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Coronavirus Pandemic

Impact of the COVID-19 pandemic on the treatment and prognosis of acute myocardial infarction in Xuzhou, China

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Abstract

Introduction: The treatment of acute myocardial infarction (AMI) during the COVID-19 pandemic has been affected to varying degrees. This study is the first to explore the impact of COVID-19 on the treatment and prognosis of rural and urban AMI in developing countries.

Methodology: A total of 128 patients with AMI in our hospital during the COVID-19 pandemic were enrolled. A total of 197 patients diagnosed with AMI before the COVID-19 pandemic were selected as the control group and one year of follow-up was performed.

Results: Hospital stay and the proportion of Killip class ≥ 2 patients were increased among rural AMI patients in the 'during COVID-19' group, compared with the 'before COVID-19' group. Among ST-segment elevation myocardial infarction (STEMI) total and rural STEMI patients, the treatment time in the during-COVID-19 group was longer than that in the before-COVID-19 group, whereas only the symptom to door (S to D) total and door to balloon (D to B) were extended in urban STEMI patients. In AMI total and rural AMI patients, major adverse cardiovascular events (MACEs) and all-cause mortality were increased in the during-COVID-19 group compared with the before-COVID-19 group. Kaplan–Meier analysis revealed that the survival and occurrence of MACEs in AMI total and rural AMI patients were significantly higher in the during-COVID-19 group.

Conclusions: The COVID-19 pandemic led to delayed treatment and worse prognosis in AMI patients. Rural areas appear to be at a greater risk.

Key words: COVID-19; acute myocardial infarction; urban areas; rural areas; MACEs.

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Introduction

Acute myocardial infarction (AMI) is a disease with high mortality and morbidity. Primary percutaneous coronary intervention (PPCI) remains the most recommended treatment [1]. Two reports have shown that reducing the reperfusion time of patients with AMI is related to improved prognosis [2,3]. The analysis of a prospective, multi-centre trial performed in Germany showed that for every 10 minutes of delay in treatment, there were of 3.31 additional deaths per 100 patients undergoing percutaneous coronary intervention [4]. In order to reduce mortality and improve prognosis, the healthcare system has been working to reduce the reperfusion treatment time for the past few decades [5,6]. Despite continuous efforts at multiple levels, delays in treatment remain a challenging factor [7]. Since December 2019, the coronavirus disease 2019 (COVID-19) that emerged in Wuhan, China has been spreading rapidly and has evolved into a pandemic [8-10], placing an enormous burden on all components of the medical system. Although many countries are constantly trying to reduce the impact of COVID-19 on AMI treatment [11], many studies have reported that its treatment during the COVID-19 pandemic has been affected to varying degrees, especially with regard to the delay of treatment [12-15]. The impact of public health emergencies, such as the outbreak of community infectious diseases, on the treatment of AMI is poorly understood. During the COVID-19 pandemic, balancing AMI management and COVID-19 control has become a major challenge for cardiovascular doctors worldwide. Many expert groups have made some recommendations for the management of AMI during the COVID-19 pandemic [16-21]. However, these recommendations lack evidence from clinical studies. During the COVID-19 pandemic in China, the Chinese government formulated strict control measures to limit the spread of COVID-19, and this successfully limited the spread of new coronary pneumonia. However, whether this management model can treat AMI during the spread of COVID-19 and its impact on prognosis management are worth investigating. At present, studies on the long-term prognosis of patients with AMI during the COVID-19 pandemic are limited, and the treatment of AMI is even more diverse. As a typical developing country, China still exhibits differences in the development levels between rural and urban areas. This study is the first to explore the treatment and prognosis of AMI in rural and urban areas during the COVID-19 pandemic.

Methodology

Study design and population

This is a single center retrospective clinical observational study. This study was approved by the ethics committee of The Affiliated Hospital of Xuzhou Medical University; all the participants were informed and signed a consent form. All methods were performed in accordance with the relevant guidelines and regulations. During the COVID-19 pandemic, all the patients with AMI were treated according to the consensus of experts at the time [18]. This study included 142 patients with AMI in our hospital during the COVID-19 pandemic (25 January 2020 – 24 March 2020). A total of 213 patients diagnosed with AMI from 25 November 2019 to 24 January 2020 were selected as the control group, and the diagnosis of AMI followed the European Society of Cardiology (ESC) definition [1]. Exclusion criteria included a history of acute myocardial infarction outside of this control area, COVID-19-positive or suspected COVID-19-positive patients and serious diseases that limited the life expectancy of the patient. A total of 325 patients were selected.

Data collection

In addition to basic clinical data, this study also focused on the proportion of reperfusion treatment, treatment time, Killip grade and length of hospital stay. The treatment time was extracted from the hospital's chest pain centre database. Symptom to door (S to D) time, door to balloon (D to B) time and symptom to balloon (S to B) time of the ST-segment elevation myocardial infarction (STEMI) patients were obtained, and the ratio of interventional treatment within 24 hours for Non-ST-segment elevation myocardial infarction (NSTEMI) patients was observed. Killip class was based on the definition and changes in patient condition during hospitalization, and the highest grade for each patient was used for analysis.

Outcomes

The follow-up time was until the end of life or 1 year, and the outcome of interest was defined as major adverse cardiovascular events (MACEs; all-cause death > reinfarction > new congestive heart failure). Reinfarction was defined according to the redefined ESC/American College of Cardiology (ACC)/American Heart Association (AHA) committee standard: ischaemic symptoms and/or new significant ST segment changes and at least one value of the increase and/or decrease in hs-cTnT was greater than the upper limit of the 99th percentile [22]. New congestive heart failure was considered the first episode of cardiac decompensation and requires intravenous diuretic treatment regardless of whether the patient is readmitted to the hospital [23]. Information regarding follow-up of the event was mainly obtained by telephone and outpatient services, and whether the patient died and their date of death was determined through the death registry of the region, a detailed mandatory official database.

Data analysis

Statistical product and service solutions (SPSS) 22.0 software was used for statistical analysis. If the data followed a normal distribution, they were expressed as the mean ± standard deviation, and the independent sample t-test was used for comparisons between groups. Abnormal distribution data were described by the median [IQR], and the Mann-Whitney U test was used for analysis. Count data were expressed as the number of cases and percentage (%), and the χ^2 test or Fisher's exact probability method was used for comparisons between groups. Kaplan-Meier curves of the clinical outcomes were compared using a log-rank test. A p value < 0.05 was considered statistically significant.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Affiliated Hospital of Xuzhou Medical University (Xuzhou, China). All methods were implemented in accordance with relevant guidelines and regulations, and all enrolled patients signed informed consent forms.

Results

Comparison of clinical data in all patients with AMI

The hospital stay was prolonged in AMI. The total number of patients in the during-COVID-19 group were compared with the before-COVID-19 group (5.12 ± 2.26 vs 5.55 ± 3.18, p = 0.178). The proportion of revascularization was decreased in the during-COVID-19 group, but the difference was not statistically significant (65.5% vs 58.6%, p = 0.209). Killip class ≥ 2 patients were significantly increased in the during-COVID-19 group (18.8% vs 32.8%, p = 0.004).

Hospital stay (5.22 ± 2.11 vs 6.29 ± 3.29, $p = 0.016$) and the proportion of Killip class ≥ 2 patients (18.1% vs 34.7%, $p = 0.01$) were higher among Rural AMI patients (Table 1).

Treatment time for STEMI patients

The S to D Total in STEMI ($p < 0.001$), Urban STEMI ($p < 0.05$) and Rural STEMI ($p < 0.05$) patients were significantly prolonged in the during-COVID-19 group compared with the before-COVID-19 group. Next, the data of patients undergoing primary percutaneous coronary intervention (PPCI) were extracted and compared. The S to D, D to B and S to B for STEMI Total ($p < 0.05$, $p < 0.001$, $p < 0.05$) and Rural STEMI ($p < 0.05$, $p < 0.001$, $p < 0.05$) patients were increased in the during-COVID-19 group compared with the before-COVID-19 group. Regarding Urban STEMI, only D to B was extended in the during-COVID-19 group ($p < 0.05$) (Figure 1).

Proportion of invasive treatment time within 24 hours in NSTEMI patients

The proportion of invasive treatment time within 24 hours in NSTEMI Total (70.9% vs. 30.8%, $p < 0.001$), Urban NSTEMI (73.7% vs. 34.5%, $p = 0.001$) and Rural NSTEMI (68.8% vs. 26.1%, $p = 0.001$) patients were obviously reduced in the during COVID-19 group compared with the before-COVID-19 group (Table 2).

Comparison of the prognosis of all patients

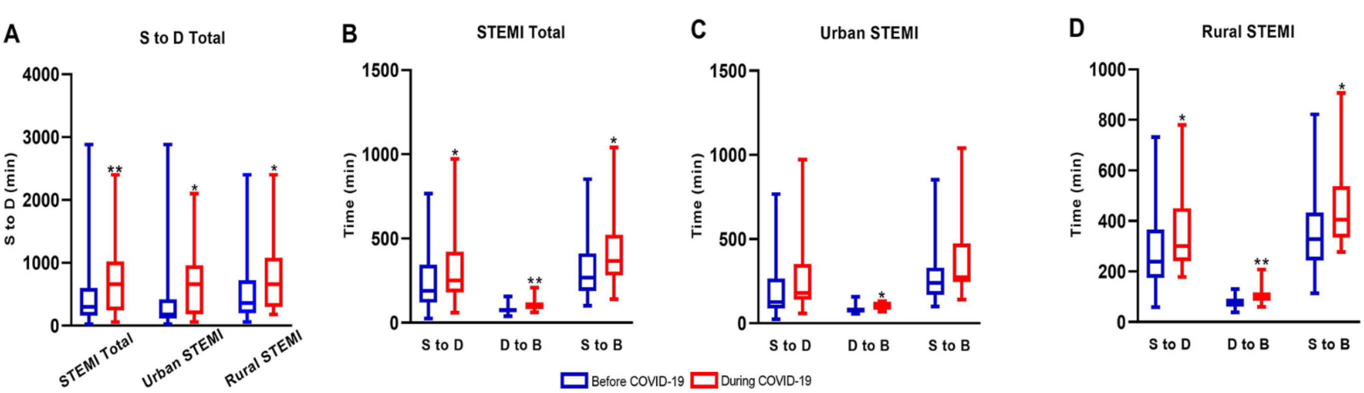
In the case of the AMI total patients, MACEs (17.3% vs. 29.7%, $p = 0.008$) and all-cause mortality (5.6% vs. 12.5%, $p = 0.027$) were increased in the during-COVID-19 group compared with the before-COVID-19 group, and similar results were observed in Rural AMI patients (19% vs. 31.9%, $p = 0.043$; 5.2% vs. 13.9%, $p = 0.037$). No significant difference in MACEs and all-cause mortality were noted in Urban AMI patients in the during-COVID-19 group compared with the before-COVID-19 group (Table 3).

Table 1. Baseline demographics of study population.

Characteristics	AMI Total			Urban AMI			Rural AMI		
	Before COVID-19 (n = 197)	**During COVID-19 (n = 128)**	***p***	**Before COVID-19 (n = 81)**	**During COVID-19 (n = 56)**	***p***	**Before COVID-19 (n = 116)**	**During COVID-19 (n = 72)**	***p***
Age (yr)	64.7 ± 12.92	66.2 ± 13.01	0.306	66.77 ± 14.26	66.02 ± 14.22	0.763	63.25 ± 11.74	66.35 ± 12.09	0.084
Male, n (%)	139 (70.6%)	90 (70.3%)	0.962	59 (72.8%)	44 (78.6%)	0.445	80 (69%)	46 (63.9%)	0.472
Currently smoking, n (%)	80 (40.6%)	54 (42.2%)	0.778	36 (44.4%)	23 (41.1%)	0.695	44 (37.9%)	31 (43.1%)	0.485
Hypertension, n (%)	87 (44.2%)	51 (39.8%)	0.442	33 (40.7%)	25 (44.6%)	0.650	54 (46.6%)	26 (36.1%)	0.159
Diabetes, n (%)	62 (31.5%)	36 (28.1%)	0.521	30 (37%)	14 (25%)	0.138	32 (27.6%)	22 (30.6%)	0.662
Stroke, n (%)	43 (21.8%)	27 (21.1%)	0.875	20 (24.7%)	9 (16.1%)	0.225	23 (19.8%)	18 (25%)	0.404
STEMI, n (%)	111 (56.3%)	76 (59.4%)	0.589	43 (53.1%)	27 (48.2%)	0.575	68 (58.6%)	49 (68.1%)	0.195
Countryside, n (%)	116 (58.9%)	72 (56.2%)	0.639	-	-	-	-	-	-
BMI (kg/m^2)	24.95 ± 3.79	24.91 ± 3.55	0.925	24.95 ± 4.00	25.65 ± 3.94	0.315	24.95 ± 3.65	24.34 ± 3.12	0.240
Hospital stay (d)	5.12 ± 2.26	5.55 ± 3.18	0.178	4.96 ± 2.46	4.61 ± 2.78	0.432	5.22 ± 2.11	6.29 ± 3.29	0.016
Killip class ≥ 2, n (%)	37 (18.8%)	42 (32.8%)	0.004	16 (19.8%)	17 (30.4%)	0.154	21 (18.1%)	25 (34.7%)	0.01
Revascularization, n (%)	129 (65.5%)	75 (58.6%)	0.209	58 (71.6%)	34 (60.7%)	0.182	71 (61.2%)	41 (56.9%)	0.563

AMI: Acute myocardial infarction; STEMI: ST-segment elevation myocardial infarction; BMI: Body Mass Index (kg/m^2).

Figure 1. Comparison of treatment time in all STEMI patients (**A**), STEMI patients undergoing PPCI (**B**), Urban STEMI patients undergoing PPCI (**C**) and Rural STEMI patients undergoing PPCI (**D**).



*p < 0.05: Comparison between before-COVID-19 group and during-COVID-19 group. **p < 0.001: Comparison between before-COVID-19 group and during COVID-19 group.

Table 2. Invasive treatment time in NSTEMI patients.

	NSTEMI Total			Urban NSTEMI			Rural NSTEMI		
	Before COVID-19 (n = 86)	During COVID-19 (n = 52)	*p*	Before COVID-19 (n = 38)	During COVID-19 (n = 29)	*p*	Before COVID-19 (n = 48)	During COVID-19 (n = 23)	*p*
Invasive treatment time < 24 h, n (%)	61 (70.9%)	16 (30.8%)	< 0.001	28 (73.7%)	10 (34.5%)	0.001	33 (68.8%)	6 (26.1%)	0.001

NSTEMI: Non-ST-segment elevation myocardial infarction.

Table 3. Comparison of the prognosis in all patients.

	AMI Total			Urban AMI			Rural AMI		
	Before COVID-19 (n = 197)	During COVID-19 (n = 128)	*p*	Before COVID-19 (n = 81)	During COVID-19 (n = 56)	*p*	Before COVID-19 (n = 116)	During COVID-19 (n = 72)	*p*
MACE, n (%)	34 (17.3%)	38 (29.7%)	0.008	12(14.8%)	15 (26.8%)	0.083	22 (19%)	23 (31.9%)	0.043
All-cause mortality, n (%)	11 (5.6%)	16 (12.5%)	0.027	5(6.2%)	6 (10.7%)	0.521	6 (5.2%)	10 (13.9%)	0.037
Reinfarction, n (%)	7 (3.6%)	7 (5.5%)	0.406	2(2.5%)	3 (5.4%)	0.672	5 (4.3%)	4 (5.6%)	0.909
NCHF, n (%)	16 (8.1%)	15 (11.7%)	0.281	5(6.2%)	6 (10.7%)	0.521	11 (9.5%)	9 (12.5%)	0.514

AMI: Acute myocardial infarction; NCHF: New congestive heart failure.

Figure 2. Kaplan–Meier survival curves for the MACEs in AMI Total (**A**), Urban AMI (**B**) and Rural AMI (**C**).

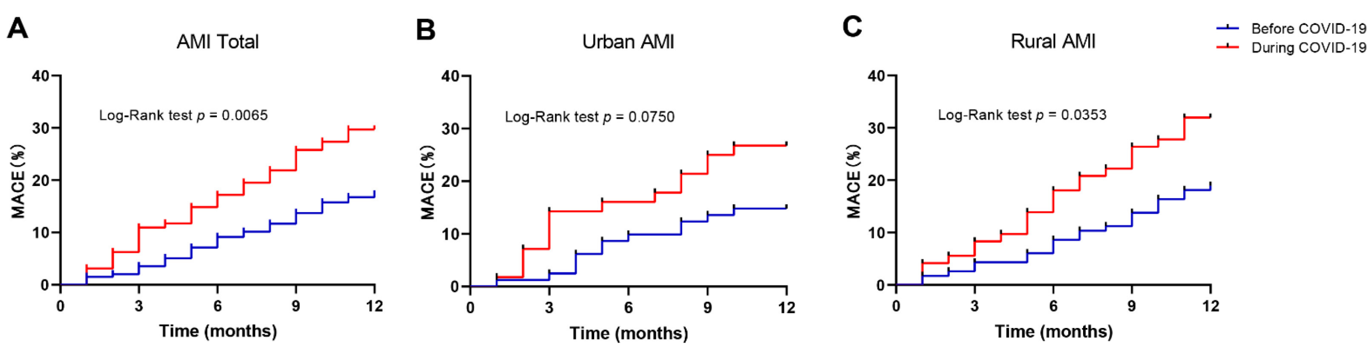
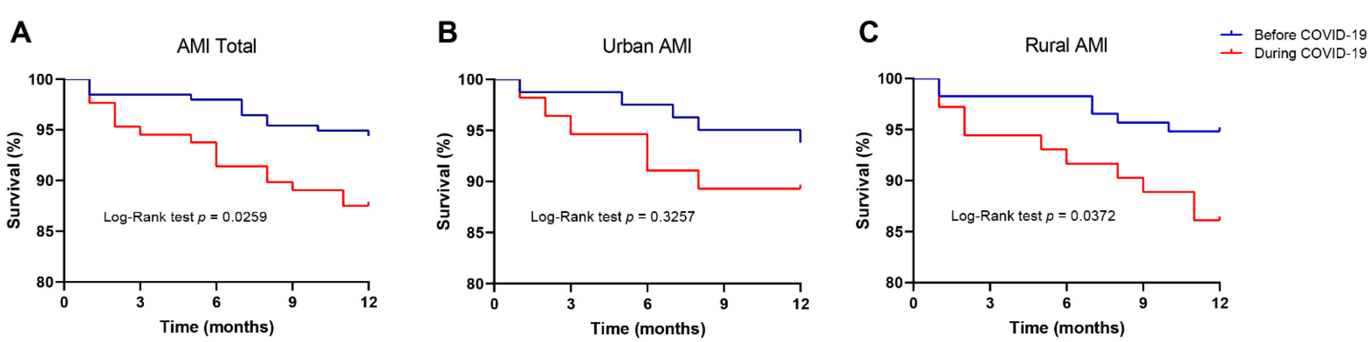


Figure 3. Kaplan–Meier survival curves for the all-cause mortality in AMI Total (**A**), Urban AMI (**B**) and Rural AMI (**C**).



MACEs of AMI patients during and before COVID-19

Kaplan–Meier analysis revealed that the occurrences of MACEs in AMI Total ($p = 0.0065$) and Rural AMI ($p = 0.0353$) patients were significantly higher in the during-COVID-19 group compared with the before-COVID-19 group. However, no significant difference in Urban AMI was noted (Figure 2).

AMI patient mortality during and before COVID-19

Kaplan–Meier analysis revealed that the survival of AMI Total ($p = 0.0259$) and Rural AMI ($p = 0.0372$) patients was significantly reduced in the during-COVID-19 group compared with the before-COVID-19 group. However, no significant difference in Urban AMI patients was noted (Figure 3).

Discussion

Acute myocardial infarction remains the main cause of cardiovascular death worldwide. Total ischaemic time is the main determinant of the prognosis of AMI patients. Reducing the reperfusion treatment time is essential to reducing mortality and improving prognosis [24,25]. At present, PPCI is still the preferred method of emergency reperfusion therapy for AMI patients after admission [26]. Over the past few decades, the reperfusion treatment time for AMI has been significantly reduced at our institution due to the construction of a chest pain centre [5]. COVID-19 is a viral infection that causes respiratory diseases [27]. Its highly contagious nature requires strict infection control measures at the national level, and the health care system is critical to limit its spread. A large number of studies have shown that novel coronavirus pneumonia has had an unprecedented impact on the treatment of AMI in various countries and regions [28-32]. Similar to the results of these studies, the treatment of AMI in this region was also affected by the spread of COVID-19. It was found that the proportion of Killip class ≥ 2 patients was significantly increased in AMI Total and Rural AMI patients in the during-COVID-19 group, and hospital stay was increased in Rural AMI patients. However, these indicators were not observed to be statistically significant in the Urban AMI patients. These findings may be due to the delay in treatment time. In STEMI Total and Rural STEMI patients, S to D, D to B and S to B in the during-COVID-19 group were longer than those in the before-COVID-19 group. In Urban STEMI patients, only D to B were extended. This delay in treatment was also shocking in NSTEMI patients. Based on the ESC guidelines for NSTEMI [33], we focused on the proportion of invasive treatment time within 24 hours. The proportion of invasive treatment time within 24 hours in NSTEMI patients was obviously reduced in the during-COVID-19 group. Based on the above research results, we found that both the prehospital visit time and the in-hospital treatment time were significantly affected, and the effects in rural areas seemed to be exacerbated. This finding may be due to the strict closure of villages and urban communities during the “first level response to pandemic situation” of COVID-19 in this province, and the hospitals with the ability to treat AMI are located far away from rural areas, resulting in prolonged SD time. Choosing to stay at home coupled with the fear of new coronary pneumonia, may lead to a longer subjective consultation time. These factors may eventually lead to delays in all aspects of the treatment of patients with acute myocardial infarction [15]. During the COVID-19 pandemic, we still regarded PPCI as the main treatment for STEMI patients. The goals of this procedure are to reduce the reperfusion time as much as possible, isolate the patient immediately after the surgery, and remove the suspicion of infection. These features may explain why the S to B of STEMI patients in cities did not exhibit a significant impact. The pathophysiological mechanisms of ST and NS are different, so the treatment procedures for the two conditions outlined in the guidelines differ [33]. Differences in the treatment management for STEMI and NSTEMI were noted in some countries or regions during the COVID-19 pandemic [16,32]. Similarly, there are stricter screening standards for NSTEMI patients, and all NSTEMI patients were confirmed to be COVID-19 negative before being admitted to the hospital for the next treatment steps. Given the sharp increase in demands of the medical system during the COVID-19 pandemic, the proportion of NSTEMI patients who received reperfusion therapy within 24 hours was significantly reduced.

Next, we conducted a 1-year follow-up of all the enrolled patients. In AMI Total and Rural AMI patients, MACEs and all-cause mortality were increased in the during-COVID-19 group. However, no significant difference in MACEs and all-cause mortality were noted in urban AMI patients. Kaplan–Meier analysis revealed that the survival and occurrence of MACEs in AMI total and rural AMI patients were significantly increased in the during-COVID-19 group. In addition to the above-mentioned differences in treatment and development levels, this finding may also be related to poor post-hospital management in rural areas.

Limitations

Our research has several limitations. First, the sample size was relatively small, which may cause some problems with statistical power. Second, this research was conducted in a single centre. Other medical centres may not have employed the same strategy to deal with COVID-19, and the treatment plan for patients with AMI may also be different. Finally, our follow-up time was one year, which may not be sufficient.

Conclusions

The COVID-19 pandemic led to delayed treatment and worse prognosis in AMI patients, and the effects in patients from rural areas seem to be more concerning. During the COVID-19 pandemic, different regions should formulate appropriate AMI management plans to improve treatment and prognosis of the patients.

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Authors' contributions

Lei Chen, Min Zhang, Yiwen Wang and Zhi Li performed the experiments and analysed the data. Yu Yang, Zhirong Wang and Yuan Lu designed the study. Lei Chen and Yuan Lu wrote the manuscript. All authors read and approved the manuscript and agree to be accountable for all aspects of the research in ensuring that the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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