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Management of ST-segment elevation myocardial infarction in predominantly rural central China

A retrospective observational study

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Abstract

The degree of adherence to current guidelines for clinical management of ST-segment elevation myocardial infarction (STEMI) is known in developed countries and large Chinese cities, but in predominantly rural areas information is lacking. We assessed the application of early reperfusion therapy for STEMI in secondary and tertiary hospitals in Henan province in central China.

Data were retrospectively collected from 5 secondary and 4 tertiary hospitals in Henan concerning STEMI patients treated from January 2011 to January 2012, including management strategy, delay time, and inhospital mortality.

Among 1311 STEMI patients, 613 and 698 were treated at secondary and tertiary hospitals, respectively. Overall, 460 (35.1%) patients received early reperfusion therapy including thrombolysis in 383 patients and primary percutaneous coronary intervention in 77. Compared with secondary centers, early (37.2% vs 32.6%) and successful reperfusion (34.5% vs 25.1%) was significantly higher, whereas thrombolysis was lower in the tertiary hospitals (26.4% vs 32.5%). Median symptom onset-to-first medical contact, and door-to-needle and door-to-balloon time was 168, 18, and 60 minutes, respectively. Delay times closely approached recommended guidelines, especially in secondary centers. Use of recommended pharmacotherapy was low, particularly in secondary hospitals. Inhospital mortality was 5.8%, and similar between secondary and tertiary hospitals (6.0% vs 5.6%; $P=0.183$).

Two-thirds of STEMI patients did not receive early reperfusion, and tertiary hospitals mostly failed to take advantage of around-the-clock primary percutaneous coronary intervention. Actions such as referrals are warranted to shorten prehospital delay, and the concerns of patients and doctors regarding reperfusion risk should be addressed.

Abbreviations: ACCF/AHA = American College of Cardiology Foundation/American Heart Association, ACEI = angiotensin-converting enzyme inhibitors, AMI = acute myocardial infarction, ARB = angiotensin receptor blockers, China PEACE = China Patient-Centered Evaluative Assessment of Cardiac Events, CPACS = Clinical Pathways for Acute Coronary Syndromes in China Study, DTB = door-to-balloon, DTN = door-to-needle, ESC = European Society of Cardiology, FMC = first medical contact, GPI = glycoprotein IIb/IIIa inhibitors, GRACE = Global Registry of Acute Coronary Events, pPCI = primary percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction.

Keywords: myocardial infarction, percutaneous coronary intervention, reperfusion, thrombolytic therapy

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1. Introduction

ST-segment elevation myocardial infarction (STEMI) is an acute and critical disease. The mainstay reperfusion treatments for STEMI are primary percutaneous coronary intervention (pPCI) and thrombolysis, according to the guidelines of the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) and European Society of Cardiology (ESC).[1,2] Clinical implementation of these current guidelines for STEMI management has been assessed in developed countries.[3–12] According to the Global Registry of Acute Coronary Events (GRACE), in the year 2000, more than half of patients with STEMI received early reperfusion treatment.[5] In the same year in Europe, the early reperfusion was administered to ~55% of patients.[4] The use of pPCI has recently increased, and in 2005 in the Czech Republic, 93% of STEMI patients received early reperfusion, with 92% receiving pPCI.[7]

In China, the rate of early reperfusion therapy for STEMI patients has been much lower than in developed countries.[13,14] The Clinical Pathways for Acute Coronary Syndromes in China Study (CPACS; a multicenter prospective survey with 2973 patients) reported that between 2004 and 2005, early reperfusion treatment was used in one-third of patients with STEMI. pPCI was applied in 16.3% and 6.6% of PCI-capable and non-PCI-capable hospitals, respectively.[13] In addition, the China Patient-Centered

Evaluative Assessment of Cardiac Events (China PEACE) retrospective study of acute myocardial infarction (AMI) included 13,815 patients with STEMI from 162 hospitals in 3 years (2001, 2006, and 2011). This study found that nearly half of the STEMI patients had not received early reperfusion in the years from 2001 (44.8%) to 2011 (45.0%), although there was an increase in the use of pPCI (10.2% in 2001; 27.6% in 2011).[14] Studies conducted in large Chinese cities such as Beijing also reported a large difference between best evidence and practice.[15,16]

Until now, there has been no survey of patients with STEMI in Henan, the most populated (94.1 million) and predominantly rural (66%) province in central China.[17] The present study assessed the features of reperfusion therapy administered to consecutive STEMI patients in reperfusion-capable hospitals in the province of Henan in central China. Specifically, secondary and tertiary hospitals were compared for patient characteristics, management practices, time delays, inhospital mortality, and adherence to current guidelines.

2. Methods

2.1. Study design

The Ethics Committee of Zhengzhou University People's Hospital approved the study protocol. This was an observational, retrospective cohort study, and used a randomized stratified cluster sampling design to select a representative sample of the population with STEMI in Henan Province, China.

The sampling process was stratified by hospital level, which has been officially defined by the Chinese government based on clinical resources.[18] Primary hospitals are community hospitals with only the most basic facilities and very limited resources to serve inpatients,[13] and do not provide reperfusion therapy; they, therefore, were not included in this STEMI study. Secondary hospitals have at least 100 inpatient beds and the ability to provide acute medical care and preventive care services to populations of at least 100,000. Tertiary hospitals are major referral centers in provincial capitals and major cities.[13] All tertiary centers are able to provide cardiac catheterization around the clock, whereas in secondary centers, the availability of such services is more limited. In Henan, secondary and tertiary institutions annually treat ~60 to 150 and ~150 to 300 STEMI patients, respectively. The criteria for patient referral to secondary or tertiary reperfusion-capable hospitals are mainly distance and patients' choice.

2.2. Sample size estimation

We firstly wanted to investigate the rate of early reperfusion use in these hospitals. Based on a previous study,[19] we initially estimated these rates at 42.3% and 57.9% in secondary and tertiary hospitals, respectively. Using for reference the design of the China PEACE-Retrospective AMI study, we assumed an intracluster correlation of 0.02,[20] and calculated the design effect to be 3 and 5 in secondary and tertiary hospitals, respectively, with an average cluster size of 100 and 200. To achieve a precision of 10% with an alpha (α) of 0.05 (1-tailed test) in each of the hospitals, we estimated a required sample size of 197 in secondary hospitals and 328 in tertiary hospitals. Therefore, to improve precision in the description of treatment patterns and outcomes in hospitals of different levels, we randomly chose 5 secondary and 4 tertiary hospitals.

2.3. Participants

We enrolled 1440 consecutive patients with STEMI admitted to 9 hospitals between January 2011 and January 2012 in Henan province, central China. The 5 secondary hospitals were the following: Qinyang People's Hospital; First People's Hospital of Lingbao; First People's Hospital of Shangqiu; People's Hospital of Xihua County; and People's Hospital of Dancheng County. The 4 tertiary hospitals were as follows: Zhengzhou University People's Hospital; Xinxiang Central Hospital; First People's Hospital of Kaifeng; and Puyang Oil Field General Hospital (Fig. 1). There are 263 secondary and 32 tertiary hospitals in Henan.[21] The 9 hospitals in the present study collectively cover 44.4% (8/18 regions) of the Henan territory.

ST-segment elevation myocardial infarction in this study was defined in accordance with the universal definition of MI, specifically as persistent ST-segment elevation ($\geq$0.1 mV at J points) in 2 or more contiguous leads or new onset of left bundle branch block.[22]

2.4. Data collection

Data were collected by trained investigators of Zhengzhou University People's Hospital using a standardized form to be

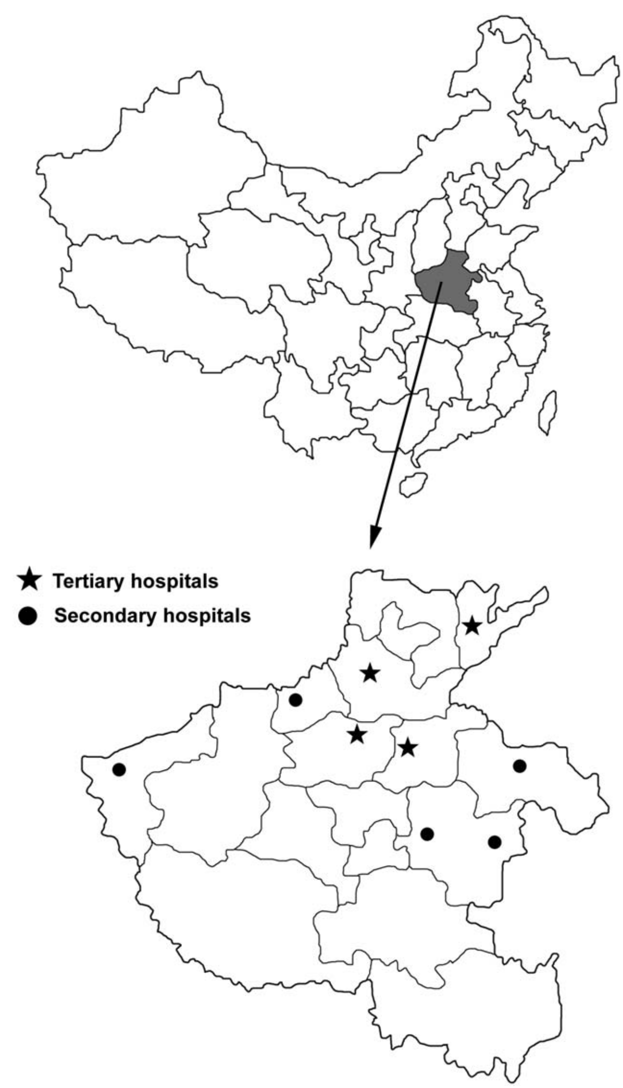

Figure 1. Geographic distribution of included hospitals.

filled in, after a 2-week training program on study objectives, data collection from medical records, and STEMI management. One secondary hospital and 4 tertiary hospitals had electronic medical records. We monitored at least 10% of the questionnaires for accuracy against medical records. If the questionnaires were not completed with 98% accuracy, all questionnaires were considered unqualified and were re-reviewed by a different investigator.

Records were collected for: demographics, cardiac risk factors and cardiac medical history, clinical characteristics on admission, delay time, management strategy, pharmacological treatments during the admission, inhospital mortality, and length of stay. The wall location of the MI was determined by electrocardiogram. Delay times were considered from symptom onset-to-first medical contact (FMC, defined as time of diagnostic ECG), from door-to-needle (DTN), and from door-to-balloon (DTB), the latter 2 defined as time from FMC to initiation of thrombolytic therapy or to wire passage into the culprit artery, respectively.

2.5. Study outcomes

The primary outcome in this study was early reperfusion use rate. The secondary outcomes were the proportion of fibrinolytic therapy, pPCI, successful reperfusion, and inhospital all-cause death. Successful reperfusion was defined as patency evaluated by the clinical standards or coronary angiography.

2.6. Statistical analysis

Categorical variables are presented as number and percentage, and were compared using the chi-square or Fisher exact tests among different-level hospitals. Continuous variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate, and differences between secondary and tertiary hospitals were compared using the *t* test or the Mann–Whitney *U* test.

In comparing study outcomes, we used multivariate logistic regression analyses to adjust for confounding factors.[23] Regarding the first 3 study outcomes, we adjusted for sociodemographics (age, sex, and race), risk factors, medical history, anterior MI, Killip class ≥2, and symptom onset-to-FMC >12 hours. Regarding all-cause death, we adjusted for sociodemographics, risk factors, medical history, anterior MI, Killip class ≥2, symptom onset-to-FMC >12 hours, successful reperfusion, and medication use during hospitalization.

Propensity score matching was chosen as a sensitivity analysis to test whether the results remain consistent using different methods. A propensity score model was constructed to eliminate covariate differences; 2 cohorts of 1:1 nearest-neighbor-matched patients were consequently obtained. The propensity score was calculated using logistic regression covariates including age, sex, risk factors, medical history, anterior MI, Killip class ≥2, and symptom onset-to-FMC >12 hours for the first 3 study outcomes. Regarding all-cause death, successful reperfusion and medication use during hospitalization were added as covariates. All baseline variables were comparable after propensity score matching.

Two-sided $P < 0.05$ denoted statistical significance. Statistical analyses were performed with SPSS version 17.0 (SPSS, Chicago, IL) and SAS 9.4 (SAS Institute Inc., Cary, NC).

3. Results

3.1. Baseline characteristics

Out of a total of 1440 consecutive patients presenting with STEMI, complete and accurate questionnaires were obtained from 1311 patients: 613 and 698 came from secondary and tertiary hospitals, respectively. Compared with STEMI patients seen at secondary hospitals, those at tertiary centers were significantly younger, with higher proportions of men, hypertension, diabetes, dyslipidemia, smoking, prior stroke, prior angina and PCI, and inferior wall and anterior-inferior wall MI at hospital admission (Table 1).

Table 1

Baseline patient characteristics.

	Total (N=1311)	Secondary (n=613)	Tertiary (n=698)	*P*
Age, y	63.0±12.2	63.5±11.6	62.6±12.7	0.026
Male, n (%)	933 (71.2)	419 (68.4)	514 (73.6)	0.035
Han Chinese, n (%)	1298 (99.0)	607 (99.0)	691 (99.0)	0.965
Risk factors, n (%)				
Hypertension	610 (46.5)	249 (40.6)	361 (51.7)	<0.001
Diabetes	214 (16.3)	73 (11.9)	141 (20.2)	<0.001
Dyslipidemia	194 (14.8)	76 (12.4)	118 (16.9)	0.022
Smoking	497 (37.9)	198 (32.3)	299 (42.8)	<0.001
Medical history, n (%)				
Myocardial infarction	77 (5.9)	32 (5.2)	45 (6.4)	0.346
Prior stroke	113 (8.6)	39 (6.4)	74 (10.6)	0.006
Prior angina	382 (29.1)	83 (13.5)	299 (42.8)	<0.001
PCI	32 (2.4)	5 (0.8)	27 (3.9)	<0.001
CABG	4 (0.3)	2 (0.3)	2 (0.3)	≈1.0
Infarct location, n (%)				
Anterior*	655 (50.0)	360 (58.7)	295 (42.3)	<0.001
Inferior†	552 (42.1)	221 (36.1)	331 (47.4)	<0.001
Antero-inferior	99 (7.6)	30 (4.9)	69 (9.9)	0.001
LBBB	5 (0.4)	2 (0.3)	3 (0.4)	≈1.0
Killip class, n (%)				
I	817 (62.3)	434 (70.8)	383 (54.9)	<0.001
II	349 (26.6)	108 (17.6)	241 (34.5)	<0.001
III	97 (7.4)	53 (8.6)	44 (6.3)	0.106
IV	48 (3.7)	18 (2.9)	30 (4.3)	0.190

CABG=coronary artery bypass grafting, LBBB=left bundle branch block, PCI=percutaneous coronary intervention.

* Includes anteroseptal wall, anterior wall, extensive anterior wall, and lateral wall.

† Includes inferior wall, posterior wall, and right ventricle.

3.2. Reperfusion strategies and delay times

Among 1311 patients, 29.2% were treated with thrombolysis and 5.9% were treated with pPCI. The percentage of patients who received fibrinolytic therapy in secondary centers (32.5%) was significantly higher than that in tertiary hospitals (26.4%; $P=0.015$), whereas the utilization rates of pPCI (0.2% vs 10.9%; $P<0.001$) and elective PCI (10.3% vs 27.5%; $P<0.001$) were lower in secondary hospitals than those in tertiary hospitals. The utilization rate of primary PCI was only 10.9% in tertiary hospitals, which was lower than that of elective PCI (27.5%) (Table 2).

Among the 851 STEMI patients who did not receive early reperfusion, 155 (18.2%) were admitted more than 12 hours after symptom onset, with no statistical difference between the admissions in secondary and tertiary hospitals (20.3% vs 16.2%; $P=0.119$); 182 (21.4%) patients refused thrombolysis or pPCI. Compared with those in secondary hospitals, patients in tertiary hospitals were more likely to refuse early reperfusion treatment (28.5% vs 13.8%; $P<0.001$). Data regarding contraindications to reperfusion therapy were difficult to extract from the medical histories.

Table 2

Reperfusion strategies and delay times.

	Total (N=1311)	Secondary (n=613)	Tertiary (n=698)	*P*
Thrombolysis, n (%)	383 (29.2)	199 (32.5)	184 (26.4)	0.015
Primary PCI, n (%)	77 (5.9)	1 (0.2)	76 (10.9)	<0.001
Elective PCI, n (%)	255 (19.5)	63 (10.3)	192 (27.5)	<0.001
Patients submitted to reperfusion				
Onset-to-FMC, min	168 (90, 270)	132 (60, 246)	180 (115, 300)	0.008
DTN, min	18 (6, 48)	18 (6, 36)	30 (12, 60)	0.005
DTB, min	60 (30, 120)	—	60 (30, 120)	—
Onset-to-thrombolysis, h	3.3 (2.1, 5.3)	3.0 (1.7, 4.7)	3.8 (2.3, 5.5)	0.002
Onset-to-pPCI, h	4.0 (2.7, 6.4)	—	4.0 (2.7, 6.2)	—
All patients				
Onset-to-elective PCI, d	10.0 (7.0, 13.8)	12.0 (8.0, 15.8)	9.0 (6.0, 13.0)	<0.001
Symptom onset-to-FMC >12 h, n (%)	166 (12.7)	88 (14.4)	78 (11.2)	0.084
Hospital stay, d	11.0 (7.0, 14.0)	10.0 (6.0, 14.0)	12.0 (8.0, 15.0)	<0.001

DTB=door-to-balloon time, DTN=door-to-needle time, FMC=first medical contact, PCI=percutaneous coronary intervention.

Times from symptom onset to FMC, DTN, and symptom onset to thrombolysis were 168, 18, and 60 minutes, respectively, which were significantly shorter in secondary hospitals than those in tertiary hospitals. Overall median hospitalization was 11 days and significantly longer in tertiary facilities (12 vs 10 days; $P<0.001$) (Table 2).

3.3. Adjunctive pharmacotherapy

Aspirin and clopidogrel were used as mainstay antiplatelet therapy in over 90% of STEMI patients, and 91.5% received low-molecular-weight heparin, and 94.7% were administered statins. However, more than 40% of patients did not receive aspirin or clopidogrel loading doses; compared with patients in secondary centers, a higher proportion of patients in tertiary hospitals received no loading dose of aspirin, or 300 or 600 mg loading dose of clopidogrel, and 48.9% of patients in secondary institutions did not receive a clopidogrel loading dose.

Other evidence-based drugs such as β-blockers, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), calcium channel blockers, the anticoagulant fondaparinux, antiplatelet agent-glycoprotein IIb/IIIa inhibitors (GPI), and proton pump inhibitors were rarely prescribed, especially in secondary facilities (Table 3).

3.4. Study outcomes

Among 1311 patients, only 35.1% received early reperfusion therapy. Before adjustment, there was no difference in early reperfusion rate between secondary and tertiary hospitals (32.6% vs 37.2%; $P=0.080$). However, after adjusting for sociodemographics, risk factors, medical history, infarct location, cardiac function, and symptom onset-to-FMC time, early reperfusion use rate was significantly higher in tertiary hospitals than that in secondary hospitals ($P=0.031$). The proportion of successful reperfusion was significantly higher in tertiary

Table 3

Medication use during hospitalization (n [%]).

	Total (N=1311)	Secondary (n=613)	Tertiary (n=698)	*P*
Aspirin	1276 (97.3)	606 (98.9)	670 (96.0)	0.001
Aspirin, LD				
None	612 (46.7)	219 (35.7)	393 (56.3)	<0.001
300 mg	630 (48.1)	340 (55.5)	290 (41.5)	<0.001
600 mg	3 (0.2)	0 (0)	3 (0.4)	0.26
Clopidogrel	1212 (92.4)	534 (87.1)	678 (97.1)	<0.001
Clopidogrel, LD				
None	571 (43.6)	300 (48.9)	271 (38.8)	0.008
300 mg	494 (37.7)	175 (28.5)	319 (45.7)	<0.001
600 mg	39 (3.0)	0 (0)	39 (5.6)	<0.001
Low-molecular-weight heparin	1200 (91.5)	579 (94.5)	621 (89.0)	<0.001
Fondaparinux	16 (1.2)	0 (0)	16 (2.3)	<0.001
Statins	1241 (94.7)	560 (91.4)	681 (97.6)	<0.001
β-blockers	769 (58.7)	328 (53.5)	441 (63.2)	<0.001
ACEI	499 (38.1)	169 (27.6)	330 (47.3)	<0.001
ARB	205 (15.6)	95 (15.5)	110 (15.8)	0.896
GPI	70 (5.3)	10 (1.6)	60 (8.6)	<0.001
Calcium channel blockers	136 (10.4)	42 (6.9)	94 (13.5)	<0.001
Proton pump inhibitors	350 (26.7)	135 (22.0)	215 (30.8)	<0.001

ACEI=angiotensin-converting enzyme inhibitor, ARB=angiotensin receptor blocker, GPI=glycoprotein IIb/IIIa inhibitor, LD=loading dose.

Table 4

Study outcomes.

	Total (N=1311)	Secondary (n=613)	Tertiary (n=698)	Unadjusted OR for tertiary hospitals	*P*	Adjusted OR for tertiary hospitals	*P*	Power
Early reperfusion, n (%)*	460 (35.1)	200 (32.6)	260 (37.2)	1.23 (0.98–1.54)	0.080	1.38 (1.03–1.85)	0.031	0.41
Fibrinolytic therapy, n (%)*	383 (29.2)	199 (32.5)	184 (26.4)	0.75 (0.59–0.95)	0.015	0.65 (0.48–0.88)	0.005	0.68
Successful reperfusion, n (%)*	395 (30.1)	154 (25.1)	241 (34.5)	1.57 (1.24–2.00)	<0.001	1.83 (1.35–2.48)	<0.001	0.96
All-cause death, n (%)†	76 (5.8)	37 (6.0)	39 (5.6)	0.92 (0.58–1.47)	0.729	1.58 (0.81–3.11)	0.183	0.06

Risk factors included hypertension, diabetes, dyslipidemia, and smoking; Medical history included stroke, angina, myocardial infarction, PCI, and CABG.
ACEI=angiotensin-converting enzyme inhibitor, ARB=angiotensin receptor blocker, FMC=first medical contact, GPI=glycoprotein IIb/IIIa inhibitor, MI=myocardial infarction, OR=odds ratio.
* Adjusted for age, sex, race, risk factors, medical history, anterior MI, Killip class ≥2, and symptom onset-to-FMC > 12 hours.
† Adjusted for age, sex, race, risk factors, medical history, anterior MI, Killip class ≥2, symptom onset-to-FMC >12 hours, successful reperfusion and medication use during hospitalization (aspirin, clopidogrel, low-molecular-weight heparin/fondaparinux, statins, β-blockers, ACEI/ARB, GPI, calcium channel blockers, and proton pump inhibitors).

hospitals compared with that in secondary hospitals before and after adjustment.

Thrombolysis is the primary reperfusion therapy in central China in both secondary and tertiary hospitals. The percentage of patients who received thrombolysis in secondary hospitals (32.5%) was significantly higher than that in tertiary hospitals (26.4%) before and after adjustment. An adjusted analysis could not be performed due to the small number of pPCI cases in secondary hospitals (Tables 4–7).

In-hospital mortality was 5.8%. There was no difference in in-hospital mortality between secondary (6.0%) and tertiary hospitals (5.6%) before and after adjusting for sociodemographics, risk factors, medical history, infarct location, cardiac function, symptom onset-to-FMC time, successful reperfusion and medication use during hospitalization (Tables 4 and 8).

3.5. Propensity score matching

After propensity score matching, all baseline variables and medication use during hospitalization between 2 groups were comparable (Tables 9 and 10). There was a significant difference in the proportion of early reperfusion ($P=0.048$), fibrinolytic therapy ($P=0.045$), and successful reperfusion ($P=0.001$) between secondary and tertiary hospitals. However, no difference was found in inhospital mortality between 2 types of hospitals ($P=0.579$) (Table 11). The results were consistent with that of multivariate logistic regression analyses.

4. Discussion

The present study investigated the management of patients with STEMI in secondary and tertiary hospitals in central China, a region of ~100 million people. We found that only ~35% of STEMI patients in these hospitals received early reperfusion therapy with thrombolysis as predominant reperfusion modality (~83% of cases). pPCI was underutilized, especially in tertiary hospitals able to provide pPCI around the clock. Patients with STEMI in tertiary hospitals had higher reperfusion use rate. Time to treatments in these centers approached the limits recommended by the ACCF/AHA and ESC guidelines,[1,2] and secondary hospitals performed better by this metric. We also found that most guideline-recommended drugs were rarely prescribed and inhospital mortality was low. These results are useful for identifying differences between guidelines and clinical practice in rural areas and to determine measures that could improve outcomes.

We noted that early reperfusion use rate was lower than that previously reported in China and other developed coun-

Table 5

Odds ratio of patients with STEMI receiving early reperfusion therapy by logistic regression analysis.

	Univariate		Multivariate	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Tertiary hospitals	1.23 (0.98–1.54)	0.080	1.38 (1.03–1.85)	0.031
Age, y	0.97 (0.96–0.98)	<0.001	0.97 (0.96–0.99)	<0.001
Male	0.56 (0.43–0.73)	<0.001	0.71 (0.51–0.99)	0.043
Han Chinese	0.63 (0.21–1.87)	0.403		
Hypertension	0.99 (0.79–1.25)	0.956		
Diabetes	0.91 (0.67–1.24)	0.537		
Dyslipidemia	1.07 (0.78–1.48)	0.677		
Smoking	1.58 (1.25–2.00)	<0.001		
Old MI	0.68 (0.41–1.13)	0.138		
Prior stroke	0.55 (0.35–0.87)	0.010	0.55 (0.32–0.95)	0.032
Prior angina	0.76 (0.59–0.98)	0.031	0.54 (0.39–0.76)	<0.001
Prior PCI	0.97 (0.46–2.03)	0.931		
Prior CABG	–	0.015		
Anterior MI	0.74 (0.59–0.93)	0.010	0.72 (0.56–0.94)	0.015
Killip class ≥2	0.76 (0.60–0.97)	0.024	0.69 (0.52–0.92)	0.010
Symptom onset-to-FMC >12 h	0.12 (0.06–0.22)	<0.001	0.08 (0.04–0.17)	<0.001

CABG=coronary artery bypass grafting, CI=confidence interval, FMC=first medical contact, MI=myocardial infarction, OR=odds ratio, PCI=percutaneous coronary intervention, STEMI=ST-segment elevation myocardial infarction.

Table 6

Odds ratio of patients with STEMI receiving fibrinolytic therapy by logistic regression analysis.

	Univariate		Multivariate	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Tertiary hospitals	0.75 (0.59–0.95)	0.015	0.65 (0.48–0.88)	0.005
Age, y	0.97 (0.96–0.98)	<0.001	0.97 (0.96–0.98)	<0.001
Male	0.57 (0.43–0.76)	<0.001	0.69 (0.49–0.98)	0.040
Han Chinese	0.48 (0.16–1.43)	0.175		
Hypertension	0.98 (0.77–1.24)	0.848		
Diabetes	0.86 (0.62–1.20)	0.368		
Dyslipidemia	0.95 (0.68–1.34)	0.781		
Smoking	1.57 (1.23–2.00)	<0.001		
Old MI	0.73 (0.42–1.25)	0.243		
Prior stroke	0.43 (0.26–0.73)	0.001	0.45 (0.24–0.85)	0.014
Prior angina	0.89 (0.68–1.16)	0.389		
Prior PCI	0.80 (0.36–1.81)	0.597		
Prior CABG	–	0.007		
Anterior MI	0.93 (0.73–1.18)	0.559		
Killip class ≥2	0.67 (0.52–0.87)	0.002		
Symptom onset-to-FMC >12 h	0.14 (0.08–0.28)	<0.001	0.10 (0.04–0.21)	<0.001

CABG = coronary artery bypass grafting, CI = confidence interval, FMC = first medical contact, MI = myocardial infarction, OR = odds ratio, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction.

tries.[3,4,11,15,16,24,25] The results of the China PEACE study showed that in 2011, 31.4% of STEMI patients received thrombolysis and 27.5% pPCI in eastern rural China, whereas 55.4% received thrombolysis and 0.3% pPCI in western rural China.[24,25] Our results confirmed that reperfusion treatment in central China is somewhere in between, corresponding with the level of economic development, for which there is great room for improvement.

In our present study, we found that pPCI was underutilized, and tertiary hospitals did not take advantage of their pPCI capability. Two reasons underlie this situation. Firstly, doctors in tertiary hospitals prefer to perform PCI, often ignoring thrombolysis as an option. In Henan, tertiary hospitals have adequate equipment and experienced doctors, and most patients with STEMI are hospitalized just for PCI. However, most STEMI patients in our study live in the countryside and have a low level of education. They are not able to quickly recognize the signs of AMI and understand or follow doctors' advice. Our study showed that the percentage of patients in tertiary hospitals who missed the recommended time window of 12 hours between onset and reperfusion therapy was 16.2%, and patient refusal was 28.5%.

Secondly, for patients who have contraindications for thrombolysis, doctors in secondary hospitals prefer to apply conservative treatment rather than transfer patients to higher-level hospitals, which has a complex mix of medical, patient-related, regulatory, and economic factors. Limited by retrospective study, we had no data on patient transfer. However, our results showed that in tertiary hospitals, the rate of elective PCI was higher than the rate of pPCI. To improve this situation, the public's understanding and recognition of STEMI must improve, and also cardiologists' knowledge of current guidelines and patient referrals should be encouraged.

Table 7

Odds ratio of patients with STEMI receiving successful reperfusion by logistic regression analysis.

	Univariate		Multivariate	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Tertiary hospitals	1.57 (1.24–2.00)	<0.001	1.83 (1.35–2.48)	<0.001
Age, y	0.97 (0.96–0.98)	<0.001	0.98 (0.96–0.99)	<0.001
Male	0.55 (0.42–0.73)	<0.001	0.69 (0.49–0.99)	0.043
Han Chinese	0.69 (0.22–2.12)	0.725		
Hypertension	1.07 (0.85–1.36)	0.560		
Diabetes	1.01 (0.74–1.39)	0.949		
Dyslipidemia	1.18 (0.85–1.64)	0.327		
Smoking	1.64 (1.29–2.09)	<0.001		
Old MI	0.59 (0.34–1.03)	0.062		
Prior stroke	0.60 (0.37–0.95)	0.028		
Prior angina	0.73 (0.56–0.96)	0.022	0.50 (0.35–0.71)	<0.001
Prior PCI	0.90 (0.41–1.97)	0.797		
Prior CABG	–	0.008		
Anterior MI	0.63 (0.50–0.80)	<0.001	0.65 (0.49–0.85)	0.002
Killip class ≥2	0.91 (0.71–1.17)	0.471		
Symptom onset-to-FMC >12 h	0.11 (0.05–0.22)	<0.001	0.09 (0.04–0.20)	<0.001

CABG = coronary artery bypass grafting, CI = confidence interval, FMC = first medical contact, MI = myocardial infarction, OR = odds ratio, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction.

Table 8

Odds ratio for inhospital mortality by logistic regression analysis.

	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Tertiary hospitals	0.92 (0.58–1.47)	0.729		
Age, y	1.08 (1.06–1.11)	<0.001	1.07 (1.04–1.10)	<0.001
Male	2.63 (1.65–4.20)	<0.001		
Han Chinese	–	≈1.0		
Hypertension	1.19 (0.75–1.89)	0.470		
Diabetes	0.77 (0.39–1.53)	0.460		
Dyslipidemia	0.65 (0.29–1.44)	0.288		
Smoking	0.56 (0.33–0.96)	0.034		
Old MI	1.15 (0.45–2.94)	0.969		
Prior stroke	2.16 (1.13–4.14)	0.018		
Prior angina	0.88 (0.52–1.48)	0.623		
Prior PCI	–	0.254		
Prior CABG	–	≈1.0		
Anterior MI	1.26 (0.78–2.01)	0.345		
Killip class ≥2	2.37 (1.48–3.79)	<0.001	2.46 (1.36–4.46)	0.003
Symptom onset-to-FMC >12 hours	1.21 (0.62–2.34)	0.578		
Successful reperfusion	0.22 (0.10–0.49)	<0.001	0.32 (0.13–0.82)	0.018
Aspirin	0.19 (0.08–0.42)	<0.001		
Clopidogrel	0.34 (0.18–0.64)	0.001		
Low-molecular-weight heparin/fondaparinux	0.45 (0.22–0.92)	0.024		
Statins	0.32 (0.16–0.65)	0.001	0.19 (0.07–0.49)	0.001
β-blockers	0.57 (0.36–0.93)	0.021		
ACEI/ARB	0.45 (0.27–0.74)	0.001	0.43 (0.23–0.80)	0.008
GPI	0.49 (0.12–2.04)	0.464		
Calcium channel blockers	0.63 (0.25–1.59)	0.321		
Proton pump inhibitors	1.14 (0.67–1.92)	0.630		

ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker, CABG = coronary artery bypass grafting, CI = confidence interval, FMC = first medical contact, GPI = glycoprotein IIb/IIIa inhibitor, MI = myocardial infarction, OR = odds ratio, PCI = percutaneous coronary intervention.

Although the application of reperfusion therapy was low in the present study, delay times to treatments more closely approached those recommended by the guidelines. Median times from symptom onset-to-FMC, DTN, and DTB are substantially lower than those reported by other studies in China. Median time from symptom onset-to-FMC was 240 minutes in a STEMI registry in 5 regions of China in 2004 and 780 minutes in the China PEACE study in 2011.[14,26] DTN and DTB times were 83 and 132

Table 9

Baseline patient characteristics.

	Total (N = 1311)	Before matching: Secondary (n = 613)	Before matching: Tertiary (n = 698)	P	Propensity score-matched*: Secondary (n = 344)	Propensity score-matched*: Tertiary (n = 344)	P	Propensity score-matched†: Secondary (n = 283)	Propensity score-matched†: Tertiary (n = 283)	P
Age, y	63.0 ± 12.2	63.5 ± 11.6	62.6 ± 12.7	0.026	62.1 ± 12.2	62.6 ± 12.9	0.580	61.9 ± 12.0	62.2 ± 12.8	0.803
Male, n (%)	933 (71.2)	419 (68.4)	514 (73.6)	0.035	253 (73.5)	244 (70.9)	0.444	201 (71.0)	200 (70.7)	0.926
Han Chinese, n (%)	1298 (99.0)	607 (99.0)	691 (99.0)	0.965	340 (98.8)	341 (99.1)	≈1.0	278 (98.2)	280 (98.9)	0.725
Risk factors, n (%)										
Hypertension	610 (46.5)	249 (40.6)	361 (51.7)	<0.001	147 (42.7)	158 (45.9)	0.399	122 (43.1)	128 (45.2)	0.612
Diabetes	214 (16.3)	73 (11.9)	141 (20.2)	<0.001	57 (16.6)	55 (16.0)	0.836	45 (15.9)	44 (15.5)	0.908
Dyslipidemia	194 (14.8)	76 (12.4)	118 (16.9)	0.022	54 (15.7)	44 (12.8)	0.275	43 (15.2)	40 (14.1)	0.721
Smoking	497 (37.9)	198 (32.3)	299 (42.8)	<0.001	136 (39.5)	125 (36.3)	0.387	108 (38.2)	105 (37.1)	0.795
Medical history, n (%)										
Prior stroke	113 (8.6)	39 (6.4)	74 (10.6)	0.006	26 (7.6)	36 (10.5)	0.183	20 (7.1)	24 (8.5)	0.530
Prior CAD	422 (32.2)	111 (18.1)	311 (44.6)	<0.001	104 (30.2)	106 (30.8)	0.868	90 (31.8)	94 (33.2)	0.720
Prior revascularization	36 (2.7)	7 (1.1)	29 (4.2)	0.001	7 (2.0)	9 (2.6)	0.613	6 (2.1)	7 (2.5)	0.779
Anterior MI	655 (50.0)	360 (58.7)	295 (42.3)	<0.001	174 (50.6)	161 (46.8)	0.321	143 (50.5)	144 (50.9)	0.933
Killip class ≥2	494 (37.7)	179 (29.2)	315 (45.1)	<0.001	147 (42.7)	136 (39.5)	0.394	120 (42.4)	119 (42.0)	0.932
Symptom onset-to-FMC >12 h	166 (12.7)	88 (14.4)	78 (11.2)	0.084	60 (17.4)	45 (13.1)	0.112	35 (12.4)	33 (11.7)	0.796
Successful reperfusion	395 (30.1)	154 (25.1)	241 (34.5)	<0.001	—	—	—	89 (31.4)	85 (30.0)	0.716

CAD = coronary artery disease, FMC = first medical contact, MI = myocardial infarction.

* Adjusted for age, sex, risk factors, medical history, anterior MI, Killip class ≥2, and symptom onset-to-FMC >12 hours.

† Adjusted for age, sex, risk factors, medical history, anterior MI, Killip class ≥2, symptom onset-to-FMC >12 hours, successful reperfusion and medication use during hospitalization (aspirin, clopidogrel, low-molecular-weight heparin/fondaparinux, statins, β-blockers, ACEI/ARB, GPI, calcium channel blockers, and proton pump inhibitors).

Table 10

Medication use during hospitalization (n [%]).

		Before matching			Propensity score-matched*		
	Total (N=1311)	Secondary (n=613)	Tertiary (n=698)	*P*	Secondary (n=283)	Tertiary (n=283)	*P*
Aspirin	1276 (97.3)	606 (98.9)	670 (96.0)	0.001	282 (99.6)	281 (99.3)	0.563
Clopidogrel	1212 (92.4)	534 (87.1)	678 (97.1)	<0.001	277 (97.9)	277 (97.9)	≈1.0
Low-molecular-weight heparin/fondaparinux	1216 (92.8)	579 (94.5)	637 (91.3)	0.026	267 (94.3)	268 (94.7)	0.853
Statins	1241 (94.7)	560 (91.4)	681 (97.6)	<0.001	273 (96.5)	272 (96.1)	0.824
β-blockers	769 (58.7)	328 (53.5)	441 (63.2)	<0.001	161 (56.9)	167 (59.0)	0.609
ACEI/ARB	675 (51.7)	264 (43.1)	440 (63.0)	<0.001	139 (49.1)	143 (50.5)	0.737
GPI	70 (5.3)	10 (1.6)	60 (8.6)	<0.001	7 (2.5)	8 (2.8)	0.794
Calcium channel blockers	136 (10.4)	42 (6.9)	94 (13.5)	<0.001	27 (9.5)	25 (8.8)	0.771
Proton pump inhibitors	350 (26.7)	135 (22.0)	215 (30.8)	<0.001	81 (28.6)	68 (24.0)	0.215

ACEI=angiotensin-converting enzyme inhibitor, ARB=angiotensin receptor blocker, GPI=glycoprotein IIb/IIIa inhibitor.
* Adjusted for age, sex, risk factors, medical history, anterior MI, Killip class ≥2, symptom onset-to-FMC >12 hours, successful reperfusion and medication use during hospitalization (aspirin, clopidogrel, low-molecular-weight heparin/fondaparinux, statins, β-blockers, ACEI/ARB, GPI, calcium channel blockers, and proton pump inhibitors).

minutes, respectively, in a STEMI registry in Beijing in 2006, and 65 and 110 minutes,respectively, in a STEMI registry in 5 regions of China.[15,26] The results of the BRIG (Bridging the Gap in Coronary Heart Disease Secondary Prevention in China) project showed that median times from symptom onset-to-FMC, DTN, and DTB were, respectively, 230, 60, and 134 minutes in secondary hospitals, and 282, 45, and 105 minutes in tertiary hospitals.[19] This result suggests good coordination of different department in secondary and tertiary hospitals in central China.

The results of this study confirm the very high use of evidence-based drugs such as aspirin, clopidogrel, low–molecular-weight heparin, and statins. However, loading doses of aspirin or clopidogrel, and drugs such as β-blockers, ACEIs, and ARBs, and antiplatelet agents such as GPI were not prescribed at the optimal rates. Tertiary hospitals applied aspirin-loading doses less, but clopidogrel-loading doses more than did secondary hospitals. This may be because the majority of patients with STEMI were first treated at secondary hospitals and survivors were then finally admitted to tertiary hospitals for PCI. However, we had no data on the medication intake before admission. In the secondary centers, patients are likely to have been on aspirin for a while, and doctors usually do not prescribe clopidogrel or give a loading dose in addition to aspirin because of fear of bleeding complications.

β-blockers and ACEIs were used in 70% to 80% of STEMI patients in the PL-ACS (Polish Registry of Acute Coronary Syndromes) study and a STEMI registry in Beijing, China[9,15]; in 70% and 67.8%, respectively, in the CPACS study[27]; and in 65% and 69% in the BLITZ study.[28] In the SNAPSHOT ACS study, β-blockers were prescribed in 82% of STEMI patients at discharge, and ACEI or ARB was used in 76%.[12] A GPI was used in 19.6% of STEMI patients in the Euro Heart Survey ACS study[4]; in 17.7% and 22.4% of thrombolysis and pPCI-treated patients, respectively, in a STEMI registry in Beijing, China[15]; and in 8% and 66% of thrombolysis and pPCI-treated patients, respectively, in the Italian BLITZ study.[28]

Inhospital mortality in our study was lower than other trials in China,[13,14,29] possibly because of the following reasons. First and most importantly, inhospital mortality is not the primary outcome in the sample size estimation, so the sample size is too small to calculate the inhospital mortality. Second, in predominantly rural central China, most severe patients died in home or outpatient, which decreased the inhospital mortality to some extent.

The present study is limited in that it is not prospective, and data were extracted from medical records that were not uniformly complete or accurate. Second, long-term follow-up data are lacking, and assessment of rescue PCI use was not possible. Third, data relating to patient referral characteristics (time, distance, and means of transportation) and medication use before admission were not available; this made factors related to prehospital delay and emergency treatment unknown. However, the symptom onset-to-FMC time was known in our study, and China PEACE study showed that no STEMI patients received prior hospital fibrinolytic therapy in non-PCI-capable hospitals.[30] Therefore, the lack of prehospital treatment data has little

Table 11

Study outcomes after propensity score-matched.

	n	Early reperfusion, n (%)*	Fibrinolytic therapy, n (%)*	Successful reperfusion, n (%)*	n	All-cause death, n (%)†
Secondary	344	115 (33.4)	114 (33.1)	91 (26.5)	283	14 (4.9)
Tertiary	344	140 (40.7)	90 (26.2)	131 (38.1)	283	17 (6.0)
P		0.048	0.045	0.001		0.579
OR (95% CI)		1.37 (1.00–1.86)	0.72 (0.51–0.99)	1.71 (1.24–2.36)		1.23 (0.59–2.54)
Power		0.51	0.90	0.51		0.09

Risk factors included hypertension, diabetes, dyslipidemia, and smoking; medical history included stroke, prior CAD, and prior revascularization.
ACEI=angiotensin-converting enzyme inhibitor, ARB=angiotensin receptor blocker, CI=confidence interval, FMC=first medical contact, GPI=glycoprotein IIb/IIIa inhibitor, MI=myocardial infarction, OR=odds ratio.
* Adjusted for age, sex, risk factors, medical history, anterior MI, Killip class ≥2 and symptom onset-to-FMC >12 hours.
† Adjusted for age, sex, risk factors, medical history, anterior MI, Killip class ≥2, symptom onset-to-FMC >12 hours, successful reperfusion and medication use during hospitalization (aspirin, clopidogrel, low-molecular-weight heparin/fondaparinux, statins, β-blockers, ACEI/ARB, GPI, calcium channel blockers, and proton pump inhibitors).

affect on the evaluation of primary outcome. Finally, sample size was relatively small, and power was not adequate to detect differences in early reperfusion rate and inhospital mortality between secondary and tertiary hospitals. Therefore, a multicenter prospective observational study, the Henan STEMI registry (NCT02641262), has been initiated to gain a deeper knowledge of the real-world use of early reperfusion in central China since December 2015. Nevertheless, to our knowledge, this is the most comprehensive study of patients admitted to hospital with STEMI in central China from 2011 to 2012.

5. Conclusions

The rate of early reperfusion therapy applied for STEMI patients in central China was lower than recommended, but time delays to treatment were close to the guidelines. Tertiary hospitals did not take full advantage of their ability to provide pPCI. Improvement in the management of STEMI patients in central China requires a joint effort between government and professional societies. The government needs to expand awareness and educational initiatives regarding STEMI and establish policies to facilitate patient referral. Professional societies need to support training and the implementation of guidelines, especially the use of thrombolysis by cardiologists in tertiary hospitals, and of pPCI overall. Ultimately, appropriate reperfusion treatment provided to STEMI patients in central China will help improve patients' quality of life in this predominantly rural region. These lessons may be useful for developing specific STEMI guidelines applicable to rural areas globally.

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