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Treatment and outcomes of acute coronary syndromes in women: An analysis of a multicenter quality improvement Chinese study

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ABSTRACT

Background: Variations in care and outcomes by sex in patients with acute coronary syndrome (ACS) have been reported worldwide. The aims of this study are to describe ACS management according to sex in China and the effects of a quality improvement program in Chinese male and female ACS patients.
Methods and results: Clinical Pathways for Acute Coronary Syndromes - Phase 2 (CPACS-2) was a cluster randomized trial to test whether a clinical pathways-based intervention would improve ACS management in China. The study enrolled 15,141 hospitalized patients [4631 (30.6%) were women] from 75 hospitals throughout China between October 2007 and August 2010. The intervention included clinical pathway implementation and performance measurement using standardized indicators with 6 monthly audit-feedback cycles. Eight key performance indicators reflecting in hospital management of ACS were measured. After adjustment for differences in patient characteristics and comorbidities at presentation, women were significantly less likely to undergo coronary angiography when indicated (RR 0.88 [0.85 to 0.92], $P < 0.001$), less likely to receive guideline recommended medical therapies at discharge (RR 0.94 [0.91 to 0.98], $P = 0.003$) and more likely to be hospitalized for shorter (mean difference −0.42 [−0.73 to −0.12] days, $P = 0.007$). However, in-hospital clinical outcomes did not differ by sex. There was no evidence of heterogeneity in the relative effects of the quality improvement initiative by sex.
Conclusions: Sex disparities were apparent in some key quality of care indicators for patients with suspected with ACS presenting to hospitals in China. The beneficial effect of the quality improvement program was consistent in women and men.
Clinical trial registration: http://www.anzctr.org.au/default.aspx. Unique identifier: ACTRN12609000491268.

1. Introduction

Sex disparities in quality and outcomes of care for acute coronary syndrome (ACS) have been previously reported in Western countries. Some studies have suggested that women with ACS face delays in diagnosis and treatment, undergo less invasive management, and receive less evidence-based medical therapies than do their male counterparts [1–5]. The US-based CRUSADE study reported that despite presenting with more adverse risk characteristics and having greater in-hospital risk of poor outcomes, women with non-ST elevation ACS were treated less aggressively than men [1]. A recent study from the Netherlands showed that sex differences were evident in terms of appropriate cardiovascular drug use, with particularly less use of antithrombotics, lipid-lowering drugs, and beta-blockers in young women, compared with young men [4]. However, such disparities are not consistently reported. A registry study involving 14 European countries has shown that women and men receive similar medications at the time of percutaneous coronary intervention (PCI), hospital discharge, and 12-month follow-up, with comparable outcomes at 1 year [6]. Similar findings have been reported from registry studies in India and Sweden [7,8]. In various settings it has also been reported that sex has no impact on door-to-ECG performance time [9,10] or use of reperfusion

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therapy after adjustment for differences in clinical and demographic characteristics at presentation [11].

A small study in the early stages of the coronary heart disease epidemic in China suggested the existence of sex disparities in treatment of ACS [12]. However in more recent years, facilities to manage ACS have grown exponentially and universal access to healthcare insurance schemes has been introduced. In this context, more reliable contemporary data are required. Clinical Pathways for Acute Coronary Syndromes - Phase 2 (CPACS-2) was a cluster randomized trial of a clinical pathways-based quality improvement initiative for ACS in China (The trial was registered at URL: http://www.anzctr.org.au/default.aspx. Unique identifier: ACTRN12609000491268). Clinical pathways are commonly used for quality improvement and proved effective in observational studies. We used data from this trial to (i) establish whether sex differences in the care and outcomes for suspected ACS exist in China and (ii) whether a quality improvement intervention had a differential effect on men and women who present to hospital with suspected ACS.

2. Methods

We used data from CPACS-2, a cluster randomized trial which enrolled 15,141 hospitalized patients with a discharge diagnosis of ACS, including unstable angina, non ST segment elevation myocardial infarction (NSTEMI) and ST segment elevation myocardial infarction (STEMI) from 50 tertiary and 25 non-tertiary hospitals in several regions of China. One patient was excluded from analysis due to missing data on sex. The design and main results of CPACS-2 have been published previously [13–15]. In brief, after developing the intervention in 5 pilot hospitals, 70 hospitals were randomly allocated to early or delayed intervention groups, with the former group implementing the quality improvement intervention one year earlier than the latter. Each participating hospital received the intervention for at least one year; comprising clinical pathway implementation, performance measurement using standardized indicators and 6 monthly audit-feedback cycles of 50 consecutively admitted patients. The primary outcomes included prespecified key performance indicators: (1) proportion of patients with final diagnosis consistent with biomarker findings, (2) proportion of patients with STEMI receiving thrombolysis or primary PCI among those arriving within 12 h of symptom onset, (3) door-to-needle time for patients with STEMI undergoing thrombolysis, (4) door-to-balloon time for patients with STEMI undergoing primary percutaneous coronary intervention (PCI), (5) proportion of high risk patients (high risk patients were those with a diagnosis of unstable angina or NSTEMI, present with any of the following characteristics: age > 75 years, systolic blood pressure < 90 mm Hg, diastolic blood pressure < 60 mm Hg, heart rate > 90 bpm, Killip classification > 3, elevated troponin T or troponin I or CK-MB, ST segment elevation >0.5 mv, new onset myocardial infarction, new onset or aggravated heart failure during hospitalization) undergoing coronary angiography, (6) proportion of low-risk patients (no ongoing symptoms, persistently normal ECG, and persistently normal biomarkers) undergoing functional testing, (7) proportion of patients discharged on combination medical therapy (including any antiplatelet therapy, β-blocker, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and statin), and (8) hospital length of stay. These key performance indicators were chose based on findings from previous studies, which indicated significant room for improvement in those aspects in ACS treatment in China [16]. The secondary outcomes were in-hospital clinical outcomes including death, cardiac death, major adverse cardiovascular events (all-cause mortality, myocardial infarction or re-infarction, or stroke), and major bleeding episodes. A qualitative evaluation using in-depth interviews with investigators was conducted in parallel with the study to understand the contextual factors associated with the success and failure of interventions. The finding was published elsewhere [15].

Local investigators were trained for data collection. During the study, data of randomly selected 10% of patients were validated with the raw data in medical records. Investigators were re-trained for those with errors rate higher than 5%.

In the current analyses, we compared the key performance indicators and in-hospital clinical outcomes between 10,508 men and 4632 women enrolled during the study. In addition, using the data in the early intervention group at 12 months (after 2 cycles) of intervention (1600 patients) and baseline data (1900 patients) from the late intervention group, we evaluated whether the effectiveness of the quality improvement intervention differed between male and female patients.

2.1. Statistical analysis

Mean and standard deviation (SD) are reported for continuous variables, while frequencies were used for categorical variables. Differences by sex in baseline variables were tested using the Student's *t*-test, the Wilcoxon rank-sum and the chi-square tests, as appropriate. In examining the relationships between sex and study outcomes, we adjusted for variables that were different between men and women at a significance (P-value) of <0.1 and variables of known prognostic importance. These included age, systolic blood pressure (SBP), heart rate and Killip classification at admission or shortly after admission, previous history of hypertension, diabetes, myocardial infarction (MI), angina pectoris, stroke or transient ischemic attack, smoking status and socioeconomic status (using data on education level and occupation) and level of hospital where the patient was treated. The GRACE score was not included because factors used in the score were individually adjusted for.

The effects of quality improvement intervention on study outcomes (key performance indicators and clinical outcomes) were estimated among men and women, respectively, and were compared between sexes by adding interaction terms between sex and intervention to the models. All analyses were conducted at the level of the patient, but accounted for clustering effects within hospitals by using generalized estimating equations (GEE) models with an exchangeable correlation structure. Gaussian and log-binomial GEE regressions models were used for continuous and binary outcomes, respectively. The model was also adjusted for pre-intervention patient characteristics that differed between randomized groups (P < 0.1). All P-values were calculated from two-tailed tests of statistical significance with a type I error rate of 5%. All analyses were performed using SAS version 9.2.

2.2. Ethics approval

Ethics approval for the trial was obtained from the Human Research Ethics Committees at the principle investigator's institute. All patients provided written informed consent to be contacted for follow-up.

3. Results

3.1. Patient characteristics

Among the 15,140 patients included in our analysis, 4631 (30.6%) were women. Women were significantly older, had significantly greater

Table 1
Baseline characteristics of patients stratified by sex.

	Female (N = 4632) n/N (%)[a]	Male (n = 10,508) n/N (%)[a]	P-value
Age, mean (SD)	68.1 (10.1)	62.0 (12.1)	<0.0001
BMI, mean (SD)	24.5 (7.9)	24.6 (3.8)	0.3629
SBP, mean (SD), mm Hg	136.9 (25.3)	130.9 (23.5)	<0.0001
DBP, mean (SD), mm Hg	79.9 (14.4)	79.5 (14.4)	0.1172
Killip	1.4 (0.75)	1.3 (0.71)	<0.0001
Grace Score	106.4 (29.0)	95.6 (29.6)	<0.0001
Heart rate, mean (SD),bpm	77.9 (16.4)	76.1 (15.9)	<0.0001
Previous history			
MI	419 (9.0%)	1414 (13.5%)	<0.0001
EAP	2111 (45.6%)	4082 (38.8%)	<0.0001
Stroke/TIA	496 (10.7%)	1016 (9.7%)	0.0487
Heart failure	378 (8.2%)	549 (5.2%)	<0.0001
Diabetes	1171 (25.3%)	1897 (18.1%)	<0.0001
Hypertension	3114(67.2%)	5497 (52.3%)	<0.0001
Dyslipidaemia	625 (13.5%)	1271 (12.1%)	0.0164
Smoking status			
Never smoked	4057 (90.1%)	3109 (30.8%)	<0.0001
Ex-smoker	208 (4.6%)	2567 (25.5%)	
Current	237 (5.3%)	4404 (43.7%)	
Main occupation†			
Manual	1089 (24.2%)	1966 (19.5%)	<0.0001
Business	108 (2.4%)	688 (6.8%)	
Retired	1866 (41.5%)	3894 (38.6%)	
Others	1431 (31.8%)	3543 (35.1%)	
Completed high school	1071 (23.1%)	4491 (42.7%)	<0.0001
Medical insurance held	3768 (81.4%)	8725 (83.0%)	0.0133
Diagnosis at discharge			<0.0001
STEMI	1312 (28.3%)	4654 (44.3%)	
NSTEMI	692 (14.9%)	1464 (13.9%)	
UAP	2627 (56.7%)	4391 (41.8%)	
Level of hospital			<0.0001
Secondary hospital	1908(41.2%)	3412(32.5%)	
Tertiary hospital	2724 (58.8%)	7096 (67.5%)	

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; mmHg, millimeters of mercury; DBP, diastolic blood pressure; bpm, beats per minute; MI, myocardial infarction; EAP, Exertional angina pectoris; TIA, transient ischemic attack; STEMI, ST segment elevated myocardial infarction; NSTEMI, Non-ST segment elevated myocardial infarction; UAP, unstable angina pectoris.

[a] Expressed as proportions and percentages, except where indicated, Denominators may be subject to missing data.

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