

Trends in Early Aspirin Use Among Patients With Acute Myocardial Infarction in China, 2001–2011: The China PEACE-Retrospective AMI Study

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Background—Aspirin is an effective, safe, and inexpensive early treatment of acute myocardial infarction (AMI) with few barriers to administration, even in countries with limited healthcare resources. However, the rates and recent trends of aspirin use for the early treatment of AMI in China are unknown.

Methods and Results—Using data from the China Patient-centered Evaluative Assessment of Cardiac Events Retrospective Study of Acute Myocardial Infarction (China PEACE-Retrospective AMI Study), we identified a cohort of 14 041 patients with AMI eligible for early aspirin therapy. Early use of aspirin for AMI increased over time (78.4% in 2001, 86.5% in 2006, and 90.0% in 2011). However, about 15% of hospitals had a rate of use of <80% in 2011. Treatment was less likely in patients who were older, presented with cardiogenic shock at admission, presented without chest discomfort, had a final diagnosis of non-ST-segment elevation acute myocardial infarction, or did not receive reperfusion therapy. Hospitalization in rural regions was also associated with aspirin underuse.

Conclusions—Despite improvements in early use of aspirin for AMI in China, there remains marked variation in practice and opportunities for improvement that are concentrated in some hospitals and patient groups.

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Key Words: acute myocardial infarction • aspirin • quality of care

Practice guidelines recommend aspirin administered early in the course of acute myocardial infarction (AMI) for every patient without contraindications to treatment. The drug is safe, effective, inexpensive, widely available, and easy to administer.^{1–4} Because of these properties, even in care

settings with limited resources and access to specialty care, there should be few barriers to the administration of aspirin.

In China, like many other low- and middle-income countries, there is a particular need to optimize the use of cost-effective medications such as aspirin. Prior studies have evaluated the early use of aspirin in selected Chinese hospitals,^{5–7} and recently a high-level analysis of a nationally representative sample of Chinese hospitals demonstrated a significant increase in the utilization of aspirin therapy among eligible patients with ST-segment elevation myocardial infarction over the past decade.⁸ However, it remains unknown whether the progress made in aspirin therapy has been experienced by all patients and in all treatment settings, including in urban and rural hospitals and across regions. A careful assessment of aspirin use over the past decade is important for learning about how best to position future interventions to ensure that each eligible patient with AMI receives aspirin.

Accordingly, to support efforts to improve the quality of care for AMI, we analyzed data from the China Patient-centered Evaluative Assessment of Cardiac Events Retrospective Study of Acute Myocardial Infarction (China PEACE-Retrospective AMI Study), a large, government-sponsored,

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nationally representative study of patients with AMI admitted to 162 randomly selected hospitals throughout China in 2001, 2006, and 2011. Our objectives were to (1) describe current rates of early aspirin use (ie, within the first 24 hours of admission) among patients with AMI; (2) examine temporal trends in early aspirin use across regions and hospitals; and (3) identify the patient and hospital characteristics associated with a lower likelihood of receiving early aspirin. These findings are critical for China, a country with a population of 1.3 billion and estimated patients with AMI to reach 23 million by 2030,⁹ given the lifesaving potential of aspirin.

Methods

Design Overview of China PEACE-Retrospective AMI Study

The design of the China PEACE-Retrospective AMI Study has been published previously.¹⁰ In brief, we created a nationally representative sample of hospitalizations for AMI during 2001, 2006, and 2011 using 2-stage random sampling. In the first stage, we identified hospitals using a simple random sampling procedure within each of the 5 study strata: Eastern-rural, Central-rural, Western-rural, Eastern-urban, and Central/Western-urban regions, since hospital volumes and clinical capacities differ between urban and rural areas as well among the 3 official economic-geographic regions (Eastern, Central, and Western) of Mainland China. We considered Central and Western urban regions together, given their similar per-capita income and health services capacity. 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). In 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) (Figure 1). Since the majority of hospitals in China are publicly owned and administered, hospital closure is rare. We selected 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 AMI in each year at each sampled hospital using systematic random sampling procedures. Patients with AMI were identified using International Classification of Diseases—Clinical Modification codes, including versions 9 (410.xx) and 10 (I21.xx), when available or through principal discharge diagnosis terms. Data were collected via standardized central medical chart abstraction using standardized data definitions. We adopted rigorous monitoring at each stage to ensure data quality.¹⁰ Data abstraction quality was monitored by randomly auditing 5% of the medical records, with overall variable accuracy exceeding 98%.

We sampled 175 hospitals; 7 did not have admissions for AMI and 6 declined participation. Examination of patient databases from the participating 162 hospitals yielded 31 601 hospitalizations for AMI in 2001, 2006, and 2011. We sampled 18 631 cases and finally acquired eligible medical records for 18 110 (97.2%). After excluding those that were uninterpretable medical chart, duplicate, non-AMI, beyond the study periods, and developed AMI during hospitalization, we identified 16 100 cases with available medical charts (Figure 1).

The central ethics committee at the China National Center for Cardiovascular Diseases approved the China PEACE-Retrospective AMI Study. All collaborating hospitals accepted the central ethics approval except for 5 hospitals, which obtained local approval by internal ethics committees. The study is registered at www.clinicaltrials.gov (NCT01624883).

Study Sample

Only those patients with a definite discharge diagnosis of AMI and eligible for aspirin therapy within 24 hours of admission were included in the study sample. The diagnosis of AMI was determined by the combination of clinical discharge diagnosis terms and ECG results. If the local diagnosis was not definitive, cardiologists at the coordinating centre reviewed the medical record and ECG to determine diagnosis. We excluded patients who were transferred from other hospitals because they might have received acute treatments at their presenting hospitals. We also excluded patients who died, were discharged, or transferred out within 24 hours of admission because we assumed that such patients might not have had an opportunity to receive aspirin. We also excluded patients with contraindications to aspirin (allergy to aspirin, active bleeding at admission, history of hemorrhagic stroke, or any physician-documented contraindications to aspirin). All remaining patients were considered eligible for the study.

Variables

Patient-level independent variables in this study included demographic information, medical history, clinical characteristics at admission, reperfusion therapy, and year of hospitalization. Hospital characteristics included teaching status, percutaneous coronary intervention capability, economic geographic region, and urban or rural location. Early aspirin use was defined as prescription of aspirin within 24 hours of admission for AMI. Details of these variables are shown in Table.

Statistical Analysis

Patient demographic information, clinical history, presenting clinical features, and treatment patterns were compared

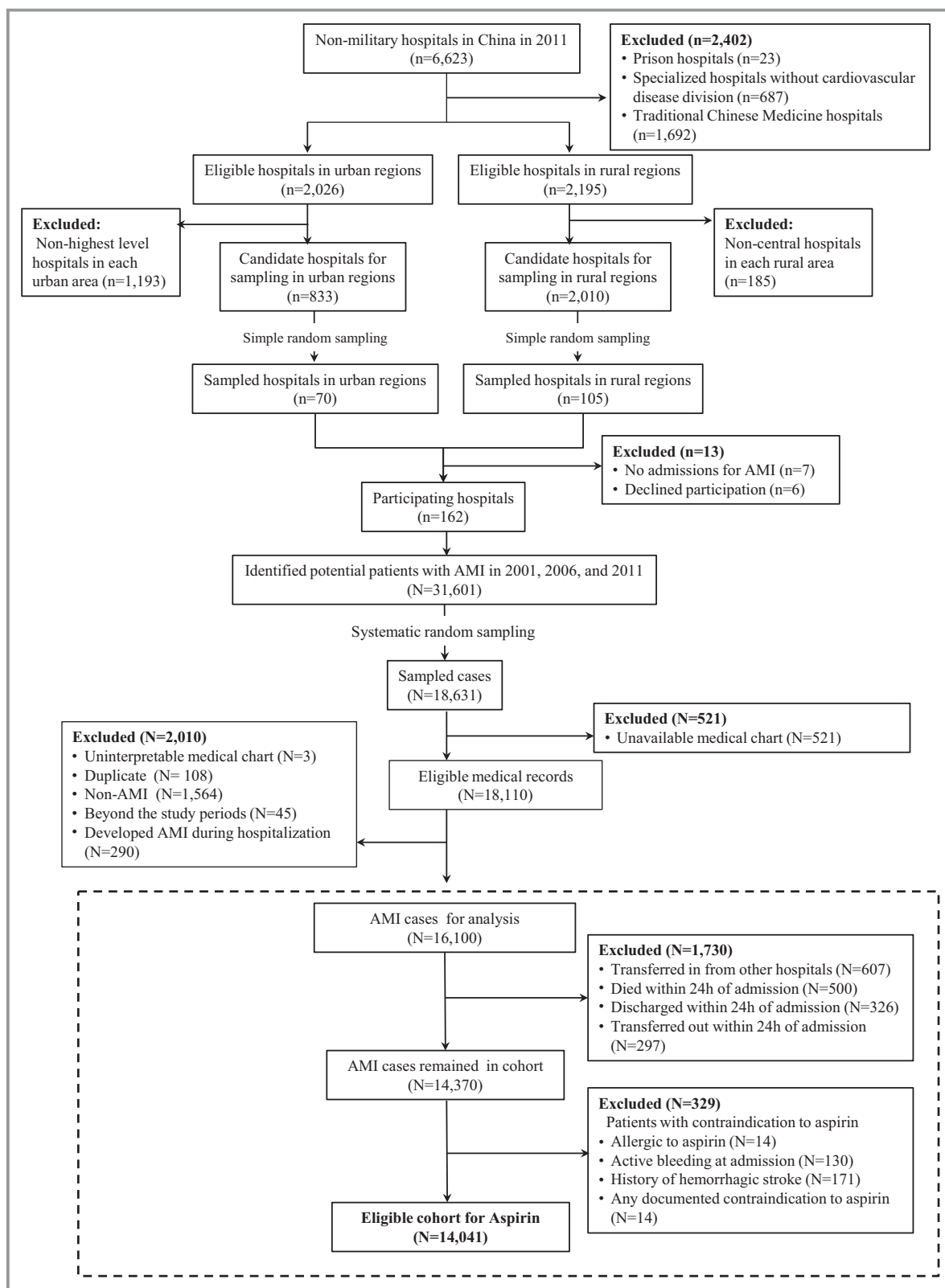


Figure 1. Flow diagram of the study sample. AMI indicates acute myocardial infarction.

between eligible patients who received aspirin within 24 hours of admission and those who did not. We employed standard parametric and nonparametric techniques for obser-

vational data, including Wilcoxon rank sum tests for continuous variables and the χ^2 test for categorical variables. For hospital rates of aspirin use, only those hospitals with at least

Table. Bivariate Analysis of Characteristics Associated With Patients Receiving Early Aspirin

Characteristics	Total (%) (N=14 041)	Early Aspirin User (%) (N=12 260)	Early Aspirin Non-User (%) (N=1781)	P Value
Demographic				
Age, y				<0.001
<55	22.1	23.0	16.3	
55 to 64	23.6	24.0	20.9	
65 to 74	30.1	29.9	31.0	
≥75	24.2	23.1	31.8	
Gender				<0.001
Male	69.9	70.7	64.4	
Female	30.1	29.3	35.7	
Cardiac risk factors				
Prior hypertension	49.5	49.9	46.8	0.015
Prior diabetes	17.4	17.3	18.1	0.388
Current smoker	34.7	35.8	27.3	<0.001
Medical histories				
Ischemic stroke	10.0	9.7	12.0	0.003
Myocardial infarction	10.8	10.9	10.3	0.460
Primary PCI	1.9	2.0	1.3	0.059
Clinical characteristics at admission				
Chest discomfort	91.9	93.5	81.5	<0.001
Cardiac arrest	1.0	0.8	2.0	<0.001
Cardiogenic shock	4.2	4.0	5.9	<0.001
Blood pressure mmHg				0.080
SBP<180 and DBP<110	91.6	91.8	90.6	
SBP≥180 or DBP≥110	8.4	8.2	9.4	
AMI type				
STEMI	85.4	86.1	80.6	<0.001
NSTEMI	14.6	13.9	19.4	
Reperfusion therapy				
No reperfusion	69.3	67.4	82.5	0.027
Fibrinolytic therapy	20.3	21.4	12.4	
Primary PCI	10.4	11.2	5.2	

Continued

Table. Continued

Characteristics	Total (%) (N=14 041)	Early Aspirin User (%) (N=12 260)	Early Aspirin Non-User (%) (N=1781)	P Value
Hospital characteristics				
Teaching hospital	80.8	80.7	75.5	<0.001
PCI-capable hospital	60.7	62.2	50.3	<0.001
Economic geographic region				
Eastern	59.2	58.6	62.7	0.915
Center	21.3	21.5	19.4	
Western	19.6	19.8	17.9	
Urban/Rural				
Urban	61.1	62.3	52.8	<0.001
Rural	38.9	37.7	47.2	
Year				
2001	15.0	13.6	24.9	<0.001
2006	28.3	28.1	29.6	
2011	56.7	58.3	45.5	

AMI indicates acute myocardial infarction; DBP, diastolic blood pressure; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; STEMI, ST-segment elevation myocardial infarction.

5 patients with AMI were included. To describe the rate of early aspirin therapy in China, we applied weights of each case to account for differences in the sampling fraction within each time period. Factors independently associated with early aspirin therapy were identified with logistic regression using the generalized estimating equation to account for the clustering of patients within hospitals. All selected variables, except those with frequencies <1%, were included in the multivariable model. Backward selection was used to identify the predictive factors of early aspirin use. Specifically, we evaluated all available variables for those that we thought might be associated with aspirin use based on prior reports, face validity, and clinical judgment. Eighteen candidate variables were identified, which we included in the initial model and then removed sequentially from least to most significant. Changes in the likelihood ratio and other parameter estimates were evaluated, and variables were retained if they were significant ($P<0.05$) in the model with likelihood ratio test. Odds ratios (OR) and 95% CI were reported. Interaction terms were tested between year of presentation and the other factors that were retained in the model. All comparisons were 2-tailed, with a $P<0.05$ considered

statistically significant. All statistical analyses were performed using SAS software (version 9.2; SAS Institute, Cary, NC).

Results

Study Sample

Of 16 100 patients with AMI, after excluding patients who transferred in ($n=607$), died ($n=500$), were discharged ($n=326$), transferred out ($n=297$) within 24 hours of admission, or had contraindications to aspirin ($n=329$), we identified a cohort of 14 041 patients with AMI eligible for early aspirin therapy (Figure 1). This cohort had a median age of 66 years (interquartile range 56 to 74) and 69.9% were men. Comorbidities were common: hypertension (49.5%), diabetes mellitus (17.4%), and previous myocardial infarction (10.8%) (Table).

Use of Early Aspirin Therapy

Overall, 87.3% of patients received early aspirin therapy. Weighted rates of use were 78.8%, 86.4%, and 90.0% in 2001, 2006, and 2011, respectively ($P<0.0001$ for trend). There were similar trends in use in all 5 regions over time ($P<0.0001$ for trend for all 5 regions); especially in Central and Western-rural areas, aspirin early use increased from $<70\%$ in 2001 to almost 90% in 2011 (Figure 2). The rate of early aspirin use in 2011 was highest in the Central/Western-urban region (92.7%) and lowest in the Eastern-rural region (87.0%).

The proportion of best-performing hospitals, defined as having at least 90% of eligible patients receiving early treatment, increased during the past decade, from 31.5% in 2001 to 48.8% in 2006 to 63.5% in 2011 (Figure 3). However, although the overall use of early aspirin therapy improved in rural hospitals, patients receiving care in these hospitals were less likely to receive early aspirin than in urban hospitals: in 2011, 17.4% of rural hospitals versus 11.3% of urban hospitals prescribed early aspirin for $<80\%$ of eligible patients.

Patient and Hospital Characteristics Associated With Early Aspirin Use

In the multivariable model, patients who were ≥ 75 years (OR 0.66; 95% CI 0.52 to 0.83 compared with younger patients), presented with cardiogenic shock (OR 0.67; 95% CI 0.52 to 0.85), had a final diagnosis of non-ST segment elevation myocardial infarction (OR 0.73; 95% CI 0.63 to 0.85 versus ST-segment elevation myocardial infarction) or were hospitalized in a rural region (OR 0.68; 95% CI 0.49 to 0.93) were significantly less likely to receive early aspirin. In contrast, patients presenting with chest discomfort (OR 2.76; 95% CI 2.32 to 3.28), were hospitalized in 2006 or 2011 (OR 1.92;

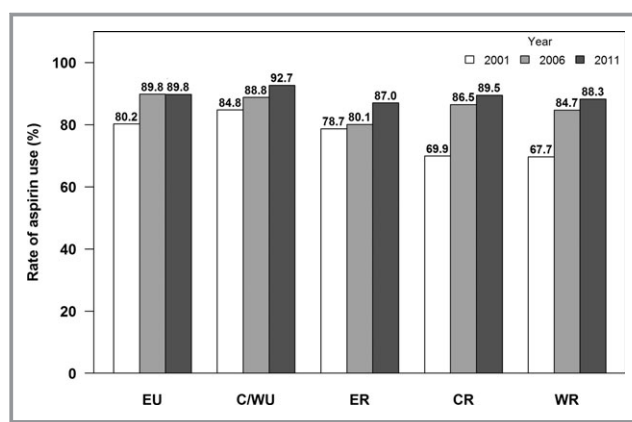


Figure 2. Trends in early aspirin use for acute myocardial infarction in 2001, 2006, and 2011 by Chinese Geographic Regions. $P<0.001$ for trend for all 5 regions. CR indicates Central-rural; C/WU, Central/Western-urban; ER, Eastern-rural; EU, Eastern-urban; WR, Western-rural.

95% CI 1.44 to 2.56, and OR 2.74; 95% CI 2.08 to 3.62, respectively, versus 2001) or received reperfusion therapies during admission were more likely to receive early aspirin (OR 1.96; 95% CI 1.63 to 2.35 for fibrinolytic therapy versus no acute reperfusion, OR 1.76; 95% CI 1.05 to 2.94 for primary percutaneous coronary intervention versus no acute reperfusion) (Figure 4). There were no significant interactions between these factors and year.

Discussion

In this study of a nationally representative sample of hospitalizations in China, we found improvements between 2001 and 2011 in the use of aspirin therapy within 24 hours of admission for AMI and concomitant attenuation in regional variation in use. However, even in the final year of our study, there were still areas for improvement. In 2011, about 1 in 10 eligible patients still did not receive early aspirin therapy, with lower rates in rural hospitals or in certain patient groups. This is the first study, to our knowledge, that characterizes contemporary trends in the early use of a readily available and effective therapy in a nationally representative population of patients with AMI in China, a country that is experiencing a marked increase in mortality and morbidity due to AMI.

In the present study, the use of early aspirin therapy is somewhat lower than that among patients with acute coronary syndrome reported by previous studies. Some multicenter studies reported that 95% of patients with acute coronary syndrome received early or in-hospital aspirin therapy in China.^{6–8} One possible explanation for the difference is that previous studies have been largely limited

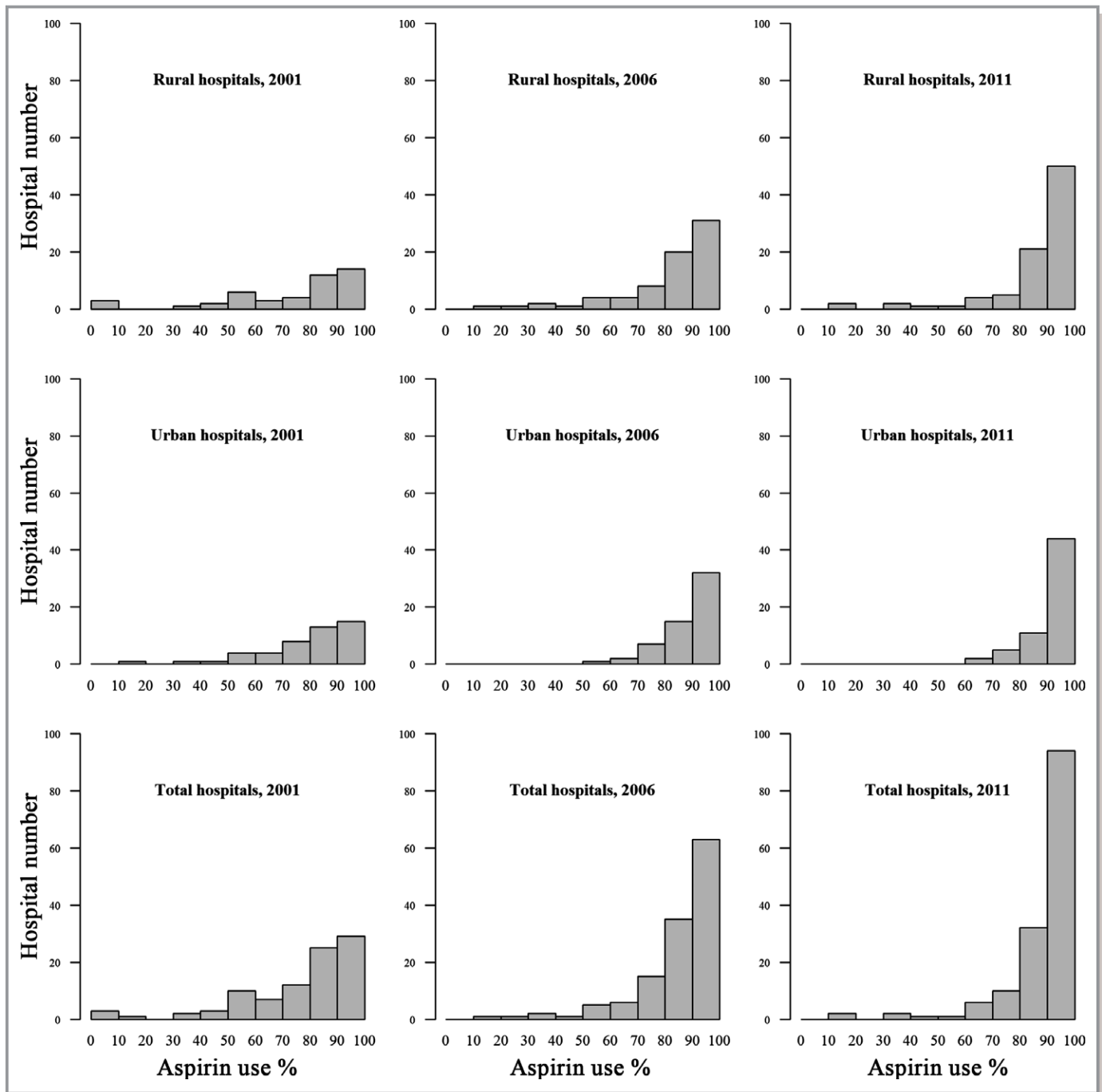


Figure 3. Trends of early aspirin therapy in rural and urban regions in 2001, 2006, and 2011 (hospitals with sample size <5 patients were excluded).

to tertiary care centers in urban regions and major metropolitan areas. The present study, with a nationally representative sample of hospitalizations for AMI in China, likely better reflects the actual practice patterns for AMI.

The increase in early aspirin use in China between 2001 and 2011 represents a substantial improvement in the use of a simple, inexpensive, and widely available evidence-based therapy for AMI. In this study, we found that there has been

marked improvement in early aspirin use over the past decade, with narrowing in the disparity in use between urban and rural regions. Moreover, the proportion of hospitals treating >90% of their eligible patients also significantly increased over time. Although we were not able to study the factors that may account for these dramatic improvements, they may be attributable to education on the utilization of evidence-based therapies for AMI and increases in

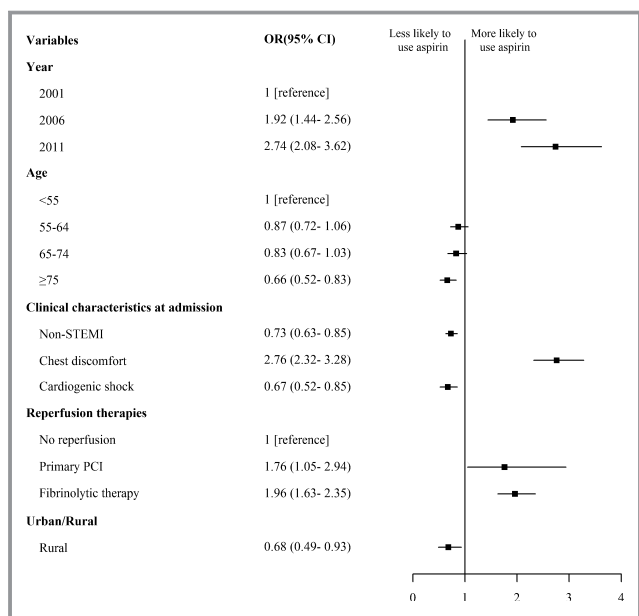


Figure 4. Factors associated with early use of aspirin in multivariable model (c-statistic 0.683). Variables in the final multivariable model are shown along the vertical axis. The strength of effect is shown along the horizontal axis with the vertical line demarking an odds ratio (OR) of 1 (OR=1, no association); estimates to the left (OR<1) indicates that patients with the characteristic have a lower likelihood of receiving aspirin than those without the characteristic, while those to the right (OR>1) indicates that patients with the characteristic have a higher likelihood of receiving aspirin than those without the characteristic. Each square and line represents the point estimate of the effect of that variable in the model, while the line shows the 95% CI. CI indicates confidence interval; NSTEMI, non-ST-segment elevation myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention.

medical insurance coverage and in healthcare expenditure by government.¹¹

Despite the overall improvement in early aspirin use, about 1 in 10 eligible patients did not receive early aspirin therapy in 2011. In developed countries, aspirin is more widely used. In the United States, rate of aspirin use within 24 hours after admission was >97% in 2009.¹² There are few recent comparisons with the early use of aspirin in other countries but in Europe, 97% of patients with AMI from 47 countries received early aspirin management in 2009.¹³ The higher rates of use in the United States and Europe may reflect the impact of quality-improvement efforts focused on this critical process of care that have not to this point been conducted in China.

Aspirin early in the course of AMI was particularly underused in specific patient groups. Consistent with previous studies, older patients were less likely to receive early aspirin.^{14,15} This may reflect concerns about the risk of bleeding. However, while elderly patients may be at high risk for adverse consequences of therapy, their risks for adverse consequences of no treatment

are also likely substantially higher; a study reported that in elderly patients, the use of aspirin was associated with 22% lower odds of 30-day mortality, which exceeded 20% in the older population.¹⁴ Therefore, the benefits of aspirin outweighed the risks for this subgroup in clinical trials. Patients who did not present with overt symptoms of AMI (such as chest discomfort) were less likely to be given aspirin, which may reflect diagnostic uncertainty. Patients with cardiogenic shock at admission were also less likely to be administered aspirin. This may have been because these patients were at a high risk for mortality and their physicians focused on emergency treatment to stabilize vital signs or interventions using advanced technology,¹⁶ while the simple use of aspirin was delayed. In addition, the early treatment of patients with aspirin was positively associated with the provision of reperfusion therapy. Thus, failure to use aspirin may be a marker for other deficits in the quality of care.

We also found that although use of aspirin improved in both urban and rural hospitals, gaps in care remained more pronounced in rural centers in 2011. China is a country with unbalanced economic development. Most of the rural hospitals, which are responsible for the care of more than 700 million people,¹⁷ have limited clinical capacity for advanced cardiac care and limited funding. However, because the cost of aspirin is minimal in China (\$0.04 for acute treatment)¹⁸ and has a dramatic effect on mortality,¹ this treatment is particularly relevant to rural hospitals. In our study, 17.4% of rural hospitals had treatment rates below 80% in 2011 compared with 11.3% of urban hospitals. Successful initiatives to improve aspirin use in China with a particular focus on rural hospitals could have an important impact on quality of care.

Certain factors should be considered in the interpretation of our results. First, the retrospective design restricted our analysis to information based on medical records. Some patients may have had contraindications to the therapy that were not documented in the records, which may have led to an underestimation of the utilization in eligible patients. However, the retrospective design and the standardized central abstraction ensured reliable data in accordance with the original medical records. Second, the missing data may vary across years, therefore biasing the analysis of trends. However, the number missing is small and therefore the effect should be minimal. Third, we excluded lower-level urban hospitals and noncentral rural hospitals from our sample. This sampling strategy was employed to ensure sample sizes within each of the participating institutions to provide adequately precise hospital-level estimates of care quality. It is possible that practice in the excluded hospitals differed from that of those in the study sample. Finally, we did not have long-term follow-up to determine whether the patterns of aspirin use were associated with health outcomes and we were underpowered to determine the early benefits and bleeding risk of aspirin therapy in the eligible cohort.

In conclusion, in China, we found a marked improvement in early aspirin therapy among patients with AMI over the past decade. However, use remained suboptimal in certain patient groups and care settings. Despite generally good performance, even this treatment could benefit from a quality improvement focus.

Appendix

Site Investigators by Hospital in China PEACE-Retrospective AMI Study

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