Invasive Management Strategies and Antithrombotic Treatments in Patients With Non–ST-Segment–Elevation Acute Coronary Syndrome in China

Findings From the Improving CCC Project (Care for Cardiovascular Disease in China)

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Background—Early invasive strategies and antithrombotic treatments are key treatments of non–ST-segment–elevation acute coronary syndrome (NSTE-ACS). Few studies have examined the use of these strategies in patients with NSTE-ACS in China. This study aimed to assess the applications of invasive strategies and antithrombotic treatments in patients with NSTE-ACS and compare their outcomes.

Methods and Results—A nationwide registry study, Improving CCC (Care for Cardiovascular Disease in China) ACS project, was launched in 2014 as a collaborative study of the American Heart Association and Chinese Society of Cardiology (CSC), with 142 participating hospitals reporting details of clinical management and outcomes of patients with NSTE-ACS. The use of invasive strategies and antithrombotic treatments was examined based on updated guidelines. Major adverse cardiovascular events were analyzed. A total of 9953 patients with NSTE-ACS were enrolled. Angiography was performed in 63.1% of these patients, and 58.2% underwent percutaneous coronary intervention (PCI). However, 40.6% of patients did not undergo early risk assessment, and very-high-risk patients had the lowest proportion of PCI (41.7%). PCI was performed within recommended times in 11.1% of very-high-risk patients and 26.3% of high risk patients. Those who underwent PCI within 2 hours had higher mortality in high-risk and very-high-risk patients who received PCI. Early dual antiplatelet treatment was given in 88.3% of patients.

Conclusions—There are notable differences between guideline recommendations and the clinical management of patients with NSTE-ACS in China. The reasons for very-high-risk NSTE-ACS patients not undergoing PCI, and the optimal timing of PCI, require further clarification.

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Key Words: acute coronary syndrome ■ American Heart Association ■ angiography ■ inpatients ■ percutaneous coronary intervention

Non–ST-segment–elevation acute coronary syndrome (NSTE-ACS) is the leading cause of morbidity and mortality from cardiovascular disease worldwide and in China, hospitalization rates having increased significantly.[1–3] NSTE-ACS, which is a working definition for non–ST-segment–elevated myocardial infarction (NSTEMI) and unstable angina, is considered a subset of the clinical spectrum of ACS in updated guidelines because their clinical presentation and management strategies are similar.[4–6] Recommendations for the management of NSTE-ACS include early invasive strategies, such as angiography and revascularization, plus antithrombotic treatments; these are key strategies with

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WHAT IS KNOWN

- Non–ST-segment–elevation acute coronary syndrome (NSTE-ACS) is the leading cause of morbidity and mortality from cardiovascular disease worldwide and in China.
- Early invasive strategies and antithrombotic treatments are key treatments of NSTE-ACS, yet few studies have reported current practical patterns of invasive strategies and antithrombotic treatments in patients with NSTE-ACS in China.

WHAT THE STUDY ADDS

- Among 9953 patients with NSTE-ACS, angiography was performed in 63.1% of these patients, and 58.2% underwent percutaneous coronary intervention, with less than half of very-high-risk patients undergoing invasive management.
- Early dual antiplatelet treatment was used in 88.3% of NSTE-ACS patients.
- The findings from this study highlight opportunities for further quality improvement of NSTE-ACS in China and the need for further investigations of optimal timing of invasive strategies of NSTE-ACS, especially for very-high-risk patients.

increasing strengths in Class of Recommendation (COR) and Level of Evidence (LOE) in updated guidelines.[4–7] However, most reports concerning quality of care from large registration studies in China have treated acute myocardial infarction, NSTEMI, and ST-segment–elevated myocardial infarction , as a single subset of ACS. Thus, few studies have reported current practical patterns of invasive management strategies and antithrombotic treatments in patients with NSTE-ACS.[2,8] Therefore, our study aimed to report the clinical characteristics of patients with NSTE-ACS in China, assess the performance of invasive management strategies and antithrombotic treatments against the key recommendations in updated guidelines, and determine the outcomes during hospitalization in patients with different invasive strategies in real clinical practice situation. These findings in this study are based on a collaborative program of the American Heart Association (AHA) and CSC: Improving CCC Project (Care for Cardiovascular Disease in China).[9]

Methods

NSTE-ACS Registry

The CCC-ACS project, a nationwide registry and quality improvement study with an ongoing database focusing on quality of ACS care, was launched in 2014 as a collaborative initiative of the AHA and CSC. Details of the design and methodology of the CCC project have been published and also shown in Methods in the Data Supplement.[9]

A standard web-based data collection platform (Oracle Clinical Remote Data Capture, Oracle) was used. Trained data abstractors in the participating hospitals reported the required data, which they abstracted from the patients' medical charts. Eligible patients were consecutively reported to the CCC-ACS database for each month before the middle of the following month. Third-party clinical research associates were hired to perform quality audits to ensure that cases were reported consecutively rather than selectively. In addition, about 5% of reported cases were randomly selected and provided data compared with the original medical records to ensure accuracy and completeness.

On the basis of principal discharge diagnosis, 11 044 inpatients with NSTE-ACS from 142 hospitals were registered from November 1, 2014 to February 29, 2016. Of these, 554 inpatients with NSTE-ACS were excluded because their cardiac enzyme results were not available, making identification of NSTE-ACS type and risk stratification impossible, and a further 537 patients were excluded because the diagnosis of NSTE-ACS was questionable according to the clinical data provided. Thus, 9953 inpatients with NSTE-ACS were included in this study, of which 74.3% had NSTEMI. Eight hospitals were not included because they reported no eligible patients. Institutional Review Board approval was granted for this research by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University. No informed consent was required.

Definition of NSTE-ACS

NSTE-ACS was initially identified based on the principal discharge diagnosis obtained by reviewing the inpatient list for NSTEMI and unstable angina. NSTE-ACS was defined according to the guidelines for diagnosis and management of patients with NSTE-ACS issued by the CSC in 2012. These guidelines are based on chest pain, ECG, and measurements of biomarkers of myocardial necrosis troponin I (TnI) or troponin T (TnT) and are consistent with the definitions of NSTE-ACS in the ACC/AHA guidelines (American College of Cardiology/American Heart Association) issued in 2014 and the European Society of Cardiology (ESC) guidelines issued in 2015.[4–6]

Collection of Clinical Data

The specific information concerning NSTE-ACS in this study can be categorized as patient characteristics, clinical diagnosis, and risk evaluation (including symptoms on arrival, ECG times, measurements of cardiac enzymes, Killip grades, blood pressure and other measurements, comorbidities, medical history, and angiography findings), invasive and noninvasive treatments, and outcomes during hospitalization.

Definitions of Variables

Risk stratification reported by clinicians and recorded in the medical records was collected. The risk for each patient was reclassified according to the risk stratification criteria proposed by the 2015 ESC guidelines for the management of NSTE-ACS.[6] Patients with ≥1 of the following conditions were classified as very high risk: hemodynamic instability or cardiogenic shock, recurrent or ongoing chest pain refractory to medical treatment, life-threatening arrhythmias or cardiac arrest, mechanical complications of myocardial infarction, acute heart failure, and recurrent dynamic ST- or T-wave changes, particularly with intermittent ST elevation. Patients with ≥1 of following conditions were classified as high risk: increase or decrease in cardiac troponin compatible with myocardial infarction, dynamic ST- or T-wave changes or GRACE score (Global Registry of Acute Coronary Events) of ≥140. Patients with ≥1 of the following conditions were classified as moderate risk: diabetes mellitus, renal insufficiency, left ventricular ejection fraction <40% or congestive heart failure, early postinfarction angina, previous percutaneous coronary intervention (PCI), previous coronary artery bypass grafting, or GRACE risk score of >109 and <140; patients without none of the variables mentioned above were defined as low risk. In the newly updated ESC guidelines, an immediate invasive strategy (<2 hours) is recommended for very-high-risk patients (COR I, LOE C), an early invasive strategy (<24 hours) for high-risk patients (COR I, LOE A), and an invasive strategy (<72 hours) for moderate-risk patients (COR I, LOE A). Noninvasive testing for ischemia is recommended for low-risk patients before deciding on invasive evaluation (COR I, LOE A).

High TnT or TnI was defined as serum TnT or TnI concentration exceeding the upper limit of the relevant normal range. High creatine kinase-MB was defined as serum creatine kinase-MB concentration exceeding double the upper limit of the normal range. Hypertension was defined as systolic blood pressure ≥140 mm Hg or DBP ≥90 mm Hg on admission, and having a history of hypertension or

receiving antihypertensive therapy. Diabetes mellitus was defined as fasting blood glucose ≥7.0 mmol/L (126 mg/dL) or HbA1c ≥6.5%, or having a history of diabetes mellitus, or receiving glucose-lowering drugs. Elevated low-density lipoprotein cholesterol concentrations were defined as serum low-density lipoprotein cholesterol ≥1.81 mmol/L (70 mg/dL). Severe clinical conditions, including heart failure, cardiac arrest, and cardiac shock, were defined as those with onset within 24 hours of the current admission. In this study, major adverse cardiovascular events (MACE) included death, reinfarction, heart failure, cardiac arrest, cardiac shock, and stroke during hospitalization.

Statistical Analysis

Continuous variables that were normally distributed were expressed as mean±SD. Otherwise, the variables were expressed as median with interquartile ranges. Unpaired *t* test or Mann–Whitney *U* test was used to test the statistical significance of differences between the means or medians where appropriate. Categorical variables were reported as number (percent), and the significance of differences was tested by the χ^2 test. Value of 2-sided $P<0.05$ was considered statistically significant, and 95% confidence intervals were calculated for the rates of MACE and death. Statistical analyses were performed using SAS software (version 9.3; SAS Institute, Cary, NC).

Results

Clinical Characteristics of Patients With NSTE-ACS

This study included 9953 NSTE-ACS patients (68.9% men) from 142 hospitals across China. For the required priority for patients with NSTEMI, 74.3% of the registered NSTE-ACS patients were NSTEMI. The median hospital stay was 8 days with significant variation among the hospitals (interquartile range, 6–12 days). Table 1 presents clinical characteristics of the NSTE-ACS patients according to sex. ECGs showed ST-segment depression in 44.3% of the patients and temporary ST-segment elevation in 4.7%. TnT or TnI concentrations had been measured in 93.6% of the patients and creatine kinase-MB concentrations in 91.0% of them. As to biomarkers of myocardial necrosis tests, 73.8% had high TnT or TnI concentrations, 57.9% being severely increased (defined as ≥5-fold of the respective upper limit). Most patients had ≥1 comorbidities: 41.1% had diabetes mellitus, 70.7% hypertension, 74.6% elevated low-density lipoprotein cholesterol concentrations, and 35.6% were smokers. A higher proportion of women than men had major cardiovascular disease risk factors, but a lower proportion had a history of acute myocardial infarction or revascularization. According to the 2015 ESC early risk stratification criteria, 79.6% of the patients were classified as high or very high risk, 18.3% as moderate risk, and no one as low risk; however, there was insufficient information to classify the risk of 2.0% of the patients.

Application of Invasive Management Strategies

Invasive angiographic examinations were performed in 63.1% of the patients with NSTE-ACS and PCI in 58.2%.

Clinical decisions on invasive management strategies may not have based on risk stratification because 40.6% of participants did not undergo early risk assessment on admission to the participating hospitals. No patients underwent risk stratification in 15 of the 142 participating hospitals (10.6%), fewer than 50% underwent risk stratification in 59 hospitals (41.5%), and all patients underwent risk stratification in 6 hospitals (4.2%). A significantly higher proportion of moderate- or

Table 1. Clinical Characteristics of Patients With NSTE-ACS on Admission

Variables	Total (n=9953)	Men (n=6855)	Women (n=3098)
Age, y*†	65.7±11.9	63.8±12.1	69.9±10.5
Hospital stays, d†‡	8 (6, 12)	8 (6, 12)	9 (6, 13)
NSTE-ACS types†			
NSTEMI	7394 (74.3)	5171 (75.4)	2223 (71.8)
UA	2559 (25.7)	1684 (24.6)	875 (28.2)
ECG†			
ST-segment depression	4409 (44.3)	2865 (41.8)	1544 (49.8)
Temporary ST-segment elevation	471 (4.7)	352 (5.1)	119 (3.8)
Pathological Q wave	747 (7.5)	604 (8.8)	143 (4.6)
Left bundle branch block	125 (1.3)	82 (1.2)	43 (1.4)
Biomarkers of myocardial necrosis			
TnT or TnI	9316 (93.6)	6429 (93.8)	2887 (93.2)
CK-MB	9055 (91.0)	6223 (90.8)	2832 (91.4)
Unknown types	58 (0.6)	40 (0.6)	18 (0.6)
Elevated TnT or TnI†	6877 (73.8)	4811 (74.8)	2066 (71.6)
5× elevated TnT or TnI†	5393 (57.9)	3805 (59.2)	1588 (55.0)
Elevated CK-MB†	2737 (30.2)	1967 (31.6)	770 (27.2)
Comorbidity			
Diabetes mellitus†	4090 (41.1)	2612 (38.1)	1478 (47.7)
Hypertension†	7036 (70.7)	4608 (67.2)	2428 (78.4)
Elevated LDL-C†	7426 (74.6)	5033 (73.4)	2393 (77.2)
Smoking†	3544 (35.6)	3317 (48.4)	227 (7.3)
Chronic kidney disease history	344 (3.5)	228 (3.3)	116 (3.7)
Myocardial infarction history†	1297 (13.0)	963 (14.0)	334 (10.8)
Previous PCI†	1321 (13.3)	1000 (14.6)	321 (10.4)
Previous CABG	113 (1.1)	86 (1.3)	27 (0.9)
Heart failure history†	502 (5.0)	299 (4.4)	203 (6.6)
Cerebrovascular disease history†	1240 (12.5)	817 (11.9)	423 (13.7)
Severe clinical conditions			
Heart failure†	1089 (10.9)	650 (9.5)	439 (14.2)
Cardiac arrest	72 (0.7)	54 (0.8)	18 (0.6)
Cardiac shock	144 (1.4)	90 (1.3)	54 (1.7)
Risk stratification at early stage†§			
Moderate risk	1822 (18.3)	1222 (17.8)	600 (19.4)
High risk	6273 (63.0)	4443 (64.8)	1830 (59.1)
Very high risk	1656 (16.6)	1075 (15.7)	581 (18.8)
Unavailable risk assessment	202 (2.0)	115 (1.7)	87 (2.8)

CABG indicates coronary artery bypass grafting; CK-MB, creatine kinase-MB; LDL-C, low-density lipoprotein cholesterol; NSTE-ACS, non–ST-segment–elevation acute coronary syndrome; NSTEMI, non–ST-segment–elevated myocardial infarction; PCI, percutaneous coronary intervention; TnI, Troponin I; TnT, Troponin T; and UA, unstable angina.

*Values are expressed as mean±SD.

†Statistically significant difference between men and women.

‡Median (interquartile range, IQR), or n (%).

§The risk criteria is based on the 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation.

high-risk patients than of very-high-risk patients underwent angiography or PCI (Figure 1A and 1B). A higher proportion of men than of women underwent angiographic examination in all risk stratification. Of note, only 35.3% of women at very high risk underwent angiography and 33.4% PCI.

The risk-relevant characteristics of patients who underwent PCI or received conservative therapy were compared by risk stratification (Table 2). Patients who received conservative therapy were older, a greater proportion were women, and had significantly higher GRACE scores than patients receiving PCI in all 3 risk groups. In the high-risk and very-high-risk groups, patients who received conservative therapy had more comorbidities, especially renal insufficiency and congestive heart failure, than those who underwent PCI.

Transradial access was the most common route of PCI in our study, being used in 85.8% of patients who underwent PCI. Drug-eluting stents were used in 93.2% and bare metal stent in only 1.1% of the patients who underwent PCI and insertion of stents. Detailed information concerning timing was available for 83.0% of patients who underwent PCI (4808/5790). Of these, 11.1% of those in the very-high-risk group underwent PCI within 2 hours, 26.3% of patients of those in the high-risk group within 24 hours, and 54.9% of those in the moderate-risk group within 72 hours of admission, these being the timing specified in the guidelines (Table 3).

Administration of Antiplatelet and Anticoagulant Medications

The use of antiplatelet and anticoagulant treatments during hospitalization is presented in Table 4. A higher proportion of patients who underwent PCI than of those who received conservative therapy received either antiplatelet or anticoagulant treatment (except for Fondaparinux). The overall proportion of patients who received dual antiplatelet treatment within 24 hours of admission was 88.3%. A much lower proportion of patients in both the PCI and conservative therapy groups received aspirin plus ticagrelor than a combination of aspirin and clopidogrel. Prasugrel is not mentioned in this study because it is not yet available in China. Glycoprotein IIb/IIIa receptor antagonists were administered to 18.9% of participants, the proportion being higher in the high-risk and very-high-risk groups than in the moderate-risk group (22.9% and 16.7% versus 7.9%, respectively; $P<0.001$). Low-molecular-weight heparin was the major anticoagulant treatment (65.2%) used in this study, the proportion of patients receiving unfractionated heparin being only 2.1%. The using rate of fondaparinux was very low (1.9% in PCI group and 2.0% in conservative therapy group, $P=0.629$)

In-Hospital Outcomes of Patients With NSTE-ACS

During hospitalization, 1194 (12.0%) patients had MACE, including 165 (1.7%) deaths. Patients who underwent PCI had lower rates of in-hospital MACE and mortality than those who received conservative therapy (MACE: 7.5% versus 18.4%, $P<0.001$; mortality: 0.5% versus 0.3.3%, $P<0.001$; Figure 2A and 2B). By risk category, patients received PCI had significantly lower MACE and mortality rates than patients received conservative therapy in high-risk and very-high-risk patient groups (Table I in the Data Supplement).When in-hospital outcomes were compared among patients received PCI in different timings, patients who underwent PCI within 24 to 72 hours of admission had the lowest risk of MACE; the patients with the high risk and very high risk who underwent PCI within 2 hours had a significantly higher mortality (Figure 2A and 2B).

Discussion

This study focused on the use of early invasive strategies and antithrombotic therapies in patients with NSTE-ACS in China and also assessed in-hospital outcomes of patients who underwent different invasive strategies. To the best of our knowledge, this is the first report of the management of NSTE-ACS in China based on a nationally representative sample of patients from tertiary hospitals.

The use of PCI technology for NSTE-ACS patients has been advancing in China. The rates of use of PCI in such patients in our study have increased when compared with the report of the Clinical Pathways for Acute Coronary Syndromes study in 2008.[3] The transradial approach that is recommended in the

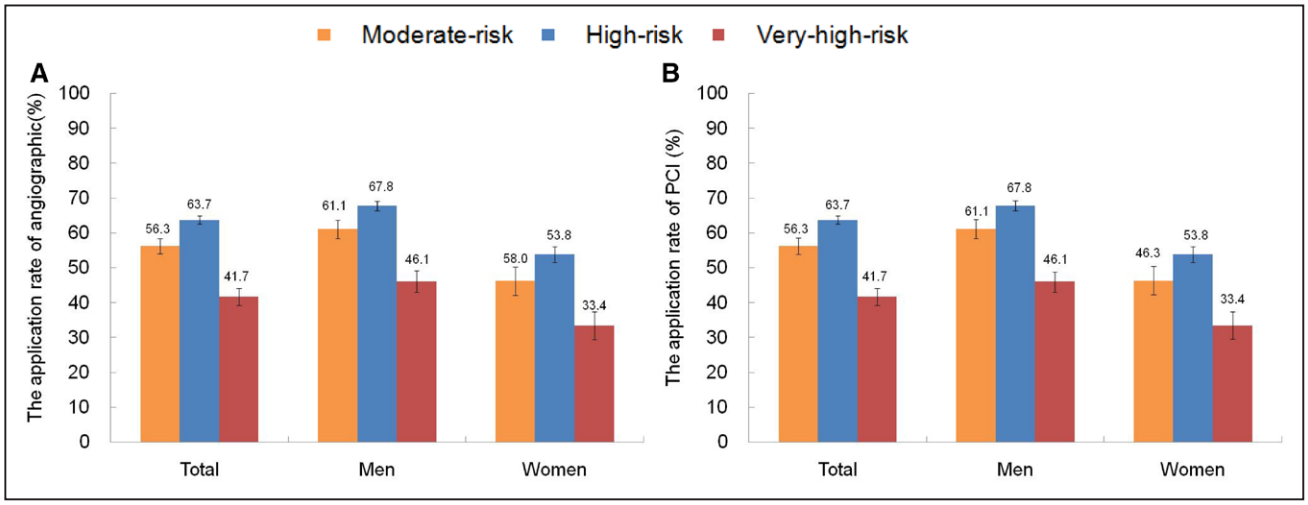

Figure 1. Invasive treatment in patients with non–ST-segment–elevation acute coronary syndrome according to risk stratification. The application of angiography and percutaneous coronary intervention (PCI) was for anytime during the hospitalization in moderate-risk, high-risk, and very-high-risk patients.

Table 2. The Risk-Relevant Characteristics of Patients With NSTE-ACS Who Underwent PCI or Received Conservative Therapy*

Variables	Moderate Risk		High Risk		Very High Risk	
	PCI (n=1025)	Conservative Therapy (n=797)	PCI (n=3998)	Conservative Therapy (n=2275)	PCI (n=690)	Conservative Therapy (n=966)
Age (mean±SD, y)	62.4±9.6	65.2±10.3†	63.3±11.7	68.8±12.3†	65.9±11.7	72.8±11.5†
Sex, women	278 (27.1)	322 (40.0)†	984 (24.6)	846 (37.2)†	194 (28.1)	387 (40.1)†
Hospital stays, d	8 (5, 10)	8 (5, 11)	8 (6, 12)	9 (6, 12)	10 (7, 14)	10 (6, 14)
GRACE score‡	104.7±20.5	107.5±19.4†	135.4±30.0	149.8±34.9†	154.2±42.0	182.0±43.5†
5× elevated TnT or TnI	0	0	2801 (70.1)	1457 (64.0)†	476 (69.0)	659 (68.2)
Diabetes mellitus	406 (39.6)	329 (41.3)	1583 (39.6)	932 (41.0)	315 (45.7)	525 (54.3)†
Renal insufficiency	87 (8.5)	74 (9.3)	471 (11.8)	589 (25.9)†	161 (23.3)	450 (46.6)†
LVEF <40%	13 (2.2)	7 (0.9)	143 (8.3)	107 (3.3)†	161 (23.0)	71 (12.5)†
Congestive heart failure	10 (1.0)	22 (2.8)†	41 (1.0)	102 (4.5)†	74 (10.7)	253 (26.2)†
Previous PCI	200 (19.5)	196 (24.6)†	429 (10.7)	293 (12.9)†	77 (11.2)	126 (13.0)
Previous CABG	7 (0.7)	16 (2.0)†	22 (0.6)	39 (1.7)†	6 (0.9)†	23 (2.4)†
Rise in cardiac troponin	0	0	3854 (96.4)	2068 (90.9)†	612 (88.7)	860 (89.0)
GRACE score >140	0	0	1612 (40.3)	1215 (53.4)†	388 (56.2)	703 (72.8)†
Hemodynamic instability	0	0	0	0	52 (7.5)	59 (6.1)
Cardiogenic shock	0	0	0	0	58 (8.4)	86 (8.9)
Cardiac arrest	0	0	0	0	30 (4.3)	42 (4.3)
Acute heart failure	0	0	0	0	360 (52.2)	729 (75.5)†
Intermittent ST-segment elevation	0	0	0	0	278 (40.3)	193 (20.0)†

CABG indicates coronary artery bypass grafting; GRACE, Global Registry of Acute Coronary Events; LVEF, left ventricular ejection fraction; NSTE-ACS, non–ST-segment–elevation acute coronary syndrome; PCI, percutaneous coronary intervention; TnI, Troponin I; and TnT, Troponin T.

*202 patients had insufficient information to stratify their risk.

†Statistically significant difference between PCI and conservative therapy.

‡1389 patients did not have GRACE scores.

guidelines because of its lower rate of complications has become the approach of choice for most Chinese cardiologists.[10,11] Transradial access was used in 75.4% of the very-high-risk patients in this study. Of the patients who underwent stent treatment, 93.2% received drug-eluting stents. As to dual antiplatelet treatment, which comprises aspirin and P2Y12 inhibitors, is recommended in the guidelines for patients with NSTE-ACS, which was administered to 88.3% of patients in our study. However, our study identified some differences between management of patients with NSTE-ACS in the clinic and the strategies recommended in the guidelines. First, CSC, AHA/ACC, and ESC guidelines all recommend risk assessment or stratification to assess the prognosis of patients with NSTE-ACS (COR I, LOE A).[4–7] In our study, 40.9% of participants did not undergo early risk stratification. This percentage being similar to the risk stratification rate in the baseline phase in the European Quality Improvement Programme for Acute Coronary Syndromes; however, the rate increased in the postquality improvement phase in European Quality Improvement Programme for Acute Coronary Syndromes.[12] We think that the rate of early risk stratification will increase as a result of the efforts of the CCC-ACS project on quality of care in China.

Second, one third of the patients with moderate to very high risk did not receive invasive assessment or treatment. In particular, a smaller proportion of very-high-risk than moderate- and high-risk patients underwent invasive treatment. The treatment–risk paradox of invasive treatment, as observed in our study, had been noted in other published international studies.[13–15] The lower use of PCI in very-high-risk patients may reflect individualized clinical decisions concerning patients with complex and serious comorbidities. It is likely impossible to achieve 100% compliance with guidelines in clinical practice. The unbalanced development of cardiac surgery and life support teams in different geographic areas, specific pressures on Chinese cardiologists from patients with a poor understanding of medicine, unrealistic expectations about treatments, and general lack of knowledge about acute coronary syndromes may limit the utilization of PCI in very-high-risk patients.[16] Further studies are needed to clarify the reasons underlying the underuse of invasive strategies in very-high-risk patients with NSTE-ACS. In this study, the proportion of PCI was even lower in women than in men. Compared with men, women were older, had higher GRACE scores (148.3 in women versus 135.8 in men), and had a higher prevalence of diabetes mellitus, hypertension, cerebrovascular disease history,

Table 3. Use of PCI Procedures in Patients With NSTE-ACS According to Risk Stratification

PCI-Related Variables	Total* (n=5790)	Moderate Risk (n=1025)	High Risk (n=3998)	Very High Risk (n=690)	*P* Value
Vascular access					
Transradial access	4969 (85.8)	907 (88.5)	3482 (87.1)	520 (75.4)	<0.001
Transfemoral access	253 (4.4)	31 (3.0)	166 (4.2)	53 (7.7)	
Transbrachial access	10 (0.2)	0 (0.0)	10 (0.3)	0 (0.0)	
Others	558 (10.6)	87 (8.5)	340 (8.5)	117 (17.0)	
Stent					
Yes	4377 (75.6)	784 (76.5)	3076 (76.9)	461 (66.8)	<0.001
No	549 (9.5)	94 (9.2)	367 (9.2)	83 (12.0)	
Unknown	864 (14.9)	147 (14.3)	555 (13.9)	146 (21.2)	
Stent types†					
DES	4079 (93.2)	735 (93.8)	2869 (93.3)	421 (91.3)	0.036
BMS	49 (1.1)	11 (1.4)	27 (0.9)	11 (2.4)	
Unknown types	249 (5.7)	38 (4.8)	180 (5.9)	29 (6.3)	
Timing of PCI‡					
<2 h	435 (9.0)	25 (2.9)	350 (10.4)	58 (11.1)	<0.001
2–24 h	711 (14.8)	88 (10.2)	534 (15.9)	88 (16.9)	
24–72 h	1507 (31.3)	359 (41.8)	998 (29.6)	122 (23.4)	
>72 h	2155 (44.8)	387 (45.1)	1487 (44.1)	254 (48.7)	

BMS indicates bare metal stent; DES, drug-eluting stents; NSTE-ACS, non–ST-segment–elevation acute coronary syndrome; and PCI, percutaneous coronary intervention.

*Patients with NSTE-ACS who underwent PCI, risk stratum unavailable for 77.

†Stent types were calculated in patients who underwent stent insertion (n=4377).

‡Time from admission to PCI, details of timing were unavailable for 982 of them.

and severe symptoms on admission. A newly published report of the ACTION Registry-GWTG (Acute Coronary Treatment and Intervention Outcomes Network; Get With The Guidelines) showed that the PCI rate in patients with NSTEMI is also lower in women than in men.[17] The underlying reasons need to be clarified in further studies.

Third, 88.9% of patients at very high risk did not undergo appropriately timed PCI according to the guidelines. In the newly updated ESC guidelines, an immediate invasive strategy is recommended in very-high-risk patients (COR I, LOE C), this recommendation being based on a consensus statement by the European Association for Percutaneous Cardiovascular

Table 4. Antiplatelet and Anticoagulant Medication Administration to Patients With NSTE-ACS

	Total (n=9953)		Moderate Risk (n=1822)		High Risk (n=6273)		Very High Risk (n=1656)	
Medicine Use	PCI	Conservative Therapy	PCI	Conservative Therapy	PCI	Conservative Therapy	PCI	Conservative Therapy
DAPT*	5384 (93.0)	3405 (81.8) †	913 (89.1)	610 (76.5)†	3370 (94.3)	1929 (84.8) †	633 (91.7)	781 (80.8)†
Aspirin+Clopidogrel*	4912 (84.8)	3187 (76.6)†	865 (84.4)	586 (73.5)†	3408 (85.2)	1784 (78.4)†	575 (83.3)	733 (75.9)†
Aspirin+Ticagrelor*	645 (11.1)	256 (6.1)†	68 (6.6)	27 (3.4)†	486 (12.2)	166 (7.3)†	84 (12.2)	62 (6.4)†
GPIs‡	1588 (27.5)	289 (7.0)†	132 (12.9)	12 (1.5)†	1227 (30.7)	209 (9.2)†	206 (30.0)	67 (7.1)†
UFH§	151 (2.6)	57 (1.4)†	18 (1.8)	7 (0.9)†	109 (2.7)	42 (1.8)†	21 (3.0)	8 (0.8)†
LMWH§	4099 (70.8)	2387 (57.3)†	550 (53.7)	230 (28.9)†	3018 (75.5)	1511 (66.4)†	498 (72.2)	617 (63.9)†
Fondaparinux§	109 (1.9)	84 (2.0)	18 (1.8)	2 (0.3)†	74 (1.9)	49 (2.2)	16 (2.3)	33 (3.4)

DAPT indicates dual antiplatelet therapy; GPIs, GP IIb/IIIa receptor inhibitors; LMWH, low-molecular-weight heparin; NSTE-ACS, non–ST-segment–elevation acute coronary syndrome; PCI, percutaneous coronary intervention; and UFH, unfractionated heparin.

*DAPT administered within 24 h of admission.

†Statistically significant difference between PCI and conservative therapy groups.

‡32 patients were excluded because of contraindication to GPIs.

§Anticoagulant medications were used in perioperative period.

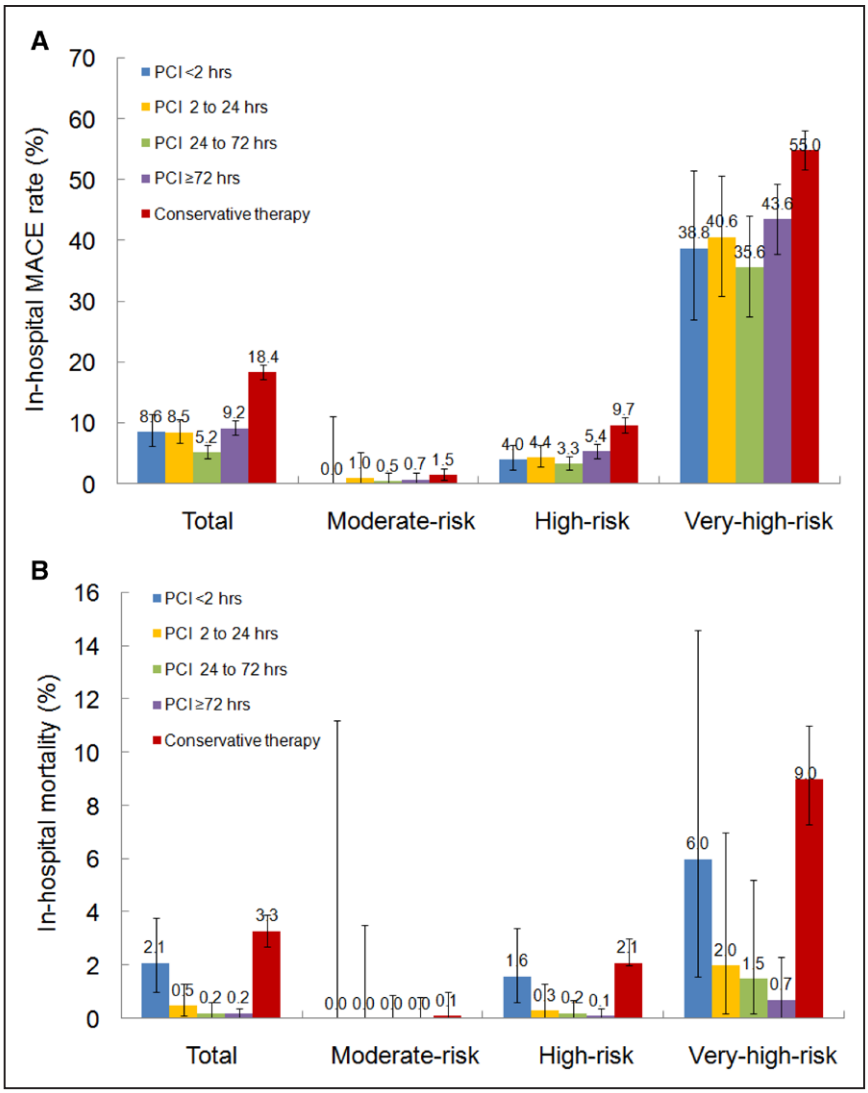

Figure 2. In-hospital outcomes of patients with non–ST-segment–elevation acute coronary syndrome in percutaneous coronary intervention (PCI) and conservative therapy groups according to risk stratification. Time intervals from hospital admission to PCI and details of timing were unavailable for 982 patients who underwent PCI. *P* value <0.05 was considered as statistically significant for any difference between the PCI and conservative therapy groups, and between different PCI timing groups. Also, 95% confidence intervals were calculated for the rates of major adverse cardiovascular events (MACE) and death.

Interventions/Stent For Life groups.[18] However, limited data are available for very-high-risk patients because they have been excluded from randomized controlled trials. In our study, the MACE rate in very-high-risk patients who underwent PCI did not differ between within 2 hours and other time intervals, whereas the in-hospital mortality rate was highest in those who underwent PCI within 2 hours. Further studies integrating risk adjustment or propensity matching and ultimately randomized prospective controlled studies are needed to determine whether very early invasive procedures produces better outcomes than later procedures.

About antithrombotic treatments, it is worth noticing that the proportion of patients receiving aspirin+ticagrelor in this study was much lower than the proportion of those receiving aspirin+clopidogrel in both the PCI and conservative therapy groups. Use of ticagrelor in preference to clopidogrel (COR IIa, LOE B) is mentioned in the AHA/ACC guidelines, whereas in the ESC guidelines, ticagrelor is recommended for patients with moderate to high risk (COR I, LOE B), and clopidogrel is considered as the second-line therapy. More evidence and more time may be needed before practice patterns shift in China. Overall, the use of low-molecular-weight heparin was 65.2% in patients with NSTE-ACS in our study, which is much higher than the 10% in patients with NSTEMI reported by a contemporaneous study from the ACC National Cardiovascular Data Registries.[19] The major explanation for this discrepancy is likely that few patients underwent immediate invasive procedures in this study, 76.1% of patients undergoing PCI >24 hours after admission. Fondaparinux as anew anticoagulant medication has been considered as the first-line anticoagulant agent for conservative strategies in the ESC guideline recommendations (COR I, LOE B); however, the proportion of patients receiving fondaparinux was low in both patients with PCI or conservative treatment groups in this study.

The median hospital stay was 8 days for patients with NSTE-ACS in our study, which is longer than the reported median of 3 to 4 days in patients in the US or European countries.[20–22] One explanation for the longer hospital stay in China is that a much smaller proportion of patients underwent early PCI than in the US or European countries, 45.0% of patients undergoing PCI ≥3 days after admission. Moreover, the lack of appropriate rehabilitation or implementation of secondary prevention measures after hospital discharge for patients with NSTE-ACS may have contributed to prolonged hospital stays.

Study Limitations

This study had several limitations. First, consecutive patients with ACS were recruited to the study each month by the participating hospitals, patients with ST-segment–elevated myocardial infarction and NSTEMI being given priority. Therefore, we are not able to examine the situation of invasive strategy use in low-risk NSTE-ACS patients. Second, this study only provided real-world data for the outcomes of the patients with or without invasive strategy and the outcomes among the patients who underwent PCI in different timing. Further studies integrating risk adjustment or propensity matching and ultimately randomized prospective controlled studies are needed to determine whether the use of very early invasive procedures produces better outcomes than later procedures. Finally, because the participating hospitals were not randomly selected, our findings cannot be generalized to all Chinese hospitals.

Conclusions

We have here reported contemporary data on real-world management of NSTE-ACS in China. There were notable differences between guidelines recommended strategies and clinical management of these patients. The underlying reasons for these differences, especially the larger proportion of very-high-risk NSTE-ACS patients not undergoing PCI, and the optimal timing of PCI require further clarification.

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Disclosures

None.

References

1. Rodriguez F, Mahaffey KW. Management of patients with NSTE-ACS: a comparison of the recent AHA/ACC and ESC guidelines. *J Am Coll Cardiol*. 2016;68:313–321. doi: 10.1016/j.jacc.2016.03.599.
2. Zhang Q, Zhao D, Xie W, Xie X, Guo M, Wang M, Wang W, Liu W, Liu J. Recent trends in hospitalization for acute myocardial infarction in Beijing: increasing overall burden and a transition from ST-segment elevation to non-ST-segment elevation myocardial infarction in a population-based study. *Medicine*. 2016;95:e2677. doi: 10.1097/MD.0000000000002677.
3. Gao R, Patel A, Gao W, Hu D, Huang D, Kong L, Qi W, Wu Y, Yang Y, Harris P, Algert C, Groenestein P, Turnbull F; CPACS Investigators. Prospective observational study of acute coronary syndromes in China: practice patterns and outcomes. *Heart*. 2008;94:554–560. doi: 10.1136/hrt.2007.119750.
4. Chinese Society of Cardiology; Editorial Board of Chinese Journal of Cardiology. 2012 CSC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Chin J Cardiol*. 2012;40:353–367. doi: 0.3760/cma.j.issn.0253-3758.2012.05.001.
5. Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Jr, Ganiats TG, Holmes DR, Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ; Members AATF. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. *Circulation*. 2014;130:e344–e426. doi: 10.1161/CIR.0000000000000134.
6. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, Gencer B, Hasenfuss G, Kjeldsen K, Lancellotti P, Landmesser U, Mehilli J, Mukherjee D, Storey RF, Windecker S, Baumgartner H, Gaemperli O, Achenbach S, Agewall S, Badimon L, Baigent C, Bueno H, Bugiardini R, Carerj S, Casselman F, Cuisset T, Erol Ç, Fitzsimons D, Halle M, Hamm C, Hildick-Smith D, Huber K, Iliodromitis E, James S, Lewis BS, Lip GY, Piepoli MF, Richter D, Rosemann T, Sechtem U, Steg PG, Vrints C, Luis Zamorano J; Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2016;37:267–315. doi: 10.1093/eurheartj/ehv320.
7. Rapezzi C, Biagini E, Branzi A. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: the task force for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes of the European Society of Cardiology. *Eur Heart J*. 2008;29:277–278. doi: 10.1093/eurheartj/ehm498.
8. Bi Y, Gao R, Patel A, Su S, Gao W, Hu D, Huang D, Kong L, Qi W, Wu Y, Yang Y, Turnbull F; CPACS Investigators. Evidence-based medication use among Chinese patients with acute coronary syndromes at the time of hospital discharge and 1 year after hospitalization: results from the Clinical Pathways for Acute Coronary Syndromes in China (CPACS) study. *Am Heart J*. 2009;157:509.e1–516.e1. doi: 10.1016/j.ahj.2008.09.026.
9. Hao Y, Liu J, Liu J, Smith SC, Jr, Huo Y, Fonarow GC, Ma C, Ge J, Taubert KA, Morgan L, Guo Y, Zhang Q, Wang W, Zhao D; CCC-ACS Investigators. Rationale and design of the Improving Care for Cardiovascular Disease in China (CCC) project: a national effort to prompt quality enhancement for acute coronary syndrome. *Am Heart J*. 2016;179:107–115. doi: 10.1016/j.ahj.2016.06.005.
10. Jolly SS, Yusuf S, Cairns J, Niemelä K, Xavier D, Widimsky P, Budaj A, Niemelä M, Valentin V, Lewis BS, Avezum A, Steg PG, Rao SV, Gao P, Afzal R, Joyner CD, Chrolavicius S, Mehta SR; RIVAL trial group. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. *Lancet*. 2011;377:1409–1420. doi: 10.1016/S0140-6736(11)60404-2.
11. Rao SV, Hess CN, Barham B, Aberle LH, Anstrom KJ, Patel TB, Jorgensen JP, Mazzaferri EL, Jr, Jolly SS, Jacobs A, Newby LK, Gibson CM, Kong DF, Mehran R, Waksman R, Gilchrist IC, McCourt BJ, Messenger JC, Peterson ED, Harrington RA, Krucoff MW. A registry-based randomized trial comparing radial and femoral approaches in women undergoing percutaneous coronary intervention: the safe-PCI for women (study of access site for enhancement of PCI for women) trial. *JACC Cardiovasc Interv*. 2014;7:857–867.
12. Flather MD, Babalis D, Booth J, Bardaji A, Machecourt J, Opolski G, Ottani F, Bueno H, Banya W, Brady AR, Bojestig M, Lindahl B. Cluster-randomized trial to evaluate the effects of a quality improvement program on management of non-ST-elevation acute coronary syndromes: The European Quality Improvement Programme for Acute Coronary Syndromes (EQUIP-ACS). *Am Heart J*. 2011;162:700.e1–707.e1. doi: 10.1016/j.ahj.2011.07.027.
13. Jedrzkiewicz S, Goodman SG, Yan RT, Welsh RC, Kornder J, DeYoung JP, Wong GC, Rose B, Grondin FR, Gallo R, Huang W, Gore JM, Yan AT; Canadian Global Registry of Acute Coronary Events (GRACE/GRACE2). Temporal trends in the use of invasive cardiac procedures for non-ST segment elevation acute coronary syndromes according to initial risk stratification. *Can J Cardiol*. 2009;25:e370–e376. doi: 10.1016/S0828-282X(09)70163-1.
14. Amsterdam EA, Peterson ED, Ou FS, Newby LK, Pollack CV, Jr, Gibler WB, Ohman EM, Roe MT. Comparative trends in guidelines adherence among patients with non-ST-segment elevation acute coronary syndromes treated with invasive versus conservative management strategies: results from the crusade quality improvement initiative. *Am Heart J*. 2009;158:748–754 e741.
15. Zia MI, Goodman SG, Peterson ED, Mulgund J, Chen AY, Langer A, Tan M, Ohman EM, Gibler WB, Pollack CV, Jr, Roe MT. Paradoxical use of invasive cardiac procedures for patients with non-ST segment elevation myocardial infarction: an international perspective from the crusade initiative and the Canadian ACS registries i and ii. *Can J Cardiol*. 2007;23:1073–1079.

16. Ending violence against doctors in China. *Lancet*. 2012;379:1764.
17. Edmund Anstey D, Li S, Thomas L, Wang TY, Wiviott SD. Race and sex differences in management and outcomes of patients after ST-elevation and non-ST-elevation myocardial infarct: results from the NCDR. *Clin Cardiol*. 2016;39:585–595. doi: 10.1002/clc.22570.
18. Noc M, Fajadet J, Lassen JF, Kala P, MacCarthy P, Olivecrona GK, Windecker S, Spaulding C; European Association for Percutaneous Cardiovascular Interventions (EAPCI); Stent for Life (SFL) Group. Invasive coronary treatment strategies for out-of-hospital cardiac arrest: a consensus statement from the European Association for Percutaneous Cardiovascular Interventions (EAPCI)/Stent for Life (SFL) groups. *EuroIntervention*. 2014;10:31–37. doi: 10.4244/EIJV10I1A7.
19. Masoudi FA, Ponirakis A, de Lemos JA, Jollis JG, Kremers M, Messenger JC, Moore JW, Moussa I, Oetgen WJ, Varosy PD, Vincent RN, Wei J, Curtis JP, Roe MT, Spertus JA. Trends in U.S. Cardiovascular Care: 2016 report from 4 ACC National Cardiovascular Data Registries. *J Am Coll Cardiol*. 2017;69:1427–1450. doi: 10.1016/j.jacc.2016.12.005.
20. Gierlotka M, Gąsior M, Wilczek K, Wasilewski J, Hawranek M, Tajstra M, Osadnik T, Banasiak W, Poloński L. Temporal trends in the treatment and outcomes of patients with non-ST-segment elevation myocardial infarction in Poland from 2004-2010 (from the Polish Registry of Acute Coronary Syndromes). *Am J Cardiol*. 2012;109:779–786. doi: 10.1016/j.amjcard.2011.10.041.
21. Kragholm K, Goldstein SA, Yang Q, Lopes RD, Schulte PJ, Bernacki GM, White HD, Mahaffey KW, Giugliano RP, Armstrong PW, Harrington RA, Tricoci P, Van de Werf F, Alexander JH, Alexander KP, Newby LK. Trends in enrollment, clinical characteristics, treatment, and outcomes according to age in non-ST-segment-elevation acute coronary syndromes clinical trials. *Circulation*. 2016;133:1560–1573. doi: 10.1161/CIRCULATIONAHA.115.017299.
22. Vavalle JP, Lopes RD, Chen AY, Newby LK, Wang TY, Shah BR, Ho PM, Wiviott SD, Peterson ED, Roe MT, Granger CB. Hospital length of stay in patients with non-ST-segment elevation myocardial infarction. *Am J Med*. 2012;125:1085–1094.

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Invasive Management Strategies and Antithrombotic Treatments in Patients With Non–ST-Segment–Elevation Acute Coronary Syndrome in China: Findings From the Improving CCC Project (Care for Cardiovascular Disease in China)

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SUPPLEMENTAL MATERIAL

Supplemental Methods

We recruited hospitals separately indifferent geographic-economic regions, representing the diversity of ACS care in China. In seven geographical regions(Northern, Northeast, Eastern, Central, Southern, Southwest, and Eastern China) in mainland China. Provinces are grouped into low, medium-low, medium-high, and high levels according to gross domestic product per capita. In each geographic-economic region, 10% of the tertiary hospitals were recruited for our study, with 150 hospitals selected in total. The first 20–30 consecutive patients in each hospital each month were recruited to the study, with priority being given to those with STEMI and NSTEMI. If fewer than 20 patients were admitted in any month, the hospital reported all of them. The reasons 20-30 ACS cases were chosen each month derive from both statistical power and feasibility considerations. This project sample size was calculated to achieve a power of 90% at a two-sided 0.05 significance level to detect a 5% improvement in composite scores of performance measures for quantifying the quality of cardiovascular care. According to the hospital survey before studying, 89% of these hospitals had more than 240 ACS inpatients annually. This means most hospitals have the ability to report over 20 ACS cases each month on average.

Supplementary Table 1. In-hospital outcomes of patients with NSTE-ACS

Hospitalization MACE	Total			Moderate-risk			High-risk			Very-high-risk		
	PCI	Conservative therapy	*p*	PCI	Conservative therapy	*p*	PCI	Conservative therapy	*p*	PCI	Conservative therapy	*p*
Total MACE	436(7.5)	765(18.4)	<0.001	7(0.7)	12(1.5)	0.086	173(4.3)	221(9.7)	<0.001	256(37.1)	531(55.0)	<0.001
Death	29(0.5)	136(3.3)	<0.001	1 (0.1)	1(0.1)	0.858	14(0.4)	48(2.1)	<0.001	14(2.0)	87(9.0)	<0.001

Supplementary Table 2. List of Participating Hospitals

ID	Hospitals	Territories	Provinces	City	Investigator
1	Shanxi Cardiovascular Hospital	Northern China	Shanxi	Taiyuan	Bao Li
2	Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School	Eastern China	Jiangsu	Nanjing	Biao Xu, Guangshu Han
3	Hainan General Hospital	Southern China	Hainan	Haikou	Bin Li
4	The Second Hospital of Jilin University	Northeast China	Jilin	Changchun	Bin Liu
5	The 2nd Affiliated Hospital of Harbin Medical University	Northeast China	Heilongjiang	Harbin	Bo Yu
6	The Ninth Hospital Affiliated to Shanghai Jiaotong University School of Medicine	Eastern China	Shanghai	Shanghai	Changqian Wang
7	Henan Provincial People's Hospital	Central China	Henan	Zhengzhou	Chuanyu Gao

8	Shanxi Provincial People's Hospital	Northern China	Shanxi	Taiyuan	Chunlin Lai
9	Xinqiao Hospital, Third Military Medical University	Southwest China	Chongqing	Chongqing	Cui Bin, Lan Huang
10	China Meitan General Hospital	Northern China	Beijing	Beijing	Di Wu
11	The 309th Hospital of Chinese People's Liberation Army	Northern China	Beijing	Beijing	Fakuan Tang, Jun Xiao
12	Zhongda Hospital, Southeast University	Eastern China	Jiangsu	Nanjing	Genshan Ma
13	The First Affiliated Hospital of Liaoning Medical University	Northeast China	Liaoning	Jinzhou	Guizhou Tao
14	Xinjiang Uygur Autonomous Region People’s Hospital	Northwest China	Xinjiang	Urumchi	Guoqing Li
15	Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University	Eastern China	Zhejiang	Hangzhou	Guosheng Fu

16	Beijing Friendship Hospital, Capital Medical University	Northern China	Beijing	Beijing	Hongwei Li
17	The First Affiliated Hospital of Bengbu Medical College	Eastern China	Anhui	Bengbu	Honhju Wang
18	General Hospital of TISCO	Northern China	Shanxi	Taiyuan	Huifeng Wang
19	Dongguan People's Hospital	Southern China	Guangdong	Dongguan	Jianfeng Ye
20	Panyu Hospital of Chinese Medicine	Southern China	Guangdong	Guangzhou	Jianhao Li
21	Peking University First Hospital	Northern China	Beijing	Beijing	Jie Jiang
22	Sun Yat-sen Memorial Hospital, Sun Yat-sen University	Southern China	Guangdong	Guangzhou	Jingfeng Wang
23	Guangdong General Hospital	Southern China	Guangdong	Guangzhou	Jiyan Chen
24	Hospital of Xinjiang Production & Construction Corps	Northwest China	Xinjiang	Urumchi	Junming Liu

25	The Military General Hospital of Beijing PLA	Northern China	Beijing	Beijing	Junxia Li
26	The First Affiliated Hospital of Guangxi Medical University	Southern China	Guangxi	Nanning	Lang Li
27	Tongren Hospital Affiliated to Shanghai Jiaotong University School of Medicine	Eastern China	Shanghai	Shanghai	Li Jiang
28	Binzou City Center Hospital	Eastern China	Shandong	Binzhou	Lijun Meng
29	The First Affiliated Hospital of Zhengzhou University	Central China	Henan	Zhengzhou	Ling Li
30	Xijing Hospital	Northwest China	Shaanxi	Xi'an	Ling Tao
31	The Affiliated Hospital of Guizhou Medical University	Southwest China	Guizhou	Guiyang	Lirong Wu

32	First Affiliated Hospital of the People's Liberation Army General Hospital	Northern China	Beijing	Beijing	Miao Tian
33	The Second People's Hospital of Yunnan Province	Southwest China	Yunnan	Kunming	Minghua Han
34	Haikou People's Hospital	Southern China	Hainan	Haikou	Moshui Chen
35	Gansu Provincial Hospital	Northwest China	Gansu	Lanzhou	Ping Xie
36	The First Affiliated Hospital of Henan University of Science and Technology	Central China	Henan	Luoyang	Pingshuan Dong
37	Chenzhou First People's Hospital	Central China	Hunan	Chenzhou	Qiaoqing Zhong
38	People’s Hospital of Qinghai Province	Northwest China	Qinghai	Xining	Rong Chang
39	Affiliated Hospital of Ningxia Medical University	Northwest China	Ningxia	Yinchuan	Shaobin Jia

40	Beijing Anzhen Hospital, Capital Medical University	Northern China	Beijing	Beijing	Shaoping Nie, Xiaohui Liu
41	North Jiangsu People's Hospital	Eastern China	Jiangsu	Yangzhou	Shenghu He
42	Shanghai Sixth People's Hospital	Eastern China	Shanghai	Shanghai	Shixin Ma
43	The First Hospital of Handan	Northern China	Hebei	Handan	Shuanli Xin
44	Huai'an First People's Hospital	Eastern China	Jiangsu	Huai'an	Shuren Ma
45	The First Affiliated Hospital of Chongqing Medical University	Southwest China	Chongqing	Chongqing	Suxin Luo
46	Navy General Hospital	Northern China	Beijing	Beijing	Tianchang Li
47	Zhejiang Provincial Hospital of TCM	Eastern China	Zhejiang	Hangzhou	Wei Mao
48	The Third Xiangya Hospital of Central South University	Central China	Hunan	Changsha	Weihong Jiang
49	Affiliated Hospital of Qinghai University	Northwest China	Qinghai	Xining	Weijun Liu

50	Teda International Cardiovascular Hospital	Northern China	Tianjin	Tianjin	Wenhua Lin
51	The Second Hospital of Hebei Medical University	Northern China	Hebei	Shijiazhuang	Xianghua Fu
52	Changhai Hospital of Shanghai	Eastern China	Shanghai	Shanghai	Xianxian Zhao
53	The Second Affiliated Hospital to Nanchang University	Eastern China	Jiangxi	Nanchang	Xiaoshu Cheng
54	Hebei General Hospital	Northern China	Hebei	Shijiazhuang	Xiaoyong Qi
55	Inner Mongolia People's Hospital	Northern China	Inner Mongolia	Hohhot	Xingsheng Zhao
56	The General Hospital of Shenyang Military Region	Northeast China	Liaoning	Shenyang	Yaling Han
57	The First Hospital of Jilin University	Northeast China	Jilin	Changchun	Yang Zheng
58	Tianjin Chest Hospital	Northern China	Tianjin	Tianjin	Yin Liu
59	Hunan Provincial People's Hospital	Central China	Hunan	Changsha	Ying Guo

60	People's Hospital of Yuxi City	Southwest China	Yunnan	Yuxi	Yinglu Hao
61	The People's Hospital of Guangxi Zhuang Autonomous Region	Southern China	Guangxi	Nanning	Yingzhong Lin
62	The First Teaching Hospital of Xinjiang Medical University	Northwest China	Xinjiang	Urumchi	Yitong Ma
63	Baogang Hospital	Northern China	Inner Mongolia	Baotou	Yongdong Li
64	Tianjin Medical University General Hospital	Northern China	Tianjin	Tianjin	Yuemin Sun
65	The Second Affiliated Hospital of Zhengzhou University	Central China	Henan	Zhengzhou	Yulan Zhao
66	Nanfang Hospital of Southern Medical University	Southern China	Guangdong	Guangzhou	Yuqing Hou
67	The First Affiliated Hospital to Nanchang University	Eastern China	Jiangxi	Nanchang	Zeqi Zheng
68	The First Affiliated Hospital of Lanzhou University	Northwest China	Gansu	Lanzhou	Zheng Zhang

69	The Third Hospital of Shijiazhuang	Northern China	Hebei	Shijiazhuang	Zhenguo Ji
70	Wuxi People's Hospital	Eastern China	Jiangsu	Wuxi	Zhenyu Yang
71	Jiangsu Province Hospital	Eastern China	Jiangsu	Nanjing	Zhijian Yang
72	The Second Hospital of Shanxi Medical University	Northern China	Shanxi	Taiyuan	Zhiming Yang
73	The Affiliated Hospital of Xuzhou Medical College	Eastern China	Jiangsu	Xuzhou	Zhirong Wang
74	Southwest Hospital, Third Military Medical University	Southwest China	Chongqing	Chongqing	Zhiyuan Song
75	The First Affiliated Hospital of Xi’an Jiaotong University	Northwest China	Shaanxi	Xi'an	Zuyi Yuan
76	Yangzhou First People's Hospital	Eastern China	Jiangsu	Yangzhou	Aihua Li
77	Hospital 463 of Chinese People's Liberation Army	Northeast China	Liaoning	Shenyang	Bosong Yang

78	The Central Hospital of Mianyang	Northwest China	Sichuan	Mianyang	Caidong Luo
79	Liaocheng People's Hospital	Eastern China	Shandong	Liaocheng	Chunyan Zhang
80	Yancheng Third People's Hospital	Eastern China	Jiangsu	Yancheng	Chunyang Wu
81	The Second Xiangya Hospital of Central South University	Central China	Hunan	Changsha	Daoquan Peng
82	The Central Hospital of Panzhihua	Northwest China	Sichuan	Panzhihua	Dawen Xu
83	The First Hospital of Qiqihaer City	Northeast China	Heilongjiang	Qiqihaer	Gang Xu
84	The Third the People‘s Hospital of Bengbu	Eastern China	Anhui	Bengbu	Gengsheng Sang
85	The First Hospital of Jiamusi	Northeast China	Heilongjiang	Jiamusi	Guixia Zhang
86	Zhoushan People's Hospital	Eastern China	Zhejiang	Zhoushan	Guoxiong Chen
87	Dalian Municipal Central Hospital	Northeast China	Liaoning	Dalian	Hailong Lin
88	Renmin Hospital of Wuhan University	Central China	Hubei	Wuhan	Hong Jiang

89	Ningxia People's Hospital	Northwest China	Ningxia	Yinchuan	Hong Luan
90	The First People's Hospital of Yunnan Province (Kunhua Hospital)	Northwest China	Yunnan	Kunming	Hong Zhang
91	The Central Hospital of Zhoukou	Central China	Henan	Zhoukou	Hualing Liu
92	Anyang District Hospital	Central China	Henan	Anyang	Hui Liu
93	Sichuan Provincial People’s Hospital	Northwest China	Sichuan	Chengdu	Jianhong Tao
94	Mudanjiang Cardiovascular Disease Hospital	Northeast China	Heilongjiang	Mudanjiang	Jianwen Liu
95	Yichang Central Hospital	Central China	Hubei	Yichang	Jiawang Ding
96	Qilu Hospital of Shandong University	Eastern China	Shandong	Jinan	Jifu Li
97	Affiliated Hospital of Jiangsu University	Eastern China	Jiangsu	Zhenjiang	Jinchuan Yan
98	The First People's Hospital of Nanning City	Southern China	Guangxi	Nanning	Jinru Wei

99	The First Affiliated Hospital of Fujian Medical University	Eastern China	Fujian	Fuzhou	Jinzi Su
100	Chengdu Third People's Hospital	Northwest China	Sichuan	Chengdu	Jiong Tang
101	Yantaishan hospital	Eastern China	Shandong	Yantai	Juexin Fan
102	Qingdao Municipal Hospital	Eastern China	Shandong	Qingdao	Jun Guan
103	Zhongshan Hospital Affiliated to Fudan University	Eastern China	Shanghai	Shanghai	Junbo Ge
104	Longyan First Hospital	Eastern China	Fujian	Longyan	Kaihong Chen
105	Affiliated Hospital of Guangdong Medical College	Southern China	Guangdong	Guangzhou	Keng Wu
106	Jiangxi Provincial People's Hospital	Eastern China	Jiangxi	Nanchang	Lang Ji
107	Anhui Provincial Hospital	Eastern China	Anhui	Hefei	Likun Ma
108	Xiangtan City Central Hospital	Central China	Hunan	Xiangtan	Lilong Tang
109	The First Hospital of Haerbin City	Northeast China	Heilongjiang	Harbin	Lin Wei

110	Central Hospital Affiliated to Shenyang Medical College	Northeast China	Liaoning	Shenyang	Man Zhang, Kaiming Chen
111	The Central Hospital of Wuhan	Central China	Hubei	Wuhan	Manhua Chen
112	Hangzhou First People's Hospital	Eastern China	Zhejiang	Hangzhou	Ningfu Wang
113	The Central Hospital of Xuzhou	Eastern China	Jiangsu	Xuzhou	Peiying Zhang
114	The Second hospital of Dalian Medical University	Northeast China	Liaoning	Dalian	Peng Qu
115	The First Affiliated Hospital of Liaoning University of Traditional Chinese Medicine	Northeast China	Liaoning	Shenyang	Ping Hou
116	Beijing Tsinghua Changgung Hospital	Northern China	Beijing	Beijing	Ping Zhang
117	Guizhou Provincial People's Hospital	Northwest China	Guizhou	Guiyang	Qiang Wu

118	The First Affiliated Hospital of Xiamen University	Eastern China	Fujian	Xiamen	Qiang Xie
119	Quanzhou First Hospital	Eastern China	Fujian	Quanzhou	Rong Lin
120	Wuzhou People's Hospital	Southern China	Guangxi	Wuzhou	Shaowu Ye
121	The Central Hospital of Jilin	Northeast China	Jilin	Changchun	Shuangbin Li
122	Xiangya Hospital Central South University	Central China	Hunan	Changsha	Tianlun Yang
123	Guangzhou Red Cross Hospital	Southern China	Guangdong	Guangzhou	Tongguo Wu
124	The First Affiliated Hospital of Guangzhou Medical College	Southern China	Guangdong	Guangzhou	Wei Wang
125	The First Affiliated Hospital of Wenzhou Medical University	Eastern China	Zhejiang	Wenzhou	Weijian Huang
126	The Second Affiliated Hospital of Soochow University	Eastern China	Jiangsu	Suzhou	Weiting Xu
127	Wuhan Asia Heart Hospital	Central China	Hubei	Wuhan	Xi Su

128	The First Affiliated Hospital of Soochow University	Eastern China	Jiangsu	Suzhou	Xiangjun Yang
129	Affiliated Hospital of Yan'an University	Northwest China	Shaanxi	Yan'an	Xiaochuan Ma
130	The First People's Hospital of Jining	Eastern China	Shandong	Jining	Xiaofei Sun
131	The Central Hospital of Taiyuan	Northern China	Shanxi	Taiyuan	Xiaoping Chen
132	West China Hospital of Sichuan University	Northwest China	Sichuan	Chengdu	Xiaoping Chen
133	The Third Affiliated Hospital of Guangzhou Medical College	Southern China	Guangdong	Guangzhou	Ximing Chen
134	The First Affiliated Hospital of Wannan Medical College	Eastern China	Anhui	Wuhu	Xingsheng Tang
135	Tangdu Hospital of The Fourth Military Medical University	Northwest China	Shaanxi	Xi'an	Xue Li
136	Shanghai East Hospital Affiliated to Tongji University	Eastern China	Shanghai	Shanghai	Xuebo Liu

137	Xiamen Cardiovascular Disease Hospital	Eastern China	Fujian	Xiamen	Yan Wang
138	Zhongnan hospital of Wuhan University	Central China	Hubei	Wuhan	Yanggan Wang
139	Fujian Provincial Hospital	Eastern China	Fujian	Fuzhou	Yansong Guo
140	The First Affiliated hospital of Dalian Medical University	Northeast China	Liaoning	Dalian	Yanzong Yang
141	The First People's Hospital of Changde	Central China	Hunan	Changde	Yi Huang
142	The First Affiliated Hospital of China Medical University	Northeast China	Liaoning	Shenyang	Yingxian Sun
143	The Fourth Affiliated Hospital of China Medical University	Northeast China	Liaoning	Shenyang	Yuanzhe Jin
144	Cangzhou Central Hospital	Northern China	Hebei	Cangzhou	Zesheng Xu
145	The Central Hospital of Shaoyang	Central China	Hunan	Shaoyang	Zewei Ouyang
146	The People's Hospital of Liaoning Province	Northeast China	Liaoning	Shenyang	Zhanquan Li

147	The First Affiliated Hospital of Jiamusi University	Northeast China	Heilongjiang	Jiamusi	Zhaofa He
148	Tangshan Gongren Hospital	Northern China	Hebei	Tangshan	Zheng Ji
149	Huaibei Miners General Hospital	Eastern China	Anhui	Huaibei	Zhenqi Su
150	Linyi People's Hospital	Eastern China	Shandong	Linyi	Zhihong Ou