Influence of the First-wave COVID-19 Pandemic on Emergency Acute Coronary Syndrome: a Multicenter Retrospective Study From a Non-epicenter Region

Qi Mao
Xinqiao Hospital  https://orcid.org/0000-0002-6040-0116

Jian-Hua Zhao
Xinqiao Hospital

Jian-Fei Chen
People's Hospital of Banan District

Qiang Xu
the Fifth People's Hospital of Chongqing

Zhong-Lin Xu
the Nineth People's Hospital of Chongqing

Yang Yu
People's Hospital of Dianjiang District

Ying Zhang
Emergency Medical Center of Chongqing

Qiang Li
People's Hospital of Nanchuan District

Xiao-Hua Pang
the Three Gorges Central Hospital

Zheng-Gong Li
Zhongshan Hospital of Chongqing

Bo-Li Ran
Third Hospital of Chongqing

Zhi-Hui Zhang
Southwest Hospital

Zhi-Feng Li
Yongchuan Hospital of Chongqing Medical University

Chun-Yu Zeng
Daping Hospital

Shi-Fei Tong
the Third Affiliated Hospital of Chongqing Medical University

Jun Jin
Research

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Abstract

Background: The COVID-19 pandemic presented severe challenges to emergency practice of acute coronary syndrome (ACS). However, poor evidence was shown on ACS in a non-hot-spot region. We sought to clarify the influence of the first-wave COVID-19 pandemic on emergency ACS from a non-epicenter region.

Methods: This retrospective multicenter study was conducted in emergency ACS patients during the pandemic (from 2020-01-23 to 2020-03-29) and the ones during the same period in 2019. Clinical characteristics, timeline parameters and treatment strategies were compared between different groups. Association of the pandemic with non-invasive therapy was further assessed.

Results: Compared with 2019, ACS had a drop in admission (267 cases vs. 475 cases) and invasive therapy (140 cases vs. 318 cases). Also, process delays were detected including the period from symptom onset to first medical contact (S-to-FMC, 5h vs. 2.5h), the period from FMC to electrocardiogram (ECG) completed (8min vs. 4min) and the period from FMC to dual antiplatelet therapy (FMC-to-DAPT, 25min vs. 19min). Primary percutaneous coronary intervention (PPCI) decreased by 54.9% in STEMI and early invasive therapy decreased by 59.2% in NSTE-ACS. The proportion of invasive therapy in NSTE-ACS decreased more than in STEMI (16.9% vs. 10.1%) with longer process delay. The pandemic was associated with increased non-PPCI in STEMI (OR=1.707, 95%CI 1.082-2.692, P=0.021) and elevated medication in NSTE-ACS (OR=2.029, 95%CI 1.268-3.247, P=0.003), respectively.

Conclusion: Even in a non-epicenter region, the first-wave COVID-19 pandemic caused a significant reduction of invasive therapy and evident process delays in emergency ACS.

Introduction

Acute coronary syndrome (ACS) is one of the most common chest pain emergencies, including ST-segment-elevation myocardial infarction (STEMI) and non-ST-segment elevation acute coronary syndrome (NSTE-ACS) [1]. Prognosis of ACS is highly dependent on standard procedures for chest pain emergency including early transfer, prompt diagnosis, risk stratification and timely intervention [2]. Since the outbreak in December 2019, coronavirus-2019 disease (COVID-19) caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has rapidly spread to the worldwide and been a devastating viral pandemic [3, 4]. As of August in 2021, a total of more than 210 million cases have been diagnosed and approximately 4.4 million confirmed deaths [5]. The COVID-19 pandemic posed severe burden and challenges to emergency network and rescue procedure.

Reasonable medical responses between COVID-19 prevention and revascularization are critical for rescuing emergency ACS [6]. After the first-wave outbreak, the findings from Europe revealed that hospital admissions for all types of ACS decreased by approximately 40%, meanwhile numbers of PCI procedures had an estimated 30%-40% reduction [7, 8]. Similarly, the data from U.S. showed a 43.7% decline in hospitalizations during the first-phase pandemic [9]. Previous evidences about the impact of the
pandemic on ACS were still mostly concentrated in high-intensity epicenters [10]. However, poor evidence on clinical characteristics and intervention strategy remained for ACS in non-hot-spot regions; and fewer studies focused on the effect of the pandemic on non-invasive therapy in STEMI and NSTE-ACS, respectively. Moreover, it is also not clear that real profile of ACS emergency during the first-wave epidemic in the absence of mature experience.

**Methods**

**Study population**

This was a retrospective multicenter study with a total of 14 hospitals involved. The first-wave COVID-19 pandemic was defined as the period from January 23 to March 29 in 2020. On January 23 of Wuhan's lockdown, our city also raised local health response to curb the spread of the epidemic. During the pandemic, a total of 576 infection cases occurred in this region including 570 cured and 6 deaths; then public health response was downgraded on March 29 owing to complete clearance of infection cases (Figure 1). In our study, emergency ACS patients during the same period in 2019 were also included to reduce the confounding effect of seasonal alternation and holiday events. In addition, the patients with confirmed or suspected COVID-19 were excluded. Our study protocol complied with the Declaration of Helsinki and was approved by Xinqiao Hospital Ethics Committee, Army Medical University.

**Emergency procedure during the pandemic**

All emergency patients were screened for SARS-COV-2 according to Clinical Guideline of Diagnosis and Treatment (7th edition) [11]. Based on fever symptoms and epidemiological history, admitted patients were first assigned to emergency or fever clinics. With the assistance of COVID-19 expert team in hospital, the patients with confirmed or suspected COVID-19 would be transferred to the designated hospitals quickly. The patients without exclusion of COVID-19 temporarily would be transferred to special wards for isolation, and if further test was positive, they would be transferred to the designated hospitals as soon as possible. Whether to perform invasive therapy mainly depended on ischemic risk assessment and guideline recommendation [12, 13]. The flowchart of chest pain procedure was shown in Figure 2.

**Data collection and definition**

Clinical data were obtained from medical records by trained clinicians in each hospital and were verified by another two investigators. Clinical characteristics included demographic data, admission signs, arrival periods, transferred methods, chest pain timelines and treatment strategy. Diagnostic criteria of ACS refer to the definitions of European Society of Cardiology guidelines for NSTE-ACS and STEMI [14, 15]. Global Registry of Acute Coronary Events (GRACE) risk score is applied for prediction of risk in ACS and is calculated based on the clinical characteristics, electrocardiogram (ECG) performance and laboratory parameters at admission [16]. Transferred methods consisted of walk-in, in-hospital onset, emergency medical services and inter-facility transports; walk-in and in-hospital onset were deemed as non-transferred, while EMS and inter-facility transports were regarded as transferred. Chest pain timelines included the period from symptom onset to first medical contact (S-to-FMC), the period from FMC to
electrocardiogram completed (FMC to ECG completed), the period from door to troponin completed and the period from FMC to dual antiplatelet therapy (FMC to DAPT) [17]. The duration of early invasive therapy is within 24 hours.

**Statistical analysis**

Continuous variables are presented as mean ± SD for symmetric distributions and median (interquartile range, IQR) for skewed distributions. Categorical variables are expressed as frequency (percentage). For comparisons between groups, the *t* test was performed for symmetric distributed variables, and nonparametric Mann-Whitney U test was applied for skewed distributed variables. Differences in categorical variables were assessed by the Chi-squared test or Fisher exact test. Taking non-invasive therapy as the dependent variable, we conducted logistic regression analysis to evaluate the association of COVID-19 pandemic with non-invasive therapy, and then sub-group analysis was utilized to further examine this correlation. Two-tailed *P* values < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS software version 24.0 (SPSS, Inc, Chicago, Illinois).

**Results**

**Clinical characteristics and therapy strategies in emergency ACS**

A total of 742 emergency ACS patients with non-COVID-19 were enrolled in this study with 267 cases during the pandemic and 475 cases during the same period in 2019 (Table 1). Compared with 2019, ACS had a reduction in cases by 43.8% totally, while the cases of emergency STEMI and NSTE-ACS decreased by 47.8% and 38.1%, respectively. Moreover, there were no differences in admission signs, GRACE scores, arrival period and transferred method (P>0.05). Significant delays appeared in S-to-FMC (5.0h vs. 2.5h), FMC to ECG completed (8 min vs. 4min), door to troponin completed (13 min vs. 12min) and FMC to DAPT (25min vs. 19min) (P<0.05) (Table 1).
| Characteristics | From 2019-01-23 to 2019-03-29 (N=475) | From 2020-01-23 to 2020-03-29 (N=267) | P value |
|-----------------|--------------------------------------|--------------------------------------|---------|
| Age (years)     | 65 (56-75)                           | 67 (56-76)                           | 0.175   |
| Male, n (%)     | 346 (72.8)                           | 194 (72.7)                           | 0.957   |
| Heart rate (/min)| 78 (68-90)                           | 78 (68-90)                           | 0.317   |
| SBP (mmHg)      | 129 (115-148)                        | 132 (112-150)                        | 0.351   |
| DBP (mmHg)      | 78 (68-88)                           | 80 (69-90)                           | 0.207   |
| Killip class    |                                      |                                      |         |
| Killip class I, n (%) | 311 (65.5)                           | 177 (66.3)                           |         |
| Killip class II, n (%)  | 106 (22.3)                           | 55 (20.6)                            |         |
| Killip class III, n (%) | 26 (5.5)                             | 10 (3.7)                             |         |
| Killip class IV, n (%)  | 25 (5.3)                             | 24 (9.0)                             |         |
| Killip class ≥ II, n (%) | 159 (33.5)                           | 89 (33.3)                            | 0.969   |
| Scr (µmol/L)    | 74.0 (62.5-91.6)                     | 74.0 (62.0-95.0)                     | 0.824   |
| GRACE score in hospital | 140 (116-164)                        | 137 (116-162)                        | 0.515   |
| STEMI, n (%)    | 278 (58.5)                           | 145 (54.3)                           | 0.265   |
| Arrival during non-office hours, n (%) | 211 (44.4)                           | 115 (43.1)                           | 0.722   |
| Non-transferred patients, n (%) | 259 (54.5)                           | 164 (61.4)                           | 0.069   |
| S-to-FMC (hours) | 2.5 (1.5-4.0)                        | 5.0 (3.0-9.0)                        | <0.001  |
| FMC to ECG completed (min) | 4 (2-6)                             | 8 (5-15)                             | <0.001  |
| Door to Troponin completed (min) | 12 (11-14)                           | 13 (12-15)                           | 0.001   |
| FMC to DAPT (min) | 19 (17-22)                           | 25 (21-32)                           | <0.001  |

Data are expressed as median (interquartile range, IQR) or number (percentage) as appropriate. ACS: acute coronary syndrome; SBP: systolic blood pressure; DBP: diastolic blood pressure; Scr: serum creatinine; STEMI: ST-segment-elevation myocardial infarction; S-to-FMC: the period from symptom onset to first medical contact; ECG: electrocardiogram; DAPT: dual antiplatelet therapy.
Primary percutaneous coronary intervention (PPCI) decreased by 54.9% in STEMI and early invasive therapy decreased by 59.2% in NSTE-ACS after the outbreak. Further analysis revealed that delays of timeline parameters occurred in both STEMI and NSTE-ACS during the pandemic (P<0.05). As compared to 2019, the proportion of PPCI significantly declined in STEMI (69.0% vs. 79.1%, P<0.05); similar but more serious trend also appeared in early invasive therapy for NSTE-ACS (32.8% vs. 49.7%, P<0.05) (Table 2).
Table 2
Comparison of clinical characteristic for different emergency ACS types before and during the pandemic

| Characteristics | STEMI From 2019-01-23 to 2019-03-29 (N=278) | NSTE-ACS From 2020-01-23 to 2020-03-29 (N=145) | P value | STEMI From 2019-01-23 to 2019-03-29 (N=197) | NSTE-ACS From 2020-01-23 to 2020-03-29 (N=122) | P value |
|-----------------|---------------------------------------------|-----------------------------------------------|---------|---------------------------------------------|-----------------------------------------------|---------|
| Characteristics | (N=278)                                     | (N=145)                                       |         | (N=197)                                     | (N=122)                                       |         |
| Age (years)     | 64 (55-74)                                  | 65 (56-76)                                    | 0.442   | 67 (58-76)                                  | 68 (60-77)                                    | 0.338   |
| Male, n (%)     | 219 (78.8)                                  | 108 (74.5)                                    | 0.317   | 127 (64.5)                                  | 86 (70.5)                                     | 0.267   |
| Heart rate (/min) | 79 (70-92)                                  | 77 (65-90)                                    | 0.178   | 78 (67-90)                                  | 78 (69-90)                                    | 0.909   |
| SBP (mmHg)      | 122 (110-143)                               | 126 (109-150)                                 | 0.685   | 133 (120-152)                               | 135 (122-151)                                 | 0.661   |
| DBP (mmHg)      | 78 (68-88)                                  | 79 (66-92)                                    | 0.584   | 80 (69-88)                                  | 80 (70-89)                                    | 0.211   |
| Killip class I, n (%) | 174 (62.6)                                  | 91 (62.8)                                     |         | 137 (69.5)                                  | 86 (70.5)                                     |         |
| Killip class II, n (%) | 66 (23.7)                                  | 31 (21.4)                                     |         | 40 (20.3)                                   | 24 (19.7)                                     |         |
| Killip class III, n (%) | 14 (5.0)                                    | 3 (2.1)                                       |         | 12 (6.1)                                    | 7 (5.7)                                       |         |
| Killip class IV, n (%) | 23 (8.3)                                    | 21 (14.5)                                     |         | 2 (1.0)                                     | 3 (2.5)                                       |         |
| Killip class ≥ II, n (%) | 104 (37.4)                                  | 55 (37.9)                                     | 0.916   | 55 (27.9)                                   | 34 (27.9)                                     | 0.992   |
| Scr (µmol/L)    | 74.0 (63.0-91.8)                            | 73.0 (61.5-92.5)                              | 0.779   | 74.8 (62.0-91.0)                            | 75.0 (62.0-101.0)                             | 0.497   |
| GRACE score in hospital | 143 (121-169)                             | 143 (120-169)                                 | 0.961   | 134 (107-163)                               | 129 (110-153)                                 | 0.555   |
| Arrival during non-office hours, n (%) | 127 (45.7)                                  | 67 (46.2)                                     | 0.918   | 84 (42.6)                                   | 48 (39.3)                                     | 0.561   |
| Non-transferred patients, n (%) | 132 (47.5)                                  | 81 (55.9)                                     | 0.102   | 127 (64.5)                                  | 83 (68.0)                                     | 0.514   |

Data are expressed as median (interquartile range, IQR) or number (percentage) as appropriate. NSTE-ACS: non-ST-segment elevation acute coronary syndrome; PPCI: primary percutaneous coronary intervention.
|                          | STEMI                                | NSTE-ACS                           |
|--------------------------|--------------------------------------|------------------------------------|
| S-to-FMC (hours)         | 2.5 (1.5-4.0)                        | 4.5 (3.0-9.0)                      |
|                          | <0.001                               | 2.5 (1.7-4.0)                      |
|                          |                                      | 6.0 (3.0-10.0)                     |
| FMC to ECG completed (min)| 4 (2-6)                              | 6 (4-13)                           |
|                          | <0.001                               | 4 (3-6)                            |
|                          |                                      | 10 (7-15)                          |
| Door to Troponin completed (min)| 12 (11-15) | 13 (12-15)                           | 0.023|
|                          |                                      | 13 (11-14)                         |
|                          |                                      | 13 (12-15)                         |
| FMC to DAPT (min)        | 19 (17-22)                           | 24 (20-32)                         |
|                          | <0.001                               | 19 (17-22)                         |
|                          |                                      | 26 (22-33)                         |
| PPCI, n (%)              | 220 (79.1)                           | 100 (69.0)                         |
|                          | 0.021                                | -                                  |
|                          |                                      | -                                  |
|                          |                                      | -                                  |
| Thrombolysis, n (%)      | 11 (4.0)                             | 10 (6.9)                           |
|                          | 0.186                                | -                                  |
|                          |                                      | -                                  |
| Early invasive strategy, n (%)| -                                | -                                  |
|                          |                                      | 98 (49.7)                          |
|                          |                                      | 40 (32.8)                          |
|                          |                                      | 0.003                              |

Data are expressed as median (interquartile range, IQR) or number (percentage) as appropriate. NSTE-ACS: non-ST-segment elevation acute coronary syndrome; PPCI: primary percutaneous coronary intervention.

**Comparisons between different groups in emergency ACS during the pandemic**

The results showed that NSTE-ACS group had older age (68 years vs. 65 years, P=0.046) and higher systolic blood pressure (135mmHg vs. 126mmHg, P=0.005) than STEMI group. STEMI group had higher GRACE scores (143 vs. 129, P=0.005) and less non-transferred patients (55.9% vs. 68.0, P=0.042) than NSTE-ACS during the pandemic. In timeline parameters, longer process delay occurred in the period from FMC to ECG completed (10min vs. 6min, P<0.001) for NSTE-ACS (Table 3).
Table 3
Comparison of clinical characteristic between different emergency ACS types during the pandemic

From 2020-01-23 to 2020-03-29

| Characteristics               | STEMI      | NSTE-ACS   | P value |
|-------------------------------|------------|------------|---------|
| Age (years)                   | 65 (56-76) | 68 (60-77) | 0.046   |
| Male, n (%)                   | 108 (74.5) | 86 (70.5)  | 0.466   |
| Heart rate (/min)             | 77 (65-90) | 78 (69-90) | 0.530   |
| SBP (mmHg)                    | 126 (109-150) | 135 (122-151) | 0.005 |
| DBP (mmHg)                    | 79 (66-92) | 80 (70-89) | 0.383   |
| Killip class                  |            |            |         |
| Killip class I, n (%)         | 91 (62.8)  | 86 (70.5)  |         |
| Killip class II, n (%)        | 31 (21.4)  | 24 (19.7)  |         |
| Killip class III, n (%)       | 3 (2.1)    | 7 (5.7)    |         |
| Killip class IV, n (%)        | 21 (14.5)  | 3 (2.5)    |         |
| Killip class ≥ II, n (%)      | 55 (37.9)  | 34 (27.9)  | 0.082   |
| Scr (µmol/L)                  | 73.0 (61.5-92.5) | 75.0 (62.0-101.0) | 0.607 |
| GRACE score in hospital       | 143 (120-169) | 129 (110-153) | 0.005 |
| Arrival during non-office hours, n (%) | 67 (46.2) | 48 (39.3) | 0.259 |
| Non-transferred patients, n (%) | 81 (55.9) | 83 (68.0) | 0.042 |
| S-to-FMC (hours)              | 4.5 (3.0-9.0) | 6.0 (3.0-10.0) | 0.193 |
| FMC to ECG completed (min)    | 6 (4-13)   | 10 (7-15)  | <0.001  |
| Door to Troponin completed (min) | 13 (12-15) | 13 (12-15) | 0.516 |
| FMC to DAPT (min)             | 24 (20-32) | 26 (22-33) | 0.096   |

Data are expressed as median (interquartile range, IQR) or number (percentage) as appropriate.

Table 4 revealed that no differences appeared in admission signs between different therapy strategies for both STEMI and NSTE-ACS. In STEMI, PPCI group had more non-transferred patients (62.0% vs. 42.2%, P=0.026) and longer S-to-FMC period (5.0h vs. 3.8h, P=0.031) than non-PPCI group; yet longer delays occurred in FMC to ECG (23min vs. 5min, P<0.001), door to troponin (14min vs. 13min, P=0.019) and
FMC to DAPT (43min vs. 22min, P<0.001) for non-PPCI group; and thrombolysis accounted for only 22.2% of non-PPCI. In NSTE-ACS, no differences existed in timeline parameters between early invasive strategy and medication (P>0.05).
Table 4
Comparison of clinical characteristic between different therapy strategies for emergency ACS during the pandemic

| Characteristics                  | STEMI From 2020-01-23 to 2020-03-29 | NSTEMI From 2020-01-23 to 2020-03-29 |
|----------------------------------|-------------------------------------|--------------------------------------|
|                                  | P value                             | P value                              |
|                                  | (N=100)                             | (N=40)                               |
| Age (years)                      | 64 (55-75)                          | 67 (58-75)                           |
|                                  | 0.091                               | 0.270                                |
| Male, n (%)                      | 77 (77.0)                           | 32 (80.0)                            |
|                                  | 0.300                               | 0.108                                |
| Heart rate (/min)                | 75 (64-88)                          | 78 (70-91)                           |
|                                  | 0.159                               | 0.499                                |
| SBP (mmHg)                       | 125 (110-150)                       | 137 (110-154)                        |
|                                  | 0.614                               | 0.713                                |
| DBP (mmHg)                       | 78 (68-91)                          | 81 (72-90)                           |
|                                  | 0.884                               | 0.645                                |
| Killip class ≥ II, n (%)         | 39 (39.0)                           | 9 (22.5)                             |
|                                  | 0.693                               | 0.356                                |
| Scr (µmol/L)                     | 71.2 (60.2-91.4)                    | 71.0 (62.0-91.5)                     |
|                                  | 0.239                               | 0.243                                |
| GRACE score in hospital          | 139 (119-166)                       | 122 (112-153)                        |
|                                  | 0.157                               | 0.672                                |
| Arrival during non-office hours, n (%) | 51 (51.0) | 20 (50.0) |
|                                  | 0.084                               | 0.092                                |
| Non-transferred patients, n (%)  | 62 (62.0)                           | 27 (67.5)                            |
|                                  | 0.026                               | 0.930                                |
| S-to-FMC (hours)                 | 5.0 (3.0-9.7)                       | 4.5 (2.5-11.0)                       |
|                                  | 0.031                               | 0.520                                |

Data are expressed as median (interquartile range, IQR) or number (percentage) as appropriate.
|                          | STEMI From 2020-01-23 to 2020-03-29 | NSTE-ACS From 2020-01-23 to 2020-03-29 |
|--------------------------|-----------------------------------|----------------------------------------|
| FMC to ECG completed (min) | 5 (3-7)                           | 23 (10-49)                             | <0.001   | 10 (8-16) | 9 (7-15) | 0.523 |
| Door to Troponin completed (min) | 13 (12-14)                        | 14 (12-19)                             | 0.019    | 14 (11-15) | 13 (12-14) | 0.630 |
| FMC to DAPT (min)         | 22 (19-25)                        | 43 (31-87)                             | <0.001   | 26 (23-32) | 25 (22-33) | 0.479 |
| Thrombolysis, n (%)       | 0                                 | 10 (22.2)                              | <0.001   | -         | -         | -     |

Data are expressed as median (interquartile range, IQR) or number (percentage) as appropriate.

Association between the pandemic and non-invasive therapy in emergency ACS

Logistic regression analysis was performed to explore the association of COVID-19 pandemic with non-invasive therapy in STEMI and NSTE-ACS. The results indicated the pandemic was associated with increased non-PPCI in STEMI (OR=1.707, 95%CI 1.082-2.692, P=0.021) and also correlated with elevated medication in NSTE-ACS significantly (OR=2.029, 95%CI 1.268-3.247, P=0.003). Sub-group analysis further confirmed this correlation (Table 5). Furthermore, compositions of ACS and therapy strategy were shown in Figure 3.
Table 5
Logistic analyses for the association of COVID-19 pandemic with non-invasive therapy in emergency ACS

|                          | Non-PPCI for STEMI | Medication for NSTE-ACS |
|--------------------------|--------------------|------------------------|
|                          | Cases   | OR      | 95% CI          | P value | Cases   | OR      | 95% CI          | P value |
| **Total**                | 423     | 1.707   | (1.082-2.692)    | 0.021   | 319     | 2.029   | (1.268-3.247)    | 0.003   |
| **Age**                  |         |         |                  |         |         |         |                  |         |
| ≥60                      | 265     | 1.846   | (1.062-3.207)    | 0.030   | 243     | 2.487   | (1.450-4.266)    | 0.001   |
| <60                      | 158     | 1.462   | (0.640-3.339)    | 0.367   | 76      | 1.067   | (0.404-2.819)    | 0.896   |
| **Gender**               |         |         |                  |         |         |         |                  |         |
| Male                     | 327     | 1.697   | (0.993-2.899)    | 0.053   | 213     | 2.140   | (1.222-3.747)    | 0.008   |
| Female                   | 96      | 1.636   | (0.680-3.936)    | 0.272   | 106     | 2.198   | (0.875-5.522)    | 0.094   |
| **Killip class**         |         |         |                  |         |         |         |                  |         |
| I                        | 264     | 1.822   | (1.026-3.237)    | 0.041   | 230     | 1.552   | (0.897-2.685)    | 0.116   |
| II-IV                    | 159     | 1.529   | (0.723-3.232)    | 0.266   | 89      | 4.167   | (1.638-10.598)   | 0.003   |
| **GRACE score**          |         |         |                  |         |         |         |                  |         |
| ≥140                     | 228     | 2.205   | (1.218-3.991)    | 0.009   | 139     | 3.411   | (1.604-7.255)    | 0.001   |
| <140                     | 195     | 1.153   | (0.553-2.404)    | 0.704   | 180     | 1.297   | (0.701-2.400)    | 0.407   |
| **Office hours or not**  |         |         |                  |         |         |         |                  |         |
| Yes                      | 229     | 2.387   | (1.299-4.388)    | 0.005   | 187     | 2.302   | (1.223-4.332)    | 0.010   |
| No                       | 194     | 1.109   | (0.550-2.236)    | 0.772   | 132     | 1.695   | (0.828-3.471)    | 0.149   |
| **Transferred or not**   |         |         |                  |         |         |         |                  |         |

OR: odds ratio; CI: confidence interval
### Discussion

Our study found that ACS had significant delays in emergency procedure and an apparent drop in invasive therapy; the pandemic was associated with increased non-invasive therapy, especially for NSTE-ACS.

ACS often has acute chest pain as the onset symptom and further leads to heart failure, arrhythmia and even cardiac arrest [18]. Early identification and intervention for ACS contributes to improve cardiovascular outcomes, thus chest pain emergency is established to cope with these conditions [19]. Under a unified procedure, ACS patients are diagnosed, transferred and treated through chest pain emergency to reduce ischemic risk [20]. In STEMI, PPCI is generally recommended as priority while sometimes thrombolysis could be also considered as supplement to ensure timely reperfusion [21]. In NSTE-ACS, therapy strategy is mainly based on evaluation of ischemic risk; high-risk patients including hemodynamic instability, recurrent or refractory chest pain, malignant arrhythmia and severe heart failure should perform early invasive treatment within 24 hours or even 2 hours; medication could be considered to be optional for "relatively stable" patients [22]. COVID-19 not only directly increased cardiovascular risk through biological mechanisms, but also affected the prognosis of ACS patients by disrupting conventional treatment procedure [23]. Although previous studies provided some evidence of the pandemic's impact on ACS, this impact still remained unclear and unquantified in a non-epicenter.

Our findings firstly revealed decreased admissions and significant process delays after the first-wave epidemic. In hot-spot regions, similar results were also reported but larger reduction of hospitalization occurred in NSTE-ACS [24, 25]. However, changes in ACS composition were not observed in our study maybe ascribed to relatively low-intensity epidemic and active admission. We proposed the main explanations for the decline in hospitalization. Firstly, the patients preferred to social distancing and medical avoidance owing to fear of infection. Secondly, strict social restrictions were not conducive for patients to obtain timely medical assistance at symptom onset. Thirdly, conventional treatment-oriented mode was transformed into epidemic control-oriented mode in medical institutions that meant more resources were spent on epidemic management thus the capacity for treatment might be weakened. Of note, although ACS had universal prolongations in emergency timelines, the delays in NSTE-ACS seemed more serious than in STEMI after the outbreak. Consistently, Metzler et al. showed a significant increase of ischemic time for ACS in Austria, yet lack of time-series analysis for emergency procedures [26]. Hamadeh et al. found the pandemic greatly affected STEMI presentation and care via process delay in a
non-hot-spot region from America, but limited to small sample size and non-first-phase pandemic [27].
Arai et al. discovered that NSTEMI had longer time for transfer and examination than STEMI in Japan,
whereas no considering season characteristics [28]. This effect should not be ignored considering that
our data derived from a non-hot-spot region. Longer delay on NSTE-ACS might be mainly attributed to
relatively lower ischemic risk and conservative response.

In terms of invasive therapy, Garcia et al. showed an estimated 38% reduction in cardiac catheterization
laboratory activations during the early phase of pandemic in U.S [29]. Kwok et al. revealed a decline in
PPCI by 43% following the lockdown in England [30]. Xiang et al. reported an approximately 60% drop in
epicenter (Hubei province) from China after the outbreak [31]. Likewise, our study found both PPCI for
STEMI and early invasive treatment for NSTE-ACS dropped significantly. PPCI was still the preferred
option for reperfusion in STEMI from our region rather than thrombolysis that also exhibited good
adaptability of catheter-labs to the epidemic. Consistent with process delays, the proportion of invasive
therapy in NSTE-ACS declined more than in STEMI suggesting conservative therapeutic behaviors. For
STEMI, non-PPCI was more severely affected by the pandemic manifested as few thrombolysis and
serious in-hospital delays that implied considerable non-PPCI patients rejected basic reperfusion therapy.
This might be due to frequent informed risks and excessive protective measures in hospital, which further
increased anxiety and insecurity of patients and reduced medical compliance. The absence of
thrombolysis as supplement for PPCI would greatly increase the risk of life-threatening adverse events,
thus it is essential for STEMI rescue to optimize in-hospital procedure [32]. Moreover, our study further
indicated whether STEMI or NSTE-ACS, the pandemic increased the probability of non-invasive therapy in
a non-epicenter. This surge in non-invasive strategy derived from both patient-level and hospital-level. On
the one hand, patient's decision on treatment become more negative subjected to individual psychology
affected by the pandemic; on the other hand, decision-making from hospital tended to be cautious in
treatment based on prevention of nosocomial infections and lack of medical resources. As a non-hot-spot
region under the first-wave epidemic, our findings might provide references for emergency ACS practice to
other current non-epicenters.

Our study had several limitations. First, this study was subject to the biases inherent to its retrospective
design. Second, clinical characteristics and timeline parameters were assessed by trained physicians in
each center without central reconfirmation, potentially resulting biases and errors. Third, our study had a
relatively small sample size and no longitudinal analysis. Fourth, the absence of PPCI parameters limited
further analysis for mechanical reperfusion procedure. Last, it remained unclear how local policies of
each hospital had altered due to the first-wave pandemic that might affect emergency procedure for chest
pain.

Conclusions

Even in a non-epicenter region, a significant reduction occurred in invasive therapy with evident
emergency process delays for ACS. In current epidemic, emergency procedure should be appropriately
adjusted and considered for integration into chest pain practice.
Abbreviations

COVID-19: Coronavirus-2019 disease; ACS: Acute coronary syndrome; STEMI: ST-segment-elevation myocardial infarction; NSTE-ACS: Non-ST-segment elevation acute coronary syndrome; PPCI: Primary percutaneous coronary intervention; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; Scr: Serum creatinine; FMC: First medical contact; S-to-FMC: Symptom onset to FMC; DAPT: Dual antiplatelet therapy; IQR: Interquartile range; OR: Odds ratio; CI: Confidence interval.

Declarations

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Authors’ contributions

All authors have read the manuscript and agreed with the content. Zhao XH was responsible for the study concept and design. Data collection and cleaning were done by Zhao JH and Mao Q. Data analysis was performed by Mao Q. Mao Q wrote the draft of this manuscript that was revised and edited by Huang L and Zhao XH. All authors contributed to the writing and revision of the paper.

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Availability of data and materials

The data used or analyzed during this study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by Xinqiao Hospital Ethics Committee, Army Medical University (No.2021-071-01). No additional ethical approval is needed.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures
Figure 1

COVID-19 outbreak and emergency response
Figure 2

Flowchart of emergency procedure
Figure 3

Constituent ratios of ACS and invasive therapy