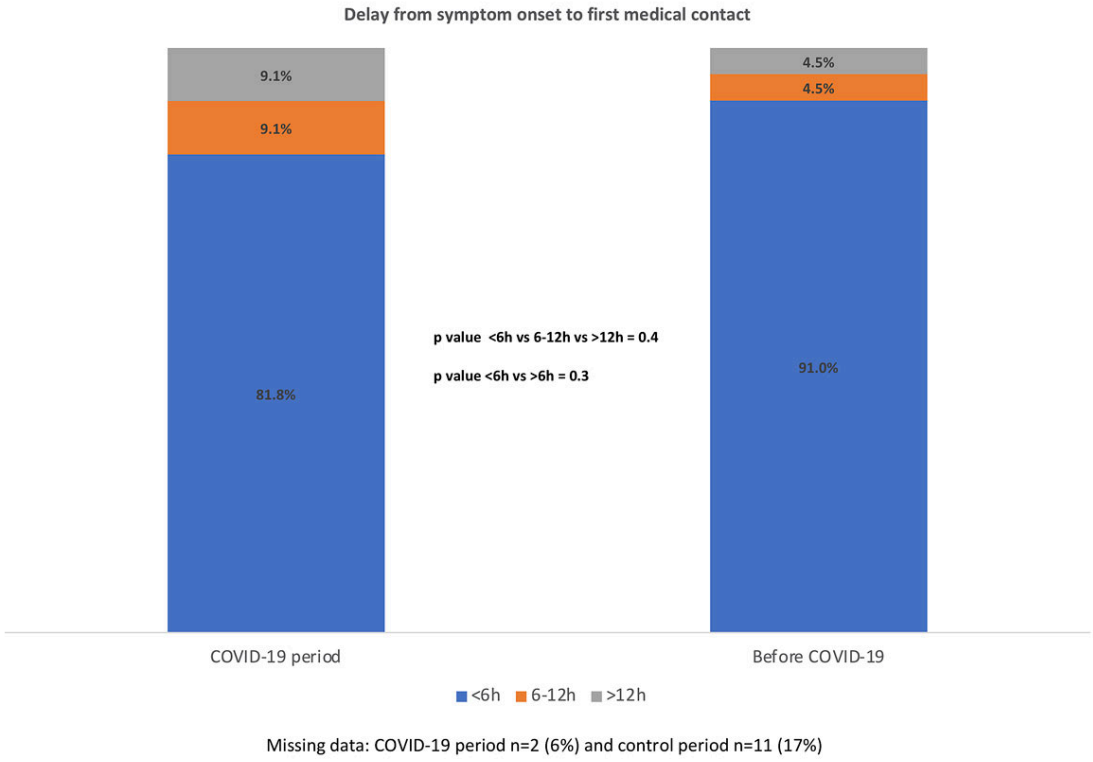
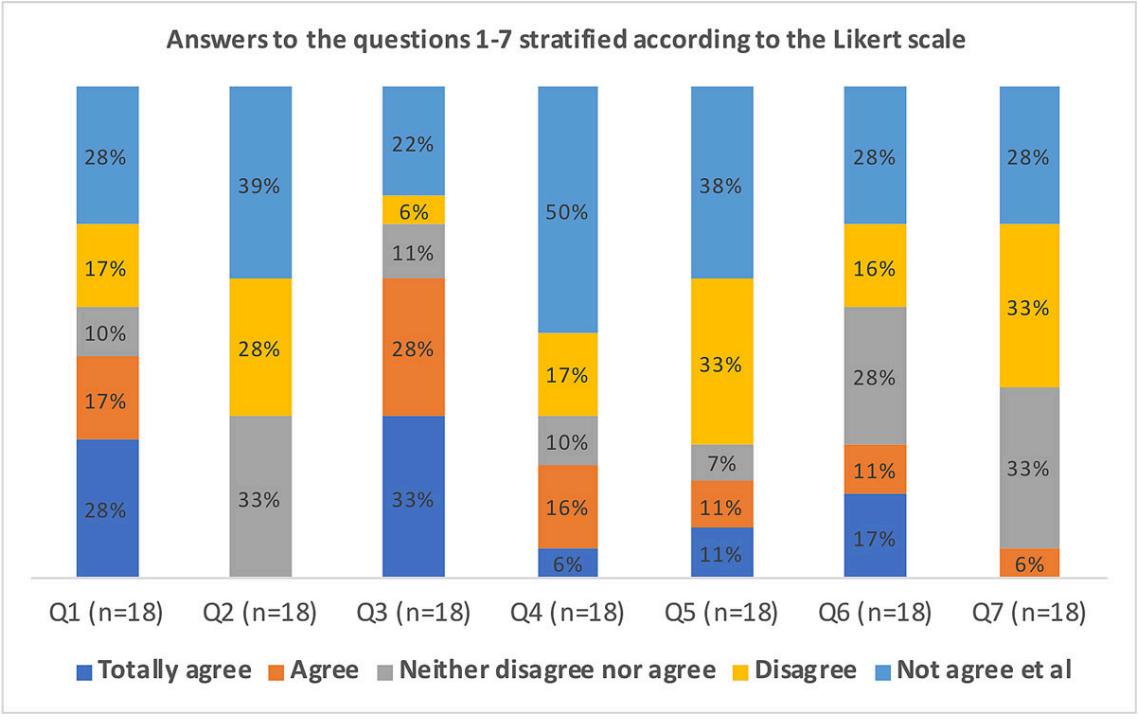


Figure 3: Answers to the questions 1–7 according to the Likert scale.



Timely myocardial revascularisation in the context of STEMI is one of the pillars of treatment to improve patient outcomes [7], and a prolonged time to hospital admission has been associated with increased in-hospital mortality [12]. Therefore, great efforts have been made to reduce as much as possible pre-hospital and intra-hospital delays by implementing locally validated STEMI protocols. Patient might contribute to increased pre-hospital delays as a result of lack of prompt recognition of symptoms or unwillingness to immediately seek medical help.

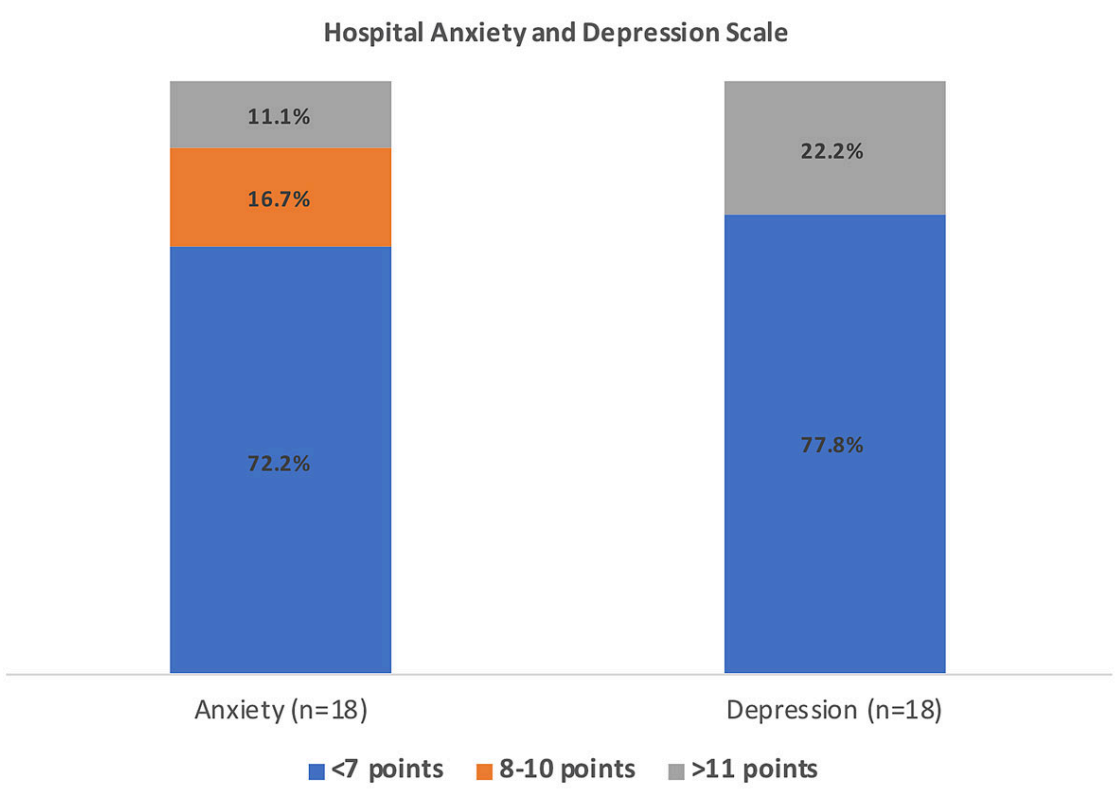
The impact of the COVID-19 pandemic on the delays from symptom onset to first medical contact remains poorly investigated. To date, limited data from single centres suggest prolonged delays from symptom onset to first medical contact in STEMI patients [13, 14]. We observed an almost doubled time from symptom onset to first medical contact during the COVID-19 pandemic as compared with the control period (112 min vs 60 min, $p < 0.05$).

Several reasons have been formulated to explain the prolonged delays during the COVID-19 pandemic, including the fear of getting or spreading the infection, unwillingness to overload the emergency medical systems or difficulty in getting a medical appointment [4]. However, to the best of our knowledge, objective questionnaire-based investigations of those delays have not been reported yet. In our study, the most prevalent reason for prolonged delays in calling the emergency services (58% of the respondents) was the misinterpretation of symptoms by the patients, even though two third of them presented typical chest pain. This might reflect either ineffective public health prevention messages or an altered patient behaviour driven by the COVID-19 pandemic. Other causes of prolonged delays identified were the fear of overloading a healthcare system already burdened by the pandemic (28% of respondents), as well as the fear of getting infected by the SARS-CoV-2 (22%) or contaminating relatives (22%) in the event of hospital admission. In addition, features of anxiety and depression, identified in approximately one quarter of the patients, may have contributed to patient-related delay.

Even though STEMI patients presented prolonged delays from symptom onset to first medical contact during the COVID-19 period, peak troponin and left ventricular ejection fraction were not different from the control group. This might be explained by the limited sample size. However, in the overall ACS population, driven by NSTE-ACS, we observed more extensive myocardial injury in the COVID-19 period as compared with the control period, with a two-fold higher high-sensitive cardiac troponin peak value (2247 ng/l vs 1076 ng/l, $p = 0.02$). This did not impact left ventricular ejection fraction, which remained similar in both groups probably as a result of the only modest, though significant from a statistical point of view, rise in high-sensitive cardiac troponins. In addition, we observed more ACS patients presenting with out-of-hospital cardiac arrest, possibly also reflecting more severe myocardial injury, even though the small number of events limits definitive conclusions.

Our results are in line with previous reports describing a significant reduction in ACS incidence during the COVID-19 pandemic [13, 15, 16], largely driven in our report by the fall in NSTE-ACS incidence (incidence rate ratio 0.324 for the COVID-19 period compared with the control period) whereas we did not find any significant reduction in STEMI incidence. A recent large analysis which

Figure 4: Hospital Anxiety and Depression Scale (HADS).



included data from all patients admitted for ACS in England, showed similar results. Even though authors reported an overall 40% reduction in ACS incidence during the COVID-19 period, they noticed an almost two-fold greater decline in NSTE-ACS incidence in comparison with STEMI incidence (percent reduction 42% vs 23%) [17]. The lack of reduction in STEMI incidence in our study needs, however, to be interpreted cautiously owing to the limited sample size. The proximity and accessibility of the emergency services in our relatively small district (15.93 km^2) might explain why patients with more severe symptoms (as is often the case during STEMI) were less reluctant to seek medical help.

Overall hospital length of stay for patients not prematurely transferred was shorter during the COVID-19 period than during the control period, likely because of the necessity to allow as many as possible hospital admissions for SARS-CoV-2 infected patients as our hospital was the designated COVID-19 hospital of the region.

For the ongoing second wave of the COVID-19 pandemic, reinforced health prevention campaigns would have been essential but did not occur. Public prevention messages should have raised awareness among the general population of the importance of rapidly seeking medical help in the case of ACS symptom onset despite the social restrictive measures.

The present study has several limitations. First, it was of single centre retrospective design with a limited number of patients included. Second, less than half of the eligible patients returned a completed version of the questionnaire. The extension of the results to the entire COVID-19 ACS population should thus be made with caution. Moreover, the results of the questionnaire were not compared between active and control groups. Third, peak troponin measurement and hospital length of stay were not available for a proportion of patients, as they were transferred early to other institutions to avoid saturation of our hospital.

In conclusion, during the COVID-19 period we observed prolonged delays from symptom onset to first medical contact in STEMI patients and a decline in overall ACS incidence driven by a lower incidence of NSTE-ACS patients. In addition, ACS patients presented with more extensive myocardial damage. Patient-related reasons for the increased delay in calling the emergency services included the fear of contracting or spreading COVID-19 in the event of hospital admission and reluctance to add additional burdens to the healthcare system. Public health campaigns should better address these issues for the potential next waves of the pandemic.

Disclosure statement

No financial support and no other potential conflict of interest relevant to this article was reported.

Data availability

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

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Appendix 1: Questionnaire

Questionnaire addressed to all surviving patients who presented an ACS during the COVID-19 period.

Appendix 2: Supplementary tables

Table S1: Baseline characteristics of the two control groups.

Table S2: Outcome measures in ST segment elevation myocardial infarction patients in the two control groups.

Table S3: Outcome measures in non-ST segment elevation myocardial infarction-acute coronary syndrome patients in the two control groups.

Table S4: Baseline characteristics of respondents and non-respondents to the questionnaire.

Table S5: Outcome measures among respondents and non-respondents to the questionnaire.

The appendices are available as separate files at https://smw.ch/article/doi/smw.2020.20448.