Using a standardized follow-up program to improve coronary heart disease secondary prevention

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Abstract

Objective: To reveal the current status and effectiveness of a standardized follow-up of the secondary prevention of coronary heart disease (CHD) at Peking University First Hospital.

Methods: The study group comprised 496 patients diagnosed with CHD between January 1, 2007 and December 31, 2009 after a standardized follow-up program began. A group of 300 patients with CHD diagnosed between January 1, 2004 and December 31, 2004 was evaluated as the control group. The study group participants were followed-up every 3 months for 1 year in the outpatient department and were interviewed by telephone between November 2012 and January 2013. Data on the control of risk-factors, medical therapy, and clinical events were collected.

Results: At discharge, 75.4% of the study group patients were non-smokers, 51.4% exercised regularly, 42.4% were overweight, 56.7% had blood pressure <140/90 mm Hg (<130/80 in those with diabetes mellitus), 51% had serum low-density-lipoprotein cholesterol <2.60 mmol/L, and 64.2% had fasting plasma glucose <6.11 mmol/L. Antiplatelet medication was used by 99.4% of the study group patients, angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers by 64.5%, beta-blockers by 79.1%, and statins by 94.3%. Major adverse cardiac events, the primary clinical outcome, occurred in 22.7% of the study group patients. The proportions of non-smokers (82.2% vs. 73.7%, p=0.014), control of serum lipids (84.4% vs. 45.6%, p<0.001), and use of statins (92.5% vs. 54.3%, p<0.001) at the end of follow-up were significantly greater in the study group than those in the control group.

Conclusion: Although some patients with CHD were still not achieving the goals of lifestyle change, control of risk factors, and medication therapy, standardized follow-up helped improve and standardize CHD secondary prevention. *(Anatol J Cardiol 2016; 16: 84-91)*

Keywords: coronary heart disease, secondary prevention, standardized management

Introduction

In 1995, the American Heart Association (AHA) published the first consensus panel statement on the prevention of heart attack and death in patients with coronary disease. Additional evidence from clinical trials was the impetus to update the original recommendations in 2001, 2006, and 2011. The statement emphasizes that aggressive risk factor management clearly improves patient survival, reduces recurrent events and the need for interventional procedures, and improves patients' quality of life (1). Appropriate medical management, including the correct use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin-receptor antagonists, and statins, provides significant benefits for patients with coronary heart disease (CHD) (2-4).

The secondary prevention of CHD has advanced because of the unremitting efforts of physicians and scientists, but it is still far from perfect. EUROASPIRE III, the Clinical Pathways for Acute Coronary Syndromes in China, and other clinical trials have revealed a significant gap between evidence-based guidelines and clinical practice (5, 6). A number of clinical projects across Europe and America suggested that the adoption of existing guidelines in clinical practice improves the control of risk factors and patient prognosis and adherence to medications (7-10).

In China, the secondary prevention of CHD and efforts to improve the application of practice guidelines are not adequate. The eleventh 5-year national key technologies R&D program for CHD-coronary heart disease secondary prevention research began in 2007 because few projects to intensify the application guidelines were implemented. The study was approved by Ethics Committee of our institute. This study investigated the current state of CHD secondary prevention in 19 tertiary hospitals in China. The aim was to standardize the management of

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CHD secondary prevention and to improve system-wide adherence to secondary prevention guidelines and regular follow-up. Our study population came from Peking University First Hospital, which is one of the 19 tertiary hospitals.

Methods

Study population

For the post-standardized follow-up, 496 study participants were recruited from a patient population diagnosed with CHD at Peking University First Hospital between January 1, 2007 and December 31, 2009. The participants had to fulfill one or more of the following inclusion criteria: (1) history of confirmed acute myocardial infarction, (2) coronary angiography showing greater than 50% stenosis of the coronary artery or its main branches, (3) typical symptoms of exertional angina with ECG ischemic change, or (4) positive exercise ECG stress test. All the participants signed an informed consent for follow-up. A group of 300 patients who were diagnosed with CHD between January 1, 2004 and December 31, 2004 at the Peking University First Hospital and who fulfilled the study inclusion criteria were evaluated as the control group.

Standardized management measures

Physicians who were responsible for the care of patients with CHD were trained to follow the AHA/ACC guidelines (2006 update) for secondary prevention in patients with coronary and other atherosclerotic vascular diseases. A questionnaire was used to evaluate the participants' knowledge on CHD secondary prevention. The participants were given a series of patient education courses on CHD to increase their knowledge on their disease. The study participants visited the hospital outpatient department for follow-up evaluation every 3 months for 1 year. The follow-ups were appointed and reminded by specialized nurses. The follow-up evaluation included a medical history review, physical examination [including height, weight, and systolic and diastolic blood pressure (SBP and DBP, respectively)], and biochemical testing [total cholesterol (TCHO), total triglycerides (TG), low- and high-density lipoprotein cholesterol (LDL-C and HDL-C, respectively), fasting blood glucose (FBG), and glycated hemoglobin A1c (GHbA1c) levels]. At each follow-up visit, the assessment of lifestyle interventions and medications were conducted.

Measurement of physical examination and biochemical variables

After resting for at least 10 min, office blood pressure (BP) was measured three times in a sitting position with the desktop mercury column sphygmomanometer. The time interval between each measurement was 2 min. The average of three BP values was calculated and used for analysis.

Blood samples were drawn from each subject after fasting for at least 12 h and an overnight rest. FBG level was measured using the oxygen electrode method; TCHO level was measured using the cholesterol oxidase method; TG level were measured using the enzymatic method; HDL-C and LDL-C levels were directly measured using the clearance method. Beckman Coulter Unicel DxC 800 was used. GHbA1c level was measured using high-performance liquid chromatography.

Data collection

A review of the hospital medical records of each participant was conducted on admission and discharge, and the following information was collected: (1) personal details, (2) risk factors of CHD, (3) personal history of CHD, (4) other medical history, (5) status of risk factor control, and (6) medical therapy.

At each follow-up visit to the outpatient department, information about the patients' (1) clinical events, (2) control of CHD risk factors, and (3) medical therapy was updated. A final follow-up interview was conducted by telephone between November 2012 and January 2013.

Definitions and outcomes

The goals of secondary prevention of CHD included 1) complete non-smoking: never smoked or stopped smoking for at least 3 months, 2) ≥30 min of moderate-intensity aerobic activity such as brisk walking per day and ≥5 days per week: patients reported their physical activity mode and duration by themselves, 3) weight management resulting in a body mass index (BMI) >18.5 kg/m^2 and <25.0 kg/m^2, 4) BP<140/90 mm Hg (or <130/80 mm Hg if the patient has diabetes or chronic kidney disease), 5) FBG <6.11 mmol/L in patients with diabetes, and 6) LDL-C<2.6 mmol/L. The major adverse cardiac events (MACE) that included the following: 1) death from all causes, 2) nonfatal myocardial infarction, 3) nonfatal stroke, 4) coronary revascularization, and 5) readmission for cardiovascular reasons.

Statistical analyses

The significance of differences in continuous data was determined by the t test, Mann–Whitney U test, or Wilcoxon test. Categorical data was analyzed with the χ^2 or McNemar test. Cox proportional hazards models were constructed by standard statistical tests on proportionality adjusted for age, gender, weight, hypertension, hyperlipidemia, diabetes mellitus, and heart failure. Statistical significance was defined as a two-tailed $p<0.05$. All statistical analyses conducted done using SPSS 20.0 statistical software.

Results

Participant characteristics

Of the 496 patients enrolled, 360 were male (72.6%), and the mean±SD age was 63.5±10.2 years (range, 24-85 years). The average duration of follow-up was 4.6 years (range, 3.5-6.0 years). Furthermore, 68.4% had a history of hypertension, and 38.7% had a history of diabetes mellitus.

Baseline of secondary prevention of CHD at discharge

Information on CHD risk factors and cardioprotective medicine use at discharge is shown in Table 1. Overall, 56.3% of the participants had a history of smoking, and 24.6% were still smoking at discharge. Most smokers (92.1%) were male. Although 76.8% of the participants knew about the risks of tobacco, more than 25.8% of them did not stop smoking.

Monitoring indices

Changes in the major surveillance indices are shown in Table 2. Some indices, including BMI, SBP, and DBP and FBG, GHbA1c, and TG levels, did not change significantly during follow-up. The average TCHO and LDL-C levels were lower than they were at discharge during both short- (≤6 months) and long-term (≥12 months) follow-up. Increase in the average HDL-C level was observed at 3 months, 6 months, 9 months, and 1 year; the HDL-C level at the last interview was not different from that at discharge.

Risk factors

Changes in the risk factor control rates are shown in Table 3. The numbers and percentages of participants who achieved the control rate goals for BP and lipids gradually increased after discharge. The control rate of diabetes mellitus significantly increased at the short-term follow-up compared with the rate at discharge, but at the long-term follow-up (i.e., 12 months and the last interview), it did not improve over the discharge value. As for the bigger picture, the proportions of participants who achieved the following control goals at each follow-up were BMI 23.1%, BP 28.6%, lipid 52.9%, and glucose 44.4%.

Medication use

Changes in medication use are shown in Table 3. The usage rates of all drugs were the highest from discharge to the third month and decreased during follow-up, but these differences were not significant. We found that 12.3% of the patients with hypertension did not take their pills regularly.

Prognosis and predictors

After the last follow-up at 3.5–6.0 years, the outcomes were as follows: cardiac death occurred in 0.7% of the participants, death from all causes in 3.0%, nonfatal myocardial infarction in 1.7%, and nonfatal stroke in 2.0%. Coronary revascularization was conducted in 8.3% of the participants, readmission for cardiovascular reasons in 20.0%, and MACE in 22.7%.

Cox proportional hazards models were constructed by standard statistical tests on proportionality adjusted for potential predictors of prognosis, including age, gender, overweight/obesity, hypertension, hyperlipidemia, diabetes mellitus, and clinical heart failure. The results are shown in Table 4. The significant predictors of MACE included male gender (HR 0.417, 95% CI 0.235-0.740, p=0.003), younger age (HR 0.417, 95% CI 0.191-0.910, p=0.028), hyperlipidemia (HR 0.399, 95% CI 0.227-0.700, p=0.001), clinical heart failure (HR 4.946, 95% CI 1.658-14.754, p=0.004). The participants with male gender, younger age, and hyperlipidemia had a lower incidence of MACE, whereas those with clinical heart failure had a higher incidence of MACE. We analyzed the data of participants and found that there was no significant difference in the risk factor control rates and usage rates of drugs between participants with and without MACE.

Table 1. Baseline of secondary prevention at discharge

	Total n=496	Male n=360	Female n=136	*P*
Monitoring indicators				
BMI, kg/m^2	25.5±3.2	25.6±3.0	25.2±3.7	0.198
SBP, mm Hg	128.5±17.2	127.9±17.1	130.2±17.5	0.223
DBP, mm Hg	75.4±10.4	76.1±10.5	73.4±10.1*	0.049
FBG, mmol/L	5.98±1.65	5.94±1.66	6.09±1.65	0.534
GHbA1c, %	6.8±1.1	6.9±1.1	6.8±1.0	0.768
TCHO, mmol/L	4.10±0.96	4.01±0.91	4.33±1.05*	0.010
TG, mmol/L	1.56±1.09	1.57±1.17	1.56±0.85	0.251
LDL-C, mmol/L	2.43±0.75	2.41±0.75	2.47±0.78	0.487
HDL-C, mmol/L	1.07±0.26	1.03±0.22	1.19±0.30**	<0.001
Control rate of risk factors, %				
Non-smoking	75.4	68.9	92.9**	<0.001
Physical activity	51.5	52.3	49.2	0.545
BMI	42.4	41.6	44.5	0.576
BP	56.7	58.1	53.0	0.353
Lipid	66.1	66.5	64.8	0.743
Glucose	64.2	66.2	59.0	0.204
Medication use rate, %				
ACEI/ARB	64.5	65.5	61.9	0.459
β-blocker	79.1	80.5	75.4	0.213
Antiplatelet medication	99.4	99.4	99.3	0.819
Lipid-lowering drug	94.3	93.2	97.0	0.108

*Females compared with males, *P*<0.05; **Females compared with males, *P*<0.01.
Data on monitoring indicators are expressed as means±SD.
ACEI/ARB - angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers; BMI - body mass index; BP - blood pressure; DBP - diastolic blood pressure; FBG - fasting blood glucose; GHbA1c - glycated hemoglobin A1c; HDL-C - high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; SBP - systolic blood pressure; TCHO - total cholesterol; TG - triglycerides

Impact of standardized management on CHD secondary prevention

A group of 300 patients diagnosed with CHD in 2004 was reviewed as the pre-standardized follow-up control group for comparison with the study population (Table 5).

There was no difference in the average age between the two groups. In the post-standardized follow-up group, the rates of non-smokers (82.2% vs. 73.7%, p=0.014), control of serum lipids (84.4% vs. 45.6%, p<0.001), and rate of statin use increased significantly (92.5% vs. 54.3%, p<0.001).

Table 2. Change of monitoring indices

Index	At discharge	3 months	6 months	9 months	1 year	Last interview
BMI, kg/m^2	25.5±3.2	25.4±3.3	25.6±3.2	26.0±3.2**	25.8±3.3	25.6±3.6
SBP, mm Hg	128.5±17.2	130.1±17.3	128.6±18.3	130.2±17.6*	129.5±15.9	126.7±12.3
DBP, mm Hg	75.4±10.4	75.9±10.4	75.2±10.0	74.7±10.7	74.5±10.5	75.4±9.1
FBG, mmol/L	5.98±1.65	6.02±1.60	5.74±1.15	5.88±1.43	6.42±2.35	6.33±1.65
GHbA1c, %	6.8±1.1	6.1±0.7	6.2±0.7	6.2±1.2	6.5±1.6	6.5±0.9
TCHO, mmol/L	4.10±0.96	3.88±0.81**	3.97±0.94**	4.03±0.86*	4.09±0.77	3.80±0.86
TG, mmol/L	1.56±1.09	1.53±0.85	1.53±0.72	1.43±0.61	1.42±0.72	1.43±1.03
LDL-C, mmol/L	2.43±0.75	2.16±0.58**	2.23±0.68**	2.31±0.73**	2.33±0.66	2.02±0.58**
HDL-C, mmol/L	1.07±0.26	1.14±0.42**	1.16±0.29**	1.19±0.32**	1.18±0.31**	1.10±0.31

*Compared with indices at discharge, $P<0.05$; **Compared with indices at discharge, $P<0.01$
Data on surveillance indices are expressed as means±SD
BMI - body mass index; DBP - diastolic blood pressure; FBG - fasting blood glucose; GHbA1c - glycated hemoglobin A1c; HDL-C - high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; SBP - systolic blood pressure; TCHO - total cholesterol; TG - triglycerides

Table 3. Change of risk factor control rates and medication use rates

	At discharge	3 months	6 months	9 months	1 year	Last interview
Risk factor control rate,%						
Non-smoking	75.4	NE	NE	NE	NE	82.2
Physical activity	51.4	NE	NE	NE	NE	49.3
BMI	42.4	42.6	41.0	37.7	38.9	41.4
BP	56.7	64.2	64.7	50.4*	65.0	77.8**
Lipid	66.1	79.4**	80.6**	75.7**	72.7	84.8**
Glucose	64.2	70.0**	77.1**	74.8	58.3	56.8
Medication, %						
ACEI/ARB	64.5	64.7	64.3	68.6	60.4	55.4
β-blocker	79.1	81.8	80.7	81.0	74.3	73.9
Antiplatelet	99.4	99.6	99.5	96.4	99.2	95.7
Lipid lowering	94.3	94.1	94.4	90.5	94.1	92.5

*Compared with rate at discharge, $P<0.05$; **Compared with rate at discharge, $P<0.01$
ACEI/ARB - angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers; BMI - body mass index; BP - blood pressure; NE - not evaluated

Discussion

Current status of CHD secondary prevention

Even in the post-standardized follow-up group, some patients did not achieve the lifestyle and risk factor control goals recommended in the 2006 AHA guidelines. More than half the study participants had a history of smoking, and nearly a quarter of them continued to smoke after experiencing cardiovascular events. At the end of the follow-up, one-fifth of the participants were smokers. Possible reasons for not quitting smoking were as follows: 1) the smoking habit was strongly addictive both pharmacologically and psychologically, 2) participants did not have complete knowledge on the benefits of smoking cessation, 3) professional counseling and pharmacological smoking cessation aids were unavailable for most smokers, and 4) there are few policies on tobacco control in China at present. We should pay more attention to health education so that more patients learn the dangers of smoking. At the same time, access to professional counseling and pharmacological aids on smoking cessation should be made more readily available (11, 12).

Obesity can cause left ventricular hypertrophy and diastolic dysfunction, increase insulin resistance, and reduce carbohydrate and fat metabolism (13). Overweight/obesity increases the risk of cardiovascular events. In our study, more than half of the participants were overweight, and over one-third of them were obese. Healthy dietary habits and regular exercise are important for the control of weight, blood lipids, and diabetes mellitus management and are associated with a decrease of cardiovascular events. Cardiac rehabilitation interventions, on the basis of physical exercise, were shown to improve survival rate. The status of diet management was unclear because it was difficult to objectively identify the types of foods and their amounts in this study. It is disappointing that the interventions did not cause significant improvement in smoking cessation, BMI, or physical activity in the post-standardized follow-up group. Some patients

Table 4. Potential predictors associated with incidence of MACE

		95% CI		
Predictors	**HR**	**Lower**	**Upper**	***P***
Male gender	0.417	0.235	0.740	0.003
Younger age	0.417	0.191	0.910	0.028
Hypertension	0.632	0.352	1.133	0.123
Hyperlipidemia	0.399	0.227	0.700	0.001
Diabetes mellitus	1.241	0.700	2.200	0.460
Clinical heart failure	4.946	1.658	14.754	0.004
Overweight/obesity	1.349	0.758	2.401	0.308

Reference predictors: Male gender 1, male; Younger age 1, male <55 years, female <65 years; Hypertension 1, with hypertension; Hyperlipidemia 1, with hyperlipidemia; Diabetes mellitus 1, with diabetes mellitus; Clinical heart failure 1, with clinical heart failure; Overweight/obesity 1, BMI≥25 kg/m^2.
BMI - body mass index; HR - hazard ratio

did not understand the risks associated with their unhealthy lifestyle, and some physicians paid less attention to lifestyle intervention than they did to medication.

Hypertension is strongly connected to cardiovascular events such as myocardial infarction, stroke, and cardiac death (14), and many clinical trials confirm that the control of hypertension significantly reduces cardiovascular events. In our study, two-thirds of the patients had hypertension. Nearly 100% of those patients were taking antihypertensive medications, but more than one-fifth of the participants did not achieve the BP control goal after follow-up. The outlook for achieving BP control is not very promising. Possible reasons for the poor control of BP were as follows: 1) most of patients did not make significant changes to their unhealthy lifestyle, and 2) some patients had poor compliance to antihypertensive drugs; we found that 12.3% of the patients with hypertension did not take their pills regularly. 3) The BP data came from the outpatient records and may have been affected by activity, stress, or mood. The rate of BP control gradually increased during follow-up, and it should be attributed to the attention physicians paid to hypertension and to the improvement of medication. Compared with another secondary prevention study EUROASPIRE III, the BP control rate was higher in our study (77.8% vs. 44.0%, p<0.01) (5).

Lowering lipid levels, especially TCHO and LDL-C levels, could delay the progress of the disease and reduce cardiovascular events (15,16). In our study, nearly two-thirds of the participants had a history of hyperlipidemia. After follow-up, less than one-sixth of the participants did not achieve the lipid management goal. In both the short- and long-term follow-up, the levels of LDL-C decreased, and the lipid control rate significantly increased compared with those at discharge. This change was attributed to a broader prescription of lipid-lowering therapy.

At the end of the study, only the BP and dyslipidemia control rates improved; this may be because physicians focused in China more on medical therapy than lifestyle changes.

Medical therapy is an important part of secondary prevention. It is clear that the application of antiplatelets, beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin-receptor antagonists, and statins could decrease the risk of cardiovascular events. There is additional evidence that beta-blockers,

Table 5. Impact of standardized management on CHD secondary prevention

	Post-standardized Follow-up: 2007-2009 n=496 (last interview)	**Pre-standardized Follow-up: 2004 n=300**	***P***
Population characteristic			
Male, %	72.6	61.7**	0.001
Age, years			
Total	63.5±10.2	64.6±11.5	0.084
Male	62.3±10.3	62.2±11.9*	0.018
Female	66.7±9.1	68.5±9.7	0.952
History			
Hypertension	68.4	67.3	0.750
Hyperlipidemia	62.6	35.7**	<0.001
Diabetes mellitus	38.7	33.0	0.108
Stroke	11.5	15.0	0.156
Clinical heart failure	2.4	11.7**	<0.001
Monitoring indices			
BMI, kg/m^2	25.6±3.2	25.6±3.3	0.744
FBG, mmol/L	6.33±1.65	5.62±1.91**	<0.001
GHbA1c, %	6.5±0.9	8.5±1.1*	0.035
TCHO, mmol/L	3.80±0.86	4.47±1.04**	<0.001
TG, mmol/L	1.43±1.03	1.59±0.92**	<0.001
LDL-C, mmol/L	2.02±0.58	2.71±0.74**	<0.001
HDL-C, mmol/L	1.10±0.31	1.00±0.28**	<0.001
Control rate of risk factors, %			
Non-smoking	82.2	73.7*	0.014
BMI	41.4	40.0	0.745
BP	77.8	78.3	0.883
Lipid	84.8	45.6**	<0.001
Glucose	56.8	76.3**	<0.001
Glucose with DM	31.1	45.4*	0.035
Medication use rate, %			
ACEI/ARB	55.4	48.7	0.107
β-blocker	73.9	76.7	0.445
Antiplatelet	95.7	96.3	0.703
Lipid lowering drug	92.5	54.3**	<c0.001

*P<0.05; **P<0.01 for comparison of pre- and post-standardized follow-up
Data on monitoring indices are expressed as means±SD.
ACEI/ARB - angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers; BMI - body mass index; BP - blood pressure; DBP - diastolic blood pressure; FBG - fast blood glucose; GHbA1c - glycated hemoglobin A1c; HDL-C - high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; SBP - systolic blood pressure; TCHO - total cholesterol; TG - triglycerides

angiotensin-converting enzyme inhibitors/angiotensin-receptor antagonists, and aldosterone antagonists can improve heart remodeling during long-term treatment (4). In this study, most patients were using antiplatelets and lipid-lowering drugs, but only 60-70% were using angiotensin-converting enzyme inhibitors and beta-blockers. Antiplatelets and lipid-lowering drugs were widely prescribed, but the use of cardioprotective medicines such as angiotensin-converting enzyme inhibitors and beta-blockers was relatively low. The use of these four classes of drugs decreased slightly during the study, but the differences were not significant compared with the usage at discharge. It is likely that economic factors are a major obstacle to increased medication use (6). When physicians stressed the importance of medical therapy, patient adherence was good.

Influence of risk factors on prognosis

After the last follow-up at 3.5-6.0 years, death from all causes was 3.0% in the study group; it can also be shown as 6.5 per 1000 pt-years. Several clinical trials, such as A Coronary Disease Trial Investigating Outcome with Nifedipine GITS, Prevention of Events with Angiotensin Converting Enzyme Inhibition, European Trial on Reduction of Cardiac Events with Perindopril in Patients with Stable Coronary Artery Disease, Treating to New Targets, and the CORONOR study, have reported annual total mortality rates in the 1.1-3.3% range (17-21). The mortality in this study was low for the relatively old CHD patients. The sample size was small, and most of the included patients were local inhabitants of Beijing and could be treated regularly and on time. They showed good compliance after receiving knowledge on CHD. Because this is a follow-up program, the patients who were seriously sick and could not participate in the follow-up were excluded. This may partly explain the low mortality in our study. However, the positive effect of our standardized management should not be neglected.

According to the results of this study, the rates of cardiac death, nonfatal myocardial infarction, nonfatal stroke, and coronary revascularization were similar in females and males, but the readmission rate for cardiovascular reasons was significantly higher in females than that in males. The analysis of these potential predictors revealed that sex, age, hyperlipidemia, and heart failure correlated with prognosis.

The risk of CHD and cardiovascular events increased with age. The presence of several common risk factors (e.g., smoking, hypertension, hyperlipidemia, and diabetes) increased with age. Physical inactivity and low socio-economic status also contributed to age-differences in risk. At the same time, age is a good marker of the duration of exposure to unknown CHD risk factors (22). In postmenopausal women, the risk of cardiovascular events increases sharply with age in the absence of the cardiovascular protective effects of estrogen.

Previous studies have shown sex differences in CHD prognosis. Male gender increases CHD risk, with the mean age of onset in males is younger than that in woman. Symptoms of CHD in female patients are often atypical and occur in the presence of multiple diseases. The advantage of female gender is attributed to the protective effect of estrogen and a lower likelihood of smoking, but after menopause, the benefit of female gender disappears, and the risk of sharply CHD increases (23, 24). In this study, males had a lower relative risk of MACE than females (HR 0.417, 95% CI 0.235-0.740, p=0.003). This was attributed to 1) the mean age of the participants, which was older in females than males; in total, 85.3% of the females were older than 55 years indicating that most women were menopausal or postmenopausal. 2) More than 90% of the patients had a history of percutaneous coronary intervention (PCI). Several clinical trials found that female patients with previous PCI have a higher mortality and more complications than males with PCI (25-27). 3) A sex difference exists in cardiometabolic risk, which sharply reduces the protection generally afforded to females compared with males and in a series of other respects. There is preference of female gender in autoimmune processes leading to diabetes. 4) In people with a proinflammatory state (including MetS, IGT, type-2 diabetes), available data indicate that current smoking reduces the risk of developing diabetes in both sexes, especially in women (28). However, in this study, less than 10% of the female participants were current smokers.

Most of the cholesterol in blood plasma is carried as LDL-C, and the risk of CHD increases with increasing LDL-C over a wide range of concentrations. However, in this study, the participants with hyperlipidemia had a lower risk of MACE than those without hyperlipidemia. The possible explanations are as follows: 1) Low circulating levels of many serum lipid constituents, such as lipoprotein(a), apolipoprotein A-I, apolipoprotein B, high-density lipoprotein, and Lp-associated phospholipase A2, are involved in autoimmune activation, which could accelerate the course of diabetes, atherosclerosis, and other chronic diseases (28). 2) Patients with hyperlipidemia had a better nutrition status as indicated by a higher BMI. In a review of 40 studies including 250,152 patients with CHD, Romero-Corral et al. (29) found that overweight patients have a lower mortality rate than both those with a normal BMI and those who were obese. 3) In patients with a history of PCI, those who were overweight had a better prognosis than those with a normal BMI because of greater nutritional reserves and fewer difficulties in performing an interventional procedure (30,31). 4) Adherence to lipid-lowering therapy in patients with hyperlipidemia was high in this study, and increased drug doses were prescribed for patients with hyperlipidemia. It is also known that in addition to lowering lipid concentrations, statins have anti-inflammatory effects and increase plaque stability. Unfortunately, additional, objective clinical evidence is needed to support these results.

Heart failure is one of the most important reasons for patient readmission and always predicts an extremely bad prognosis. The Framingham Heart Study found that the median survival time following a diagnosis of heart failure is only 1.66

years for males and 3.17 years for females (32). CHD is a common cause of heart failure, and over one-third of patients with CHD die because of it (33). This data is consistent with the study results showing that heart failure predicted an increased risk of MACE.

Although hypertension was not the significant risk factor for MACE, hypertension leads to a lower association with MACE. One possible explanation may be that patients with hypertension pay more attention to their BP and salt intake. In our study, 38.7% of the patients had a history of diabetes mellitus. According to a contemporary guideline, the goal of BP control in a population with diabetes mellitus is lower than 130/80 mm Hg even in patients without hypertension. However, this lower SBP goal is not supported by any RCT that randomized participants into two or more groups, in which treatment was initiated at an SBP threshold lower than 140 mm Hg, or into treatment groups, in which the SBP goal was lower than 140 mm Hg, and that assessed the effects of a lower SBP threshold or goal on important health outcomes. Therefore, in JNC 8, an SBP goal lower than 140 mm Hg and a DBP goal lower than 90 mm Hg is recommended (34). In our study, regardless of hypertension or normotension, the BP goal is recommended as lower than 130/80 mm Hg; this may weaken the benefit of normotension.

Impact of standardized management on CHD secondary prevention

In the post-standardized follow-up group, the use of antiplatelet agents, angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers, and beta-blockers did not significantly improve compared with the control group before the beginning of standardized follow-up. However, the use of lipid-lowering drugs significantly increased (92.5% vs. 54.3%). Even though the proportion of patients with hyperlipidemia was higher after the standardized follow-up, the TCHO and LDL-C levels were significantly lower and the use of lipid-lowering agents and lipid control rate were at a relatively high level. The factors that may have contributed to this improvement include 1) The China Adult dyslipidemia Prevention Guidelines published in 2007 and other CHD guidelines may have increased the awareness of lipid-lowering therapy. 2) Domestic patients had a greater access to lipid-lowering therapy with statins following their entry into the Chinese market in the 1990s. 3) The safety and efficacy of statins in the Chinese population were confirmed by their increased use (6). 4) In the post-standardized follow-up group, physicians emphasized the importance of these medications during each outpatient visit.

The rate of BP control did not improve in the post-standardized follow-up group. This result may be attributed to 1) increased morbidity of hypertension, 2) unhealthy lifestyle and social stress, 3) poor adherence to medications, and 4) inappropriate prescription (35). However, it is difficult to confirm the effect of these factors on BP control because of the lack of objective data on medication use, lifestyle, and social stress.

Study limitations

The study population was enrolled at a single center, and the sample size was small. There was lack of objective data on medicine use, lifestyle and social stress, and vaccination history. The participants of the two groups were of different age groups. Only education courses were delivered face-to-face to the patients; no other types of education resource such as network were used.

Conclusion

Although some patients with CHD were still not achieving the goals of lifestyle change, control of risk factors, and medication therapy, the standardized follow-up helped standardize CHD secondary prevention, improve patients' compliance, increase the control rate of risk factors, and improve prognosis.

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Peer-review: Externally peer-reviewed.

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