



# A new cooperative approach for ST-elevation myocardial infarction patients to receive timely and effective percutaneous coronary reperfusion in China

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## Abstract

**Background** Acute myocardial infarction (AMI) is the most serious type of coronary heart disease. However, less than 30% of these patients have been treated effectively in China. Delayed treatment is a leading cause. This study aimed to evaluate a new regional cooperative model for improving the first medical contact-to-device time and the therapeutic effects on AMI patients. **Methods** A retrospective analysis of 458 ST-elevation myocardial infarction (STEMI) patients was performed. Patients were divided into two groups in terms of before or after the model were implemented. First medical contact-to-device time (FMC2D), Door to device time (D2D), referral time, cardiac functions, mean cost, days of hospitalization, and major adverse cardiac events (MACE) were analyzed. **Results** The mean FMC2D time, D2D time and referral time of the model group were significantly lower than the control group. The left ventricular ejection fraction of the model group increased but the left ventricular end-diastolic dimension decreased compared with the control group at 6 months after discharge. These results also showed that mean costs and days of hospitalization were reduced. The MACE rate was reduced in the model group. **Conclusions** These results suggested that the new model decreased the FMC2D time, which could improve the cardiac function and therapeutic effect of STEMI patients as well as decreased the financial burden.

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**Keywords:** Acute myocardial infarction; First medical contact; Regional cooperative rescue model

## 1 Introduction

Approximately 20 million patients with coronary heart disease (CHD) are documented in China. Among these CHDs, acute myocardial infarction (AMI) is considered to be the most serious type. Approximately 650,000 new cases of AMI are recorded annually, but only 160,000 patients or 25% are treated effectively and account for < 30% of all patients with AMI.<sup>[1]</sup> Treatment delay is the leading cause of death and severe outcomes in terms of mortality.<sup>[1]</sup> Thus, delay should be shortened. Time is crucial when AMI occurs, and an effective prognosis is provided for patients with AMI when percutaneous coronary intervention (PCI) is administered at an early stage.<sup>[2–6]</sup> Pre-hospital treatment is given more and more attention in AMI rescues. Current European Society of Cardiology (ESC) guidelines state that

if the reperfusion therapy is primary PCI, the goal should be a delay [the first medical contact (FMC) to wire passage into the culprit artery] of  $\leq 90$  min.<sup>[7]</sup> Thus, the first medical contact-to-device (FMC2D) time has been substituted for the original standard of door to device (D2D) time.<sup>[8]</sup>

Our cardiology center has started to investigate a new model for shortening the delay time of reperfusion for AMI patients and some achievements have been made. In a previous study involving our practice of AMI treatment with a “seamlessly linked” mode constructed by our cardiovascular center and Emergency Medical Services (EMS), we reported that the training of general practitioners in identifying and diagnosing of AMI as well as in adopting a seamlessly linked mode of transportation to our catheterization laboratory could result in the following: a decreased time of delay of AMI, a significant reduction in average door to device time to less than 90 min, and an improved survival rate and therapeutic effect.<sup>[9]</sup> Based on these findings, we established the new regional cooperative emergency model between primary hospitals and the cardiology center of Affiliated Hospital of Jiangsu University.<sup>[10]</sup> The present study aimed to investigate whether the new regional cooperative emergency model improves FMC2D time and the therapeutic

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tic effects on patients with ST-elevation myocardial infarction (STEMI).

## 2 Methods

### 2.1 The new regional cooperative emergency model

The new regional cooperative emergency model was established as described by our previous study.<sup>[10]</sup> Briefly, physicians in primary hospitals in the remote city of Zhenjiang, Jiangsu Province in China were educated about AMI identification and diagnosis every year and real-time 12-lead ECG transmission equipment (the IVT corporation) was placed at these facilities. A Bluetooth 3.0 communication system was established to transmit the ECG data to the tablet computer in our cardiology center. A GPS positioning system and real-time traffic tracking query system was installed inside the emergency ambulance.

### 2.2 Patient population

All STEMI patients who first visited the six primary hospitals by themselves and then transported to the cardiology center within 24 h of the onset of symptoms and were admitted for PCI from February 2010 to November 2014 were included in this analysis. These six primary hospitals were involved in the regional cooperative emergency model since January 2013. Thus, patients were divided in two groups: the model group ( $n = 285$ ) (from January 2013 to November 2014), and the control group ( $n = 173$ ) (from February 2010 to December 2012). The control group consisted of STEMI patients transferred from the same primary hospitals to our PCI center before the regional cooperative emergency model was established.

The inclusion criteria were as previously described.<sup>[10]</sup> Briefly, patients were diagnosed as STEMI in the primary hospital and then transferred to our cardiology center to perform emergent coronary angiography and angioplasty. The coronary angiography exhibited infarction-related arteries exhibiting total occlusion or subtotal occlusion.

The exclusion criteria included the following: (1) patients with non-ST-elevation AMI; (2) patients with greater than 24 h of acute onset of chest pain and without chest pain; (3) patients subjected to pre-hospital thrombolytic treatment and recanalization; (4) patients with reperfusion delay for unstable conditions; or (5) patients with reperfusion delay due to refusal to accept further treatment.

The study was reviewed and approved by the institutional review committee of Jiangsu University (approval number: 2014/1268), and written informed consent was obtained from all patients.

### 2.3 STEMI management

All of the patients were administered with oral load aspirin (0.3 g) and Plavix (0.3 g) before PCI. Blood clots were pumped using a suction catheter and PCI was performed. Emergency cardiac catheterization and PCI procedures were performed using standard methods. Tirofiban was used by a continuous vein pump during for 12 to 18 h after the PCI. After the PCI was conducted, the patients were routinely treated with anti-platelet aspirin (0.1 g) and Plavix (75 mg). Plavix was administered for at least 12 months.

### 2.4 Detection of troponin I

In all patients, blood samples were obtained from the forearm at the time of admission to our PCI center. The concentration of troponin I was determined by the Triage and Biosite system (lower detection limit, 0.04 ng/mL).

### 2.5 Data collection

We established the following time segments as primary outcomes: FMC2D time was defined as the time between the patient's initial contact with the first physician who made the diagnosis and the first angioplasty balloon inflation. D2D time was defined as the time between the patient's admission to the interventional cardiovascular center (whether to the emergency department or directly to the catheterization laboratory) and the first angioplasty balloon inflation; transfer time was defined as the time between FMC and arrival at the interventional cardiovascular center; informed consent time was defined as the time between when the physicians in the interventional cardiovascular center started to speak with the patients and/or the relatives about performing the PCI and obtained the consent. Secondary outcomes: (1) to analyze the treatment effect, we evaluated cardiac function and major adverse cardiac events (MACE) in the next six months after the PCI. The left ventricular ejection fraction (LVEF) and left ventricular end-diastolic dimension (LVED) at two days, one month and six months after PCI were measured by ultrasonic cardiogram (UCG). LVED was measured by M-mode method,<sup>[11]</sup> and the apical 4-chamber and 2-chamber were used to calculate LVEF with Simpson method.<sup>[12]</sup> (2) MACE was defined as cardiac death, recurrent nonfatal myocardial infarction or unplanned revascularization. (3) To analyze the economic benefits, we assessed the mean cost in hospital and hospitalization days.

### 2.6 Statistical analysis

Statistical graph were performed with GraphPad software (Prism.3.0) and statistical analysis was performed with SPSS11.5 software. Quantitative variables were expressed

as the mean  $\pm$  SD and analyzed by Student's *t* test; if they did not follow a normal distribution, they were reported as median  $\pm$  interquartile range and compared using the Wilcoxon test. Categorical variables were compared using the Pearson  $\chi^2$  test and described using absolute numbers and percentages. Multivariate linear regression model with LVEF or LVED as univariate was applied to identify significant factors contributing to recovery from LVEF and LVED. A value of  $P < 0.05$  was considered statistically significant.

### 3 Results

#### 3.1 Patient population and baseline characteristics

The baseline characteristics of the two groups are provided in Table 1. The model and control groups exhibited no significant differences in sex, age, lesion number, infarction area, risk factors (hypertension, hypercholesterolemia, smoking status, and diabetes) and complications including prior AMI/CABG (coronary artery bypass grafting)/PCI, chronic heart failure (CHF) and chronic kidney disease (CKD). However, a significant difference in levels of troponin I was noted in the hospital.

#### 3.2 Time segments

The different time intervals in each group are summarized in Table 2. The control group exhibited an increased delay in informed consent and transfer time whereas the

**Table 1. Patients characteristics.**

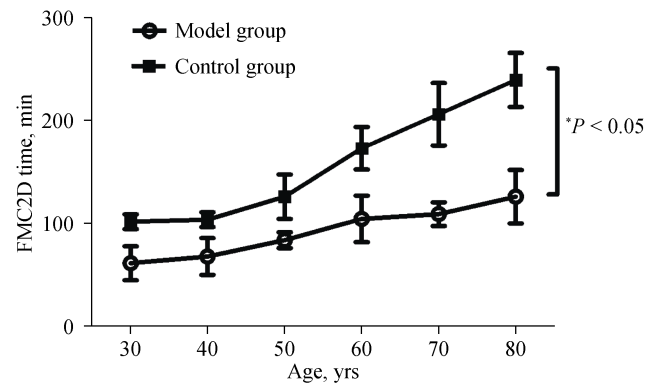
Characteristics	Model group ( <i>n</i> = 285)	Control group ( <i>n</i> = 173)	<i>P</i> value
Men/women	64.6%/35.4%	64.2%/35.8%	NS
Age, yrs	58.7 $\pm$ 9.4	59.7 $\pm$ 7.6	NS
Single/multi vessel diseases	34.7%/65.3%	34.6%/65.4%	NS
Anterior MI	169 (59.2%)	101 (58.4%)	NS
Non anterior MI	116 (40.7%)	72 (41.6%)	NS
Prior MI/CABG/PCI	16	13	NS
Prior CHF	23		NS
CKD	28	21	NS
Diabetes	82 (28.8%)	50 (28.9%)	NS
Hypertension	101 (35.4%)	61 (35.2%)	NS
Hypercholesterolemia	91 (31.9%)	54 (31.2%)	NS
Smoker	132 (46.3%)	79 (45.6%)	NS
Troponin I, ng/mL	20.7 $\pm$ 5.8	26.6 $\pm$ 7.2	< 0.001

Data are presented as mean  $\pm$  SD, *n*, or *n* (%). CABG: coronary artery bypass grafting; CHF: chronic heart failure; CKD: chronic kidney disease; MI: myocardial infarction; NS: not significant; PCI: percutaneous coronary intervention.

**Table 2. Times and delays of the patients.**

	<i>n</i>	FMC2D	D2D	Transfer time	Informed consent time
Model group, min	285	97 $\pm$ 20	22 $\pm$ 8	61 $\pm$ 17	7 $\pm$ 3
Control group, min	173	211 $\pm$ 27	105 $\pm$ 14	101 $\pm$ 19	28 $\pm$ 7
<i>P</i> value		0.001	0.001	0.001	0.05

Data are presented as mean  $\pm$  SD unless other indicated. D2D: door to device time; FMC2D: first medical contact-to-device time.



**Figure 1. The FMC2D time is different in different ages.** The FMC2D time increased as age increased, and a large gap between the model group and the control group was noted ( $*P < 0.05$ ). FMC2D: first medical contact-to-device.

model group exhibited shorter total time due to a pre-hospital delay. Moreover, FMC2D time and D2D time were significantly decreased. In Figure 1, the FMC2D time increased as age increased, and a large gap between the model group and the control group was also noted.

#### 3.3 The cardiac function

LVEF at two days, one month and six months after PCI increased, but LVED decreased in the model group compared with the corresponding index in the control group (Table 3). As shown in Table 4 & 5, patients who participated in the regional cooperative rescue model, who were younger, and suffered single vessel lesions exhibit a much better recovery. Gender and whether were smoking status appeared not to affect the cardiac function. Other factors effects on characteristics contributing to the recovery of cardiac function at different periods (two days, one month and six months) require future study.

#### 3.4 MACE in the six month period after PCI

The patients in the two groups were followed up at six months after PCI. The MACE rate in the model group was significantly reduced compared with the control group (Table 6).

**Table 3. Cardiac function of the patients.**

	Total/lost to follow-up	LVEF, %			LVED, mm		
		2 days	1 month	6 months	2 days	1 month	6 months
Model group	285/3	49.8 ± 8.3	56.7 ± 6.8	55.2 ± 9.3	49.8 ± 7.2	49.3 ± 8.3	48.2 ± 6.4
Control group	173/2	46.1 ± 5.9	47.3 ± 8.1	48.2 ± 5.7	51.2 ± 7.8	52.1 ± 6.7	52.8 ± 8.3
<i>P</i> value		0.05	0.05	0.01	0.05	0.02	0.05

Data are presented as mean ± SD unless other indicated. LVED: left ventricular end diastolic; LVEF: left ventricular ejection fraction.

**Table 4. Significant factors contributed to recovery of cardiac function.**

	LVEF			LVED		
	2 day	1 moth	6 moths	2 day	1 moth	6 moths
Model group	+	+	+	+	+	+
Age	+	+	+	+	+	+
Gender, Male/Female	-	-	-	-	-	-
Single vessel lesions	+	+	+	+	+	+
Anterior MI	+	+	+	-	-	-
Diabetes	+	-	-	-	-	-
Hypertension	-	+	+	+	+	-
Hypercholesterolemia	-	+	+	+	-	-
Smoker	-	-	-	-	-	-

+: *P* < 0.05; -: *P* ≥ 0.05. LVED: left ventricular end diastolic; LVEF: left ventricular ejection fraction; MI: myocardial infarction.

**Table 5. Multivariate linear regression coefficient results of the factor contributed to LVEF and LVED.**

	LVEF						LVED					
	2 days		1 month		6 moths		2 days		1 month		6 months	
	<i>b</i>	<i>P</i>	<i>b</i>	<i>P</i>	<i>b</i>	<i>P</i>	<i>b</i>	<i>P</i>	<i>b</i>	<i>P</i>	<i>b</i>	<i>P</i>
Model group	1.768	0.003	1.754	0.002	1.835	0.002	1.751	0.003	1.723	0.003	1.789	0.003
Age	1.325	0.006	1.423	0.005	1.421	0.002	1.354	0.006	1.389	0.004	1.378	0.003
Gender, Male/Female	0.968	0.056	0.923	0.054	0.987	0.002	0.934	0.059	0.921	0.053	0.952	0.057
Single vessel lesions	1.548	0.002	1.654	0.003	1.702	0.002	1.887	0.004	1.879	0.004	1.859	0.004
Anterior MI	1.873	0.002	1.942	0.002	1.987	0.001	0.983	0.065	0.976	0.063	0.093	0.063
Diabetes	1.465	0.006	0.978	0.054	0.926	0.056	0.876	0.054	0.809	0.055	0.877	0.056
Hypertension	0.893	0.059	1.357	0.007	1.386	0.007	1.543	0.008	1.592	0.008	1.601	0.007
Hypercholesterolemia	0.865	0.063	1.398	0.007	1.389	0.007	1.363	0.019	0.954	0.056	0.958	0.064
Smoker	0.899	0.062	0.956	0.054	0.987	0.053	0.876	0.076	0.823	0.077	0.889	0.069

LVED: left ventricular end diastolic; LVEF: left ventricular ejection fraction; MI: myocardial infarction.

**Table 6. MACE of different groups.**

MACE	In-hospital		1 month		Six months	
	Model group	Control group	Model group	Control group	Model group	Control group
Total MACE	6 (2.1%)*	11 (6.4%)	4 (1.4%)*	9 (5.2%)	19 (6.7%)*	26 (14.9%)
Cardiac death	3 (1.1%)*	5 (2.9%)	1 (0.4%)*	2 (1.2%)	4 (1.4%)*	6 (3.4%)
Non-fatal MI	1 (0.4%)*	2 (1.2%)	0 (0%)	1 (0.6%)	3 (1.1%)*	4 (2.3%)
revascularization	2 (0.7%)*	4 (2.3%)	3 (1.1%)*	6 (3.5%)	12 (4.2%)*	16 (9.2%)

Data are presented as *n* (%). \*Compared with Control group, *P* < 0.05. MACE: major adverse cardiac events; MI: myocardial infarction.

### 3.5 Cost and days of hospitalization

The median hospitalization days of the model group was 8 days, which exhibited a decrease by three days compared

with the control group (*Z* = -11.24, *P* < 0.05). The median cost of the model group was 42,935 China Yuan, which exhibited a decrease by 7536 China Yuan compared with control group (*Z* = -3.26, *P* < 0.05).

## 4 Discussion

By comparing outcomes before and after the new regional cooperative rescue model was implemented, several encouraging findings were obtained. First, the pre-hospital delay, FMC2D time, D2D time, and total time after the model implemented were significantly reduced compared with corresponding indexes before the model was used. Second, a significant improvement in cardiac function was noted. LVEF increased and LVED decreased in the model group. In addition, the MACE rate in the model group was reduced. Third, patients involved in the new model benefited not only in prognosis but also in economic costs. The regional cooperative rescue model could significantly decrease days of hospitalization and mean costs in hospital.

Numerous studies including randomized trials and meta-analyses have demonstrated that the first few hours are vital for AMI patients in improving outcomes and reducing MACE rates. Reducing time to reperfusion to salvage the myocardium is important and challenging not only to cardiologist but also to the government. The time from when the patient seeks medical care to the opening of the culprit vessel can influence the development of the disease and prognosis.<sup>[13]</sup> Many countries are making effort to shorten the FMC.<sup>[14–17]</sup> In China, some hospitals in large cities such as Beijing and Guangzhou are investigating methods to shorten the delay time, such as building a chest pain center. With this healthcare facility, D2D may be significantly reduced. However, in small- and medium-sized cities, the situation is different and more complicated. Many factors such as economy, transport, and the education of the physicians and patients can influence the results. Many patients with AMI initially visit rural/community hospitals, where diagnosis, treatment guidelines, and rescue process are limited.

Zhenjiang is a typical medium city and is one of the first two health-care reform cities in China. The city has an area of 3843 square kilometers and a population of over 300 million. There are two PCI-centers and both located in the downtown. In our new model, the farthest distance which the primary hospital is 105 km away from our PCI center. The EMS consists of 120, its sub site and ambulance systems which affiliated hospitals. All the constituent parts should cooperative effectively and are well organized. Our cardiology center is the largest center in the city. Since 2008, when we established the new regional cooperative emergency cardiovascular care model for STEMI patients, a large number of patients have benefitted from the new model.<sup>[10]</sup> More and more primary hospitals are becoming involved in the new model, and the model has become more and more stable. In addition, our cardiology center has made

great efforts to train physicians in primary hospitals and residents in surrounding areas. Here, we retrospectively analyzed the differences in six primary hospitals before and after becoming involved in the new model. FMC2D, D2D, transfer time and informed consent time were all reduced. Because of the new model, we diagnosed patients with STEMI in time and activated the cardiac catheterization team immediately. Moreover, a GPS positioning system and real-time traffic tracking query system was installed in the emergency ambulance. The ambulance driver was able to avoid busy roads and select the most efficient transfer path to quickly reach the catheter room of our hospital. Thus, the pre-hospital delay can be reduced. Patients could also be directly sent to the interventional catheterization room bypassing the emergency room and the Coronary Care Unit, thus potentially decreasing the D2D time. Surprisingly, informed consent time was also decreased. This result may be associated with better education about AMI for the physicians and patients in primary hospitals. Given our efforts, physicians and residents knew more about AMI and reperfusion. Thus when patients are sent to our center, patients and/or relatives were prepared for the need to perform the PCI. In total, the FMC2D time delay was shortened. Moreover, to some extent, the onset of symptoms to FMC time may also be reduced due to more educated patients.

As the ischemic time was reduced, we observed a significant improvement in cardiac function. LVEF was increased and LVED was decreased in the model group. Furthermore, the incidence rate of MACE in the model group was reduced. In addition, of the patients who participated in regional cooperative rescue model, those who were younger, or suffered single vessel lesions exhibit better recovery. Gender and smoking status does not appear to affect cardiac function. Other factors' effects on characteristics contributing to recovery of cardiac function at different period require future study. Patients involved in the new model benefitted not only in outcomes but also in economic costs. The regional cooperative rescue model could significantly decrease days of hospitalization and the mean hospital costs. The result may reveal an association with the reduced incidence of MACEs and the improvement of cardiac function in the hospital. As reported in Circulation Cardiovascular Quality and Outcomes,<sup>[18]</sup> the result is not optimistic for project-clinical pathways established for acute coronary artery syndrome-2 (CPACS-2) since July 2008 in China. The effectiveness was otherwise limited and the D2D time and in-hospital days and incidence of MACEs were not significantly improved. A stepped-wedge cluster-randomized trial including remote level 2 hospitals called CPACS-3 has been designed in China and the results are eagerly an-

ticipated.<sup>[19]</sup> Our cardiology team now is the first to propose a regional cooperative rescue model for STEMI in a medium-size city. This model can effectively improve STEMI treatment by reducing FMC-to device time.

Overall, our results are promising. This system provides a new approach to reduce time to reperfusion and cardiovascular mortality. However, as this study is a retrospective cohort analysis, larger complicated factors that can influence outcomes of STEMI patients who were not included in the analysis, such as socioeconomic data, skill levels of the cardiac catheterization team, and the self-health care awareness in residents. Different cities have different situations, our single center and single city may not be applicable to other cities and other centers. More governmental support and societal attention will foster further study and application.

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