

# Impact of Physician-Coordinated Intensive Follow-Up on Long-Term Medical Costs in Patients with Unstable Angina Undergoing Percutaneous Coronary Intervention

Jing-Jing Jia, Ping-Shuan Dong, Lai-Jing Du, Zhi-Guo Li, Li-Hong Lai, Xu-Ming Yang, Shao-Xin Wang, Xi-Shan Yang, Zhi-Juan Li, Xi-Yan Shang and Xi-Mei Fan

**Background:** To investigate the impact of professional physician-coordinated intensive follow-up on long-term expenditures after percutaneous coronary intervention (PCI) in unstable angina (UA) patients.

**Methods:** In this study, there were 669 UA patients who underwent successful PCI and followed up for 3 years, then divided into the intensive follow-up group (N = 337), and the usual follow-up group (N = 332). Patients were provided with detailed discharge information and individualized follow-up schedules. The intensive group received the extra follow-up times and medical consultations, and all patients were followed up for approximately 3 years.

**Results:** At the 3-year mark after PCI, the cumulative major adverse cardiac events (MACE), recurrence of myocardial ischemia, cardiac death, all-cause death and revascularization in the intensive group were lower than in the usual group. Additionally, the proportion of good medication adherence was significantly higher than in the usual group (56.4% vs. 46.1%,  $p < 0.001$ ). The hospitalization daytime, total hospitalization cost and total medical cost in the intensive group were lower. Multiple linear regression showed that diabetes, hypertension, intensive follow-up and good medication adherence were associated with emergency and regular clinical cost ( $p < 0.05$ ), the re-hospitalization cost ( $p < 0.05$ ) and the total medical cost ( $p < 0.05$ ) of patient care. Intensive follow-up and good adherence were negatively correlated with the cost of re-hospitalization (standardized coefficients = -0.132, -0.128,  $p < 0.05$ ) and total medical costs (standardized coefficients = -0.072, -0.086,  $p < 0.05$ ).

**Conclusions:** Intensive follow-up can reduce MACE, improve medication adherence and save long-term total medical costs, just by increasing the emergency and regular clinical visits cost in UA patients after PCI.

**Key Words:** Coronary artery disease • Disease management • Medical cost • Percutaneous coronary intervention

## INTRODUCTION

Coronary artery disease (CAD) accounts for nearly

15% of all deaths worldwide.<sup>1</sup> Due to such an elevated mortality rate, it is apparent that coronary artery disease globally has significant social and economic implications. The economic implications of management of CAD are increasingly important, because the direct and indirect costs of such management are enormous.<sup>2</sup> Expenses related to the treatments for CAD represent a considerable burden for healthcare systems. In the United States, the total medical cost estimated for CAD was US \$204.4 billion in 2010, of which US \$97.2 billion

Received: June 5, 2015 Accepted: May 21, 2016  
Department of Cardiology, The First Affiliated Hospital, and College of Clinical Medicine of Henan University of Science and Technology, Luoyang 471003, China.

Corresponding author: Dr. Ping-Shuan Dong, Department of Cardiology, The First Affiliated Hospital, and College of Clinical Medicine of Henan University of Science and Technology, Luoyang 471003, China. Tel: +86 379 64815776; Fax: +86 379 64815776; E-mail: cnjdoc@126.com

was correlated to the loss of productivity or mortality. By 2030, the costs of CAD are projected to increase by about 100%.<sup>3</sup> Coronary artery revascularisation procedures constitute an important component of the overall health costs of CAD. Increasingly, the troubling short and long-term medical costs of CAD are getting more and more attention.

In the management of CAD, costs were further characterized by: 1) cardiac (or complications related to treatment, drugs or procedures); 2) other CAD and related risk factors (hypertension, diabetes, renal disease, chronic obstructive pulmonary disease); and 3) not CAD or related conditions. There are many parameters affecting the costs of CAD, such as diagnosis, age, sex, socio-economic status, aboriginality, hospital type (public or private), admission type, cardio-protective drug therapy and comorbidity therapy.<sup>4</sup> Furthermore, other potential factors also have a significant impact on the costs of CAD. Altowajri et al.<sup>5</sup> showed that pharmacists can decrease total health care costs through improving CAD risk factor controls and patient outcomes. Choudhry et al.<sup>6</sup> suggested that providing full coverage for combination therapy to post-myocardial infarction medicare beneficiaries would both save lives and reduce cost from the societal perspective. Medicine adherence, major adverse cardiac events (MACE) after procedure can also affect patient health cost and prognosis. To date, an increasing number of factors affecting costs have been reported.

At present, there are few studies in the literature that address the different intervention methods affecting long-term costs of CAD. However, the true relationship between follow-up and medical cost remains uncertain. This research focuses on intensive follow-up for CAD patients with percutaneous coronary intervention (PCI) after discharge by special professional physicians, to explore their impact on costs and also analyze factors related to the costs. This can assist physicians in their therapeutic decisions so that the maximum possible benefit is reached with the lowest possible cost.

## MATERIALS AND METHODS

### Study population

Our research protocol was approved by the ethics

committees of the First Hospital Affiliated to Henan University of Science and Technology. All subjects who attended this study were unstable angina (UA) patients undergoing PCI procedure between Aug. 1, 2010 and Sep. 30, 2011, at the First Affiliated Hospital of Henan University of Science and Technology. Written informed consent was obtained from all participants. All subjects were randomly divided into intensive follow-up group and usual follow-up group. Additionally, all the participants were advised to take anti-platelet therapy (aspirin with concomitant therapy with clopidogrel) and cholesterol lowering statin drugs after PCI. Other medications including  $\beta$ -blockers, angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker, calcium channel inhibitor were recommended when necessary.

Inclusion criteria were patients with UA who underwent PCI procedure in the First Affiliated Hospital of Henan University of Science and Technology.

Major exclusion criteria were: 1) ST-elevation myocardial infarction (STEMI) or non-ST elevation myocardial infarction (NSTEMI) within the last month; 2) severe valvular heart diseases, hypertrophic cardiomyopathy and dilated cardiomyopathy, previous artificial heart valve replacement; 3) severe diseases which affect the survival duration (malignant tumor and renal failure); 4) chronic obstructive pulmonary diseases, pulmonary artery hypertension, right ventricular dysfunction; 5) congestive heart failure (New York Heart Association class III or IV) or left ventricle ejection fraction (LVEF) < 40% according to the echocardiogram; 6) unable to communicate in Chinese language (cognitive impairment or other causes) are excluded; and 7) unable or unwilling to participate in follow-up.

### Data collection and interventions

To participate in this study, the physicians received training. Additionally, each physician held a MBBS (Bachelor of Medicine) degree, with the majority also holding Master of Science in Medical Science degrees. These physicians met all the patients face-to-face, who each signed their informed consent within 1 week after admission. According to the follow-up tables, the physicians filled in the basic information, living and working environments, with noted risk factors including smoking, blood pressure, blood glucose, family history, body-weight and obesity. Physicians collected laboratory data

consisting of total cholesterol (TC), blood triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting blood glucose, and serum creatinine. The height, weight and blood pressure were measured one or two days before discharge.

We adopted a health service perspective and calculated total cost for PCI procedure and overheads, post-procedure services and follow-up expenditure. Medical costs were defined as all medical expenditures after discharge from hospital for PCI intervention, although pre-PCI costs were excluded. These medical costs included the expenditures for emergency and regular clinical visits (lab cost and daily drug cost), and the costs for re-hospitalization. The costs for re-hospitalization contained: 1) costs related to intervention, including operation, disposable material, and stent costs; and 2) clinical support services such as nursing care, therapeutic cost, radiology and laboratory services; the traditional Chinese medicine cost was not included. Cost units were calculated in Yuan (Renminbi, RMB). All patient information was collected from hospital records, and the records of patients and their family or local community doctor. All obtained information was directly filled into the forms, and subsequently entered into a dedicated cardiology database.

Each patient was randomly assigned to one of the two groups blindly, and follow-up appointments were scheduled for individual patients. For the usual follow-up, research nurses contacted the patients by telephone 1, 3, 6, 12 and 36 months after they were discharged from the hospital. For each follow-up, the nurses evaluated the medication adherence, diet, weight and smoking from each patient. At the 12- and 36-month follow-ups, blood pressure, lipid and glucose metabolism data were collected. For intensive follow-up, the special professional physicians contacted the patients regularly by telephone and scheduled face-to-face visits as necessary. At each follow-up, physicians collected the information on diet, weight, smoking, blood pressure, lipid and glucose metabolisms and medication adherence. They also provided additional health education, including consultations on the current treatment and reminded patients to complete the following-up in outpatient clinics after hospital discharge. Physicians also regularly checked patients' hepatic and renal function, blood li-

pids, blood glucose, cardiac ultrasound and electrocardiogram, adjusting medications and providing necessary interventions in view of any abnormal laboratory results.

Three years after PCI, MACE [which is defined as cardiac death, non-fatal acute coronary syndrome (ACS) including UA, STEMI and NSTEMI] and coronary revascularization by PCI were collected. Data regarding patient bleeding events, control of risk factors, and medication adherence were all collected from the hospital records, which were supplemented by records of patients and their family members, and records of local community doctors.

### Definitions

The diagnostic criteria of UA was pathological ST-T changes in resting electrocardiogram, ST-segment depression  $\geq 0.05$  mV during angina attack and normal in remission stage. A positive exercise test is defined as ST-segment depression  $\geq 0.1$  mV (horizontal or downward sloping)  $\geq 2$  min during the activities.

Body mass index (BMI),  $24 \text{ kg/m}^2 > \text{BMI} \geq 18.5 \text{ kg/m}^2$  was normal,  $28 \text{ kg/m}^2 > \text{BMI} \geq 24 \text{ kg/m}^2$  was overweight, and  $\text{BMI} \geq 28 \text{ kg/m}^2$  was defined as obesity.<sup>7</sup> Diabetes mellitus was defined as fasting plasma glucose  $\geq 7.0$  mmol/l or 2 h postprandial blood glucose  $\geq 11.0$  mmol/l, preexisting diagnosis of diabetes mellitus, or use of medications for diabetes. Hypertension was defined as a systolic blood pressure  $\geq 140$  mmHg, diastolic blood pressure  $\geq 90$  mmHg, preexisting diagnosis of hypertension, or use of antihypertensive medications. Smoking was defined as continuous or accumulated smoking for 6 months or more, and smoking cessation was absolutely giving up smoking. Dyslipidemia was defined as TC  $\geq 5.18$  mmol/l (200 mg/dl), or HDL-C  $< 1.04$  mmol/l (40 mg/dl), or LDL-C  $\geq 3.37$  mmol/l (130 mg/dl).<sup>8</sup> Patients with LDL-C  $< 80$  mg/dl during the follow-ups were defined as "LDL-C control", and patients with HDL-C  $\geq 40$  mg/dl during the follow-ups were defined as "HDL-C control".

Selective coronary angiographies were performed via the right or left radial artery according to standard Judkins techniques. The coronary angiography procedures were all performed by experienced interventional physicians. The results were analyzed by at least two interventional physician. More than two vessels of the left anterior descending artery, left circumflex ar-

tery, and right coronary artery with luminal stenosis 50% or more were defined as multi-vessel disease. The left anterior descending artery, left circumflex artery, and right coronary artery with luminal stenosis 50% or more were examined to evaluate the number of stenotic coronary arteries as 1- to 3-vessel disease. If the left main trunk was involved, this was evaluated as a 2-vessel disease by itself.

Medication adherence was measured by Morisky-Green questionnaire.<sup>9</sup> This questionnaire had been widely used to measure medication adherence due to its good quality internal consistency and accuracy.<sup>8,10</sup> The questionnaire contained 4 items: 1) Do you sometimes forget to take your medication? 2) Are you careless at times about taking your medicine? 3) When you feel better, do you sometimes stop taking your medicine? And 4) Sometimes when you feel worse, do you stop taking your medicine? Each 'Yes' answer scored 1 point. Consequently, a score of 0 would suggest that a patient had no problem with medicine-taking and hence good compliance, whereas the maximum score of 4 could indicate major difficulties and suggest poor compliance. In general, good medication adherence is 0-2 score.

Special clinical medical insurance is a cost-sharing strategy, where a patient pays a set percentage of the cost per drug or per prescription after PCI; this represents the national health insurance hospital support mechanism.

### Statistical analysis

The SPSS program (version 16.0, Chicago, IL, USA) was used to perform all statistical analysis. Categorical variables are summarized in terms of frequencies and percentages, and continuous variables in terms of means  $\pm$  standard deviation (SD). The 2 groups of patients were compared in terms of baseline characteristics, using the chi-square test for categorical variables and percentage, and the parametric two-sample t-test for continuous variables. The medical costs were addressed by skew distribution, so this variable was summarized as median value, and the medical costs in the two groups were compared using nonparametric Mann-Whitney U test. Including the variables with supposed clinical relevance into the linear regression equation, residual error was approximately the normal distribution. The multiple linear regression analysis was performed to analyze those

factors that affect the medical cost. All analyses were 2-sided, and significance was established at the 0.05 level.

## RESULTS

### Baseline patient characteristics

We recruited 714 patients who underwent successful PCI. Eighteen patients were lost in the intensive follow-up, and 27 patients were lost in the usual follow-up. Indeed, 669 UA patients who underwent successful PCI and were followed up for 3 years were divided into the intensive follow-up group (N = 337) and the usual follow-up group (N = 332). Ultimately, 669 patients were enrolled in this study. There were no differences in the age, gender, obesity, diabetes mellitus, hypertension, current smoking, previous myocardial infarction, and cerebrovascular disorder between the two groups. Additionally, there was no difference in the number of stenotic coronary arteries, chronic total occlusion (CTO) lesions and left main lesions, number of stents, LVEF and left ventricular end diastolic diameter between the two groups. The plasma biochemistry analysis indicated similar lipid profiles and renal functions between the two groups (Table 1).

### The MACE 3 years after PCI

52 patients died during the 36 months follow-up, including 16 from the intensive follow-up group and 36 from the usual follow-up group. The mean follow-up time was  $1139.9 \pm 340.2$  days, and the two groups showed no difference regarding mean follow-up time ( $1140.1 \pm 333.9$  days in the intensive follow-up and  $1139.6 \pm 347.5$  days in the usual follow-up,  $p = 0.99$ ). Subsequently, 36 months after PCI, the cumulative MACE, recurrence of myocardial ischemia, cardiac death, all-cause death, revascularization and number of readmission were lower than the usual control group ( $p < 0.05$ ) (Table 2).

### The medical cost in 3 years after PCI

3 years after PCI, in the intensive follow-up group, number of readmission, rehospitalization day, the rehospitalization cost, the disposable material and stent cost in hospital and the total medical cost were obviously lower than the usual follow-up group. However,

**Table 1.** Baseline characteristics of study participants \*

	Intensive follow-up (n = 337)	Usual follow-up (n = 332)	p-value
Clinical variables			
Age-yr	61.0 ± 11.0	62.0 ± 10.8	0.22
Female sex – no. (%)	103 (30.6)	104 (31.3)	0.83
Body mass index (kg/m <sup>2</sup> )	25.1 ± 3.0	25.3 ± 3.0	0.53
Obesity – no. (%)	55 (16.3)	59 (17.8)	0.62
Hypertension – no. (%)	131 (38.9)	127 (38.3)	0.87
Systolic BP – mmHg	126.8 ± 22.3	126.8 ± 22.8	0.98
Diabetes – no. (%)	104 (30.9)	98 (29.5)	0.71
Fasting blood glucose – mmol/L	6.4 ± 3.8	6.4 ± 3.8	0.84
Stroke – no. (%)	9 (2.7)	8 (2.4)	0.83
Smoking – no. (%)	197 (58.5)	188 (56.6)	0.63
Angiographic characteristics and procedure			
Single vessel lesion – no. (%)	119 (35.3)	124 (37.3)	0.58
Left main lesion – no. (%)	57 (16.9)	54 (16.3)	0.82
Chronic occluded lesion – no. (%)	13 (3.9)	14 (4.2)	0.81
Average stent number	2.0 ± 0.9	1.9 ± 0.9	0.31
Plasma biochemistry			
Uric acid (μmol/l)	326.1 ± 107.4	321.9 ± 117.0	0.63
Triglycerides (mmol/l)	2.7 ± 1.2	2.7 ± 1.2	0.95
Total cholesterol (mmol/l)	4.7 ± 1.1	4.7 ± 1.1	0.90
HDL-C (mmol/l)	1.1 ± 0.2	1.1 ± 0.2	0.79
LDL-C (mmol/l)	2.8 ± 1.0	2.7 ± 1.0	0.31
Creatinine (mmol/l)	81.7 ± 27.5	81.2 ± 18.4	0.80
LVEDD (mm)	49.7 ± 5.3	49.7 ± 5.9	0.90
LVEF (%)	53.8 ± 7.9	52.3 ± 8.1	0.20
Special clinical – no. (%)	189 (56.9)	190 (56.4)	0.89

\* Plus-minus values are means ± standard deviation.

BP, blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; Special clinical, special disease outpatient service of basic medical insurance.

**Table 2.** Comparison of major clinical endpoints and medical adherence in two groups (36 months) – no. (%)

	Intensive follow-up (n = 337)	Usual follow-up (n = 332)	p-value
Good medication adherence	190 (56.4)	133 (40.1)	< 0.001
MACE			
Recurrent angina	73 (21.7)	104 (31.3)	0.005
Nonfatal myocardial infarction	6 (1.8)	13 (3.9)	0.10
Coronary revascularization	10 (3.0)	24 (7.2)	0.01
Cardiovascular mortality	13 (3.9)	31 (9.3)	0.004
All-cause mortality	16 (4.7)	36 (10.8)	0.003
Bleeding			
Minimal/minor	17 (5.0)	24 (7.2)	0.24
Major	8 (2.4)	12 (3.6)	0.35

MACE, major adverse cardiac events.

emergency and regular clinical cost was higher (Table 3).

### Factors related to the medical cost

Variables in the model included age, gender, BMI, special clinical medical insurance, coronary artery lesions (single vessel lesions, CTO lesions and left main lesions), number of stents, hypertension, diabetes mellitus, current smoking, dyslipidemia (TC increase, LDL-C increase, HDL-C decrease), and medication adherence with supposed clinical relevance were entered into the linear regression equation. The rehospitalization cost, emergency and regular clinical cost, and the total cost after first PCI were the dependent variables, respectively. Thereafter, the step-by-step procedure was performed. The residual error was approximate normal distribution, which revealed that the dependent variable was a fit for the regression model. For the emergency and regular clinical cost, the obviously significant factors

**Table 3.** Cardiac rehospitalization and clinical/emergency cost of two groups

	Intensive follow-up (n = 337)			Usual follow-up (n=332)			p-value
	25%	Median	75%	25%	Median	75%	
Cardiac rehospitalization – no. (%)		54(16.0)			79 (23.8)		0.012
Hospitalization day*	7	9	15	9	11	15	0.019
Total hospitalization cost (USD) <sup>#</sup>	1312.4	1642.2	2955.5	1720.2	3249.0	7241.0	< 0.001
Therapeutic cost (USD)	50.0	119.0	331.6	89.8	225.0	429.5	0.080
Interventional operation cost (USD)	204.5	272.6	283.4	272.6	272.6	5213.8	0.007
Lab cost (USD)	238.5	276.1	348.1	238.5	273.1	326.2	0.973
Drug cost (USD)	253.4	334.8	484.2	325.3	409.9	636.3	0.962
Clinical/emergency cost (USD) <sup>†</sup>	2520.6	3296.1	3719.4	2396.6	3101.0	3536.7	0.001
Drug cost (USD)	2196.3	2799.4	3223.9	2145.4	2678.3	3096.6	0.003
Lab cost (USD)	287.0	492.2	537.3	222.7	382.7	513.8	< 0.001
Total medical cost (USD) <sup>‡</sup>	4090.9	4994.4	7221.5	4392.0	5994.1	10116.7	0.020

\* Quartile of rehospitalized patients'; # Quartile of rehospitalized patients'; † Quartile of all patients'; ‡ Total medical cost = both clinical/emergency cost and total hospitalization cost; USD, the United States dollars.

according to the absolute value of standard partial regression coefficient were diabetes mellitus, hypertension, intensive follow-up, medication adherence and HDL decrease, whether MACE was excluded or included (Table 4, 5). For the total medical cost and total rehospitalization cost after PCI, the obviously significant factors were diabetes mellitus, hypertension, intensive follow-up and medication adherence with MACE excluded. When MACE was included, diabetes mellitus, hypertension, MACE and intensive follow-up were related to the total rehospitalization cost. However, diabetes mellitus, hypertension and MACE were related to the total medical cost. For intensive follow-up, medication adherence was negatively correlated with the rehospitalization cost and the total medical cost after first PCI. This ultimately revealed that good medication adherence and intensive follow-up can potentially lead to a decrease in medical cost.

## DISCUSSION

To our knowledge, this is the first prospective randomized controlled study to demonstrate the impact of professional physician-coordinated intensive follow-up on the long-term medical cost of PCI in UA patients in China. Intensive follow-up can reduce MACE and long-term total medical cost, but also increase the emergency and regular clinical visits cost. Moreover, we also revealed that risk factors such as hypertension, diabetes

mellitus and medication adherence were closely related to the medical cost. In clinical treatment, it appears that intensive follow-up can facilitate risk factor management, reduce total medical cost and improve patient prognosis.

The clinical treatment of CAD involves not only the use of anti-platelet agents and statins, but also  $\beta$ -blockers, ACEI, nitrates and non-pharmacological measures such as diet, smoking cessation, weight control and regular physical activity. They all have a noteworthy significance on medical cost.<sup>11</sup> The complexity of measuring all these treatments and their impact on costs is an important issue to be considered when interpreting the results of studies which compare different strategies.

Medical costs were defined as all the medical expenditures after discharge from hospital for PCI intervention. They included the expenditures for emergency and regular clinical visits cost (lab cost and daily drug cost), related exams and the costs for re-hospitalization. The disposable material and stent cost is the main portion in the total hospitalization cost. The total hospitalization and total medical costs in the intensive follow-up group were lower than in the usual group, and the significance was obvious. However, the cost of emergency and regular clinical visits (lab cost and daily drug cost) was higher, and the hospitalization day was shorter. The reasons for the differences between two groups may depend upon the medication adherence, risk factors control and MACE incidence. The better the medication adherence, the higher the emergency and regular clinical

**Table 4.** Multiple linear regression analysis of the medical cost

	Clinical/emergency cost				Total rehospitalization cost				Total medical cost			
	Adjusted R square	p value	Standardized coefficients	p value	Adjusted R square	p value	Standardized coefficients	p value	Adjusted R square	p value	Standardized coefficients	p value
Diabetes mellitus	0.132	< 0.001	0.376	< 0.001	0.077	< 0.001	0.226	< 0.001	0.189	< 0.001	0.388	< 0.001
Intensive follow-up	0.153	< 0.001	0.128	< 0.001	0.100	< 0.001	-0.132	< 0.001	0.219	< 0.001	-0.072	0.04
Hypertension	0.169	< 0.001	0.140	< 0.001	0.114	0.001	0.120	0.001	0.227	0.005	0.177	< 0.001
Good medical adherence	0.174	0.021	0.090	0.02	0.126	0.001	-0.128	0.001	0.231	0.04	-0.086	0.02
Low HDL-c level	0.179	0.036	0.074	0.04								

HDL-C, high density lipoprotein cholesterol.

**Table 5.** Multiple linear regression analysis after adjusted MACE

	Clinical/emergency cost				Total rehospitalization cost				Total medical cost			
	Adjusted R square	p value	Standardized coefficients	p value	Adjusted R square	p value	Standardized coefficients	p value	Adjusted R square	p value	Standardized coefficients	p value
Diabetes mellitus	0.132	< 0.001	0.377	< 0.001	0.322	< 0.001	0.200	< 0.001	0.189	< 0.001	0.365	< 0.001
Intensive follow-up	0.222	0.002	0.109	0.002	0.339	0.02	-0.077	0.02				
Hypertension	0.20	< 0.001	0.141	< 0.001	0.335	< 0.001	0.115	< 0.001	0.361	< 0.001	0.174	< 0.001
Low HDL-c level	0.227	0.03	0.073	0.03								
MACE	1	< 0.001	-0.277	< 0.001	0.279	< 0.001	0.486	< 0.001	0.332	< 0.001	0.380	< 0.001

HDL-C, high density lipoprotein cholesterol; MACE, major adverse cardiac events.

visits cost; however, the MACE incidence was lower. Though the follow-up costs (lab cost and daily drug cost) were high in the intensive follow-up group, the risk factors were well controlled. This may be attributed to the use of a special physician which allows for closer disease status monitoring, a more timely and professional adjustment of medications, thus avoiding more severe outcomes. Stukel et al. showed<sup>12</sup> that higher prescription medication costs among those who adhered well to their medications were more than offset by medical cost reductions from decreased emergency room use and hospitalizations, leading to a net reduction in overall health care costs.

The number of cumulative MACE, cardiac death, nonfatal myocardial infarction and coronary vessel revascularization in 3 years in the intensive follow-up group was significantly lower than in the usual follow-up

group; there, the patient adherence to medication regimen was good. MACE and medication adherence may be the main factors that affect long-term costs. The GOSPEL study<sup>13</sup> demonstrated that a multifactorial, continually reinforced intervention up to 3 years after rehabilitation following MI is effective in decreasing the risk of several important cardiovascular outcomes, although the overall effect is small. Li et al.<sup>14</sup> showed that the direct and active involvement of cardiologists in secondary prevention in patients after PCI can reduce the cardiovascular risk factors and MACE rate. Indeed, intensive follow-up can improve the medication adherence and prognosis, which may ultimately reduce medical costs.

The existing research shows that hypertension, diabetes mellitus, intensive follow-up and medication adherence have an impact on medical cost. Generally,

medical costs correspond to three items of expenditure: hospitalization (for invasive treatment and/or care of complications of the disease), outpatient care (medical visits, radiological and biological tests, etc.) and outpatient medications (anti-platelet drugs, anti-anginal drugs, etc). The MACE incidence is the most important factor that affects the total medical cost for involving the readmission. When we exclude MACE, medication adherence, intensive follow-up and risk factors, hypertension and diabetes mellitus were closely related to the total medical and total rehospitalization cost. Choudhry et al.<sup>1</sup> indicated that the cost savings from clinical events that are avoided by improved medication adherence may more than offset the incremental cost of full drug coverage and full coverage for post-myocardial infarction secondary prevention therapies, and would result in greater functional life expectancy (0.35 quality-adjusted life-year) and less resource use (\$2500).<sup>6</sup> Cost analysis will be undertaken to assess the impact of factors such as diagnosis, age, sex, socio-economic status, aboriginality, hospital type (public or private), admission type, cardioprotective drug therapy and comorbidity on the total cost of care.<sup>4</sup> Mann et al. showed<sup>16</sup> that in patients aged 65 or older with hypertension, hypercholesterolemia, and/or diabetes, medication insurance increased the odds of adherence to guideline-recommended medications by 19-136% compared to those without drug insurance coverage. However, this study showed that special clinical medical insurance was not related to the emergency and regular clinical visits (lab cost and daily drug cost). The reason may be that the medical insurance in our country is diverse yet unified, and the cost-sharing strategies of medical insurance is also a small part of the total patient healthcare cost equation. In China, medical insurance is divided into basic medical insurance, new-type rural cooperative medical insurance system, commercial insurer, people's self-pay insurance and insurance purchased through the expense of the public. Different medical insurance strategies typically determine the total medical cost after discharge. There are many other factors affecting the medical cost of CAD patients after PCI. Low adherence could be explained by a lack of adjustment for comorbidities, because these patients had a wide range of comorbidities with high hospitalization rates.<sup>17-19</sup> Compared to other studies, our intensive follow-up program is coordi-

nated by profession physicians. This allows a closer monitoring of disease status, a more timely and professional adjustment of medications, which led to the decrease of total medical cost.

Similarly, medical cost also affects patient medication adherence and prognosis. Cubanski et al.<sup>20</sup> showed that even with the advent of prescription drug coverage under Medicare, patients face substantial cost sharing through tiered copayments and a coverage gap or "doughnut hole," so out-of-pocket costs may reduce the use of prescribed medication. Heisler et al.<sup>21</sup> found that hospitalization rates among middle-aged and older adults with cardiovascular disease who reported restricting medication use significantly increased due to cost. Tuppin et al.<sup>22</sup> showed that nonadherence to evidence-based pharmacotherapy is associated with a marked increase in all-cause mortality and readmission for ACS. Cost-effective strategies for adherence improvement should be developed among patient groups with poor adherence.

#### Limitation

This study was a single-center study, thus reflecting the patients in our specific district (Luoyang, Henan Province), rather than the total population in China. The medication adherence relating to a specific drug, including antiplatelet, cholesterol lowering and blood pressure lowering drugs have not previously been compared between the two groups. There are problems dealing with censored data (patients who die do not continue to incur costs) and the nature of cost accrual, which is irregular and may depend upon different factors at different times. In this study, the follow-up cost of the physician is free, and the travel and accommodation fee was undertaken by patients. The stents used by patients were all drug-eluting stents, which were made in China.

#### CONCLUSIONS

Intensive follow-up can reduce MACE and long-term total medical cost, though there would be a corollary increase in the emergency and regular clinical visit cost. Moreover, we also revealed that risk factors such as hypertension, diabetes mellitus and medication adherence were related to the medical cost. In conclusion, inten-

sive follow-up can lead to enhanced management of patient risk factors, and lead to reduced medical cost and improved prognosis.

## ACKNOWLEDGEMENTS

This study was supported by The Program for Science and Technology Innovation of the Henan Province, China (#112102310142).

## CONFLICTS OF INTEREST

All of the authors declare that they have no conflicts of interest regarding this paper.

## REFERENCES

- de Waure C, Lauret GJ, Ricciardi W, et al. Lifestyle interventions in patients with coronary heart disease: a systematic review. *Am J Prev Med* 2013;45:207-16.
- Scudeler TL, Rezende PC, Hueb W. The cost-effectiveness of strategies in coronary artery disease. *Expert Rev Pharmacoecon Outcomes Res* 2014;14:805-13.
- Go AS, Mazaffan D, Roger VL, et al. Heart disease and stroke statistics--2014 update: a report from the American Heart Association. *Circulation* 2014;129:e28-292.
- Gardner C, Rankin JM, Geelhoed E, et al. Evaluation of long-term clinical and health service outcomes following coronary artery revascularisation in Western Australia (WACARP): a population-based cohort study protocol. *BMJ Open* 2014;4:e006337.
- Altowajri A, Phillips CJ, Fitzsimmons D. A systematic review of the clinical and economic effectiveness of clinical pharmacist intervention in secondary prevention of cardiovascular disease. *J Manag Care Pharm* 2013;19:408-16.
- Choudhry NK, Patrick AR, Antman EM, et al. Cost-effectiveness of providing full drug coverage to increase medication adherence in post-myocardial infarction Medicare beneficiaries. *Circulation* 2008;117:1261-8.
- Joint Committee for Developing Chinese guidelines on Prevention and Treatment of Dyslipidemia in Adults. Chinese guidelines on prevention and treatment of dyslipidemia in adults. *Zhonghua Xin Xue Guan Bing Za Zhi* 2007;35:390-419.
- Knobel H, Alonso J, Casado JL, et al. Validation of a simplified medication adherence questionnaire in a large cohort of HIV-infected patients: the GEEMA Study. *AIDS* 2002;16:605-13.
- Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;24:67-74.
- Kirchberger I, Meisinger C, Seidl H, et al. Nurse-based case management for aged patients with myocardial infarction: study protocol of a randomized controlled trial. *BMC Geriatr* 2010;10:29.
- Thomas D. Smoking and cardiovascular diseases. *Rev Prat* 2012;62:339-43.
- Stukel TA, Fisher ES, Alter DA, et al. Association of hospital spending intensity with mortality and readmission rates in Ontario hospitals. *JAMA* 2012;307:1037-45.
- Giannuzzi P, Temporelli PL, Marchioli R, et al. Global secondary prevention strategies to limit event recurrence after myocardial infarction: results of the GOSPEL study, a multicenter, randomized controlled trial from the Italian Cardiac Rehabilitation Network. *Arch Intern Med* 2008;168:2194-204.
- Li FX, Zhao Y, Zhao HQ. Effect of different ways of follow up on patients with primary percutaneous coronary intervention treatment. *Shanxi Med J* 2008;12:1617-9.
- Choudhry NK, Avorn J, Antman EM, et al. Should patients receive secondary prevention medications for free after a myocardial infarction? An economic analysis. *Health Aff (Millwood)* 2007;26:186-94.
- Mann BS, Barnieh L, Tang K, et al. Association between drug insurance cost sharing strategies and outcomes in patients with chronic diseases: a systematic review. *PLoS One* 2014;9:e89168.
- Ho PM, Magid DJ, Shetterly SM, et al. Medication nonadherence is associated with a broad range of adverse outcomes in patients with coronary artery disease. *Am Heart J* 2008;155:772-9.
- Jackevicius CA, Li P, Tu JV. Prevalence, predictors, and outcomes of primary nonadherence after acute myocardial infarction. *Circulation* 2008;117:1028-36.
- Winkelmayer WC, Charytan DM, Levin R, Avorn J. Poor short-term survival and low use of cardiovascular medications in elderly dialysis patients after acute myocardial infarction. *Am J Kidney Dis* 2006;47:301-8.
- Cubanski J, Neuman P. Status report on Medicare Part D enrollment in 2006: analysis of plan-specific market share and coverage. *Health Aff (Millwood)* 2007;26:w1-12.
- Heisler M, Choi H, Rosen AB, et al. Hospitalizations and deaths among adults with cardiovascular disease who underuse medications because of cost: a longitudinal analysis. *Med Care* 2010;48:87-94.
- Tuppin P, Neumann A, Danchin N, et al. Evidence-based pharmacotherapy after myocardial infarction in France: adherence-associated factors and relationship with 30-month mortality and rehospitalization. *Arch Cardiovasc Dis* 2010;103:363-75.