Time to hospital arrival among patients with acute myocardial infarction in China: a report from China PEACE prospective study

Wenchi Guan1†, Arjun K. Venkatesh2,3†, Xueke Bai1, Si Xuan4, Jing Li1, Xi Li1, Haibo Zhang1, Xin Zheng1, Frederick A. Masoudi5, John A. Spertus6, Harlan M. Krumholz2,7,8‡, and Lixin Jiang1*‡, for the China PEACE Prospective Collaborative Group

1National Clinical Research Center of Cardiovascular Diseases, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, 167 Beilishi Road, Beijing 100037, China; 2Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, 1 Church Street, Suite 200, New Haven, CT 06510-3330, USA; 3Department of Emergency Medicine, Yale University School of Medicine, 464 Congress Ave, Ste 260, New Haven, CT 06519-1315, USA; 4Department of Pharmaceutical & Health Economics, School of Pharmacy, University of Southern California, 635 Downey Way, Los Angeles, California, 90089-3333, USA; 5Division of Cardiology, University of Colorado Anschutz Medical Campus, Campus Box B132, 12401 East 17th Avenue, Room 522, Aurora, CO 80045, USA; 6Saint Luke’s Mid America Heart Institute/University of Missouri Kansas City, 4401 Wornall Road, Kansas City, MO 64111, USA; 7Department of Health Policy and Management, Yale University School of Public Health, 60 College Street, PO Box 208034, New Haven, CT 06520-8034, USA; and 8Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University School of Medicine, 333 Cedar Street, SHM I-456 PO Box 208088, New Haven, CT, 06520, USA

Received 19 March 2018; revised 10 May 2018; editorial decision 22 May 2018; accepted 24 May 2018; online publish-ahead-of-print 24 June 2018

Aims
Few contemporary studies have reported the time between acute myocardial infarction (AMI) symptoms onset and hospital arrival, associated factors, and patient perceptions of AMI symptoms and care seeking. We sought to study these issues using data from China, where AMI hospitalizations are increasing.

Methods and results
We used data from the China PEACE prospective AMI study of 53 hospitals across 21 provinces in China. Patients were interviewed during index hospitalization for information of symptom onset, and perceived barriers to accessing care. Regression analyses were conducted to explore factors associated with the time between symptom onset and hospital arrival. The final sample included 3434 patients (mean age 61 years). The median time from symptom onset to hospital arrival was 4 h (interquartile range 2–7.5 h). While 94% of patients reported chest pain or chest discomfort, only 43% perceived symptoms as heart-related. In multivariable analyses, time to hospital arrival was longer by 14% and 39% for patients failing to recognize symptoms as cardiac and those with rural medical insurance, respectively (both $P < 0.001$). Compared with patients with household income over 100 000 RMB, those with income of 10 000–50 000 RMB, and <10 000 RMB had 16% and 23% longer times, respectively (both $P = 0.03$).

Conclusion
We reported an average time to hospital arrival of 4 h for AMI in China, with longer time associated with rural medical insurance, failing to recognize symptoms as cardiac, and low household income. Strategies to improve the timeliness of presentation may be essential to improving outcomes for AMI in China.

Clinical trial registration
https://clinicaltrials.gov/ct2/show/NCT01624909.

Keywords
Time to hospital arrival • Acute myocardial infarction • Access to care

* Corresponding author. Tel: +86 10 8839 6203, Fax: +86 10 8836 5201, Email: jiangl@fwoxford.org
† The first two authors are joint first authors.
‡ The last two authors are joint senior authors.
© The Author(s) 2018. Published by Oxford University Press on behalf of the European Society of Cardiology. This is an Open Access article distributed under the terms of the Creative Commons Attribution-Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
Introduction

The benefits of reperfusion therapy for patients with acute myocardial infarction (AMI) depend on timely patient presentation for acute care.1,2 Prolonged time intervals have been associated with worse outcomes3,4 and are an international problem. In the United States and other Western countries, the median time from symptoms onset to hospital arrival is 2–3 h [2 h for ST-elevated myocardial infarction (STEMI), 3 h for non-ST-elevated myocardial infarction (NSTEMI)].5,6 Yet approximately 10% of patients still arrive at the hospital greater than 12 h after noticing symptoms.7,8 In countries with limited access to advanced health care, less developed emergency response systems, and limited personal and public financial resources for health care, time intervals to hospital arrival are reportedly worse.9–11

Few contemporary studies of delays to hospital arrival incorporate patients’ perspectives and perceptions regarding seeking care. Moreover, we know little about whether patient characteristics such as education, medical insurance, income, or psychosocial status are associated with delays. Understanding both the extent of time to hospital arrival and the factors contributing to prolonged time intervals may help identify barriers to timely presentation, and help guide future improvement strategies and interventions. This issue is particularly important in China where rates of AMI are increasing rapidly; by 2030 the country is estimated to have over 23 million AMIs each year, nearly three times as many as those in 2010.12

The China Patient-Centered Evaluative Assessment of Cardiac Events Prospective Study of Acute Myocardial Infarction (China PEACE-Prospective AMI Study) was specifically designed to study, among other topics, the time to hospital arrival and factors associated with it, as a means of developing future improvement programs. The study captured details of symptom onset and factors known to be related to health care access for AMI, to examine care seeking delays and associated factors. Specifically, we aim to describe the time from symptom onset to hospital arrival, patient perceptions regarding AMI symptoms and care-seeking, and factors associated with longer time to hospital arrival.

Methods

Study design of China PEACE-prospective AMI study

The design of the China PEACE-Prospective AMI Study has been published previously.13 In brief, the study consecutively registered patients aged 18 or older and were hospitalized for AMI within 24 h of symptom onset from 53 acute-care hospitals (35 tertiary and 18 secondary hospitals) in 21 Chinese provinces. Eligible patients who provided informed consent were enrolled and interviewed during index hospitalization, and followed up at 1, 6, and 12 months following hospital discharge. The first patient was enrolled in December 2012 and the last patient was enrolled in May 2014.

Data were collected via centralized medical chart abstraction, while interviews and physical examinations were conducted locally by site investigators. Medical chart abstraction quality was monitored by randomly auditing 5% of the medical charts. The chart abstraction achieved an overall accuracy of over 98%. Interviews were completed using tablet computers that employed data entry validation to ensure the accuracy and completeness of data.

Categorical variables were expressed as frequencies and percentages and analysed using χ² tests; continuous variables were described as means with 95% confidence intervals.
medians and interquartile ranges (IQRs) and analysed by the Kruskal–Wallis test. To characterize the patient characteristics for different time groups, we first examined the distribution of the primary outcome and then classified patients into one of three mutually exclusive categories: (i) less than or equal to 2 h; (ii) 2–6 h; and (iii) greater than 6 h. We chose 2 h and 6 h as cut-offs because these time points were commonly used in previous studies as well as in clinical practice; we also defined time to hospital arrival >6 h as ‘extreme delay’.

We subsequently fit a mixed model to estimate the associations between time to hospital arrival and patient characteristics. Because the distribution of time to hospital arrival was skewed, we applied a log-transformation to normalize its distribution prior to regression analysis. The estimated coefficients represent the percentage change for the time to hospital arrival for each 1-unit change in an independent variable. Candidate variables included age, sex, marriage status, work status, education level, household income, medical insurance, diabetes mellitus (DM), hypertension, hypercholesterolaemia, current smoking, medical history (AMI, percutaneous coronary intervention, coronary artery bypass grafting, angina, heart failure, and stroke), time of symptoms onset, onset symptoms, perceiving symptoms as cardiac, EQ5D index score, EuroQol five dimensions questionnaire visual analog scale (EQ5D-VAS), depression, stress level, social support, and SAQ-AF score. Missing data occurred only for time of symptoms onset (7.5%) and was reported as a separate group in the model. The model was fitted with hospital-specific random intercepts to account for within-hospital and between-hospital variations. We also did secondary analysis to identify factors associated with extreme delay using logistic regression; candidate variables included in the logistic model were the same as those in the mixed model. All comparisons were two-tailed, with a \( P < 0.05 \) considered statistically significant. All statistical analyses were performed using SAS software (version 9.4, SAS Institute, Cary, NC, USA).

## Results

### Study cohort

The final study sample included 3434 patients (81.5% of the total AMI cohort; Figure 1: baseline characteristics of patients included and excluded in this study were shown in Appendix, Table A1), 43% had documented timestamps of both symptom onset and hospital arrival, and 57% reported duration from symptom onset to hospital arrival. Among them, 799 (23%) of patients were female, 2808 (81.8%) were STEMI, and the mean age was 61 years (SD 12 years). Across the cohort, 1435 (42%) were currently employed; 1137 (33%) had an education level equal to or greater than high school; 1944 (57%) had household income lower than 50,000 RMB (~7142 USD) per year. Together, medical insurance for urban workers and residents and rural medical insurance accounted for the two major insurance types (56% and 36%, respectively). Cardiovascular risk factors were common: hypertension (56%), DM (23%), current smoking (58%) and hypercholesterolaemia (30%). Two-thirds of the patients had symptom onset during weekdays (Table 1).

### Time from symptom onset to hospital arrival

The median time to hospital arrival was 4 h (IQR 2–7.5 h). The distribution of time to hospital arrival is shown in Figure 2. There were 29% of patients had time from symptom onset to hospital arrival greater than 6 h.

### Patient-reported symptoms and reasons for delay in seeking care

Almost all patients (94%) reported typical symptoms of chest pain or chest discomfort (Table 2), and 84% also reported other ischaemic
symptoms in addition to chest pain/discomfort. However, less than half of patients (43%) perceived the symptoms as heart-related problems. Among all patients, 50% of the cohort reported delays in seeking medical care and a large proportion of prolonged time to acute care could be attributed to ‘symptoms did not seem bad enough for emergency care’ (27%), and ‘symptoms would come and go over time’ (24%); these factors were also more pronounced among patients with extreme delay (i.e. greater than 6 h) (Table 3).

### Table 1  Baseline characteristics of study cohort

| Characteristics                              | Number of patients (%) | ≤2 h, n (%) | 2–6 h, n (%) | >6 h, n (%) | P-value |
|----------------------------------------------|------------------------|-------------|--------------|-------------|---------|
| **Socio-demographics**                       |                        |             |              |             |         |
| Age                                          | 60.7 (11.9)            | 60.5 (12.0) | 60.7 (11.8)  | 61.0 (11.9) | 0.539   |
| Female                                       | 799 (23.3)             | 256 (22.3)  | 282 (21.8)   | 261 (26.2)  | 0.031   |
| Married                                      | 3007 (87.6)            | 1020 (88.9) | 1137 (88.1)  | 850 (85.4)  | 0.045   |
| Working full or part time                    | 1435 (41.8)            | 478 (41.6)  | 541 (41.9)   | 416 (41.8)  | 0.991   |
| Education level ≥ high school                | 1137 (33.1)            | 450 (39.2)  | 400 (31.0)   | 287 (28.8)  | <0.001  |
| **Health insurance**                         |                        |             |              |             | <0.001  |
| Rural medical insurance                      | 1225 (35.7)            | 327 (28.5)  | 470 (36.4)   | 428 (43.0)  |         |
| Household income                             |                        |             |              |             | <0.001  |
| <10 000 RMB                                  | 430 (12.5)             | 123 (10.7)  | 145 (11.2)   | 162 (16.3)  |         |
| 10 000–50 000 RMB                            | 1514 (44.1)            | 500 (43.6)  | 586 (45.4)   | 428 (43.0)  |         |
| 50 000–100 000 RMB                           | 501 (14.6)             | 203 (17.7)  | 183 (14.2)   | 115 (11.6)  |         |
| >100 000 RMB                                 | 215 (6.3)              | 97 (8.4)    | 65 (5.0)     | 53 (5.3)    |         |
| Patient unclear or refuse to answer          | 774 (22.5)             | 225 (19.6)  | 312 (24.2)   | 237 (23.8)  |         |
| **CVD risk factors**                         |                        |             |              |             |         |
| Diabetes mellitus                            | 798 (23.2)             | 266 (23.2)  | 293 (22.7)   | 239 (24.0)  | 0.757   |
| Hypertension                                 | 1909 (55.6)            | 652 (56.8)  | 706 (54.7)   | 551 (55.4)  | 0.571   |
| Hypercholesterolaemia                        | 1017 (29.6)            | 386 (33.6)  | 374 (29.0)   | 257 (25.8)  | <0.001  |
| Current smoking                              | 2001 (58.3)            | 680 (59.2)  | 781 (60.5)   | 540 (54.3)  | 0.008   |
| Abnormal waist circumference                 | 1760 (51.3)            | 603 (52.5)  | 668 (51.7)   | 489 (49.1)  | 0.268   |
| **Medical history**                          |                        |             |              |             |         |
| Prior heart failure                          | 232 (6.8)              | 86 (7.5)    | 79 (6.1)     | 67 (6.7)    | 0.403   |
| Prior stroke                                 | 567 (16.5)             | 197 (17.2)  | 233 (18.0)   | 137 (13.8)  | 0.018   |
| Prior angina                                 | 136 (4.0)              | 41 (3.6)    | 49 (3.8)     | 46 (4.6)    | 0.428   |
| Prior AMI                                    | 275 (8.0)              | 105 (9.1)   | 115 (8.9)    | 55 (5.5)    | 0.003   |
| Prior PCI                                    | 238 (6.9)              | 84 (7.3)    | 109 (8.4)    | 45 (4.5)    | 0.001   |
| Prior CABG                                   | 5 (0.1)                | 2 (0.2)     | 2 (0.2)      | 1 (0.1)     | 0.900   |
| **Time of symptoms onset**                   |                        |             |              |             | 0.034   |
| Weekday                                      | 2287 (66.6)            | 740 (64.5)  | 864 (66.9)   | 683 (68.6)  |         |
| Weekend                                      | 889 (25.9)             | 301 (26.2)  | 334 (25.9)   | 254 (25.5)  |         |
| Unclear                                      | 258 (7.5)              | 107 (9.3)   | 93 (7.2)     | 58 (5.8)    |         |
| **Onset symptoms**                           |                        |             |              |             |         |
| Chest pain or discomfort                     | 3233 (94.1)            | 1070 (93.2) | 1233 (95.5)  | 930 (93.5)  | 0.030   |
| Other ischaemic symptoms                     | 2874 (83.7)            | 952 (82.9)  | 1093 (84.7)  | 829 (83.3)  | 0.475   |
| Symptoms perceived as heart-related problems | 1491 (43.4)            | 533 (46.4)  | 593 (45.9)   | 365 (36.7)  | <0.001  |
| **Psychosocial factors**                     |                        |             |              |             |         |
| Health-related quality of life (EQ5D index score, mean) | 0.9 (0.2) | 0.9 (0.2) | 0.9 (0.2) | 0.9 (0.2) | 0.210 |
| Health-related quality of life (EQ5D-VAS, mean) | 76.1 (16.6) | 75.8 (17.4) | 76.8 (16.1) | 75.6 (16.3) | 0.269 |
| Depression (PHQ-8)                           | 212 (6.2)              | 75 (6.5)    | 70 (5.4)     | 67 (6.7)    | 0.358   |
| Low social support (ESSI)                    | 760 (22.1)             | 271 (23.6)  | 275 (21.3)   | 214 (21.5)  | 0.335   |
| Stress (PSS-4)                                | 2667 (77.7)            | 904 (78.7)  | 1010 (78.2)  | 753 (75.7)  | 0.194   |
| SAQ Angina Frequency                         | 87.2 (20.5)            | 87.5 (20.9) | 88.1 (19.7)  | 85.8 (21.2) | 0.009   |

CVD, cardiovascular disease; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; EQ5D, EuroQol five dimensions questionnaire; EQ5D-VAS, EuroQol five dimensions questionnaire visual analog scale; PHQ-8, Patient Health Questionnaire depression scale; ESSI, ENRICH-D Social Support Instrument; PSS, Perceived Stress Scale; SAQ, Seattle Angina Questionnaire.
Patient factors associated with prolonged times in care seeking

Several patient-reported perceptions and patient factors were associated with longer time to hospital arrival in unadjusted analyses, as shown in Table 1. Results from the log-transformed mixed model are given in Figure 3A. Patients who had rural medical insurance had 39% longer times than those with other types of medical insurance (mainly urban medical insurance) ($P < 0.001$). Compared with patients with household income over 100 thousand RMB, those in the 10–50 thousand RMB group and less than 10 thousand RMB group had 16% and 23% longer adjusted times, respectively (both $P = 0.03$). Time to hospital arrival was longer by 14% for patients that failed to recognize symptoms as cardiac ($P < 0.001$). Conversely, patients with a stroke history had 8% shorter times than those without prior stroke ($P = 0.048$).

Similarly, in the secondary analyses assessing factors associated with extreme delay, patients who had rural medical insurance, and those who failed to recognize symptoms as cardiac were more likely to have time to hospital arrival $>$6 h [odds ratio (OR) 1.7, 95% confidence interval (CI) 1.4–2.1; OR 1.5, 95% CI 1.2–1.8, respectively; both $P < 0.001$] (Figure 3B).

Discussion

In this large prospectively enrolled sample of patients with AMI, we found that both patient socio-demographic factors such as rural medical insurance and lower household income, and patient-reported factors, such as failing to recognize symptoms as cardiac, were associated with longer time to hospital arrival. These findings reveal important vulnerabilities in accessing timely acute cardiovascular care. However, the magnitude of effect from each factor was overshadowed by the overall duration of delay in China. Furthermore, we identified significant problem of unawareness of AMI-related symptoms, which were associated with longer times. Our study identifies important opportunities for future improvement initiatives and policy
efforts to improve timely care seeking, particularly for time-sensitive conditions such as AMI.

Time to hospital arrival in China is longer than what has been reported in both China and Western countries. We describe a median time of 4 h in China; by contrast, the international Global Registry of Acute Coronary Events (GRACE) study reported that in 2006, the median care seeking time ranged between 1.7–2.3 h for STEMI and 1.9–2.7 h for NSTEMI in Western countries. The prolonged time to hospital arrival attenuates the benefit of reperfusion therapy for patients with STEMI, which is particularly important as STEMI accounts for about 80% of patients with AMI in China.23

The time to hospital arrival is also longer than those previously reported in China. However, prior studies were usually retrospective, conducted in cities, and were limited to single hospital/region with small sample size (less than 1000 patients). In contrast, our work is the largest and first multi-centre study that includes hospitals in both urban and rural areas, incorporates patients’ perspectives from prospective interviews, and therefore, provides a comprehensive assessment of care seeking times for AMI in China. It is no doubt that there are substantial variations in distances to hospital in a huge country like China, which may affect the time to hospital arrival. However, AMI is an acute condition that requires seeking

| Table 3 | Patient-reported reasons for delays in seeking medical care (among those reported to delay before seeking care) |
|-------------------|-------------------------------------------------|
| **Self-reported delayed reasons for seeking medical care** | **Number of patients (%)** | **≤2 h, n (%)** | **2–6 h, n (%)** | **>6 h, n (%)** | **P-value** |
| Didn’t have time to go to the doctor | 78 (2.3) | 18 (1.6) | 24 (1.9) | 36 (3.6) | 0.266 |
| Symptoms did not seem bad enough for emergency care | 912 (26.6) | 244 (21.2) | 310 (24.0) | 358 (36.0) | 0.182 |
| Symptoms would come and go over time (not persistent) | 836 (24.3) | 244 (21.2) | 297 (23.0) | 295 (30.0) | 0.065 |
| Transportation-waited for someone to drive me to hospital | 181 (5.3) | 32 (2.8) | 67 (5.2) | 82 (8.2) | 0.008 |
| A concerns about the cost | 49 (1.4) | 8 (0.7) | 21 (1.6) | 20 (2.0) | 0.229 |
| Embarrassment or fear | 8 (0.2) | 4 (0.4) | 3 (0.2) | 1 (0.1) | 0.229 |
| None of above | 40 (1.1) | 15 (1.3) | 16 (1.2) | 9 (0.9) | 0.111 |
| Other reasons | 162 (4.6) | 46 (4.0) | 50 (3.9) | 66 (6.6) | 0.392 |

**Figure 3** (A) Factors associated with time from symptom onset to hospital arrival in log-transformed mixed model. Variables associated with longer or shorter time to hospital arrival among patients with acute myocardial infarction are shown along the vertical axis. The percentage of 0 shows no difference in time from symptoms onset to hospital arrival for different subgroups. Each dot represents the point estimate of the effect of that variable in the model; the line shows the 95% confidence interval. (B) Factors associated with extreme delay in hospital arrival (greater than 6 h) in multivariable logistic model. Variables associated with extreme delay in hospital arrival (greater than 6 h) among patients with acute myocardial infarction are shown along the vertical axis. The adjusted odds ratio of 1 shows no difference in time from symptoms onset to hospital arrival for different subgroups. Each dot represents the point estimate of the effect of that variable in the model; the line shows the 95% confidence interval. CI, confidence interval; CVD, cardiovascular disease; PCI, percutaneous coronary intervention.
medical help in the nearest hospital. In China, even in rural areas, patients with AMI could arrive at the nearest county hospital for treatment within a relatively short time period.

We found several patient-level factors that were associated with delayed presentations, such as rural medical insurance. Rural insurance covers 97% of rural residents (rural or urban residents were determined by the Hukou policy in China), however, this finding is not easily explained by distance to care. Patients with rural medical insurance live in both rural and urban areas due to China’s urbanization, and patients with rural medical insurance in both geographies had longer time to hospital arrival. Out-of-pocket financial concerns may partially explain the result, as household incomes as well as reimbursement rates vary for patients with different types of medical insurance; it is also possible that patients with rural medical insurance had poorer health literacy of AMI than those from urban areas. Lower income is also associated with delayed presentation times independent of insurance type, which indicated that economic status could help to identify vulnerable groups for more educational support. Contrary to our expectations, we did not find associations between psychosocial factors and prolonged time to arrival; it is possible that psychosocial factors play a more important role in long-term prognosis rather than acute care-seeking behaviors.

Factors associated with prolonged time to hospital arrival in our study are different from those reported in Western studies. Factors such as older age, DM, female, prior angina, prior AMI, have been commonly reported to be related to delayed presentation in previous Western studies; however, these factors were not associated with delays to hospital arrival in our work. Meanwhile, few previous studies have examined the effect of social and psychosocial factors. It is possible that in China, social factors such as medical insurance and income play a more important role, overshadowing the impact of demographic and clinical factors. Future study is needed to examine our hypothesis and understand the underlying mechanism.

A particularly important insight from this work is the association of patient-reported symptoms and reasons for delaying in seeking care reveal substantial barriers in AMI awareness. Over half of the patients with AMI did not perceive their symptoms as heart-related, although almost all reported typical symptoms of chest pain; nearly half of the patients reporting delays in seeking medical care services also reported lack of awareness of the symptoms’ severity. Such findings reveal that many patients may lack the knowledge of AMI symptoms and risks of AMI, which remains a major concern because awareness of AMI symptoms is a prerequisite to shorten time to hospital arrival. To our knowledge, little is known about efforts to narrow patient education gaps in China. Public education campaigns in Western countries designed to reduce time to hospital arrival for patients with AMI have shown mixed results. The largest study to date, the Rapid Early Action for Coronary Treatment (REACT) trial, failed to shorten time to hospital arrival in the USA. However, authors of the REACT study noted that this campaign would be more likely to succeed in a context where there are relatively long time to hospital arrival at baseline, a less competitive media environment, and a centrally organized health care system. Due to its central coordinating and planning system, China may have a greater capacity to implement strategies and policies more rapidly and consistently. Moreover, STEMI, which usually presents with more typical symptoms than NSTEMI, is preponderant in China; therefore, it is possible that awareness regarding unrelenting chest pain as a prompt to recognize AMI in the circumstances of education campaign may carry more impact in China.

Our findings suggest several principles for future improvement efforts for patients with AMI in China and perhaps other countries. First, substantial opportunity exists to reduce time to hospital arrival in China, particularly through interventions aimed at improving patient awareness of symptoms and responsiveness to seek care. Given that the overall duration of time to hospital arrival in China is worrying, such interventions should target all patients at risk for AMI, not just those who have individual risk factors for longer delays. Second, a mix of socio-demographic and patient-reported factors should be acknowledged as contributing to longer time to hospital arrival; there should be intensive strategies tailored to these vulnerable groups. Third, novel, multi-dimensional strategies should be developed and tested in order to address the knowledge gaps. The current dramatic growth of electronic media and mobile health applications offer powerful platforms for effective education at a lower cost. By making clear strategies as well as testing these new tools, China may implement effective improvement initiatives to shorten delays to hospital and provide solutions for other countries facing similar challenges of acute care access.

Limitations

Certain limitations should be considered when interpreting our results. First, although a strength of our design is the prospective interview of patients, those enrolled patients may have been subject to recall bias regarding symptom onset time. However, documenting time to hospital arrival by patients’ recall has been widely used in other studies, and there is no better way to collect this information. Second, our findings are limited to those who successfully survived through pre-hospital period to hospital arrival, suggesting that the clinical ramifications of our findings may be interpreted as conservative. Third, we are unable to assess time for transportation, and the use of ambulance services; therefore, investigations on transportation delays are warranted in future studies.

Conclusion

We reported a median time of 4 h for time to access care for AMI in China, which was worse than previously reported, especially among patients with rural insurance, low household income, and those failing to recognize symptoms as cardiac. Notably, the poor awareness of AMI symptoms and severity contributed to delays in seeking hospital care for AMI. Future initiatives are needed to improve the responsiveness to seek AMI care.

Acknowledgements

We appreciate the multiple contributions made by study teams at the China Oxford Centre for International Health Research and the Yale-New Haven Hospital Center for Outcomes Research and Evaluation in the realms of study design and operation, particularly the data collection by Li Li, Jianmin Liu, Xiaofang Yan, Ying Sun, Siying Niu, Qian Xiao, Xuekun Wu, Yuan Yu, Fang Feng, Ning Zhang, Qian Xie, Jia Li, Jianxin Zhang, Hao Dai, Hui Zhong, Liping Zhang, Yang Yang, Yang Gao, Sinming Wang, Shuang Hu, Xiqian Huo, and Bin Wang. We appreciate the analytical advice from Yongfei Wang and Yun Wang, and the analytic review check by Yetong Li.
We appreciate the editing by Paul Horak, Julia Zou, Claire Masters, George Linderman, and Tianna Zhou. We are grateful for the support provided by the Chinese government.

**Funding**

This study was supported by the Research Special Fund for Public Welfare Industry of Health (201502009) from the National Health and Family Planning Commission of China, the National Key Technology R&D Program (2015BAI12B01, 2015BAI12B02) from the Ministry of Science and Technology of China and the 111 Project (B16005). The content is solely the responsibility of the authors and does not necessarily represent the official views of these organizations.

**Conflict of interest:** H.M.K. is the recipient of a research grant from Medtronic and Johnson & Johnson, through Yale University, to develop methods of clinical trial data sharing; chairs a cardiac science advisory board for United Health; works under contract with the Centers for Medicare & Medicaid Services to develop and maintain performance measures that are publicly reported; is a participant/participant representative of the IBM Watson Health Life Sciences Board; is a member of the Advisory Board for Element Science and the Physician Advisory Board for Aetna; and is the founder of Hugo, a personal health information platform. F.A.M. receives salary support from the American College of Cardiology for his role as the Chief Science Officer of the National Cardiovascular Data Registry. J.A.S. has served as a consultant to United Healthcare, Novartis, AstraZeneca, Bayer, Corvia, V-wave and Janssen; owns the copyright to the SAQ, KCCQ and PAQ and has an equity interest in Health Outcomes Collaboration. G.H.R. receives financial support from the Chinese government.

We appreciate the editing by Paul Horak, Julia Zou, Claire Masters, George Linderman, and Tianna Zhou. We are grateful for the support provided by the Chinese government.

**Conflict of interest:** H.M.K. is the recipient of a research grant from Medtronic and Johnson & Johnson, through Yale University, to develop methods of clinical trial data sharing; chairs a cardiac science advisory board for United Health; works under contract with the Centers for Medicare & Medicaid Services to develop and maintain performance measures that are publicly reported; is a participant/participant representative of the IBM Watson Health Life Sciences Board; is a member of the Advisory Board for Element Science and the Physician Advisory Board for Aetna; and is the founder of Hugo, a personal health information platform. F.A.M. receives salary support from the American College of Cardiology for his role as the Chief Science Officer of the National Cardiovascular Data Registry. J.A.S. has served as a consultant to United Healthcare, Novartis, AstraZeneca, Bayer, Corvia, V-wave and Janssen; owns the copyright to the SAQ, KCCQ and PAQ and has an equity interest in Health Outcomes Collaboration. G.H.R. receives financial support from the Chinese government.

**References**

1. Moser DK, Kimble LP, Alberts MJ, Alonsoa A, Craft J, Dracup K, Evenson KR, Go AS, Hand MM, Kothari RU, Mensah GA, Morris DL, Pancioli AM,iegel B, Zerjic W. Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: a scientific statement from the American Heart Association Council on cardiovascular nursing and stroke council. Circulation 2006;114:168–182.

2. Rawles JM. Quantification of the benefit of earlier thrombolytic therapy: five-year results of the Grampian Region Early Anstreptase Trial (GRETAT). J Am Coll Cardiol 1997;30:1181–1186.

3. Newby LK, Rutsch WR, Calif RM, Simoons ML, Aylward PE, Armstrong PW, Woodfill LH, Lee KL, Topol EJ, Van de Werf F. Time from symptom onset to treatment and outcomes after thrombolytic therapy. GUSTO-I Investigators. J Am Coll Cardiol 1996;27:1646–1655.

4. Berger PB, Ellis SG, Holmes DR, Granger CB, Crigrer DA, Betriu A, Topol EJ, Calr RM. Relationship between delay in performing direct coronary angioplasty and early clinical outcome in patients with acute myocardial infarction: results from the global use of strategies to open occluded coronary arteries (GUSTO-I) trial. Circulation 1999;100:14–20.

5. Goldberg RJ, Spencer FA, Fox KAA, Binger D, Seng PG, Gurlek E, Dedrick R, Gore JM. Prehospital delay in patients with acute coronary syndromes (from the Global Registry of Acute Coronary Events [GRACE]). Eur J Intern Med 2009;20:598–603.

6. Welsh RC, Chang W, Goldstein P, Adgey J, Granger CB, Verheugt FW, Wallentin L, Van de Werf F, Armstrong PW. Time to treatment and the impact of a physician on prehospital management of acute ST elevation myocardial infarction: insights from the ASSENT-3 PLUS trial. Heart 2005;91:1400–1406.

7. Ting HH, Chen AY, Roe MT, Chan PS, Spertus JA, Nallamothu BK, Sullivan MD, DeLong ER, Bradley EH, Krumholz HM, Peterson ED. Delay from symptom onset to hospital presentation for patients with non-ST-segment elevation myocardial infarction. Arch Intern Med 2010;170:1834–1841.

8. Ting HH, Bradley EH, Wang Y, Lichtman JH, Nallamothu BK, Sullivan MD, Gersh BJ, Roger W, Calpas M, Krumholz HM. Factors associated with longer time from symptom onset to hospital presentation for patients with ST-elevation myocardial infarction. Arch Intern Med 2008;168:959–968.
### Table A1  Baseline characteristics of patients included and excluded in the article

| Variables                          | Total     | Enrolled  | Not enrolled | P-value |
|------------------------------------|-----------|-----------|--------------|---------|
| **Socio-demographics**             |           |           |              |         |
| Age                                | 60.9 (11.8)| 60.7 (11.9)| 61.6 (11.6)  | 0.108   |
| Female                             | 995 (23.6)| 799 (23.3)| 196 (25.2)   | 0.254   |
| Married                            | 3674 (87.2)| 3007 (87.6)| 667 (85.7)   | 0.167   |
| Working full or part time          | 1727 (41.0)| 1435 (41.8)| 292 (37.5)   | 0.029   |
| Education level ≥ high school      | 1403 (33.3)| 1137 (33.1)| 266 (34.2)   | 0.564   |
| **Health insurance**               |           |           |              |         |
| Rural medical insurance            | 1648 (39.1)| 1339 (39.0)| 309 (39.7)   | 0.708   |
| **Household income**               |           |           |              |         |
| <10 000 RMB                        | 537 (12.7)| 430 (12.5)| 107 (13.8)   | 0.284   |
| 10 000–50 000 RMB                  | 1824 (43.3)| 1514 (44.1)| 310 (39.8)   |         |
| 50 000–10 000 RMB                  | 622 (14.8)| 501 (14.6)| 121 (15.6)   |         |
| >100 000 RMB                       | 258 (6.1)| 215 (6.3)| 43 (5.5)     |         |
| Patient unclear or refuse to answer| 649 (15.4)| 498 (14.5)| 151 (19.4)   |         |
| **CVD risk factors**               |           |           |              |         |
| Diabetes mellitus                  | 999 (23.7)| 798 (23.2)| 201 (25.8)   | 0.124   |
| Hypertension                       | 1840 (43.7)| 1477 (43.0)| 363 (46.7)   | 0.064   |
| Hypercholesterolaemia              | 1114 (26.4)| 880 (25.6)| 234 (30.1)   | 0.011   |
| Current smoking                    | 2 (0.0)  | 1 (0.0)  | 1 (0.1)      | 0.25    |
| Abnormal waist circumference       | 2130 (50.6)| 1760 (51.3)| 370 (47.6)   | 0.063   |
| **Medical history**                |           |           |              |         |
| Prior heart failure                | 323 (7.7)| 232 (6.8)| 91 (11.7)    | <0.001  |
| Prior stroke                       | 675 (16.0)| 571 (16.6)| 104 (13.4)   | 0.025   |
| Prior angina                       | 167 (4.0)| 136 (4.0)| 31 (4.0)     | 0.975   |
| Prior AMI                          | 328 (7.8)| 275 (8.0)| 53 (6.8)     | 0.261   |
| Prior PCI                          | 273 (6.5)| 238 (6.9)| 35 (4.5)     | 0.013   |
| Prior CABG                         | 5 (0.1)  | 5 (0.1)  | 0 (0.0)      | 0.287   |
| **Time of symptoms onset**         |           |           |              |         |
| Weekday                            | 2811 (66.7)| 2287 (66.6)| 524 (67.4)   | 0.843   |
| Weekend                            | 1089 (25.9)| 889 (25.9)| 200 (25.7)   |         |
| Unclear                            | 312 (7.4)| 258 (7.5)| 54 (6.9)     |         |
| **Onset symptoms**                 |           |           |              |         |
| Chest pain or discomfort           | 3927 (93.2)| 3233 (94.1)| 694 (89.2)   | <0.001  |
| Other ischaemic symptoms           | 3503 (83.2)| 2874 (83.7)| 629 (80.8)   | 0.056   |
| **Symptoms perceived as heart-related problems** | 1818 (43.2)| 1491 (43.4)| 327 (42.0)   | 0.48    |
| **Psychosocial factors**           |           |           |              |         |
| Health-related quality of life (EQSD index score, mean) | 0.9 (0.2) | 0.9 (0.2) | 0.8 (0.2) | 0.051 |
| Depression (PHQ-8)                 | 76.1 (16.9)| 76.1 (16.6)| 76.1 (18.2)  | 0.387   |
| Low social support (ESSI)          | 256 (6.1)| 212 (6.2)| 44 (5.7)     | 0.585   |
| Stress (PSS-4)                     | 671 (15.9)| 525 (15.3)| 146 (18.8)   | 0.009   |
| **SAQ Angina Frequency**           | 3192 (75.8)| 2667 (77.7)| 525 (67.5)   | <0.001  |

PSS, Perceived Stress Scale; CVD, cardiovascular disease; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; EQSD, EuroQol five dimensions questionnaire; EQSD-VAS, EuroQol five dimensions questionnaire visual analog scale; PHQ-8, Patient Health Questionnaire depression scale; ESSI, ENRICH-D Social Support Instrument; SAQ, Seattle Angina Questionnaire.