



Effect of coronary artery revascularization on in-hospital outcomes and long-term prognoses in acute myocardial infarction patients with prior ischemic stroke

Bo-Yu LI¹, Xiao-Ming LI¹, Yan ZHANG², Zhan-Yun WEI³, Jing LI¹, Qi HUA¹

¹Department of Cardiology, Xuanwu Hospital, Capital Medical University, Beijing, China

²School of Nursing, Capital Medical University, Beijing, China

³Department of Geriatrics, Xuanwu Hospital, Capital Medical University, Beijing, China

Abstract

Objective To investigate whether coronary artery revascularization therapies (CART), including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), can improve the in-hospital and long-term outcomes for acute myocardial infarction (AMI) patients with prior ischemic stroke (IS). **Methods** A total of 387 AMI patients with prior IS were enrolled consecutively from January 15, 2005 to December 24, 2011 in this cohort study. All patients were categorized into the CART group ($n = 204$) or the conservative medications (CM) group ($n = 183$). In-hospital cardiocerebral events and long-term mortality of the two groups after an average follow-up of 36 months were recorded by Kaplan-Meier survival curves and compared by Logistic regression and the Cox regression model. **Results** The CART patients were younger (66.5 ± 9.7 years vs. 71.7 ± 9.7 years, $P < 0.01$), had less non-ST segment elevation myocardial infarction (11.8% vs. 20.8%, $P = 0.016$) and more multiple-vascular coronary lesions (50% vs. 69.4%, $P = 0.031$). The hospitalization incidence of cardiocerebral events in the CART group was 9.3% while 26.2% in the CM group ($P < 0.01$). CART significantly reduced the risk of in-hospital cardiocerebral events by 65% [adjusted odds ratio (OR) = 0.35, 95% CI: 0.13–0.92]. By the end of follow-up, 57 cases (41.6%) died in CM group ($n = 137$) and 24 cases (12.2%) died in CART group ($n = 197$). Cox regression indicated that CART decreased the long-term mortality by 72% [adjusted hazard ratio (HR) = 0.28, 95% CI: 0.06–0.46], while categorical analysis indicated no significant difference between PCI and CABG. **Conclusions** CART has a significant effect on improving the in-hospital and long-term prognoses for AMI patients with prior IS.

J Geriatr Cardiol 2016; 13: 145–151. doi:10.11909/j.issn.1671-5411.2015.06.017

Keywords: Acute myocardial infarction; Conservative medications; Coronary artery bypass grafting; Coronary artery revascularization; Ischemic stroke; Percutaneous coronary intervention

1 Introduction

Acute myocardial infarction (AMI) is a life-threatening disease and the coronary artery revascularization therapies (CART), including the percutaneous intervention (PCI) and coronary artery bypass grafting (CABG), have a prompt and definite effect on restoring the blood flow to the coronary arteries and improving the patients' prognoses.^[1–4] The drug-eluting stents accompanied with antiplatelet therapy have decreased the occurrence of in-stent restenosis and long-term cardiovascular events.^[5] The application of new tech-

niques and equipment such as arterial bridge, off-pumping, micro invasive techniques and Da Vinci robots in CABG have substantially reduced the operational trauma and risks for the patients.^[6–9] The safety and efficacy of CART have been demonstrated in many clinical trials.^[10]

For patients suffering from AMI with prior ischemic stroke (IS), however, little available data indicate they could benefit from CART. Most of them are characterized with poor basic body conditions and suffered from severe clinical complications.^[11] It is very common for clinical trials to exclude those patients and most current guidelines recommend cautious therapeutic strategies for these patients. In contrast to those without prior stroke, the patients who suffered from coronary artery disease with prior stroke had higher cardiogenic mortality and recurrence of cerebral infarction.^[12,13] Up to 27.6% patients after CABG had post-operational cerebral infarctions on MRI, and a history of

Correspondence to: Qi HUA, MD, PhD, Department of Cardiology, Xuanwu Hospital, Capital Medical University, Changchun Street 45#, Beijing 100053, China. E-mail: huaqi5371@medmail.com.cn

Telephone: +86-10-83198899-8438 **Fax:** +86-10-83162560

Received: July 6, 2015 **Revised:** October 29, 2015

Accepted: October 31, 2015 **Published online:** November 16, 2015

prior stroke has proven to be an independent indicator.^[14] So cardiologists often face the dilemma of choosing perfect therapy strategies for AMI patients with IS after assessing their risks and benefits.^[15] In this study, we conducted a cohort study to assess whether CART was more effective than CM in treating AMI patients with prior IS.

2 Methods

2.1 Study design and sample

We conducted a cohort study comparing in-hospital and long-term outcomes between patients of AMI with prior IS treated with CM or CART in Xuanwu Hospital in Beijing, China. Our institution is a 1200-bed teaching hospital affiliated with Capital Medical University and is equipped with 140-bed intensive care units including a 12-bed cardiac care unit. The study protocol was approved by the Institutional Review Board of Medical Ethics Committee. All the discharge information during the period from January 15, 2005 to December 24, 2011 was retrieved from the clinical information files, and patients who had AMI with prior IS were identified. For the diagnosis of AMI, patients had to meet the European Society of Cardiology/American College of Cardiology clinical criteria for the AMI standard which included elevation of biochemical markers of myocardial necrosis (preferably troponin) in addition to at least one of the following: (a) ischemic symptoms; (b) development of pathologic Q waves on the ECG; (c) ECG changes indicative of ischemia (ST segment elevation or depression); and (d) coronary artery intervention (e.g., coronary angioplasty).^[16] The onset of AMI should have occurred before patient's arrival at the hospital. For the diagnosis of IS, patients had to meet the American Heart Association/American Stroke Association Council on Stroke clinical criteria for IS, including: (a) large-artery atherosclerotic infarction, which may be extracranial or intracranial; (b) embolism from a cardiac source; (c) small-vessel disease; (d) other determined cause such as dissection, hypercoagulation states, or sickle cell disease; and (e) infarcts of undetermined cause.^[17] Imaging evidence such as CT or MRI was required to confirm the diagnosis of IS.

The exclusion criteria were as following: (a) patients with cognitive impairment or unwilling/incapable to sign the informed consent; (b) patients with prior histories of myocardial infarction; (c) IS of patients occurring in three months before the enrollment; (d) patients with AMI secondary to shock, thrombus or PCI procedure; and (e) patients with malignant tumor.

2.2 Types of treatment and clinical characteristics

After admission to hospital, patients received assess-

ments and basic therapies such as oxygenation, nitroglycerin, antiplatelet drugs (aspirin and/or clopidogrel), low molecular weight heparin (LMWH), angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), β -blockers and statins. The subsequent treatment strategies of CM, PCI or CABG for these patients were chosen mainly at the discretion of the attending cardiologists based on the patients' clinical conditions.

Demographic data (including sex and age), clinical characteristics (including medical history, body mass index, pulse pressure, type of AMI, Killip classification, left ventricular ejection fraction, complications), and laboratory data (complete blood cell, liver and renal function, initial myocardial enzymes) were also collected through reviewing data collected by reviewing paper and electronic medical records.

2.3 Outcome assessments

The indicators for in-hospital outcomes were in-hospital stroke (including acute ischemic stroke and hemorrhagic stroke), all-cause death and cardiocerebral events. After being discharged from the hospital, patients were followed up by interviews via telephone or clinic visits every three months until death, lost to follow-up or March 2012, whichever came first. The indicators for long-term outcomes included recurrence of myocardial infarction and stroke, death, re-admission for cardiogenic reasons and cardiocerebral events.

2.4 Statistical analysis

The demographic data and clinical characteristics of patients were acquired. Categorical variables are expressed as percentages and compared using the Pearson Chi-square test. Continuous variables are expressed as mean \pm SD and compared using student-*t* test.

A logistic regression model was used to analyze the independent effectiveness of CART on in-hospital outcomes of AMI patients with prior IS through adjustment for the main baseline variables related to outcome identified in the univariate analyses. The potential confounding variables included sex, age, duration of cardiovascular disease (CVD), movement disorder after CVD (including paralysis, ataxia, dystonia and involuntary movements), heart rate, pulse pressure (PP), left ventricular ejection fraction (LVEF), time from AMI onset to hospital, arrhythmia, using of ACEI/ARB and β -blocker. Odds ratio (OR) and 95% CI were used to measure the magnitude of association between types of treatment and in-hospital recurrence of cardiocerebral events

The Kaplan-Meier survival curve was used to describe

the long-term mortality between the CART and CM groups. The Cox regression was used to evaluate the independent effectiveness of CART on long-term survival of AMI patients with prior IS. A hazard ratio (HR) and 95% CI measured the magnitude of association between types of treatment and long-term mortality. All analyses were conducted with SPSS 16.0 (SPSS Inc, Chicago, Ill).

3 Results

3.1 Baseline characteristics

Three hundred and eighty seven AMI patients with prior IS were included in this study, 183 of which were in the CM group and 204 patients in the CART group. The baseline characteristics of these patients are shown in Table 1. There were more men in the CART group (73.0%) than in the CM

Table 1. Clinical characteristics, laboratory findings and medications of AMI patients with prior IS by treatment groups.

Variable	CM group (n = 183)	CART group (n = 204)	P value
Clinical characteristics			
Age, yrs	71.7 ± 9.7	66.5 ± 9.7	< 0.001
Male	113 (61.7%)	149 (73.0%)	0.018
Lacunar infarction	98 (53.6%)	132 (64.7%)	0.026
Duration of stroke history, yrs	5.8 ± 5.3	6.1 ± 4.9	0.233
Movement disorder	89 (48.6%)	80 (39.2%)	0.062
Laboratory findings			
BMI, kg/m ²	24.3 ± 3.5	25.3 ± 3.0	0.021
Heart rate, beats/min	82.0 ± 19.6	76.5 ± 17.0	0.004
PP, mmHg	62.13 ± 24.72	56.40 ± 20.50	0.013
LVEF	52.5% ± 12.2%	56.1% ± 9.4%	0.003
Non-STEMI	38 (20.8%)	24 (11.8%)	0.016
Anterior wall involved	85 (46.4%)	103 (50.5%)	0.427
Multiple vascular coronary lesions	25 (69.4%)	101 (50.0%)	0.031
Medications			
ACEI/ARB	140 (76.5%)	155 (76.0%)	0.904
β-blocker	132 (72.1%)	164 (80.4%)	0.056
Statins	153 (83.6%)	176 (86.3%)	0.463
Aspirin	163 (89.1%)	200 (98.0%)	< 0.001
LMWH	108 (59.0%)	152 (74.5%)	0.001
Warfarin	4 (2.2%)	2 (1.0%)	0.585

Data are presented as mean ± SD or n (%). ACEI: angiotensin converting enzyme inhibitor; AF: atrial fibrillation; ARB: angiotensin receptor blocker; BMI: body mass index; CART: coronary artery revascularization therapies; CM: conservative medications; IS: ischemic stroke; LMWH: low molecular weight heparin; LVEF: left ventricular ejection fraction; PP: pulse pressure; STEMI: ST-segment elevation myocardial infarction.

group (61.7%). The average age was 71.7 ± 9.7 years among CM patients and 66.5 ± 9.7 years among CART group. Patients with prior history of lacunar infarction in CM group and CART group, respectively, accounted for 53.6% and 64.7%. The mean duration from AMI onset to admission of CM patients was 16 h, which was much longer than the 6 h of CART patients. There were fewer non ST-segment elevation myocardial infarctions (11.8% vs. 20.8%) and multiple-vascular coronary lesions (50% vs. 69.4%) in the CART group while much more atrial fibrillation (AF) (14.2% vs. 7.4%) in the CM group. Compared to the CM patients, the CART ones had higher BMI (25.3 ± 3.0 vs. 24.3 ± 3.5 kg/m²) and LVEF (56.1% ± 9.4% vs. 52.5% ± 12.2%) but lower HR (76.5 ± 17.0 vs. 82.0 ± 19.6 beats/min) and PP (56.4 ± 20.5 vs. 62.1 ± 24.7 mmHg).

Regarding medication use, use of aspirin (98% vs. 89.1%) and LMWH (74.5% vs. 59%) were much more common in the CART group than in the CM group ($P < 0.01$), while there were no significant difference in using statins, β-blockers or ACEI/ARBs between the two groups ($P > 0.05$).

3.2 In-hospital outcomes

During hospitalization, the incidence of cardiocerebral events in CART group was 9.3% and 26.2% in CM group ($P < 0.01$). There were totally 13 deaths (6.4%) in CART group, 11 of which died of cardiac rupture, pump failure or malignant arrhythmia and two cases died of cerebral hemorrhage. There were 40 deaths (21.9%) in CM group, 37 of which died of cardiac complication, one case died of cerebral hemorrhage and two cases died of recurrence of IS. The incidence of cerebral hemorrhage or IS in the CART group was 4.4% in contrast to 7.1% in the CM group.

The relationship of in-hospital incidence of cardiocerebral events to treatment type and other clinical characteristics are shown in Table 2. Compared to CM, CART significantly reduced the risk of in-hospital cardiocerebral events by 65% (adjusted OR = 0.35, 95% CI: 0.13–0.92;

Table 2. Correlates of in-hospital incidence of cardiocerebral events among AMI patients with IS.

	OR value	95% CI	P value
CART vs. CM	0.35	0.13–0.92	0.034
Duration of stroke history, yrs	0.88	0.78–0.99	0.028
Movement disorder, %	3.25	1.22–8.63	0.018
PP, mmHg	0.96	0.94–0.99	0.003
LVEF, %	0.95	0.91–0.99	0.015
Arrhythmia, yes vs. no	6.60	1.88–23.08	0.003

AMI: acute myocardial infarction; CART: coronary artery revascularization therapies; CM: conservative medications; IS: ischemic stroke; LVEF: left ventricular ejection fraction; PP: pulse pressure.

$P = 0.034$). Other factors that were significantly correlated with an increased risk of in-hospital cardiocerebral events included a shorter duration of stroke history, presence of movement disorder after CVD, lower pulse pressure, lower LVEF and presence of arrhythmia.

3.3 Long-term outcomes

A total of 143 patients from the CM group and 191 from the CART group survived to hospital discharge and were followed up to observe their long-term prognoses. During the follow-up of the CM group, 11 cases (7.7%) were lost to follow-up and five patients were treated with PCI and one with CABG, so they were included in the CART group in analyses. There were 12 cases (6.3%) lost to follow-up from the CART group. The average survival time was 30.8 ± 23.6 months among patients in the CM group and 42.8 ± 24.3 months among patients in the CART group.

Long-term prognoses of AMI patients with previous IS stratified by treatment types are shown in Table 3. By the end of the follow-up, 57 cases (41.6%) died in the CM group, 53 of whom died of cardiac rupture, pump failure or malignant arrhythmia. There were 24 cases (12.2%) deaths in the CART group of which 20 cases died of cardiac rupture, pump failure or malignant arrhythmia. Recurrence of myocardial infarction was much more common in the CM group than in the CART group (28.5% vs. 8.1%), as were heart failure (31.4% vs. 17.8%), re-admission to hospital (45.3% vs. 29.9%), and cardiovascular events (48.2% vs. 17.3%). There was less recurrence of stroke in CART group than that in CM group (4.1% vs. 7.3%).

The long-term outcomes of PCI patients were much better than CABG patients with regards to re-stroke (3.2%

Table 3. Long-term prognoses of AMI patients with previous IS stratified by treatment types.

	CM (<i>n</i> = 137)	PCI (<i>n</i> = 158)	CABG (<i>n</i> = 39)	<i>P</i> value
Male	85 (62.0%)	116 (73.4%)	32 (82.1%)	0.022
Age, yrs	72.0 ± 9.0	66.3 ± 9.8	65.4 ± 9.3	< 0.001
Survival time, months	30.8 ± 23.6	43.0 ± 24.5	42.2 ± 23.8	< 0.001
All-cause mortality	57 (41.6%)	18 (11.4%)	6 (15.4%)	< 0.001
Stroke recurrence	10 (7.3%)	5 (3.2%)	3 (7.7%)	0.222
MI recurrence	39 (28.5%)	11 (7.0%)	5 (12.8%)	< 0.001
HF incidence	43 (31.4%)	27 (17.1%)	8 (20.5%)	0.009
Hospital re-admission	62 (45.3%)	48 (30.4%)	11 (28.2%)	0.008
Cardiocerebral events	66 (48.2%)	26 (16.5%)	8 (20.5%)	< 0.001

Data are presented as mean \pm SD or *n* (%). AMI: acute myocardial infarction; CABG: coronary artery bypass grafting; CM: conservative medications; HF: heart failure; IS: ischemic stroke; PCI: percutaneous coronary intervention.

vs. 7.7%), recurrence of myocardial infarction (7.4% vs. 12.8%) and heart failure (17.1% vs. 20.5%). And the all-cause death in PCI was lower than that in CABG group (11.4% vs. 15.4%).

Figure 1 describes the Kaplan-Meier survival curves by different treatment types. Patients treated with PCI or CABG had much better survival than those treated with CM, and this superiority became evident from the start of follow-up and sustained throughout the study period. In addition, cumulative survival of patients in CABG group appeared better than that in PCI group after the 18th months but the curves overlapped at around the 47th month. After being followed up for 53 months, the cumulative survival in PCI group was better than the CABG and this trend sustained till the end of the study. Overall, there was no statistical difference in cumulative survival between the two groups (Log-rank test $P = 0.557$).

After adjusting for potential confounding variables with the Cox regression model, patients treated with CART had a significantly reduced mortality than those treated with CM (adjusted HR = 0.28, 95% CI: 0.06–0.46; $P < 0.001$). After categorizing the CART patients into patients treated with PCI and CABG, Cox regression indicated that CABG and PCI reduced the long-term mortality by 60% and 75% respectively, (adjusted HR for CABG = 0.40, 95% CI: 0.17–0.94; $P = 0.036$ and adjusted HR for PCI = 0.25, 95% CI: 0.14–0.44; $P < 0.01$) in comparison to CM, and there was no statistically significant different in mortality

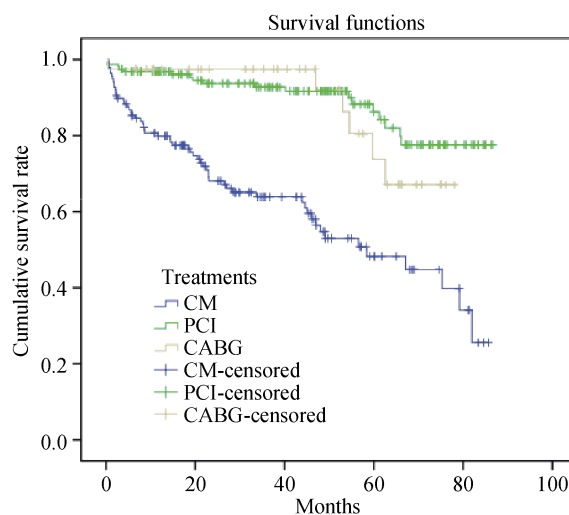


Figure 1. Kaplan-Meier curves of different treatments among AMI patients with prior IS (including patients who were lost to follow-up). AMI: acute myocardial infarction; CM: conservative medications; CABG: coronary artery bypass grafting; HF: heart failure; IS: ischemic stroke; PCI: percutaneous coronary intervention.

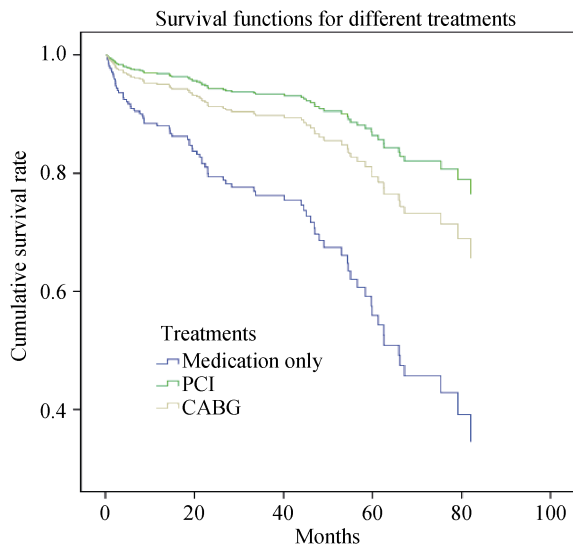


Figure 2. Cox-Regression curves of different treatments among AMI patients with prior IS. AMI: acute myocardial infarction; CABG: coronary artery bypass grafting; IS: ischemic stroke; PCI: percutaneous coronary intervention.

between PCI and CABG (adjusted HR = 0.64, 95% CI: 0.25–1.62; $P = 0.342$) (Figure 2). Other factors that were significantly associated with an increased risk of long-term all-cause mortality included older age (adjusted HR = 1.07, 95% CI: 1.04–1.10; $P < 0.001$) and higher serum creatinine (adjusted HR = 1.01, 95% CI: 1.00–1.11; $P = 0.006$).

4 Discussion

Among the AMI patients with a history of prior IS, we observed that the CART could significantly improve the in-hospital and long-term prognoses. Compared to CM, CART significantly reduced the risk of having in-hospital cardiocerebral events by 65%. After an average follow-up of 36 months, compared with patients treated with CM, patients treated with PCI and CABG had significantly reduced the long-term mortality of all-cause. Difference in survivals between patients treated with PCI and CART was not statistically significant.

Previous studies have shown a definite effectiveness of invasive strategies including PCI and CABG on reducing MI and cardiovascular death among patients with acute coronary syndrome.^[18–20] Primary PCI can save the ischemic cardiac muscle, decrease mortality and reduce recurrence of cardiac ischemia significantly for AMI patients,^[21] and elective PCI can decrease the ischemic onset and improve the recovery of cardiac function by restoring the blood flow to infarction related arteries and other vessels with stenoses.^[22] Similarly, several clinical trials demon-

strated that CABG had superiorities in reducing revascularization of target vessels and major adverse cardiac events for patients with left main coronary artery diseases,^[23] multiple-vessel diseases^[24,25] and impaired left ventricular systolic function.^[26]

Despite the established benefits of revascularization for patients with AMI, the benefits for those with prior IS were seldom assessed, perhaps because AMI patients with prior IS are at higher risk for recurrence of cerebral infarction and death. A study in Korea reported that AMI patients with prior IS had more risk factors such as older age, hypertension and diabetes, more severe complications and higher incidence of cardiac death (adjusted OR = 1.42, 95% CI: 1.14–1.76) and total death (adjusted OR = 1.50, 95% CI: 1.25–1.81) than those without IS.^[27] Similarly, a study in China draw the similar conclusion after a follow-up of 35.0 ± 19.6 months that cardiac death rate (8.5% vs. 3.9%, $P = 0.002$) and re-cerebral infarction rate (5.8% vs. 1.4%, $P < 0.001$) were higher in patients with prior IS than those without IS.^[28] These findings may explain why most clinical trials have excluded those patients and thus, appropriate treatment strategies for these patients have not yet been made so clear.

The finding that revascularization procedures were associated with better prognoses is consistent with the report that medical treatments, especially thrombolytic therapy might increase the risk of hemorrhage among patients with IS. For example, the TRITON-TIMI 38 trial indicated that prasugrel could increase the incidence of hemorrhage (HR = 1.54, $P = 0.04$) for those patient with IS while it can benefit others without IS.^[29]

We found that recurrence of stroke after CABG (8.1%) was higher than PCI (3.4%). This is also reported by other studies in Chinese patients with prior IS. One study indicated that after non-extracorporeal circulation surgery, patients with IS history had delayed recovery time, longer stay in intensive care unit and higher risk for developing stroke and deliria.^[30] Another study reported that patients undergoing CABG compared with PCI had a higher risk of post-operative stroke, probably due to the formation of thrombus and aortic cannulation.^[25] These findings indicated patients undergoing CABG are more liable to have a recurrent stroke during and after the procedure.

Besides treatment types, other factors that were significantly correlated with the risk of in-hospital cardiocerebral events included LVEF, arrhythmia, duration of CVD history and movement disorder after CVD. Prior studies showed that the complications and cardiac ejection function after myocardial infarction could influence the in-hospital prognosis,^[31,32] and our study indicates that both the duration of

stroke history and dyskinesia after the stroke are independent predictors for in-hospital incidence of cardiocerebral events, which has not been reported by previous studies. The reasons may be complex. Patients with a long history of stroke and dyskinesia always have severe clinical conditions, e.g., thrombosis or cerebral embolism. In addition, myocardial infarction always accompanies abnormal coagulation and fibrinolytic function, which can lead to recurrence of stroke especially under the circumstances of poor brain perfusion because of decreased cardiac output or inappropriate use of vascular-dilating drugs.^[33]

There are some limitations in this study. First, it is a non-experimental study in which confounding bias cannot be completely avoided. Even though we measured and adjusted for a variety of clinical characteristics that might determine the treatment choice and predict the study outcomes, residual confounding cannot be ruled out. Second, results in our study may not be widely promoted to other populations because it is a single-center study and when we separated the CRT group, the number of CABG cases was less than the other two groups. Further studies with more study centers, more enrolled patients and longer follow-up are warranted to draw a more definite conclusion.

Acknowledgements

This study was supported by the National Natural Science Foundation of China (81470491). We thank all the staff of the Department of Cardiology in Xuanwu Hospital affiliated to the Capital Medical University for their contribution to this study.

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