Current Trends for ST-segment Elevation Myocardial Infarction during the Past 5 Years in Rural Areas of China's Liaoning Province: A Multicenter Study

Guang-Xiao Li[1], Bo Zhou[1], Guo-Xian Qi[2], Bo Zhang[3], Da-Ming Jiang[4], Gui-Mei Wu[5], Bing Ma[1], Peng Zhang[1], Qiong-Rui Zhao[1], Juan Li[1], Ying Li[6], Jing-Pu Shi[1]

[1]Department of Clinical Epidemiology, Institute of Cardiovascular Diseases, The First Affiliated Hospital, China Medical University, Shenyang, Liaoning 110001, China
[2]Department of Geriatric Cardiology, The First Affiliated Hospital, China Medical University, Shenyang, Liaoning 110001, China
[3]Department of Cardiology, The First Affiliated Hospital, Dalian Medical University, Dalian, Liaoning 116000, China
[4]Department of Cardiology, Dandong Center Hospital, Dandong, Liaoning 118000, China
[5]Department of Special Clinic, The First Affiliated Hospital, China Medical University, Shenyang, Liaoning 110001, China
[6]Department of Experiment Teaching Center, School of Public Health, China Medical University, Shenyang, Liaoning 110001, China

Abstract

Background: Since 2010, two versions of National Guidelines aimed at promoting the management of ST-segment elevation myocardial infarction (STEMI) have been formulated by the Chinese Society of Cardiology. However, little is known about the changes in clinical characteristics, management, and in-hospital outcomes in rural areas.

Methods: In the present multicenter, cross-sectional study, participants were enrolled from rural hospitals located in Liaoning province in Northeast China, during two different periods (from June 2009 to June 2010 and from January 2015 to December 2015). Data collection was conducted using a standardized questionnaire. In total, 607 and 637 STEMI patients were recruited in the 2010 and 2015 cohorts, respectively.

Results: STEMI patients in rural hospitals were older in the second group (63 years vs. 65 years, $P = 0.039$). We found increases in the prevalence of hypertension, prior percutaneous coronary intervention (PCI), and prior stroke. Over the past 5 years, the cost during hospitalization almost doubled. The proportion of STEMI patients who underwent emergency reperfusion had significantly increased from 42.34% to 54.47% ($P < 0.0001$). Concurrently, the proportion of primary PCI increased from 3.62% to 10.52% ($P < 0.0001$). The past 5 years have also seen marked increases in the use of guideline-recommended drugs and clinical examinations. However, in-hospital mortality and major adverse cardiac events did not significantly change over time (13.01% vs. 10.20%, $P = 0.121$; 13.34% vs. 13.66%, $P = 0.872$).

Conclusions: Despite the great progress that has been made in guideline-recommended therapies, in-hospital outcomes among rural STEMI patients have not significantly improved. Therefore, there is still substantial room for improvement in the quality of care.

Key words: Epidemiology; Mortality; Myocardial Infarction; Rural Health

INTRODUCTION

Globally, acute myocardial infarction (AMI) causes tremendous medical, social, and economic burdens.[1,2] In China, with the rapid economic growth and the transition of lifestyles, the incidence of AMI and AMI-related mortality has dramatically increased over the last few decades. It was estimated that the number of patients with myocardial infarction (MI) in China would increase to 23 million by 2030.[3] According to the China cardiovascular report in 2015,[4] the mortality rate for AMI in urban areas was 55.32/100,000, while the mortality rate for AMI in rural areas was 68.86/100,000. Hence, AMI has become a

major public health problem in China, particularly in the rural areas.

Compared with urban residents, rural residents usually face several barriers to receive optimal care after the occurrence of AMI.[5] First, the majority of cardiology care services and facilities are located in urban areas. Fewer hospitals in rural areas are capable of primary percutaneous coronary intervention (PCI). Second, those who live in rural areas usually experience a longer transfer delay before the arriving at hospitals.[6] Third, residents living in rural areas tend to have a lower socioeconomic status and choose a more conservative treatment programs than those living in the urban areas. Fourth, there are disparities in the delivery of recommended treatment between rural and urban hospitals.[7] These disparities are believed to be more apparent in Liaoning province, a relatively undeveloped region located in Northeast China.

Evidence showed that ST-segment elevation myocardial infarction (STEMI) accounted for more than 80% of MI patients in China.[8,9] Since 2010, two versions of the National Guidelines for STEMI[10,11] have been subsequently formulated by the Chinese Society of Cardiology to improve the diagnosis and treatment of STEMI. Previous studies were mainly conducted in large or teaching hospitals in urban areas. However, much less is known about the current trends for ST-segment MI in rural areas.[3]

A multicenter study has the advantage of accumulating large volumes of data in a short period.[12] Furthermore, patients are enrolled without any preselection in a multicenter study, which makes it highly representative of real-world patients. Therefore, a multicenter study was conducted to (1) provide insight into the differences in rural STEMI patient characteristics during the past 5 years; (2) evaluate temporal changes in STEMI management and in-hospital outcomes; and (3) identify independent indicators of major in-hospital outcomes in rural areas of China's Liaoning province using a real-world situation.

METHODS

Study subjects

In this multicenter study, participants were enrolled at two different periods. As previously described,[13] in the first period, STEMI patients who presented at 12 secondary hospitals located in rural areas of China's Liaoning province were consecutively recruited from June 2009 to June 2010. Physicians would complete a purposed-designed questionnaire after written informed consent was obtained from patients or their families. During the second period, patients admitted to 8 secondary hospitals (chosen from the initial 12 secondary hospitals) were enrolled through a retrospective review of medical records from January 2015 to December 2015. Data extraction was conducted by trained physicians using a minimally modified questionnaire that was highly similar to the one used in the first stage. All patients were diagnosed and treated at the discretion of the local physicians without any intervention from researchers.

The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of China Medical University. Ethics approvals were also obtained from all collaborating hospitals.

Inclusion and exclusion criteria for patient selection

Patients who met the following criteria were included: (1) symptoms of chest pain or chest discomfort that persisted for longer than 30 min; (2) ST-segment elevation in two or more contiguous leads that was observed on a standard 12-lead electrocardiography (0.1 mV limb leads, 0.2 mV precordial leads); (3) concentrations of creatine kinase (CK) and CK-MB were twice the normal upper limit or troponin concentration was high enough (at least 99th percentile above the upper limit of the normal local laboratory value) to be diagnosed as MI within 12 h after symptom onset; and (4) new-onset left bundle branch block was treated as STEMI equivalent.

Patients were excluded according to criteria as follows: (1) the time course from symptom onset to hospital presentation that was >24 h; (2) STEMI that resulted from invasive diagnosis and/or treatment that blocked coronary blood flow; and (3) patients who had a history of malignant diseases (such as cancers).

Data collection

Data collection was conducted using a standardized questionnaire. Information concerning demographic characteristics, cardiovascular risk factors, medical history, clinical characteristics on admission, length of hospital stay, costs during hospitalization, reperfusion therapy, drugs used, clinical examinations, and clinical outcomes was recorded.

Definitions

Hyperlipidemia was defined as a history of hyperlipidemia or positive laboratory test reports (total cholesterol ≥6.2 mmol/L, low-density lipoprotein ≥4.1 mmol/L, or triglyceride ≥2.3 mmol/L).[14] A serum creatinine ≥178 μmol/L was considered to be positive for renal insufficiency.[15] The diagnosis of recurrent MI was judged by the local physicians, based on new-onset chest pain, indicators of new ischemia on the electrocardiogram (ECG), and a significant increase in CK, CK-MB, or troponin levels (at least 50% higher than that of the previous test).[15] Major adverse cardiac events (MACEs) were defined as the combination of death, recurrent MI, stroke, and target vessel revascularization.[16,17] Thrombolytic therapies were considered successful if at least two of the following criteria were met:[17] chest pain that disappeared within 2 h; ST-segment on the ECG that resolved by at least 50% within 2 h; reperfusion arrhythmia that occurred after thrombolytic therapy; or peak serum myocardial enzymes that were detected in advance.

Statistical analysis

Data entry was conducted using EpiData 3.1 software (The EpiData Association, Denmark). Categorical variables

were expressed as frequencies (percentage) and Chi-square tests were used for comparisons between two time points (2010 and 2015). Continuous variables were presented as the mean (standard deviation) or median (interquartile range). Student's t-test or nonparametric analyses (Kruskal–Wallis H-test) were performed where appropriate. To identify independent predictors of in-hospital mortality and in-hospital MACE, univariate and multivariate logistic regression analyses were sequentially performed. Independent variables included demographic characteristics (age and sex), cardiovascular risk factors (diabetes, hypertension, hyperlipidemia, renal insufficiency, and whether the patient was a current smoker), medical history (prior MI, prior coronary artery disease, prior PCI, and prior stroke), clinical characteristics (symptom-to-door time, chest discomfort, MI location, Killip class, and systolic blood pressure), reperfusion strategies, and drugs used. Only variables with $P \leq 0.1$ identified by the univariate analysis would serve as potential explanatory variables in subsequent multivariate models. In addition, a stepwise variable selection option was chosen to construct the final logistic regression models.

All statistical analyses were conducted using SAS software (version 9.3, SAS Institute, Cary, NC, USA). All comparisons were two-sided, with $P < 0.05$ considered statistically significant.

RESULTS

Characteristics of patients

The flowchart for patient selection is depicted in Figure 1. Overall, 607 and 637 STEMI patients were consecutively recruited in the 2010 and 2015 cohorts, respectively. As shown in Table 1, the median age of patients increased from 63 to 65 years of age from 2010 to 2015 ($P = 0.039$). The proportion of male patients remained relatively stable. Over the preceding 5 years, the prevalence of hypertension increased from 45.96% to 51.65% ($P = 0.045$). However, heterogeneity was not observed in the prevalence of other cardiovascular risk factors (diabetes, hyperlipidemia, renal insufficiency, and current smoker). STEMI patients in 2015 were more likely to present with a history of PCI and stroke when compared with that in 2010 ($P = 0.035$ and $P = 0.006$, respectively). The distribution of symptom-to-door time, MI location, heart rate, and systolic blood pressure on admission was comparable between the two cohorts. When compared with patients in 2010, patients in 2015 were less likely to present to the hospital with obvious chest discomfort ($P = 0.005$). In addition, STEMI patients tended to have higher Killip classifications in 2015 ($P = 0.017$). The length of hospital stay did not differ between the study periods. However, the median cost during hospitalization almost doubled (from 6957 RMB Yuan to 11,680 RMB Yuan).

Reperfusion therapies, drugs used, clinical examinations, and clinical outcomes during hospitalization

Among patients with STEMI, 42.34% underwent emergency reperfusion in 2010 compared to 54.47% in 2015 ($P < 0.0001$). Similarly, the proportion of patients who underwent primary PCI increased markedly from 3.62% in 2010 to 10.52% in 2015 ($P < 0.0001$). Concurrently, the door-to-balloon time declined almost by half (from 260 to 132 min, $P < 0.0001$). The rate of STEMI patients who received fibrinolytic therapy showed no significant difference. Meanwhile, the median door-to-needle time was
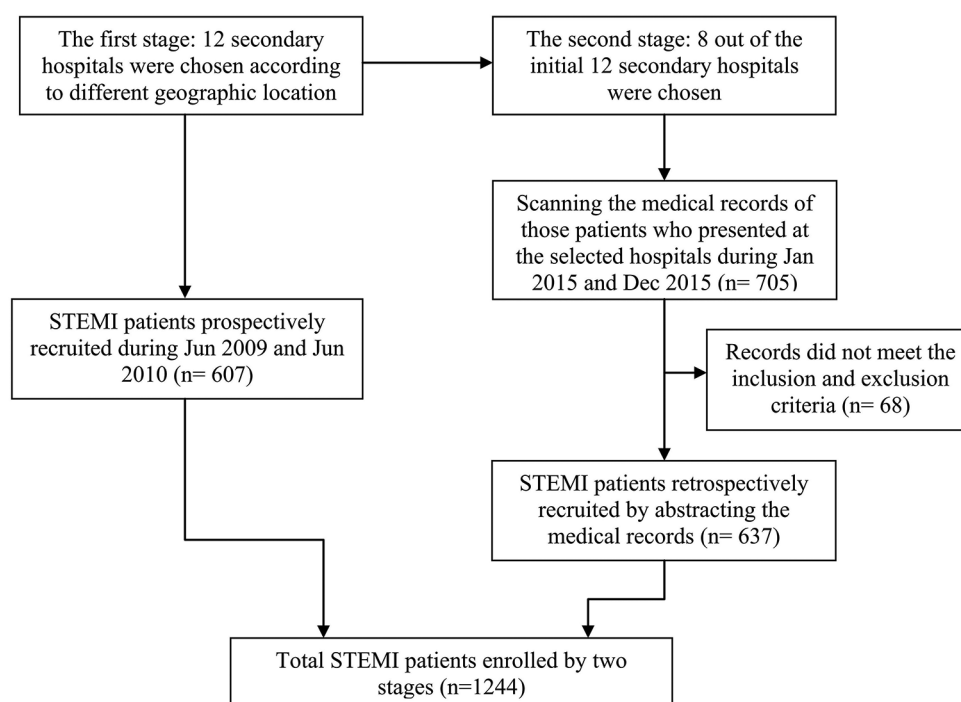

Figure 1: Flowchart showing the process of patient selection. STEMI: ST-segment myocardial infarction.

Table 1: Characteristics of patients with STEMI in the year 2010 and 2015 cohorts

Characteristics	Year 2010 (*n* = 607)	Year 2015 (*n* = 637)	Statistics	*P*
Demographic				
Age (years)	63 (55, 73)	65 (56,74)	−2.07*	0.039
Male	420 (69.19)	452 (70.96)	0.46†	0.497
Cardiovascular risk factors				
Diabetes	132 (21.75)	140 (21.98)	0.01†	0.921
Hypertension	279 (45.96)	329 (51.65)	4.02†	0.045
Hyperlipidemia	206 (33.94)	218 (34.22)	0.01†	0.915
Renal insufficiency	17 (2.80)	18 (2.83)	0.00†	0.979
Current smoker	230 (37.89)	261 (40.97)	1.24†	0.266
Medical history				
MI	36 (5.93)	53 (8.32)	2.67†	0.102
CAD	183 (30.15)	179 (28.10)	0.63†	0.427
PCI	7 (1.15)	18 (2.83)	4.42†	0.036
Stroke	73 (12.03)	112 (17.58)	7.58†	0.006
Clinical characteristics				
Symptom-to-door time				
<3 h	315 (51.89)	302 (47.41)	3.30†	0.192
3–6 h	231 (38.06)	255 (40.03)		
>6 h	61 (10.05)	80 (12.56)		
All	150 (70, 300)	180 (60, 360)	−0.94†	0.345
Chest discomfort	553 (91.10)	548 (86.03)	7.87†	0.005
Anterior MI	330 (54.37)	344 (54.00)	0.02†	0.898
Killip class >1	177 (29.16)	226 (35.48)	5.67†	0.017
Heart rate				
<100 beats/min	530 (87.31)	538 (84.46)	2.09†	0.149
≥100 beats/min	77 (12.69)	99 (15.54)		
All	74 (62, 89)	75 (64, 90)	−0.75*	0.451
Systolic blood pressure				
<140 mmHg	348 (57.33)	351 (55.10)	0.63†	0.428
≥140 mmHg	259 (42.67)	286 (44.90)		
All	130 (110, 153)	132 (115, 158)	−1.70*	0.088
Length of hospital stay (days)	9 (3, 13)	9 (4, 12)	1.56*	0.119
Cost (RMB Yuan)‡	6957 (4876, 9000)	11,680 (7587, 17,090)	134.54*	<0.0001

Data are shown as *n* (%) or median (25th, 75th). *Z values; †χ² values; ‡Only among patients with measurements available. 1 mmHg = 0.133 kPa. CAD: Coronary artery disease; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; STEMI: ST-segment myocardial infarction.

similar at different time points. However, the thrombolytic recanalization rate in 2015 was slightly higher than in 2010 (84.64% vs. 75.21%, *P* = 0.007) [Table 2].

No differences were observed in the prescriptions of aspirin, low molecular weight heparin, or calcium antagonists between 2010 and 2015. However, the number of STEMI patients who used clopidogrel, statins, GPIIb/IIIa receptor inhibitors, and traditional Chinese medicines increased dramatically from 2010 to 2015 [Table 2]. By contrast, the use of β blockers and angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEI/ARB) decreased slightly in 2015. The past 5 years have seen a significant increase in troponin testings (from 31.63 to 95.60%, *P* < 0.0001), cardiac enzymes (from 88.80 to 93.72%, *P* = 0.002), creatinine (from 81.38 to 92.78%, *P* < 0.0001), and echocardiogram (from 14.17 to 56.99%, *P* < 0.0001) [Table 2].

Our results showed no difference in the rates of in-hospital mortality, mortality within 24 h, recurrent MI, hemorrhage,

and MACE between 2010 and 2015. However, the occurrence of cardiogenic shock and acute stroke in 2015 was more frequent than in 2010 (*P* = 0.008 and *P* < 0.0001, respectively). In contrast, cardiac arrest less frequently occurred in 2015 than in the population from 5 years ago (*P* < 0.0001) [Table 2].

Multivariate analysis

Results from multivariate logistic regression analyses indicated that sex, Killip class, and administrations of ACEI/ARB and statins were significantly associated with the risk of in-hospital mortality in both 2010 and 2015 cohorts, while a history of prior stroke and administration of β blockers were only associated with the risk of in-hospital mortality in the 2015 cohort [Table 3]. With respect to in-hospital MACE, sex, Killip class, and administrations of statins were associated with an increased risk of in-hospital MACE in both 2010 and 2015 cohorts. Prior stroke, chest discomfort, and the use of β blockers and traditional Chinese medicines were independent indicators of in-hospital MACE

Table 2: Treatments, clinical examinations, and outcomes for patients with STEMI during their hospitalization

Variables	Year 2010 (n = 607)	Year 2015 (n = 637)	Statistics	P
Emergency reperfusion therapies	257 (42.34)	347 (54.47)	18.32[†]	<0.0001
Primary PCI	22 (3.62)	67 (10.52)	22.24[†]	<0.0001
Door-to-balloon time (min)	260 (190, 420)	132 (78, 211)	4.36*	<0.0001
Fibrinolytic therapies	242 (39.87)	281 (44.11)	2.30[†]	0.130
Thrombolytic agents				
Urokinase	205 (84.71)	66 (23.49)	310.28[†]	<0.0001
rt-PA	3 (1.24)	0		
r-PA	34 (14.05)	215 (76.51)		
Door-to-needle time (min)	50 (30, 85)	44 (24, 75)	1.57*	0.118
Thrombolytic recanalization	182 (75.21)	237 (84.64)	7.30[†]	0.007
Drugs				
Aspirin	577 (95.06)	611 (95.92)	0.54[†]	0.464
Clopidogrel	410 (67.55)	598 (93.88)	140.20[†]	<0.0001
LMWH	507 (83.53)	547 (85.87)	1.32[†]	0.250
β-blockers	374 (61.61)	355 (55.73)	4.44[†]	0.035
ACEI/ARB	371 (61.12)	322 (50.55)	14.08[†]	<0.001
Statins	513 (84.51)	578 (90.74)	11.16[†]	0.001
Calcium antagonists	33 (5.44)	40 (6.28)	0.40[†]	0.527
GPIIb/IIIa receptor inhibitor	16 (2.64)	102 (16.01)	64.78[†]	<0.0001
Traditional Chinese medicines	279 (45.96)	539 (84.62)	206.22[†]	<0.0001
Clinical examinations				
Troponin	192 (31.63)	609 (95.60)	554.77[†]	<0.0001
Cardiac enzymes	539 (88.80)	597 (93.72)	9.50[†]	0.002
Creatinine	494 (81.38)	591 (92.78)	36.20[†]	<0.0001
Echocardiogram	86 (14.17)	363 (56.99)	247.05[†]	<0.0001
Outcomes				
Mortality	79 (13.01)	65 (10.20)	2.40[†]	0.121
Mortality within 24 h	55 (9.06)	41 (6.44)	3.01[†]	0.083
Cardiogenic shock	65 (10.71)	101 (15.86)	7.12[†]	0.008
Cardiac arrest	71 (11.70)	44 (6.91)	8.50[†]	0.004
Acute stroke	3 (0.49)	23 (3.61)	14.75[†]	<0.0001
Recurrent MI	5 (0.82)	5 (0.78)	0.01[†]	0.939
Hemorrhage	11 (1.81)	17 (2.67)	1.04[†]	0.309
MACE	81 (13.34)	87 (13.66)	0.03[†]	0.872

Data are shown as n (%) or median (25th, 75th). *Z values; †χ^2 values. ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; LMWH: Low molecular weight heparin; MI: Myocardial infarction; MACE: Major adverse cardiac event; PCI: Percutaneous coronary intervention; r-PA: Reteplase; rt-PA: Alteplase; STEMI: ST-segment myocardial infarction.

for the 2015 cohort, but not for the 2010 cohort. By contrast, the use of ACEI/ARB was negatively associated with the risk of in-hospital MACE in the 2010 cohort, but not in the 2015 cohort [Table 4].

DISCUSSION

In this multicenter study, we aimed to describe the temporal trends in clinical characteristics, treatment, the quality of care, and in-hospital outcomes of STEMI patients who presented at rural hospitals in China's Liaoning province. Our findings suggested that STEMI patients in the 2015 cohort were moderately older than those in 2010 cohort. The increased prevalence of hypertension, prior PCI, and stroke was noted throughout the study. The costs during hospitalization also rapidly increased. Furthermore, increasing numbers of STEMI patients in the rural areas of the Liaoning province

received emergency reperfusion, especially primary PCI. Although the past 5 years has witnessed a substantial improvement in other guideline-recommended therapies, in-hospital outcomes have not significantly improved. Sex, prior stroke, chest discomfort, Killip class, and prescriptions of β-blockers, ACEI/ARB, statins, and traditional Chinese medicines were identified as independent predictors of in-hospital outcomes.

The progressive change in the age of STEMI patients might partially result from the rapidly aging population. According to China's 2010 census, residents who were aged 60 years and above accounted for 13.3% of the total population in 2010.[18] The increasing prevalence of hypertension, prior PCI, and stroke was noted in our study, which was consistent with that in the China PEACE study.[3] Several factors might account for the rising cost during hospitalization. First, health

Table 3: The multivariate logistic regression model for in-hospital mortality

Predictors	Year 2010 (*n* = 607)				Year 2015 (*n* = 637)			
	Mortality, *n* (%)	*OR* (95% *CI*)	Wald χ^2	*P*	Mortality, *n* (%)	*OR* (95% *CI*)	Wald χ^2	*P*
Sex								
Female	44 (23.53)	Reference	–	–	33 (17.84)	Reference	–	–
Male	35 (8.33)	0.37 (0.20, 0.71)	9.07	0.003	32 (7.08)	0.25 (0.12, 0.49)	15.81	<0.0001
Prior stroke								
No	–	–	–	–	44 (8.38)	Reference	–	–
Yes	–	–	–	–	21 (18.75)	3.52 (1.64, 7.54)	10.41	<0.001
Killip class >1								
No	17 (3.95)	Reference	–	–	12 (2.92)	Reference	–	–
Yes	62 (35.03)	12.00 (6.12, 23.84)	51.53	<0.0001	53 (23.45)	8.94 (4.20, 19.06)	32.22	<0.0001
β-blockers								
No	–	–	–	–	55 (19.50)	Reference	–	–
Yes	–	–	–	–	10 (2.82)	0.39 (0.17, 0.89)	4.97	0.026
ACEI/ARB								
No	61 (25.85)	Reference	–	–	59 (18.73)	Reference	–	–
Yes	18 (4.85)	0.24 (0.12, 0.47)	17.08	<0.0001	6 (1.86)	0.14 (0.06, 0.38)	15.42	<0.001
Statins								
No	45 (47.87)	Reference	–	–	28 (46.46)	Reference	–	–
Yes	34 (6.63)	0.10 (0.05, 0.20)	42.01	<0.0001	37 (6.40)	0.11 (0.05, 0.25)	28.28	<0.0001

–: Not applicable. ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; *CI*: Confidence interval; *OR*: Odds ratio.

Table 4: The multivariate logistic model for in-hospital MACE

Predictors	Year 2010 (*n* = 607)				Year 2015 (*n* = 637)			
	MACE, *n* (%)	*OR* (95% *CI*)	Wald χ^2	*P*	MACE, *n* (%)	*OR* (95% *CI*)	Wald χ^2	*P*
Sex								
Female	44 (23.53)	Reference	–	–	43 (23.24)	Reference	–	–
Male	37 (8.81)	0.41 (0.22, 0.77)	7.85	0.005	44 (9.73)	0.32 (0.18, 0.57)	15.37	<0.0001
Prior stroke								
No	–	–	–	–	59 (11.24)	Reference	–	–
Yes	–	–	–	–	28 (25.00)	2.65 (1.42, 4.96)	9.28	0.002
Chest discomfort								
No	–	–	–	–	32 (35.96)	Reference	–	–
Yes	–	–	–	–	55 (10.04)	0.39 (0.21, 0.73)	8.67	0.003
Killip class >1								
No	19 (4.42)	Reference	–	–	22 (5.35)	Reference	–	–
Yes	62 (35.03)	10.36 (5.42, 19.80)	50.04	<0.0001	65 (28.76)	5.20 (2.91, 9.29)	30.94	<0.0001
β-blockers								
No	–	–	–	–	66 (23.40)	Reference	–	–
Yes	–	–	–	–	21 (5.92)	0.39 (0.21, 0.72)	9.17	0.003
ACEI/ARB								
No	62 (26.27)	Reference	–	–	–	–	–	–
Yes	19 (5.12)	0.25 (0.13, 0.48)	17.48	<0.0001	–	–	–	–
Statins								
No	45 (47.87)	Reference	–	–	29 (49.15)	Reference	–	–
Yes	36 (7.02)	0.11 (0.06, 0.22)	40.54	<0.0001	58 (10.03)	0.19 (0.09, 0.40)	19.99	<0.0001
Traditional Chinese medicines								
No	–	–	–	–	29 (29.59)	Reference	–	–
Yes	–	–	–	–	58 (10.76)	0.35 (0.18, 0.66)	10.36	0.001

–: Not applicable. ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; *CI*: Confidence interval; MACE: Major adverse cardiac event; *OR*: Odds ratio.

insurance coverage has become more extensive, particularly the newly-established rural corporative medical guarantee system, with the persistent efforts by China's government to improve the quality of healthcare. Second, high cost might

also attribute to the popularity of PCI treatment and the use of new generation thrombolytic agents. Third, the increasing usage of other guideline-recommended drugs and clinical examinations would cost STEMI patients more money.

The past 5 years has seen great progress in reperfusion therapy in rural hospitals in the Liaoning district, but substantial gaps still exist. In 2015, both emergency reperfusion and primary PCI rates were significantly higher than in 2010. In addition, the median door-to-balloon time markedly declined from 260 to 132 min. A similar trend was reported in rural eastern China,[19] in which emergency reperfusion increased from 49.7% to 58.8% and primary PCI from 0% to 27.5% in the period between 2001 and 2011. For fibrinolytic therapies, the major thrombolytic agents underwent a transition from urokinase to reteplase (r-PA) during the past 5 years. Accordingly, the thrombolytic recanalization rate increased from 75.21% in 2010 to 84.64% in 2015. However, the proportion of rural STEMI patients who received primary PCI was still far lower than the national level of 28.1% in 2011.[3] Only a few secondary hospitals had the interventional cardiology capabilities and the qualifications to conduct PCI. The median door-to-balloon time for primary PCI was longer than 90 min, which was the benchmark recommended by the treatment guideline.[11] STEMI care networks in rural areas may have several disadvantages in achieving this benchmark for the following reasons.[20] First, emergency medical systems in rural hospitals usually have lower staffing level of paramedics or emergency medical technicians, which limits the capability of STEMI diagnosis. Second, PCI capabilities in rural hospitals do not have enough resources for 24/7 in-house staffing in the cardiac catheterization laboratory, which results in longer response time to catheterization laboratory activation. Finally, since STEMI is a relatively infrequent event in rural areas, it prevents staff from ever becoming completely familiar with a process that must be managed quickly.

The quality of care has improved during the past 5 years. Increases in the prescriptions of clopidogrel, GPIIb/IIIa receptor inhibitor, and traditional Chinese medicines are encouraging. Similarly, increases in troponin, cardiac enzymes, and creatinine testings as well as echocardiograms are striking. The results were consistent with previous investigations in both rural and urban areas in China.[19,21,22] However, β-blockers and ACEI/ARB were prescribed to fewer patients in the 2010 cohort when compared to those in the 2015 cohort, even though their favorable effects have been previously reported.[23-25]

It is noteworthy that the in-hospital mortality rate of rural STEMI patients has not significantly improved, despite the increasing intensity of treatments, procedures, and clinical examinations over the past 5 years. A similar contradictory trend has been previously reported in Chinese mainland and Taiwan.[3,26] By contrast, the mortality of AMI during the same period has continued to decrease in developed western countries.[27-31] Therefore, there are abundant opportunities for quality improvement in the rural hospitals in Liaoning

province. There might be several possible explanations for the reason mortality did not significantly decline. First, no significant improvement in prehospital delay was observed during 2010 and 2015 (median symptom-to-door time, 150 min vs. 180 min, $P = 0.345$). Second, though progress has been made in emergency reperfusion therapy, its rate remained relatively low when compared to those in other studies, particularly the primary PCI therapy.[32-34] Third, higher degree of Killip class was observed in 2015 than that in 2010 (35.48% vs. 29.16%), indicating increased severity of STEMI on presentation. This in turn would offset the beneficial effects gained from improved reperfusion therapy and the quality of care. Fourth, the lack of change in mortality may be partly attributable to the declining administration of lifesaving drugs such as β-blockers and ACEI/ARB that had been proven effective in preventing ventricular remodeling after MI.[35,36] Finally, the control of major cardiovascular risk factors may be suboptimal, which was supported by our results as the prevalence of STEMI patients with diabetes, hyperlipidemia, renal insufficiency, and smoking did not significantly decrease in the past 5 years. These concomitant risk factors were closely related to the severity of coronary artery disease.[37-39] It has been reported that about half of the decline in MI mortality was due to the primary prevention of an MI (reduction in the proportions of cardiovascular risk factors).[26]

To accelerate the improvement in STEMI management, future efforts should focus on the following aspects. STEMI networks should be established to optimize prehospital treatment, triage and transport of STEMI patients, and collaborations between hospitals and emergency medical services.[40] Prehospital diagnosis and fibrinolysis should be recommended in remote rural hospitals without PCI capability since they have been reported as effective strategies in shortening total ischemic time and reducing early mortality.[40,41] Furthermore, new generation of thrombolytic drugs (rt-PA and r-PA) which are proven to be more efficient and safer than urokinase should be covered by the medical insurance systems in China. Sufficient cardiologists are needed in rural hospitals. The shortage of cardiologists and emergency services in rural areas means that rural STEMI patients are more likely to see generalist physicians rather than cardiologists.[5] Evidence has shown that generalist physicians were less likely than cardiologists to prescribe recommended AMI medications.[42,43] It is also critical to educate the public regarding the importance of being at the right place at the right time in case of an AMI because time is muscle and mortality is directly correlated with the time to treatment.[44]

Findings from the multivariate logistic regression showed that male gender and administrations of β-blockers, ACEI/ARB, statins, and traditional Chinese medicines were independent predictors for improving in-hospital survival and MACE. In contrast, prior stroke and high Killip class were identified as independent predictors for the elevated risk of in-hospital mortality and MACE, which was in

accordance with previous studies.[45,46] The favorable effects that guideline-recommended medicines have on in-hospital cardiovascular risks were easily understood.[23-25,47-49] However, as nonguideline-recommended medicine, traditional Chinese medicines have been reported to have some advantages for the treatments of AMI.[50] However, the safety and components of these traditional therapies remain uncertain.[51] Well-designed and performed randomized controlled trials are needed to validate the beneficial effects of traditional Chinese medicines on the management of STEMI.

Several limitations should be noted when interpreting the results of this study. First, as an observational study, the possible confounding bias could not be completely ruled out. However, we have considered the traditional clinical factors when constructing the regression models that predicted the risk of in-hospital outcomes. Second, definitions and diagnoses of some disorders might vary among hospitals even though all physicians had received uniform training from the researchers. Third, we could not evaluate STEMI patients who were not admitted to hospitals, and the proportion of prehospital death was unavailable. Finally, only in-hospital outcomes were measured since we could not link patient-level data to the national death registration system to investigate long-term outcomes.[3] Despite these limitations, we believe that the study population was highly representative of STEMI patients admitted to rural hospitals in Liaoning province. Our study provided valuable real-world STEMI data in evaluating the temporal trends for STEMI in the rural areas of Northeast China over the past 5 years.

In conclusion, even though great progress has been made in guideline-recommended treatments, procedures, and clinical examinations, in-hospital outcomes among rural STEMI patients have not significantly improved during the past 5 years. Therefore, there is still substantial room for improvement in the quality of care. Our study provides evidence for health-policy makers to optimize the management of STEMI patients, particularly in China's rural areas.

Conflicts of interest

There are no conflicts of interest.

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