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Changes in ST segment elevation myocardial infarction hospitalisations in China from 2011 to 2015

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ABSTRACT

Objective Access to acute cardiovascular care has improved and health services capacity has increased over the past decades. We assessed national changes in (1) patient characteristics, (2) in-hospital management and (3) patient outcomes among patients presenting with ST segment elevation myocardial infarction (STEMI) in 2011–2015 in China.

Methods In a nationally representative sample of hospitals in China, we created two random cohorts of patients in 2011 and 2015 separately. We weighted our findings to estimate nationally representative numbers and assessed changes from 2011 to 2015. Data were abstracted from medical charts centrally using standardised definitions.

Results While the proportion of patients with STEMI among all patients with acute myocardial infarction decreased over time from 82.5% (95% CI 81.7 to 83.3) in 2011 to 68.5% (95% CI 67.7 to 69.3) in 2015 (p<0.0001), the weighted national estimate of patients with STEMI increased from 210 000 to 380 000. The rate of reperfusion eligibility among patients with STEMI decreased from 49.3% (95% CI 48.1 to 50.5) to 42.2% (95% CI 41.1 to 43.4) in 2015 (p<0.0001); ineligibility was principally driven by larger proportions with prehospital delay exceeding 12 hours (67.4%–76.7%, p<0.0001). Among eligible patients, the proportion receiving reperfusion therapies increased from 54% (95% CI 52.3 to 55.7) to 59.7% (95% CI 57.9 to 61.4) (p<0.0001). Crude and risk-adjusted rates of in-hospital death did not differ significantly between 2011 and 2015.

Conclusions In this most recent nationally representative study of STEMI in China, the use of acute reperfusion increased, but no significant improvement occurred in outcomes. There is a need to continue efforts to prevent cardiovascular diseases, to monitor changes in in-hospital treatments and outcomes, and to reduce prehospital delay.

Key questions

What is already known about this subject?

- Access to acute cardiovascular care improved and health services capacity increased in China between 2001 and 2011.

What does this study add?

- This most recent nationally representative study of ST segment elevation myocardial infarction in China found the use of acute reperfusion increased between 2011 and 2015, but no significant improvement occurred in outcomes.

How might this impact on clinical practice?

- There is a need to continue efforts to prevent cardiovascular diseases, to monitor changes in in-hospital treatments and outcomes, and to reduce prehospital delay.

INTRODUCTION

Over the past two decades in China access to acute cardiovascular care has improved and health services capacity has increased. Insurance reform began in 2003 and achieved the goal of minimum universal coverage by 2011.[1] This period was also marked by an increasing burden of acute cardiovascular events and a focus on effective in-hospital management strategies. In response, several guideline updates for acute myocardial infarction (AMI) care were released during this period.[2 3]

Dynamic changes also occurred in the epidemiology and quality of care for ST segment elevation myocardial infarction (STEMI) hospitalisations in China between 2001 and 2011.[4] Although a previous study found marked improvements in use of primary percutaneous coronary intervention (pPCI) as well as adjunctive STEMI therapies, the overall reperfusion rate and patient outcomes had not changed.[4]

The focus of healthcare reform in China has evolved from increasing access to care and expanding capacity to improving efficiency and quality of acute cardiovascular care.[5] In this latest iteration of the China Patient-Centered Evaluative Assessment of Cardiac

Events (PEACE) Retrospective AMI Study, we report data from 2015 to evaluate changes in patient characteristics, presentations, use of guideline-based therapies and outcomes. Our focus is to determine whether the improvements in quality of care observed from 2001 to 2011 have continued and whether outcomes changed, and to identify areas for improvement.

Accordingly, our aims were to assess national changes among patients presenting with STEMI in 2011 and 2015 in (1) patient characteristics (demographic, cardiovascular risk factors, medical history, clinical characteristics), (2) in-hospital management (use of recommended treatments, procedures and diagnostic tests, and inappropriate use of non-evidence-based treatments), and (3) patient outcomes (in-hospital and 7-day mortality and complications).

METHODS

Data source and study design

The design of the China PEACE-Retrospective AMI Study had been previously described.[6] In addition to a nationally representative sample of patients admitted for AMI in China during 2011, which was created in the China PEACE-Retrospective AMI Study, we also included a more recent sample of patients admitted in 2015 from the same nationally representative hospital cohort, using the same random sampling process (online supplemental methods).

In the first stage, we created a sample of hospitals that are representative of hospitals in China, excluding military hospitals, prison hospitals, specialised hospitals without a division for cardiovascular disease and hospitals for traditional Chinese medicine. We stratified the sample by five economic geographical regions (online supplemental methods). In the second stage, using systematic random sampling procedures we selected patients with AMI from the local hospital database of each sampled hospital (online supplemental methods). Discharges with AMI were identified according to the International Classification of Diseases-Clinical Modification codes, including versions 9 (410.xx) and 10 (I21.xx), when available, or through principal diagnosis terms noted at discharge. Data were collected by central abstraction of medical charts with use of standardised data definitions. At each sampling stage, data quality was monitored by random auditing of 5% of the medical records, with overall variable accuracy exceeding 98%. A waiver of patients' written consent was approved since it was not feasible to approach patients hospitalised several years ago in a retrospective study. All collaborating hospitals accepted the central ethics approval except for five hospitals, which obtained local approval from internal ethics committees (online supplemental methods).

Participants

Only patients with a definite discharge diagnosis of STEMI were included in the study sample. The diagnosis of STEMI was determined by the combination of clinical discharge diagnosis terms and ECG results and validated by review of ECGs from randomly selected records by a cardiologist not involved in data abstraction. We treated left bundle branch block as a STEMI equivalent.

We excluded all patients whose STEMI occurred during the course of the hospitalisation because STEMI during hospitalisation could be considered one severe and rare complication of other clinical conditions (ie, coronary artery bypass graft and trauma), so the treatment could be very different, making it difficult to measure quality of care. For the analysis of treatments, procedures and tests, we excluded patients who had transferred in from other hospitals or who had a length of stay of 24 hours or shorter. For the analysis of in-hospital outcomes, we excluded patients who were transferred in from another hospital because we sought to characterise patients admitted directly to the hospital. We also excluded patients who were transferred out because their admissions were truncated. We further excluded patients who were discharged alive within 24 hours because they may have left against medical advice and there was very little time for treatment.

Patient-level characteristics

Variables included patient-level characteristics (age, sex, cardiovascular risk factors, medical history and clinical characteristics at admission), defined as documentation on the admission notes, discharge diagnosis or positive laboratory test results (total cholesterol >5.18 mmol/L or low-density lipoprotein ≥3.37 mmol/L, or high-density lipoprotein <1.04 mmol/L in men or <1.30 mmol/L in women).

Quality metrics

We assessed use of treatments recommended by the 2010 China National Guideline for STEMI,[2] which were consistent with those recommended by the guidelines in the USA.[7] These treatments included reperfusion therapy, aspirin within 24 hours of admission, clopidogrel or ticagrelor within 24 hours of admission, β blockers within 24 hours of admission, ACE inhibitors or angiotensin receptor blockers during hospital admission, and statins during hospital admission. We excluded patients with documented contraindications (online supplemental methods).[2] We also assessed use of magnesium sulfate (a treatment with no documented survival benefits in the setting of STEMI),[8] traditional Chinese medicine, other procedures and tests. We included the seven main categories of traditional Chinese medicine used for coronary heart disease (online supplemental methods). We did not include some care processes (eg, door-to-balloon time and counselling for smoking cessation) due to inadequate documentation on the medical records.

We compared patients' in-hospital outcomes with three measures: death, death or withdrawal from treatment due to terminal status at discharge (referred to as treatment withdrawal), and composite complications (including death, treatment withdrawal, reinfarction, cardiogenic shock, ischaemic stroke or congestive heart failure, defined in online supplemental methods). Treatment withdrawal is common in China due to reluctance of many patients to die in the hospital. The Chinese Government uses in-hospital death or treatment withdrawal as a quality measure for hospitals.[9] Cardiologists in the coordinating study centre adjudicated the clinical status of patients who withdrew from treatment using medical records.

Statistical analysis

We examined patient characteristics, treatments, tests, procedures and crude rates of outcomes across different study years using the χ^2 test for categorical variables and the Mann-Whitney test for continuous variables. We used percentages with 95% CI to describe categorical variables and median with IQR to describe continuous variables. We used multiple imputation for missing age values. To estimate nationally representative numbers of hospitalisations for 2011 and 2015, we applied sampling weights proportional to the inverse sampling fraction of hospitals within each stratum and the sampling fraction of patients within each hospital.

We did multilevel logistic regressions accounting for clustering of patients within hospitals. We included year 2015 as key explanatory variable, while adjusting for patients' demographics (age and sex), risk factors or medical history (hypertension, diabetes, current smoker, previous myocardial infarction, previous coronary heart disease and previous stroke), and clinical characteristics at admission (chest discomfort, cardiac arrest, acute stroke, heart rate and systolic blood pressure). The dependent variables were in-hospital death, in-hospital death or treatment withdrawal, and in-hospital composite complications. We transformed continuous variables (eg, age, heart rate and systolic blood pressure) into categorical variables according to clinically meaningful cut-off values. We report OR and 95% CI from the multilevel logistic regression related to the year indicators. In view of the small decrease in length of hospital stay over time, a sensitivity analysis was performed using 7-day outcomes using the same approach as for in-hospital outcomes. We also repeat outcome analyses using a sample of patients that includes patients transferred in from other facilities.

All comparisons were two-sided, with statistical significance defined as $p<0.05$. Statistical analysis was done with SAS V.9.2 software and R V.3.0.2.

Patient and public involvement

This research was done without patient or public involvement.

RESULTS

Demographical and clinical characteristics

During 2011 and 2015, we identified 21 167 patients with AMI, including 15 807 patients with STEMI, in 166 hospitals in China (figure 1A, online supplemental figure S1). The absolute number of STEMI hospitalisations increased in our sample from 7696 in 2011 to 8111 in 2015 (figure 1A). Applying sample weighting showed the number of patients hospitalised with STEMI increased from 0.21 million in 2011 to 0.38 million in 2015 (figure 1B). In our sample, the proportion of patients with STEMI among all patients with AMI decreased from 82.5% (95% CI 81.7 to 83.3) in 2011 to 68.5% (95% CI 67.7 to 69.3) in 2015 ($p<0.0001$; online supplemental

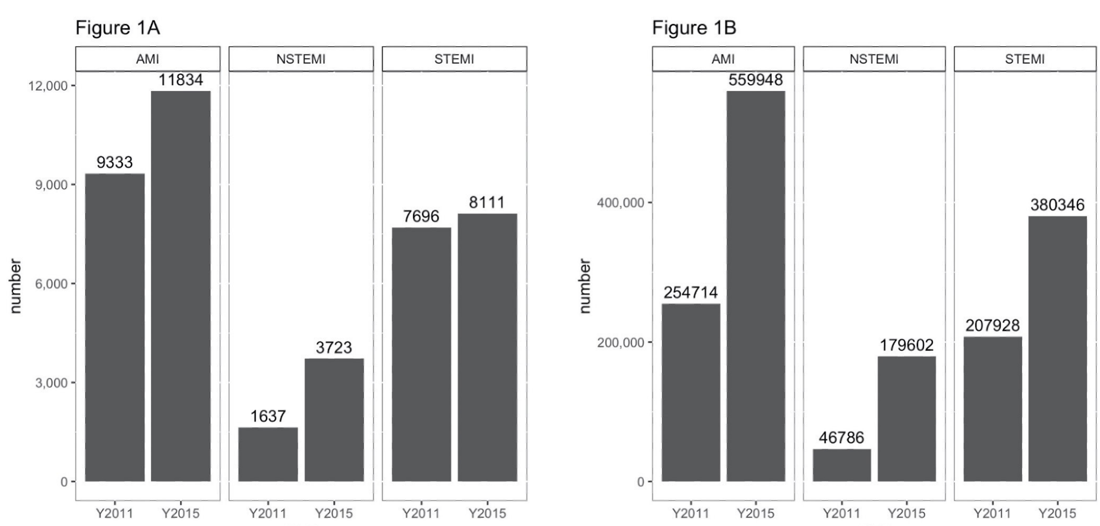

Figure 1 Number of patients by year and condition. (A) Number of patients in PEACE-Retrospective AMI Study. (B) Weighted number of patients in China. To estimate nationally representative numbers of hospitalisations for 2011 and 2015, we applied sampling weights proportional to the inverse sampling fraction of hospitals within each stratum and the sampling fraction of patients within each hospital to account for differences in the sampling fraction for 2011 in all analyses. AMI, acute myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; PEACE, China Patient-Centered Evaluative Assessment of Cardiac Events; STEMI, ST segment elevation myocardial infarction.

Table 1 Characteristics of patients with STEMI in 2011 and 2015

	2011 (n=7696)	2015 (n=8111)	P value
Demographics			
Age (years)	65 (55–75)	65 (55–74)	0.9
Women	2247 (29.2)	2311 (28.5)	0.3
Cardiovascular risk factors			
Hypertension	3890 (50.5)	4197 (51.7)	0.1
Diabetes	1558 (20.2)	1818 (22.4)	0.0009
Dyslipidaemia	4843 (62.9)	6452 (79.5)	<0.0001
Current smoker	2854 (37.1)	2853 (35.2)	0.01
Clustering of risk factors			
≥3	1612 (20.9)	2027 (25)	<0.0001
2	2878 (37.4)	3360 (41.4)	<0.0001
1	2357 (30.6)	2275 (28)	0.0004
None	849 (11)	449 (5.5)	<0.0001
Medical history			
Myocardial infarction	814 (10.6)	569 (7)	<0.0001
Coronary heart disease	1568 (20.4)	1897 (23.4)	<0.0001
PCI	180 (2.3)	251 (3.1)	0.004
Coronary artery bypass graft	21 (0.3)	14 (0.2)	0.2
Stroke	897 (11.7)	1022 (12.6)	0.07
Clinical characteristics			
Symptom onset to admission (hours)	12 (3–72)	24 (4–96)	<0.0001
Chest discomfort	7118 (92.5)	7478 (92.2)	0.5
Left bundle branch block	97 (1.3)	65 (0.8)	0.004
Cardiac arrest	125 (1.6)	104 (1.3)	0.07
Cardiogenic shock	508 (6.6)	630 (7.8)	0.005
Acute stroke	83 (1.1)	217 (2.7)	<0.0001
Heart rate (beats per minute)			
<50	384 (5)	306 (3.8)	0.0002
50–110	6917 (89.9)	7278 (89.7)	0.8
>110	395 (5.1)	527 (6.5)	0.0003
Heart rate	76 (65–89.5)	78 (66–90)	0.0009
Systolic blood pressure (mm Hg)			
<90	408 (5.3)	430 (5.3)	>0.9
90–139	4658 (60.5)	5017 (61.9)	0.09
≥140	2630 (34.2)	2664 (32.8)	0.08
Mini-GRACE risk score	142 (122–160)	141 (120–160)	0.06

Data are median (IQR) or n (%), for which n is the number of patients in the study sample and % is a nationally representative rate.
GRACE, Global Registry of Acute Coronary Events; PCI, percutaneous coronary intervention; STEMI, ST segment elevation myocardial infarction.

table S1). Between 2011 and 2015, the median age of patients and the proportion of women did not change (table 1). In 2015, the median age was 65 years (IQR 55–74) and 28.5% of patients were women (table 1).

Among patients with STEMI, the prevalence of diabetes and dyslipidaemia increased (p<0.001), the prevalence of smoking decreased (p<0.05), and the prevalence of hypertension did not change (p=0.1; table 1). In 2015, 51.7% of patients had hypertension, 22.4% had diabetes, 79.5% had dyslipidaemia and 35.2% were current smokers (table 1). The proportion of patients with a medical history of myocardial infarction decreased from 10.6% in 2011 to 7% in 2015, while a medical history of coronary heart disease and percutaneous coronary intervention became more prevalent (p<0.01; table 1).

Between 2011 and 2015, the median time between symptom onset and hospital admission increased from 12 hours (IQR 3–72) to 24 hours (IQR 4–96) (p<0.0001; table 1). In 2015, 56.9% (95% CI 55.7 to 58) of patients had a long prehospital delay, defined as >12 hours between symptom onset and admission (online supplemental table S2). The prevalence of left bundle branch block on admission decreased, while the prevalence of cardiogenic shock, acute stroke and tachycardia (defined as heart rate >110 beats per minute) increased (p<0.05; table 1). The median Mini-Global Registry of Acute Coronary Events scores did not change significantly between 2011 and 2015 (table 1).

Among all patients with STEMI, the rate of reperfusion eligibility decreased from 49.3% (95% CI 48.1 to 50.5) in 2011 to 42.2% (95% CI 41.1 to 43.4) in 2015 (p<0.0001; online supplemental table S3). Among ineligible patients, ineligibility was principally driven by increased prevalence of long prehospital delay (online supplemental table S4).

Use of treatments, procedures and diagnostic tests

After exclusion of 630 patients transferred in from other facilities and 1416 patients with length of stay ≤24 hours, 13 761 patients with STEMI were included in the analysis of treatments, procedures and tests (online supplemental figure S1).

Use of troponin tests increased from 63.1% (95% CI 62 to 64.3) in 2011 to 80.0% (95% CI 79.1 to 80.9) in 2015 (p<0.0001; table 2). Use of other cardiac enzyme tests decreased between 2001 and 2015 (p<0.0001; table 2). Use of echocardiography increased from 63.1% (95% CI 61.9 to 64.2) in 2011 to 72.1% (95% CI 71 to 73.1) in 2015 (p<0.0001; table 2).

Among patients eligible for reperfusion, the proportion receiving reperfusion therapies increased from 54.0% (95% CI 52.3 to 55.7) in 2011 to 59.7% (95% CI 57.9 to 61.4) in 2015, in which use of pPCI increased from 21.1% (95% CI 19.7 to 22.5) to 33.7% (95% CI 32.1 to 35.4) and use of fibrinolytic therapy decreased from 32.9% (95% CI 31.3 to 34.5) to 25.9% (95% CI 24.4 to 27.5) (p<0.01; table 2). Meanwhile, the prehospital delay of patients who received reperfusion therapy was longer in 2015 than in 2011 (3 hours (IQR 2–6) vs 3 hours (IQR 2–5), p<0.0001).

Use of statins and use of clopidogrel or ticagrelor increased between 2011 and 2015 (p<0.0001; table 2). Use of ACE inhibitors or angiotensin receptor blockers

Table 2 Use of treatments, procedures and tests among patients with STEMI

	2011		2015		
	Relative frequency	% (95% CI)	Relative frequency	% (95% CI)	P value
Reperfusion therapies					
Any reperfusion*	1769/3278	54 (52.3 to 55.7)	1793/3005	59.7 (57.9 to 61.4)	<0.0001
Primary PCI*	691/3278	21.1 (19.7 to 22.5)	1014/3005	33.7 (32.1 to 35.4)	<0.0001
Fibrinolytic therapy*	1078/3278	32.9 (31.3 to 34.5)	779/3005	25.9 (24.4 to 27.5)	<0.0001
Acute drugs					
Aspirin within 24 hours*	5904/6490	91 (90.3 to 91.7)	6354/6924	91.8 (91.1 to 92.4)	0.1002
Clopidogrel or ticagrelor within 24 hours*	5069/6498	78 (77 to 79)	6298/6964	90.4 (89.7 to 91.1)	<0.0001
β blockers within 24 hours*	1846/3106	59.4 (57.7 to 61.2)	1969/3379	58.3 (56.6 to 59.9)	0.3423
Statins*†	6045/6642	91 (90.3 to 91.7)	6711/7118	94.3 (93.7 to 94.8)	<0.0001
ACE inhibitors or angiotensin receptor blockers*†	4224/6440	65.6 (64.4 to 66.8)	4028/6803	59.2 (58 to 60.4)	<0.0001
Traditional Chinese medicine†	4827/6643	72.7 (71.6 to 73.7)	5101/7118	71.7 (70.6 to 72.7)	0.1912
Magnesium sulfate†	1159/6643	17.4 (16.5 to 18.4)	1477/7118	20.8 (19.8 to 21.7)	<0.0001
Stents†‡					
Drug-eluting stents only	1436/1466	98 (97.2 to 98.7)	1974/1985	99.4 (99.1 to 99.8)	0.0001
Bare metal stents only	28/1466	1.9 (1.2 to 2.6)	11/1985	0.6 (0.2 to 0.9)	0.0002
Both	2/1466	0.1 (–0.1 to 0.3)	0/1985	0 (0 to 0)	0.0997
Procedures†					
Coronary angiography	2204/6643	33.2 (32 to 34.3)	3239/7118	45.5 (44.3 to 46.7)	<0.0001
PCI (non-primary)	1077/6643	16.2 (15.3 to 17.1)	1237/7118	17.4 (16.5 to 18.3)	0.0676
Coronary artery bypass graft	30/6643	0.5 (0.3 to 0.6)	5/7118	0.1 (0 to 0.1)	<0.0001
Intra-aortic balloon pump	137/6643	2.1 (1.7 to 2.4)	110/7118	1.5 (1.3 to 1.8)	0.0225
Tests†					
Troponin	4195/6643	63.1 (62 to 64.3)	5695/7118	80 (79.1 to 80.9)	<0.0001
Cardiac enzymes	6443/6643	97 (96.6 to 97.4)	6407/7118	90 (89.3 to 90.7)	<0.0001
Echocardiogram	4191/6643	63.1 (61.9 to 64.2)	5129/7118	72.1 (71 to 73.1)	<0.0001

Data are n/N or % (95% CI), for which n is the number of patients in the study sample and % is a nationally representative rate, unless otherwise stated.
*Only among patients eligible for the treatment (ie, patients with no documented contraindications).
†During hospital admission.
‡Among patients who received at least one stent.
PCI, percutaneous coronary intervention; STEMI, ST segment elevation myocardial infarction.

decreased (p<0.0001; table 2). Use of magnesium sulfate increased (p<0.001) and use of traditional Chinese medicine did not significantly change (p=0.2; table 2). Use of coronary angiography during hospitalisation increased (p<0.0001; table 2).

In-hospital and 7-day outcomes

After exclusion of 630 patients transferred in from other facilities, 2281 patients transferred out to other facilities and 132 patients discharged alive within 24 hours, 12 764 patients with STEMI were included in the analysis of in-hospital and 7-day outcomes (6472 in year 2011 and 6292 in year 2015; online supplemental figure S1).

The median length of stay decreased from 11 days (IQR 7–15) to 10 days (IQR 7–13) (p<0.0001; online supplemental table S5). Crude rates of in-hospital death were unchanged between 2011 and 2015 (p=0.9; online supplemental table S5). Adjustment for patient demographic and clinical characteristics in the multilevel logistic regression model did not differ significantly between 2011 and 2015 with respect to death, treatment withdrawal or complications during hospitalisation (p>0.05; figure 2). Adjusted outcomes calculated with a 7-day timeframe showed similar results as the in-hospital analysis (figure 3). With the inclusion of 630 patients transferred in from other facilities, adjusted in-hospital outcomes and 7-day outcomes remained similar to the main analyses (online supplemental figures S2 and S3).

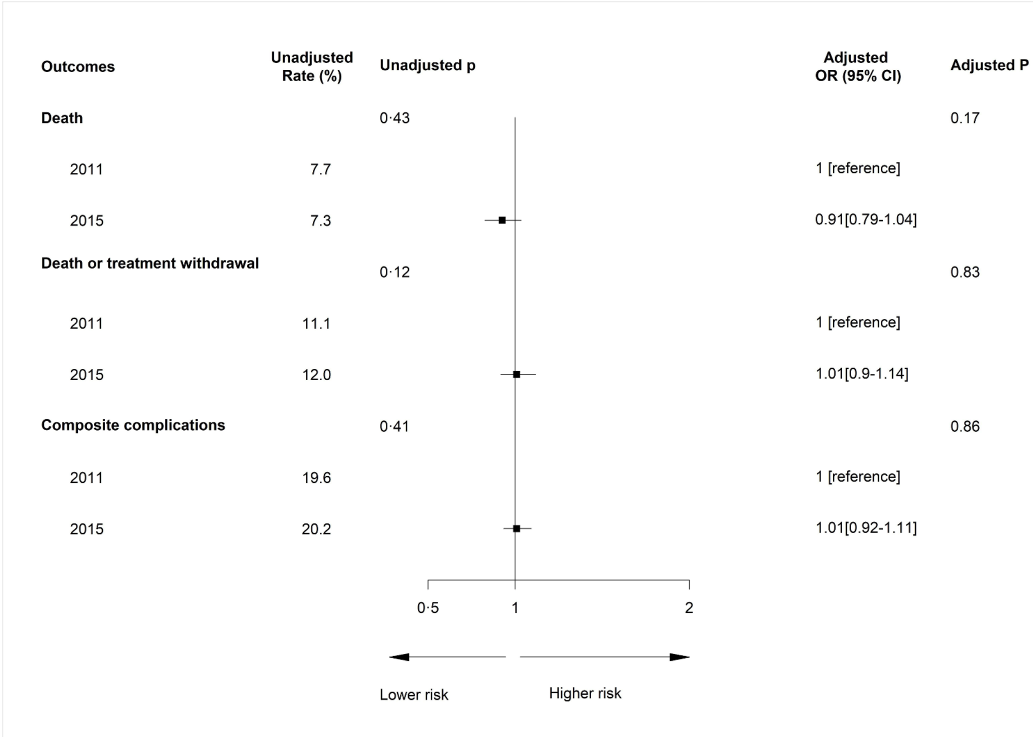

Figure 2 Adjusted in-hospital outcomes for patients with STEMI. Adjusted OR of 1 shows no difference from year 2011. We included 12 764 patients (6472 in year 2011 and 6292 in year 2015). We excluded 630 patients transferred in from other facilities, 2281 patients transferred out to other hospitals at any timepoint and 132 patients discharged alive within 24 hours. C=0.774 for mortality, C=0.793 for death or treatment withdrawal, and C=0.694 for composite complications. STEMI, ST segment elevation myocardial infarction.

DISCUSSION

In this nationally representative retrospective study in China, our findings had implications for measuring and improving quality of care for STEMI. First, the number of AMI hospitalisations doubled from 2011 to 2015. Although the proportion of those with STEMI decreased,

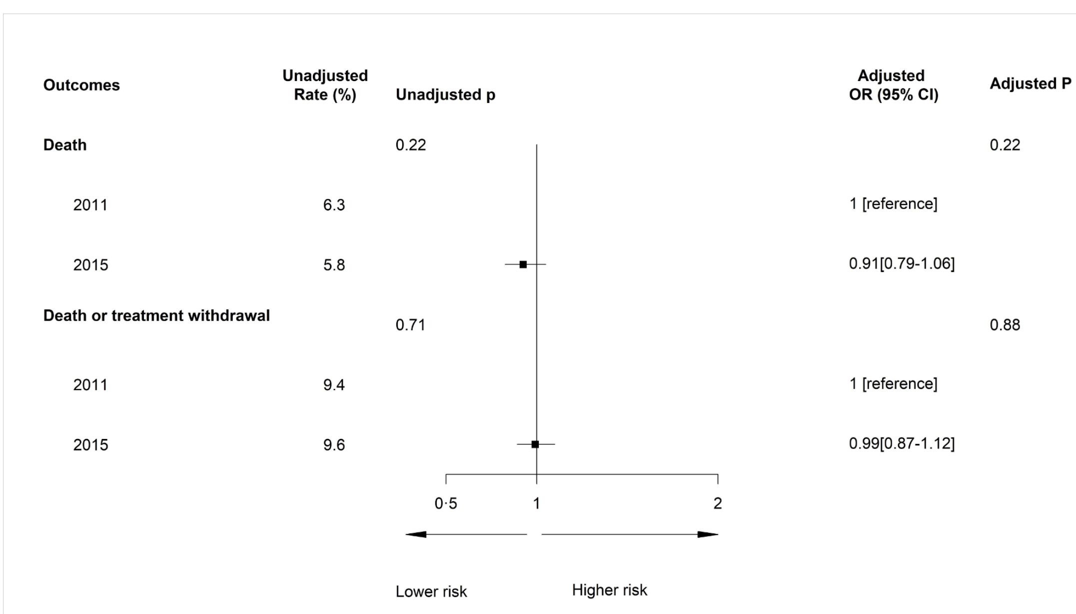

Figure 3 Adjusted 7-day outcomes among patients with STEMI. Adjusted OR of 1 shows no difference from year 2011. We included 13 518 patients (6715 in year 2011 and 6803 in year 2015). We excluded 630 patients transferred in from other facilities, 1527 patients transferred out to other hospitals within 7 days of admission and 132 patients discharged alive within 24 hours. C=0.773 for mortality and C=0.791 for death or treatment withdrawal. STEMI, ST segment elevation myocardial infarction.

the total number of patients with STEMI nearly doubled. Second, among patients with STEMI, the proportion of patients eligible for reperfusion decreased, primarily due to an increase in prehospital delay. Third, among those eligible for reperfusion, while significantly more received guideline-recommended therapy, substantial room for improvement remained. Fourth, among those receiving reperfusion therapy, we observed a continued shift away from fibrinolytic therapy towards pPCI. Finally, patient in-hospital outcomes did not improve between 2011 and 2015.

Regarding epidemiology, we note that from 2011 to 2015, non-ST segment elevation myocardial infarction (NSTEMI) cases as a proportion of all AMI cases increased, continuing the trend observed between 2001 and 2011. As we have previously reported, this is likely due to both an increased use of sensitive biomarkers for myocardial injury in China,[10] which would increase the diagnoses of NSTEMI,[11] as well as a concomitant change in the Chinese population at risk of AMI.[12] Despite increasing numbers of NSTEMI, the predominant AMI presentation in China continues to be STEMI, in contrast to high-income countries. This could be attributable to China's comparatively higher rates of smoking and lower rates of use of preventive therapy (eg, aspirin, statins), which are factors more strongly associated with STEMI than NSTEMI.[13–15] Similarly, this study found an increased proportion of patients with concomitant stroke in 2015, which might be explained by the unchanged or worsened prevalence of stroke-related risk factors, such as hypertension, diabetes and dyslipidaemia.[16]

We found processes of care improved, consistent with prior studies.[17 18] For example, we found a notable increase in use of antiplatelet therapies, which may be attributable to the introduction of ticagrelor as a guideline-based medical therapy (GDMT) for AMI during the study period.[19] However, obstacles remain, such as the persistent use of ineffective therapies such as magnesium sulfate, which had been shown to vary by hospital and physician characteristics in China.[20 21] To improve the uptake of GDMT and other evidence-based processes in AMI care, a deeper understanding of the sources of practice variation is needed, many of which may be related to local and regional differences in resource allocation. Similarly, although the rate of cardiogenic shock increased over time, use of mechanical support devices such as intra-aortic balloon pump (IABP) decreased. This could be explained by a prior finding that in clinical practice in China, IABP is more often used as preventive implantation before pPCI and less often used for cardiogenic shock.[22] Further, the Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock II (IABP-SHOCK II) trial results were published in 2012 and may have influenced clinical practice away from use of IABP for cardiogenic shock.[23]

Despite an increase in use of reperfusion therapies and guideline-based medications, we found no significant improvement in patient outcomes (in-hospital and 7-day mortality and complications) in 2015 compared with 2011. It is likely that there are multiple mechanisms for this finding. First, clinical outcomes may be confounded by variables not captured in this study. A prior study on geographical variation in China's quality of care for STEMI reported a similar paradox. The western region, which had the best performance in processes of care, such as use of clopidogrel, ACE inhibitors/angiotensin receptor blockers and statins, had worse mortality than hospitals in the central region, which had worse performance on processes of care.[24] However, second, we did find a decrease in the proportion of patients eligible for reperfusion on admission, with one of the drivers being increased prehospital delay, which may have masked the potential benefit of increased reperfusion rate among those eligible as observed at a cohort level. Further, we found that although marked shifts in acute reperfusion therapy occurred with a move from fibrinolysis to pPCI, among reperfused patients the time to reperfusion increased in 2015.

Prior studies vary in their reports of the prevalence of prehospital delay, with studies reporting from 8.6% to 34.1% of patients with STEMI in China present to the hospital >12 hours after symptom onset.[25 26] Prehospital delay can be influenced by accessibility (eg, transportation or distance to hospitals), affordability and patient preferences, factors not captured by many quality of care studies including our study. Further, these three factors may vary across time and geography and interact with one another. For example, as transportation and affordability improve, some patients may choose to bypass local hospitals for more distant hospitals perceived to offer better care. Prior studies on patient choice have shown that for severe conditions, patients prefer large hospitals with advanced equipment and expert physicians.[27–29] Regardless, this is a finding worthy of further indepth study, as timely reperfusion is key for optimal outcomes for STEMI. To reliably deliver good outcomes in timebound STEMI care, a unified STEMI network is ideal with the involvement of physician societies, state governments, ambulance agencies and hospitals.

Our findings have important implications for practice and policy. Given the increasing number of STEMI hospitalisations, prevention of cardiovascular diseases remains a public health priority. To improve outcomes for patients with existing cardiovascular conditions, China has instituted several hospital-based initiatives, such as the establishment of national (and provincial) medical quality control centres to routinely measure the performance of local hospitals on major diseases, as well as healthcare alliance with vertical collaborations between hospitals of varied levels to facilitate dissemination of clinical knowledge and experiences.[30 31] Efforts to improve reperfusion of eligible patients remain important. Prehospital delay in China is higher than in high-income countries.[32–34] Studies have shown that 24% of Chinese patients with STEMI present without typical chest pain and often seek non-emergent medical care when no chest pain occurs, which delays definitive treatment.[33 35] This highlights the need to increase population awareness of the symptoms of myocardial infarction, especially atypical symptoms, and the importance of seeking timely care STEMI care; such efforts require involvement of physician societies, state governments, ambulance agencies and hospitals.[36 37] In general, exploration of a broader range of care processes, beyond hospital treatment, would enhance quality improvement efforts.

The present study has several limitations. First, as a fixed cohort of hospitals that was representative in 2011, the China PEACE network's 2015 iteration may not reflect the national increase in hospitals treating STEMI between 2011 and 2015. Second, the quality of our data depends on the accuracy and completeness of prior documentation and abstraction. Nevertheless, the standardised procedures for abstraction of medical records ensure the reliability of our results in describing the treatments and outcomes. Third, changes in the clinical characteristics, care and outcomes are likely to have occurred between 2015 and the present. However, our data remain the most recently available data that are nationally representative. Fourth, some quality metrics of STEMI care, such as door-to-balloon, were missing since they were not routinely documented on the medical records.

In conclusion, our study identifies several changes in patient characteristics, treatment patterns and outcomes for STEMI in China from 2011 to 2015. The overall number of STEMI hospitalisations has increased substantially even though the proportion of STEMI continues to reduce. Prehospital delay renders a larger proportion of patients ineligible for reperfusion, highlighting an urgent need for improvement.[38 39] Further, increasing reperfusion rates and use of pPCI have not translated to an improvement in mortality, which warrants further study. The health system of China can benefit from an integrated data repository which can enable real-time assessments of treatment patterns and outcomes to improve the quality of care.

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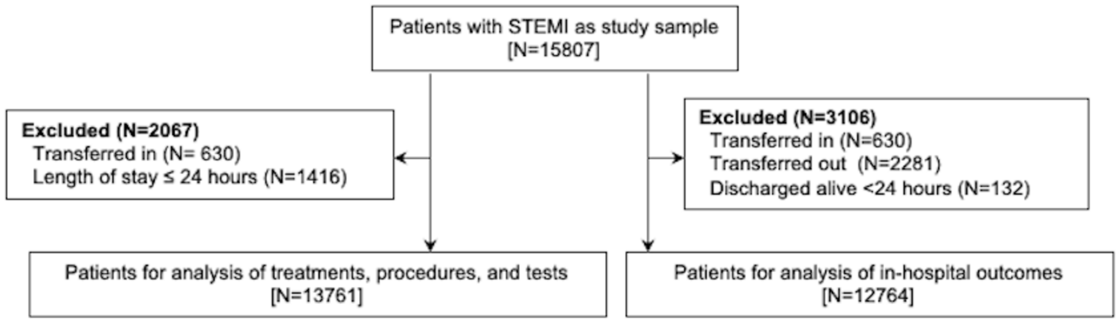
SUPPLEMENTARY MATERIAL

Supplementary Figure S1

Supplementary Table S1 – S5

Supplementary Methods

SUPPLEMENTARY FIGURES AND FIGURE LEGENDS



Supplementary Figure S1: Study profile

AMI = acute myocardial infarction. STEMI = ST-segment elevation myocardial infarction. NSTEMI = non-ST-segment elevation myocardial infarction. Number of hospitals of the 16052 patients in this paper: 166.

SUPPLEMENTARY TABLES

Supplementary Table S1: STEMI patients as a proportion of all AMI patients (unweighted)

	2011		2015		P
	Relative Frequency	Percent (95% CI)	Relative Frequency	Percent (95% CI)	
% STEMI among all AMI	7696/9333	82.5%(81.7-83.3)	8111/11834	68.5%(67.7-69.3)	<0.0001

Supplementary Table S2: Pre-hospital delay among different groups of patients.

	2011		2015		p value
	Relative frequency	Percent (95% CI)	Frequency	Percent (95% CI)	
Long delay*/Among STEMI	3285/6643	49.5%(48.2-50.7)	4050/7118	56.9%(55.7-58)	<0.0001
Long delay*/Among reperfusion ineligible	3285/3365	97.6%(97.1-98.1)	4050/4113	98.5%(98.1-98.8)	0.0079
Long delay*/Among no reperfusion	3285/4874	67.4%(66.1-68.7)	4050/5279	76.7%(75.6-77.9)	<0.0001

*Long delay is >12 hours between symptom onset and admission

Supplementary Table S3: Reperfusion eligibility and contraindications among all STEMI patients*

	2011		2015		
	Frequency	Percent (95% CI)	Frequency	Percent (95% CI)	p value
Patients eligible for reperfusion / all patients with STEMI	3278/6643	49.3%(48.1-50.5)	3005/7118	42.2%(41.1-43.4)	<0.0001
Ineligible patients					
Late presenters (>12h) / all patients with STEMI	3285/6643	49.5%(48.2-50.7)	4050/7118	56.9%(55.7-58)	<0.0001
Hemorrhage stroke at admission / all patients with STEMI	6/6643	0.1%(0-0.2)	12/7118	0.2%(0.1-0.3)	0.2
Gastrointestinal bleeding at admission / all patients with STEMI	48/6643	0.7%(0.5-0.9)	53/7118	0.7%(0.5-0.9)	0.9
Hemorrhage stroke history / all patients with STEMI	90/6643	1.4%(1.1-1.6)	93/7118	1.3%(1-1.6)	0.8

*all patients with STEMI for analysis of treatment process (n=13761), which is patients with STEMI, after excluding those who were transferred in and had length of stay <24h

Supplementary Table S4: Reperfusion contraindications among reperfusion-ineligible patients

	2011		2015		
	Frequency	Percent (95% CI)	Frequency	Percent (95% CI)	p value
Late presenters (>12h) / ineligible patients	3285/4874	67.4%(66.1-68.7)	4050/5279	76.7%(75.6-77.9)	<0.0001
Other contraindications (among reperfusion-ineligible patients and excluding late presenters)					
Hemorrhage stroke at admission / (ineligible patients – late presenters)	2/1589	0.1%(0-0.3)	4/1229	0.3%(0-0.6)	0.2543
Gastrointestinal bleeding at admission / (ineligible patients – late presenters)	14/1589	0.9%(0.4-1.3)	12/1229	1%(0.4-1.5)	0.7929
Hemorrhage stroke history / (ineligible patients – late presenters)	35/1589	2.2%(1.5-2.9)	27/1229	2.2%(1.4-3)	0.9918

Supplementary Table S5: Unadjusted STEMI outcomes

	2011	2015	P
Length of stay	11(7-15)	10(7-13)	<0.0001
In-hospital death	496(7.7%[7.1-8.3])	499(7.7%[7.1-8.3])	0.9
Treatment withdrawal	224(3.5%[3.1-3.9])	321(5%[4.5-5.5])	<0.0001

SUPPLEMENTARY METHODS

China PEACE-Retrospective AMI Study Sampling Design

We intended study hospitals to reflect diverse sites of care in China. As hospital volumes and clinical capacities differ between urban and rural areas as well among the 3 official economic-geographic regions of China, we separately identified hospitals in 5 strata: Eastern-rural, Central-rural, Western-rural, Eastern-urban, and Central/Western-urban regions. We considered an area urban if it is part of a downtown or suburban area within a direct-controlled municipality (Beijing, Tianjin, Shanghai, Chongqing) or 1 of 283 prefectural-level cities. We considered surrounding county-level regions, including counties and county-level cities, to be rural. Within this framework, China is composed of 287 urban regions and 2010 rural regions. We considered Central and Western urban regions together given their similar per capita income and health services capacity as shown below:

Population, Economy, and Hospitals in Different Geographic Strata of Mainland China

	Eastern	**Central**	**Western**
Rural Setting			
Population*	256,899,053	205,567,264	222,491,738
Income per capita (RMB)†	9,256	6,351	5,604
Level of central hospital			
Tertiary (%)	33 (5%)	12 (2%)	30 (3%)
Secondary (%)	586 (92%)	462 (92%)	739 (85%)
Primary (%)	20 (3%)	26 (5%)	102 (12%)
Total	639	500	871

Urban Setting			
Population*	336,364,491	150,467,917	144,803,916
Income per capita (RMB)†	21,547	15,539	15,523
Median # of hospitals per urban area (IQR)‡			
Tertiary	3 (2-6)	2 (1-3)	2 (1-4)
Secondary	5 (3-8)	4 (3-6)	3 (2-6)

* Statistics in 2009 from the National Bureau of Statistics of China (http://www.stats.gov.cn/tjsj/ndsj/2010/indexch.htm)

† Statistics in 2009 from the National Bureau of Statistics of China (http://www.stats.gov.cn/tjsj/ndsj/2010/indexch.htm)

‡ Median (interquartile range)

We identified cases for study inclusion using a stratified 2-stage cluster sampling design. In the first stage, we identified hospitals using a simple random sampling procedure within each of the 5 study strata. In the 3 rural strata, the sampling framework consisted of the central hospital in each of the predefined rural regions (2010 central hospitals in 2010 rural regions). Within each rural region, the central hospital is the largest general hospital with the greatest clinical capacity for treating acute illness. In each of the 2 urban strata, the sampling framework consisted of the highest-level hospitals in each of the predefined urban regions (833 hospitals in 287 urban regions). Hospital level is officially defined by the Chinese government based on clinical resource capacity. For example, secondary hospitals have at least 100 inpatient beds and the capacity to provide acute medical care and preventive care services to populations of at least 100,000, while tertiary hospitals are large referral centers in provincial capitals and major cities.

We excluded military hospitals prison hospitals, specialized hospitals without a cardiovascular disease division, and traditional Chinese medicine hospitals. Since the majority of hospitals in China are publicly owned and administered, hospital closure is rare, and hospital number has remained stable over the past decade. We therefore decided to select representative hospitals from 2011 to reflect current practices and trace this cohort backward to 2006 and 2001 to describe temporal trends.

In the second stage, we drew cases based on the local hospital database for patients with acute myocardial infarction at each sampled hospital. We ordered each hospital's list of eligible cases by date of admission and selected cases using systematic random sampling with equal probabilities. We selected a case at random, after which we selected every k^{th}casebased on sample size requirements, where k is the sampling interval.

In each of the 5 study strata, we determined the sample size required to achieve a 2% precision for describing the primary outcome, in-hospital mortality, which we had estimated to be approximately 9% in urban hospitals and 7% in rural county-level hospitals.

The following *Equation 1* can be used to define the sample size required (n) for a given proportion of the primary outcome (P), desired precision (d), and specific choice of α.

Equation1:

$$n = \frac{{z_{\propto}}^2 \cdot P(1-P)}{d^2}$$

However, because random cases sampled within the same hospital are likely to be more similar to one another than to random cases from another hospital, the effective sample size is reduced. Consequently, a design effect adjustment should be introduced as follows:

Equation2:

$$n = \frac{z_{\propto}{}^{2} \cdot P(1-P)}{d^{2}} \times \ deff$$

Where the design effect (*deff*) is given by

Equation3:

$$deff = 1 + \ \delta\ (\overline{n'} - 1)$$

where δ is the intraclass correlation for the statistic in question and$\overline{n'}$is the average number of sampled cases within each hospital.$\overline{n'}$is also known as the cluster size.

With this framework in mind, to achieve a precision of 2% with an α of 0.05 in each of the 3 rural strata, assuming an intraclass correlation of 0.02 and design effect of 1.8, we would need to sample 1150 medical records among hospitals with an average cluster size of 40. Analogously, to achieve a precision of 2% with an α of 0.05 in each of the 2 urban strata, assuming an intraclass correlation of 0.02 and design effect of 2.2, we would need to sample 1750 medical records among hospitals with an average cluster size of 60. These cluster sizes in rural and urban settings appeared reasonable based upon our previous survey of treatment for acute coronary syndromes at more than 1000 hospitals in 2010, which demonstrated that the median volume of hospitalization for acute myocardial infarction was approximately 180 cases per year in urban hospitals and 95 cases per year in rural county-level hospitals. Assuming an anticipated participation rate of 85% among selected hospitals, we approached 35 hospitals for participation in each stratum for a total of 175 hospitals (70 urban and 105 rural). We doubled cluster sizes for 2011 and 2015 to improve precision in the description of hospital-level treatment patterns and outcomes.

Ideal candidates for the treatments

Patients who were transferred in or whose lengths of hospital stay did not exceed 24 hours were excluded for all the following treatments.

For the reperfusion therapy, we included patients who were admitted within 12 hours of symptom onset and did not receive reperfusion therapy before hospital presentation. Then we excluded patients with any contraindications (history of hemorrhagic stroke, active bleeding at presentation, or any other physician documented contraindications for fibrinolytic therapy if the patient was treated in non-percutaneous coronary intervention (PCI) capable hospital; allergy to contrast agents or any other documented contraindication to PCI if the patient was treated in PCI-capable hospital).

For aspirin, we excluded patients with any contraindications for aspirin (allergy to aspirin, active bleeding on admission, history of hemorrhagic stroke, or other documented contraindications).

For clopidogrel, we excluded patients who participated in the ClOpidogrel and Metoprolol in Myocardial Infarction Trial (COMMIT) or patients with any contraindications for clopidogrel (allergy to clopidogrel, active bleeding on admission, history of hemorrhagic stroke, or other documented contraindications).

For beta-blockers, we excluded patients who participated in the ClOpidogrel and Metoprolol in Myocardial Infarction Trial (COMMIT) or patients with any contraindications for beta-blockers (allergy to beta-blockers, cardiogenic shock on admission, heart failure on admission, second or third degree atrioventricular block with no pacemaker implanted, systolic blood pressure <100mmHg on admission, bradycardia [heart rate <60 beats/min] on admission without taking a beta-blocker, or other documented contraindications).

For angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB), we excluded patients with any contraindications for ACE inhibitors (allergy to ACE inhibitors, hyperkalemia (serum potassium >5·5 mmol/L during hospitalization), creatinine >265 umol/L during hospitalization, pregnancy or breast feeding, or other documented contraindications).

For statins, we excluded patients who were allergy to statins.

The seven categories of traditional Chinese medicines commonly used in China among patients with acute myocardial infarction

(1) Salvia miltiorrhiza/Red Ginseng/Ginseng (e.g. Danshen dripping pill, Tanshinone)*

(2) Gingko (e.g. Ginkgo biloba, Ginkgo biloba extract)*

(3) Panax notoginseng (e.g. Panax notoginseng saponins, Xueshuantong injection)*

(4) Hirudo (e.g. Lepirudin, Shuxuetong injection)*

(5) Erigeron Breviscapus (e.g. Erigeron breviscapus injection, Breviscapinun)*

(6) Lipid lowing agents (e.g. Xuezhikang, Taizhian)

(7) Other (e.g. Puerarin, Suxiao jiuxin pills, Kyushin pills)

* based on the main functional ingredient.

Definition of in-hospital complications

1) Re-infarction

Indicate if there is physician documentation of recurrent myocardial infarction during hospitalization.

2) Cardiogenic shock

Indicate if there is physician documentation of cardiogenic shock during hospitalization.

3) Ischemic stroke

Indicate if there are physician documentations of new-onset ischemia stroke and stroke-related symptoms during hospitalization. The stroke-related symptoms include: trouble walking/loss of balance/incoordination, one-sided numbness or hemi-anesthesia, one-sided facial numbness or hemi-anesthesia, mouth askew and drooling, dysarthria or slurred speech, loss of vision or blurred version in one or both eyes, dizziness with vomiting, severe headache and vomiting, unconsciousness, and hyperspasmia.

4) Congestive heart failure

Indicate if there is physician documentation of heart failure during hospital stay. This include those without a history of heart failure but develop heart failure during hospitalization, and those with a history of heart failure as a chronic comorbidity and develop worsening heart failure during hospitalization.

China PEACE-Retrospective AMI Study Site Investigators by Hospital

All collaborating hospitals accepted the central ethics approval except for five hospitals (***bold and italicized***), which obtained local approval from internal ethics committees.

Aba Tibetan and Qiang Autonomous Prefecture People's Hospital, ShipingWeng, ShuyingXie; Affiliated Hospital of Guiyang Medical College, Lirong Wu, Jiulin Chen; Affiliated Hospital of Hainan Medical College, Tianfa Li, Jun Wang; ***Affiliated Zhongshan Hospital of Dalian University,*** Qin Yu, Xiaofei Li; Alxa League Central Hospital, Zhong Li, ShiguoHao, Yuzhen Zhang, Xuemei Wu; Baiquan County People's Hospital, Yachen Zhang, Zhifeng Liu; Biyang People's Hospital, Zhongxin Wang, HaoJia; Bortala Mongol Autonomous Prefecture People's Hospital, Bayin Bate, BadengQiqige; Changda Hospital Of Anshan, Xiang Jin, Ting Cai; Chengwu County People's Hospital, Fengqin Liu, Dayong Xu; Chenxi County People's Hospital, Xuejin He, Shui Yang; Chongren County People's Hospital, Chun Yuan, Jiping Wang; County People's Hospital of Jinning, LihuaGu, Lin Li, Shijiao Chen; Dalian Municipal Central Hospital, YongchaoZhi, Lili Sun; Dao County People's Hospital, Shengcheng Zhou, Lingjiao Jin; Daofu County People's Hospital, Yong Leng, Liangchuan Zhang, Tianyun Deng; Dingyuan County People's Hospital of Anhui Province, Yuanjin Wang, Wenhua Zhang, Xinmin Ma; Dongyang People's Hospital, Weimin Li, Liang Lu, Xuan Ge; Dulong and Nu Autonomous County People's Hospital of Gongshan, Xiaoping Wu, Yanming He; Dunhua City Hospital of Jilin Province, FanjuMeng, Jia Li; Fenghuang County People's Hospital, Dexi Liao, Guangyong Liu, Wen Qin; Fengshan County People’s Hospital, Wen Long, Xiangwen Chen; Fourth Hospital of Baotou City, Baohong Zhang, Yonghou Yin, Bin Tian; Fourth People's Hospital of Zigong City, Yong Yi, Chaoyong Wu; Fugu County People's Hospital of Shaanxi Province, Baoqi Liu, Zhihui Zhao, Haiming Li; Fujian Provincial Hospital, YansongGuo, Xinjing Chen; Fuling Center Hospital of Chongqing City, Liquan Xiang, Lin Ning; Gannan County People's Hospital, Mei Chen, Xin Jin, Guiling Li; General Hospital of the Yangtze River Shipping, Xiuqi Li, Xing'an Wu; Gongcheng Yao Autonomous County People's Hospital, Congjun Tan, Mingfang Feng, Meili Wang; Guangchang County People's Hospital, Liangfa Wen, Xiang Fu, QunxingXie; Guilin People's Hospital, Wei Zhang, Yanni Zhuang, Hua Lu;Guiping People's Hospital, Jiaqian Lu, Yu Huang; Haerbin 242 Hospital, Yin Zhou, Qiuling Hu; Haiyan People's Hospital, Chunhui Xiao, Xiaoli Hu; Heling Ge Er County People's Hospital, Yongshuan Wu, Qiuli Wang; Helong Municipal People's Hospital, Youlin Xu, Xuefei Yu; Henan Provincial People's Hospital, Chuanyu Gao, Jianhong Zhang, You Zhang; Heze Municipal Hospital, WentangNiu, Xiaolei Ma, Yong Wang; HGKY Group Company General Hospital, Xiaowen Pan, Yanlong Liu; ***Hua Xin Hospital (First Hospital of Tsinghua University),*** Lifu Miao, Yanping Yin, Zhiying Zhang; Huairen People's Hospital, Shutang Feng; Huayin People's Hospital, Aiping Wang, Jiangli Zhang, Feipeng Li; Huaying People's Hospital , Hong Wang; Hunchun Hospital, Lijun Yu, Xinxin Zhao; Huizhou Municipal Central Hospital, Yuansheng Shen, Zhiming Li, Lizhen He; Hunan Province Mawangdui Hospital, ZhiyiRong, Wei Luo; Ji'an Municipal Central People's hospital, Xueqiao Wang; Jianghua Yao Autonomous County People's Hospital, Rongjun Wan, Jianglin Tang, Guanghan Wu; Jiangsu Haimen People's Hospital, Jie Wu, Bin Xu; Jiangxi Provincial People's Hospital, Qing Huang, Xiaohe Wu; Jiangzi County People's Hospital, Sang Ge, Pian Pu, PingcuoDuoji; ***Jilin Province People's Hospital,*** Hui Dai, Yuming Du, Wei Guo; Jilin Integrated Traditional Chinese & Western Medicine Hospital, Jilin Province, Jianping Shi; Jinghai County Hospital, Peihua Zhao, Jingsheng Sun; Jingxi County People's Hospital, Hongxiang Li, Wen Liang; Jingxing County Hospital, Zhiwen Dong, Zhenhai Zhao; Jingzhou Central Hospital, Xin

Li, Qin Xu; Jiuquan City People’s Hospital, Yaofeng Yuan, Zhirong Li; Jixi People's Hospital of The Jixi Municipal People's Hospital Medical Group, Jinbo Gao; Jize County Hospital, Qiu’eGuo; Kangbao County People's Hospital, Ruiqing Zhao, Guangjun Song; Keshiketengqi Hospital of Chifeng City, Lize Wang, Haiyun Song; Lanping Bai and Pumi Autonomous County People's Hospital, Jinwen He, Jinming He; Laoting County Hospital, Keyong Shang, Changjiang Liu, Kuituan Xi; Liaoyang Central Hospital, Rihui Liu, Peng Guo; Liaoyuan Central Hospital, ChaoyangGuo, Xiangjun Liu, Rujun Zhao, Zeyong Yu; Lindian County Hospital, Wenzhou Li, Xudong Jing, Huanling Wang; Linxiang People's Hospital, Xiyuan Zhao, Chao Zhang, Long Chen; Liujiang County People's Hospital, Meifa Wei, Yan Liu, Shengde Chen; Longyan First Hospital, Kaihong Chen, Yong Fang, Ying Liao; Luancheng County Hospital, Junli Wang, Tianyu Liu, Suzhe Cheng; Lucheng People's Hospital, Yunke Zhou, XiaoxiaNiu, Huifang Cao; Luchuan County People's Hospital, Zebin Feng, Min Feng; Luxi County People's Hospital, FeilongDuan, Haiming Yi; Luyi County People's Hospital, Yuanxun Xu, AnranGuo; Macheng People's Hospital, Xianshun Zhou, HongzhuanCai, Peng Zheng; Mengcheng First People's Hospital, GaofengGuo; MenglianLahudaiwa autonomous counties People's Hospital, Xiang Li; Min County People's Hospital, MinwuBao, Yuhong Liu; Nanjing First Hospital, Shaoliang Chen, HaiboJia, Hongjuan Peng; Nan’an Hospital, Duanping Dai, Shaoxiong Hong; Nantong Third People's Hospital, Song Chen, Dongya Zhang, Ying Wang; Nanyang Central Hospital, Yudong Li, Jianbu Gao, Shouzhong Yang; Ningwu County People's Hospital, Junhu An; Peking University People's Hospital, Chenyang Shen, Yunfeng Liu; Peking University Shenzhen Hospital, Chun Wu, Huan Qu, Saiyong Chen; People's Hospital of Jingyu, Yuhui Lin, Dehai Jiao; People's Hospital of Yueqing City, Manhong Wang, Qiu Wang; Pianguan County People's Hospital, YingliangXue, Ruijun Zhang; Puding County People's Hospital, Cheng Yuan, Lei Wu;

Qinghai Red Cross Hospital, Jianqing Zhang, Chunmei Wei, Yanmei Shen; Qinshui County People's Hospital, Hehua Zhang, Hongmei Pan, Yong Gao; Qinyang People's Hospital, Xiaowen Ma, Yanli Liang, Tianbiao Wang; Queshan County People's Hospital, Daguo Zhao; Quzhou People's Hospital, XiaomingTu, Zhenyan Gao; Rongjiang County People's Hospital, Fangning Wang, Qiang Yang; Rudong County People's Hospital, Xiaoping Kang, Jianbin Fang, Dongmei Liu; Ruyang County People's Hospital, Chengning Shen, Mengfei Li; Shangluo Central Hospital, Yingmin Guan, Wenfeng Wang, Ting Xiao; ShangqiuChangzheng People's Hospital, Qian Wang; Shaoyang County People's Hospital, Fengyun Jiang, Kaiyou Wu; Shengsi People's Hospital, Songguo Wang; Shenyang Weikang Hospital, Xujie Fu, Shu Zhang,Lifang Gao; ShougangShuicheng Iron & Steel (Group) Co·, Ltd. General Hospital, Min Zhang, Kai Fu, XiaojingDuan; Shuangshan Hospital Of Anshan, Rui Xiao, Ruixia Wu, Bin Li; Siziwang County People's Hospital, Hongtu Zhang, Yuerong Ma, Zhonghui Cao; SunanYugur Autonomous County People's Hospital, Zhansheng Ba, Wanhai Fu; Taizhou Hospital of Zhejiang Province, Jianjun Jiang, YafeiMi, Weiwei Zhou; The Affiliated Hospital of Beihua University, Feng Sun, Qi Zhang, Shiyu Zheng; The Fifth People's Hospital of Dalian, Jing Zhang, Yang Zhong; The First Affiliated Hospital of Hebei North University, Fangjiang Li, Xiaoyuan Wang; The First Affiliated Hospital of Henan University of Science & Technology, Pingshuan Dong, Laijing Du, Wei Liu; The First Affiliated Hospital Of Jia Mu Si University, Zhaofa He, Meihua Jin; The First Hospital of Fuzhou City, Ting Jiang, Zhuoyan Chen; The First Hospital of Xi'an, Manli Cheng, YuqiangJi; The First People's Hospital of Danzhou, Youhua Zhou, Jvyuan Li; The First People's Hospital of Guangzhou, Yizhi Pan, Jian Liu; ***The First People's Hospital of Guangyuan,*** Tianxun Wang, Ping Yang; The Fourth People's Hospital of Shangqiu Shi, Guiyu Huang, JianjunPan,QingliangCai,Qianying Wang; The General Hospital of Yongzhou, Hunan Province, MingliLv; The people's hospital of Wuchuan, Yuanming Yi, Xuelian Deng; The People's Hospital of Yuanling, Wenhua Chen, RongCai; The People's Hospital of Zhijiang City, Bing Zhang; The Second Affiliated Hospital of Harbin Medical University, Bo Yu, Yousheng Xu, Zhengqiu Wang; The Second Affiliated Hospital of Kunming Medical University, Jun Shu, Ge Zhang, Kai Li; The Second Central Hospital of Baoding City, Guang Ma, PuxiaSuo; The Second People's Hospital of Liaoyuan City, Aimin Zhang, Yongfen Kang; ***Tianjin Medical University General Hospital,*** Zheng Wan,Yuemin Sun, Bo Bian; Tibet Autonomous Region People's Hospital, Xuejun Hu, DawaCiren; Tongchuan Mining Bureau Central Hospital, GuojiongJia, Jieli Pan; Tongliang County People's Hospital, Guofu Li, Hongliang Zhang, Longliang Zhan; Tongliao City Horqin District First People's Hospital, Junping Fang, Xinli Yu; Ulanqab Central Hospital, Dacheng Wang, Dajun Liu, Xinhong Cao; Wencheng County People's Hospital, Yi Tian, HaishengZhu,Wanchuan Liu; Wuhai People's Hospital, Zhaohai Zhou, Lei Shi; Wuhu Second People's Hospital, Wuwang Fang, Manxin Chen; Wulate County People's Hospital, ,FuqinHan,JianyeFu,Yunmei Wang; Wuqiang County People's Hospital, Binglu Liu, YanliangZhang,Xiupin Yuan; Wuyishan Municipal Hospital, Qingfei Lin, Yun Chen; Xiangtan County People's Hospital, Yuliang Zhu, ZhiqiangCai; Xing County People's Hospital, Xingping Li, LirongAo; Xingshan County People's Hospital, Shubing Wu, Hui Zhang; Xinmi First People's Hospital, Fusheng Zhao, Guangming Yang; Xinshao County People's Hospital, Renfei Liu, Wenwei Ai; Xiuwu County People's Hospital, JianbaoChang,Haijie Zhao; Xuanhan County People's Hospital, Qijun Ran, Xuan Ma; Xupu County People's Hospital, Shijun Jiang, Xiaochun Shu; Yanggao County People's Hospital, Zhiru Peng, Yan Han; Yanqing County Hospital, Jianbin Wang, Li Yang; Ying County People's Hospital, Yu Shen, Xingcun Shang; Yitong Manchu Autonomous County First People's Hospital, Haifeng Wang; Yongxing County People's

Hospital, Hongyan Li, Zhisong Liao, Yang Cao; Yuanzhou District People's Hospital of Guyuan City, Xiaoping Gao, MeiyingCai, Lining You; Yuncheng Central Hospital, Xuexin Li, Shuqin Li, Yingjia Li; Yunlong County People's Hospital, Jianxun Yang, Song Ai, Jianfei Ma; Yuyao People's Hospital, Lailin Deng; ZhangjiachuanHui Autonomous County First People's Hospital, Keyu Wang, Shitang Gao, Jian Guan; Zhouning County Hospital, Banghua He, Youyi Lu; Zhuoni County People's Hospital, Weirong Yang, Hong Li; Zhuozi County People's Hospital, Zhizhong Zhang, Xiaohong Chi; Zuoyun County People's Hospital, Ru Duan, Guangli Wang.

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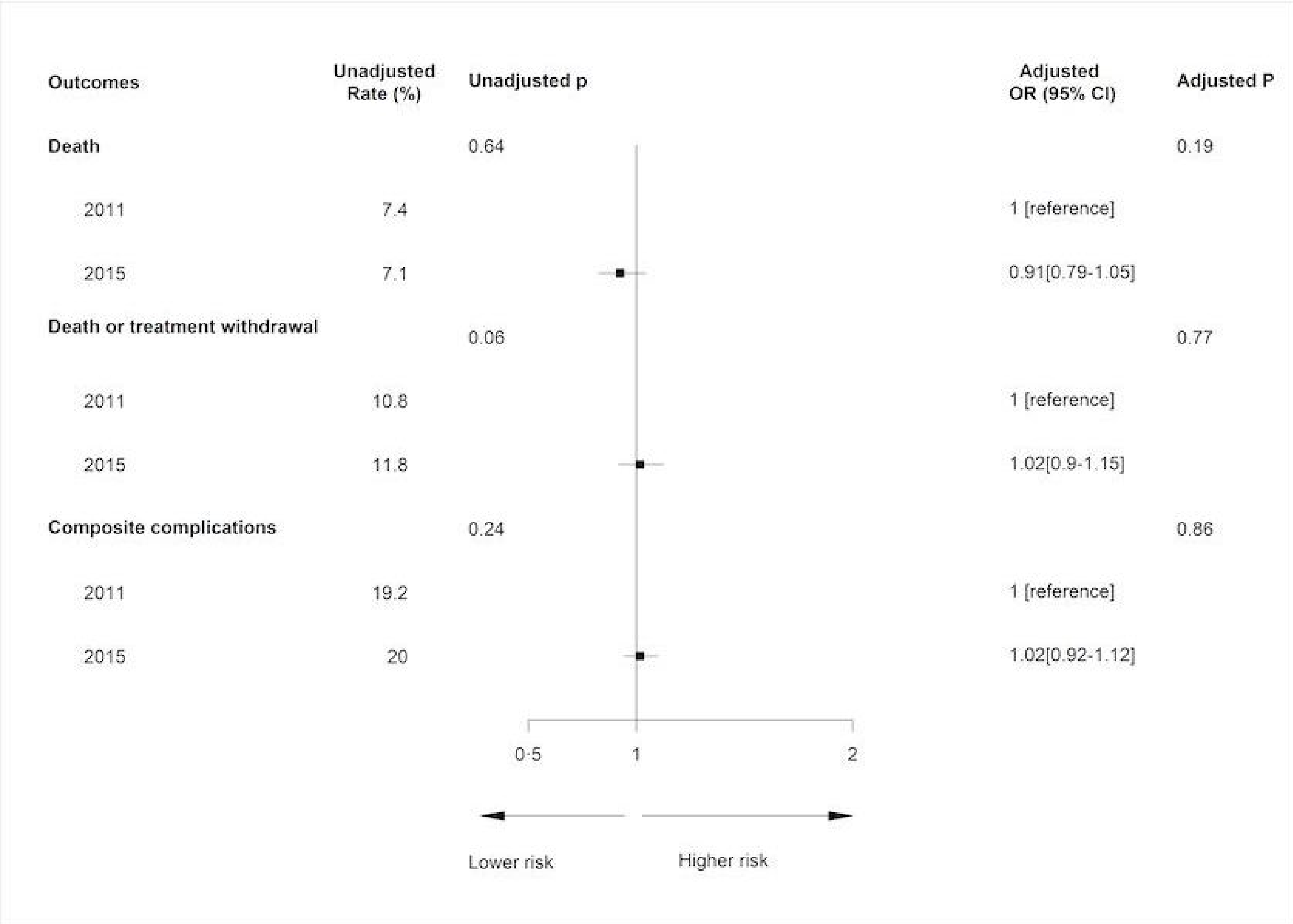
Outcomes
Unadjusted Rate (%)
Unadjusted p
Adjusted OR (95% CI)
Adjusted P
Death
0.64
0.19
2011
7.4
1 [reference]
2015
7.1
0.91[0.79-1.05]
Death or treatment withdrawal
0.06
0.77
2011
10.8
1 [reference]
2015
11.8
1.02[0.9-1.15]
Composite complications
0.24
0.86
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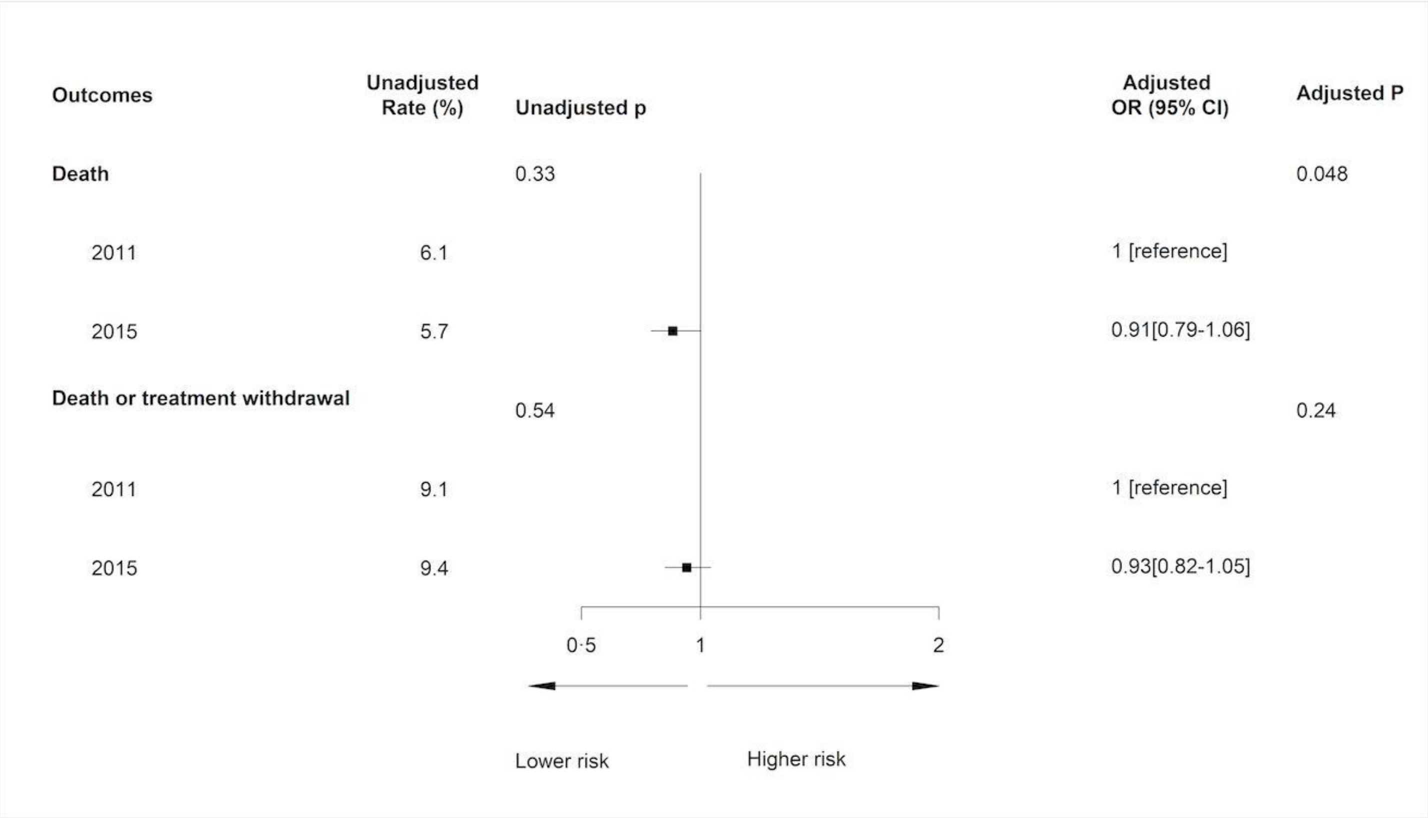
2015
20
1.02[0.92-1.12]
0·5
1
2
Lower risk
Higher risk


Outcomes
Unadjusted Rate (%)
Unadjusted p
Adjusted OR (95% CI)
Adjusted P
Death
0.33
0.048
2011
6.1
1 [reference]
2015
5.7
0.91[0.79-1.06]
Death or treatment withdrawal
0.54
0.24
2011
9.1
1 [reference]
2015
9.4
0.93[0.82-1.05]
0·5
1
2
Lower risk
Higher risk