Rational and design of a stepped-wedge cluster randomized trial evaluating quality improvement initiative for reducing cardiovascular events among patients with acute coronary syndromes in resource-constrained hospitals in China

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Background Acute coronary syndromes (ACSs) are a major cause of morbidity and mortality, yet effective ACS treatments are frequently underused in clinical practice. Randomized trials including the CPACS-2 study suggest that quality improvement initiatives can increase the use of effective treatments, but whether such programs can impact hard clinical outcomes has never been demonstrated in a well-powered randomized controlled trial.

Design The CPACS-3 study is a stepped-wedge cluster-randomized trial conducted in 104 remote level 2 hospitals without PCI facilities in China. All hospitalized ACS patients will be recruited consecutively over a 30-month period to an anticipated total study population of more than 25,000 patients. After a 6-month baseline period, hospitals will be randomized to 1 of 4 groups, and a 6-component quality improvement intervention will be implemented sequentially in each group every 6 months. These components include the following: establishment of a quality improvement team, implementation of a clinical pathway, training of physicians and nurses, hospital performance audit and feedback, online technical support, and patient education. All patients will be followed up for 6 months postdischarge. The primary outcome will be the incidence of in-hospital major adverse cardiovascular events comprising all-cause mortality, myocardial infarction or reinfarction, and nonfatal stroke.

Conclusions The CPACS-3 study will be the first large randomized trial with sufficient power to assess the effects of a multifaceted quality of care improvement initiative on hard clinical outcomes, in patients with ACS. (Am Heart J 2015;169:349-55.)

Background

Coronary heart disease is the leading cause of death worldwide[1] and now also in China.[2] Between 2010 and 2019, China is predicted to experience a 69% increase in the incidence of acute coronary disease amounting to nearly 8 million additional episodes of myocardial infarction or unstable angina pectoris, compared with the decade 2000 to 2009.[3] More than two-thirds of the burden of death and disability from these acute coronary syndromes (ACSs) will occur in adults younger than 65 years.[3] This rapidly escalating burden of disease among individuals in the prime of life will have increasingly profound economic and social implications for China.[4,5]

Despite the widespread promulgation and endorsement of ACS treatment guidelines[6,7] and the strong evidence base for guideline recommendations,[8–10] substantial evidence-practice gaps exist in low- and middle-income countries, including China.[11–14] In the first phase of the Clinical Pathways in Acute Coronary Syndromes program (CPACS-1), evidence-practice gaps and in-hospital mortality were found to be larger in lower

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David A. Morrow, MD, MPH, served as guest editor for this article.
NCT01398228
Submitted June 13, 2014; accepted December 15, 2014.

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0002-8703

http://dx.doi.org/10.1016/j.ahj.2014.12.005

level, nontertiary hospitals, as compared with tertiary hospitals in large urban centers.[15] However, about one-half of China's population resides in rural regions, with access only to nontertiary hospital care.[16]

Many strategies aimed at narrowing evidence-practice gaps in ACS care have been evaluated.[8,17–20] The second phase of CPACS (CPACS-2) had shown the intervention that clinical pathways with regular audit-feedback cycles of key ACS quality of care performance indicators significantly increased the evidence-based medications use from 51.2% to 62.8%.[21] Besides, another lifesaving treatment, reperfusion therapy, was increased from 31.8% to 42.7% among ST-elevation myocardial infarction (STEMI) patients with borderline significance ($P = .07$).[21]

Although quality of care improvement (QCI) initiatives have been shown to improve process outcomes for ACS management in other countries,[17–19] the effects of such programs on hard clinical events remain uncertain. Theoretically, the effect of the QCI must be far beyond the observed significant increase in medications use, and the intervention should also improve other aspects of the ACS care, such as increase of the dosage of the medications and the knowledge of patients on self-care through improved communications between the doctors and patients. These factors should also have impact on hard clinical outcomes but unfortunately very hard to measure. The totality of the effects of quality improvement could only be measured ideally by major adverse cardiovascular events (MACEs) or cardiovascular mortality. The CPACS-2 study had shown that multivariable adjusted odds ratio of in-hospital MACE was reduced by 59%, although the reduction was not statistically significant due to the small sample size.[21] Thus, although the observational studies[10,22–24] have shown significant reductions in clinical outcomes after initiation of quality improvement interventions, to our knowledge, there is no clear evidence from randomized trials.

Since 2009, the government of China has initiated major health care reforms.[25] One major objective is to strengthen the rural primary health care system, which places county hospitals as regional centers.[26] As an official implementation research project of the National Health and Family Planning Commission (NHFPC; former Ministry of Health), the third phase of CPACS (CPACS-3) has been initiated to evaluate a multifaceted intervention aimed at improving clinical outcomes among patients with ACS treated in resource-constrained hospitals

Methods

Study aims

The primary aim of CPACS-3 study is to test whether the routine use of a multifaceted QCI initiative will lead to a measurable reduction in the number of in-hospital MACE in patients with ACS presenting to resource-constrained hospitals in China.

The secondary aims include the following:

1. To determine whether the routine use of the initiative will improve quality of care
2. To determine the major system-level facilitators and barriers to implementation and uptake of the initiative in these resource-constrained settings
3. To determine the cost-effectiveness of the initiative compared with usual care, from the perspective of the health care provider

Study design

A stepped-wedge cluster randomized trial design will be used to evaluate the impact of the intervention.[27] Eligible hospitals (clusters) are randomly assigned into 4 wedges (groups) using a centralized randomization process, stratified by province. The intervention will be implemented sequentially from groups 1 to 4 at 6-month time intervals, referred to here as "steps" (Figure), until the intervention has been initiated in all hospitals. The intervention will be applied at the level of the hospital, with outcomes measured at the patient level. This study was registered on www.clinicaltrails.gov, and the registration number is NCT01398228.

Hospitals selection

A total of 104 county hospitals from 15 provinces (Anhui, Gansu, Guizhou, Guangzhou, Hebei, Henan, Hubei, Jiangsu, Jilin, Liaoning, Neimeng, Shandong, Shanxi, Shannxi, Sichuan) were chosen, according to the following criteria, through recommendations by NHFPC in collaboration with local provincial Bureaus of Health. Hospitals were eligible to participate if:

1. the time taken to transfer an ACS patient to the nearest large tertiary hospital with a cardiac catheterization laboratory is more than 90 minutes;
2. the hospital is not planning to develop capacity to perform onsite percutaneous coronary intervention (PCI) within the next 4 years;
3. there are more than 40 ACS patients hospitalized every 6 months; and
4. the hospital did not participate in CPACS-2 study.

Patient recruitment

Study participants are all patients 18 years or older admitted prospectively after December 1, 2011, to participating hospitals with a final diagnosis of ACS at the time of death or discharge. Patients will be excluded if they are dead on arrival or die within 10 minutes of arriving at hospital. Patients transferred to the Cardiology Department from other departments of the same hospital will also be excluded.