

Impact of daily lifestyle on coronary heart disease

YAN-FANG WAN, XIAO-LI MA, CHEN YUAN, LING FEI, JING YANG and JUN ZHANG

Department of Cardiology, Cangzhou Central Hospital, Hebei Medical University, Cangzhou, Hebei 061001, P.R. China

Received August 1, 2014; Accepted March 5, 2015

DOI: 10.3892/etm.2015.2646

Abstract. Limited data are available with regard to the impact of daily lifestyle choices in patients with coronary heart disease (CHD) who have undergone stent placement. Thus, the aim of the present study was to investigate the impact of daily lifestyle factors in patients with CHD following stent implantation. Between March 2005 and March 2006, 129 consecutive patients with CHD were admitted to Cangzhou Central Hospital at Hebei Medical University (Cangzhou, China). The patients underwent coronary stenting and participated in a 7-year clinical follow-up that analyzed the impact of their daily lifestyle choices on CHD following the stent placement. Rates of dinner satiety [95% confidence interval (CI), 1.121-10.97, $P=0.005$], smoking (95% CI, 4.05-34.90, $P=2.01 \times 10^{-7}$) and heavy alcohol use (95% CI, 1.32-11.05, $P=0.006$) were significantly higher in the repeated (re)-revascularization group when compared with the non-revascularization group. In addition, the exercise rate was significantly lower in the re-revascularization group when compared with the non-revascularization group (95% CI, 0.02-0.65, $P=0.005$). However, no statistically significant differences were observed between the groups with regard to sleeping patterns (95% CI, 0.03-0.71, $P=0.270$) or anxiety rates ($P=0.289$). A coronary angiography performed during re-revascularization revealed in-stent restenosis in 26% of the patients, stenoses at the entrance to or exit from the stent in 29% of the patients and new lesions in 19% of the patients. Furthermore, original lesions exhibited deterioration in 26% of the patients. The clinical endpoint was reached in 55% of the patients between 3 and 5 years of the follow-up period. In conclusion, poor daily lifestyle habits can increase the in-stent restenosis rate, accelerate the progression of the original lesion and promote the emergence of new lesions in patients with CHD following stent placement.

Introduction

The incidence of coronary heart disease (CHD) is increasing in Chinese society. To date, CHD is among the main causes of mortality in Chinese adults (1). Since the introduction of coronary intervention technology, the technique has become one of the primary methods for the treatment of CHD. Coronary intervention has been used successfully to treat a large number of patients with acute myocardial infarction (MI), and the therapy substantially improves the quality of life of patients with unstable angina (2). Therefore, the number of patients undergoing coronary intervention is increasing (3,4). Concurrently, the prognosis of stenting has significantly improved as a result of the widespread use of drug-eluting stents and anticoagulation (2-4). In the Cangzhou region of China, the number of patients who underwent percutaneous coronary intervention (PCI) increased rapidly from 102 to 1,628 cases per year between 2000 and 2010 (unpublished data).

In recent decades, lifestyle factors have been recognized as important determinants of health status and have increasingly become a focus of research interest worldwide. Previous studies have demonstrated (5-7) that healthy lifestyle habits reduce disease and mortality rates, and that sociodemographic parameters, such as gender, age, marital status, economical level and paid employment, correlate with a healthy lifestyle (8,9). In China, the substantial societal changes brought on by modernization have altered lifestyle habits. Compared with 10 years ago, Chinese individuals of today eat more, drink more, smoke more, have increased anxiety and exercise less. Therefore, the aim of the present retrospective analysis was to investigate the impact of various daily lifestyle indicators, including the dinner satiety rate, tobacco use, heavy alcohol use, sleep pattern, anxiety and exercise, in patients with CHD who had undergone a stent implantation over a 7-year follow-up period.

Patients and methods

Patients and procedures. In total, 129 consecutive patients with CHD and indications for PCI and stent implantation, who were admitted to the Cangzhou Central Hospital at Hebei Medical University (Cangzhou, China) between March 2005 and March 2006, were recruited for the study. The patients received lifelong oral aspirin (100 mg daily) initiating subsequent to the procedure, and clopidogrel (75 mg daily) starting prior to the procedure and ending one year subsequent to

Correspondence to: Professor Jun Zhang, Department of Cardiology, Cangzhou Central Hospital, Hebei Medical University, 16 Xinhua West Road, Cangzhou, Hebei 061001, P.R. China
E-mail: junzhangcn@126.com

Key words: lifestyle, coronary artery disease, stent placement, coronary angiography, primary angioplasty

the procedure. The study was conducted in accordance with the Declaration of Helsinki and with approval from the Ethics Committee of Hebei Medical University. Written informed consent was obtained from all the participants. Patients were eligible for inclusion if they met the following criteria: i) Angiographically confirmed stenosis of $\geq 75\%$ in at least one proximal epicardial coronary artery; and ii) underwent stent implantation according to the American College of Cardiology/American Heart Association PCI guidelines (10). Patients were excluded from the study if they were aged <18 or >70 years, and had a history of other organic diseases, diabetes, heart failure or stage III hypertension. In addition, exclusion criteria included unsatisfactory stent placement, such as poor adherence, artery dissection and low flow, and mortality or MI within one month following stent placement. Patients were also excluded if coronary artery bypass grafting (CABG) was indicated initially, however, PCI was performed instead.

Data collection and follow-up. Data entered into the database were collected from patient charts or through bedside inquiry and physical examination. In-hospital outcome data were complete for all the patients. Following hospital discharge, the patients were monitored by telephone, clinic visits and calls to their primary care physicians; this information was corroborated with hospital records. The clinical endpoint was a composite of target lesion revascularization, defined as repeated PCI and CABG. The follow-up period continued for 7 years (2006-2013), and the success rate was 88.37% (114/129).

Dinner satiety was defined as eating ≥ 200 g for dinner almost daily, and tobacco use was defined as smoking ≥ 10 cigarettes a day. Heavy alcohol consumption was defined as consuming ≥ 20 units alcohol at least three times a week or >60 units weekly. Regular sleep was defined as ≥ 4 days of regular sleep each week. Anxiety was defined as a Hamilton Depression Rating Scale score of <17 and a Hamilton Anxiety Rating Scale score or >14 (11). Exercise was defined as physical activity ≥ 3 days a week for a minimum of 1 h.

Groups. Patients were grouped according to the occurrence of the clinical endpoint and to the association between daily lifestyle indicators and CHD prognosis following PCI.

Statistical analysis. Median (range), mean (forecast standard deviation) and percentage values were calculated for the overall sample. The χ^2 test was used to assess differences in the categorical and continuous baseline variables between the subgroups.

Independent prognostic variables were assessed using multivariate logistic regression models that included dinner satiety, tobacco use, heavy alcohol use, sleep pattern, anxiety and exercise. $P < 0.05$ was considered to indicate a statistically significant difference, and statistical analysis was performed using SPSS software (version 16.0; SPSS, Inc., Chicago, IL, USA).

Results

Baseline characteristics. During the enrollment period, 129 consecutive patients with PCI were surveyed. Patients were divided into two groups according to whether they reached the clinical endpoint. The repeat (re)-revascularization group

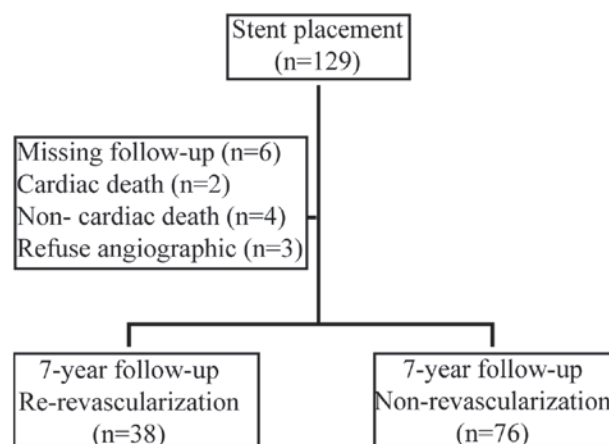


Figure 1. Flowchart of the study. Re-revascularization, repeat revascularization.

included 38 patients who underwent re-revascularization. The non-revascularization group included 76 patients who did not reach the clinical endpoint. The mean age of the patients was 55.9 ± 7.8 years, and 66.7% of the patients were male. No statistically significant differences were observed in baseline demographics and clinical characteristics between the two groups ($P > 0.05$; Tables I and II).

The study flow chart is shown in Fig. 1. At the end of the 7-year follow-up, six patients had missed their follow-up, two patients had succumbed to acute MI after three and five years, four patients had succumbed to a non-cardiac disease and three patients with angina had refused to undergo a repeat angiography.

Baseline data and procedure results. Incidence rates of dinner satiety (84.21%), tobacco use (65.79%) and heavy alcohol use (52.63%) were significantly higher in the re-revascularization group compared with the non-revascularization group (57.89, 17.11 and 26.32%, respectively). In addition, the exercise rate was significantly lower in the re-revascularization group (5.26%) compared with the non-revascularization group (27.63%; $P < 0.05$) (Table I and Fig. 2).

Angiographic follow-up data. A repeat angiography revealed in-stent restenosis in 26% of the patients, stenoses at the entrance to or exit from a stent in 29% of the patients and new lesions in 19% of the patients. In 26% of the patients, the original lesions were found to have deteriorated (Table III and Fig. 3).

Clinical outcome. A multivariate logistic regression analysis revealed that dinner satiety, tobacco use, heavy alcohol use and exercise significantly impacted CHD ($P < 0.05$; Table IV). The clinical endpoint was reached in 55% of the cases between 3 and 5 years of the follow-up period (Fig. 4).

Discussion

Numerous aspects influence patient prognosis following coronary stent placement. A previous study (12) focused on a variety of causes for in-stent restenosis; however, the present study found that the in-stent restenosis rate (including stenosis

Table I. Baseline demographic and clinical characteristics of the study patients.

Characteristic	Re-revascularization (n=38)	Non-revascularization (n=76)	P-value
Age ^a , years	55.8±8.21	56.4±7.56	0.176
Male gender, n (%)	27 (71.05)	49 (64.47)	0.482
BMI ^a , kg/m ²	24.97±4.44	24.76±4.44	0.79
Family history of CAD, n (%)	4 (10.53)	9 (11.84)	>0.05
Hyperlipidemia, n (%)	25 (65.79)	49 (64.47)	>0.05
Previous stroke, n (%)	4 (10.53)	6 (7.89)	>0.05
Stages I-II hypertension, n (%)	26 (68.42)	45 (59.21)	0.98
Prior cardiovascular disease, n (%)			
Prior MI	10 (26.32)	14 (18.42)	>0.05
Prior PCI	4 (10.53)	7 (9.21)	>0.05
Clinical presentation			
Acute MI, n (%)	15 (39.47)	29 (38.16)	>0.05
Unstable angina, n (%)	14 (36.84)	30 (39.47)	>0.05
Chronic stable angina, n (%)	7 (18.42)	12 (15.79)	>0.05
Silent ischemia, n (%)	2 (5.26)	5 (6.58)	>0.05
Left ventricular ejection fraction ^a	50.3±7.9	51.4±6.6	>0.05
Medication at discharge, n (%)			
β-blocker	22 (57.89)	39 (51.32)	>0.05
ACEI or ARB	19 (50)	34 (44.74)	>0.05
Statins	32 (84.21)	71 (93.42)	>0.05
Aspirin	38 (100)	76 (100)	>0.05
Clopidogrel	36 (94.73)	70 (92.11)	>0.05
Dinner satiety, n (%)	32 (84.21)	44 (57.89)	0.005
Tobacco use, n (%)	25 (65.79)	13 (17.11)	2.01E-07
Heavy alcohol use, n (%)	20 (52.63)	20 (26.32)	0.006
Regular sleep, n (%)	27 (60.53)	46 (71.05)	0.270
Anxiety, n (%)	22 (57.89)	36 (47.37)	0.289
Exercise, n (%)	2 (5.26)	21 (27.63)	0.005
Type of stent, n (%)			
ZETA	5 (13.16)	11 (14.47)	>0.05
HEListent	2 (5.26)	4 (5.26)	>0.05
Driver	5 (13.16)	12 (18.42)	>0.05
Vision	3 (7.89)	5 (6.58)	>0.05
Cipher	14 (36.84)	24 (31.58)	>0.05
Firebird	9 (23.68)	20 (26.32)	>0.05
Numbers of stents, n (%)			
1	21 (55.26)	49 (64.47)	>0.05
2	13 (34.21)	21 (27.63)	>0.05
3	4 (10.53)	6 (7.89)	>0.05
4	0	0	

^aData are presented as the mean ± standard deviation. Re-revascularization, repeat revascularization; BMI, body mass index; CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; ACEI, acetylcholinesterase inhibitor; ARB, angiotensin II receptor blockers.

at the entrance to and exit from the stent) was only 55%. In addition, new lesions were identified in 19% of the cases and deterioration of the original lesions accounted for 26% of the cases. Thus, patient prognosis following coronary stent place-

ment was not only found to concern in-stent restenosis, but was also shown to depend on new lesions and the deterioration of original lesions. In the present study, poor daily lifestyle habits were demonstrated to increase the in-stent restenosis rate,

Table II. Angiographic characteristics.

Target lesion coronary artery	Re-revascularization (n=38)	Non-revascularization (n=76)
Left main	0	0
Left anterior descending	19	40
Left circumflex	8	15
Right	11	21

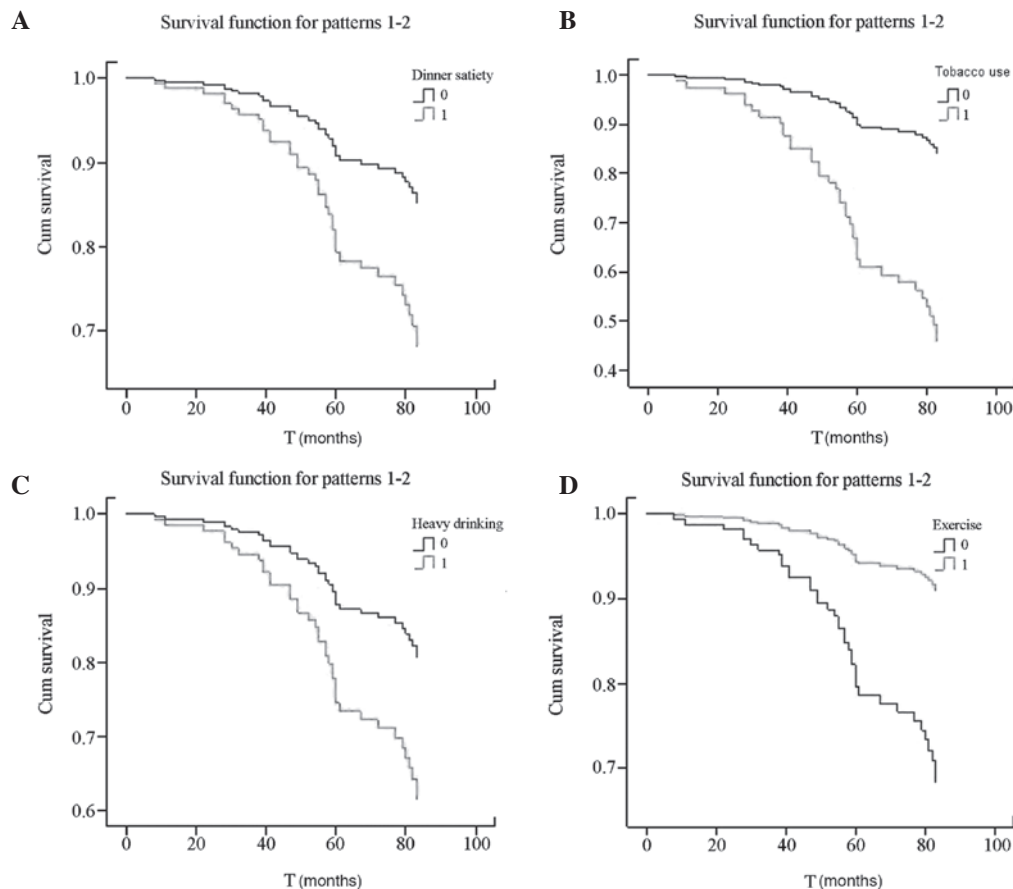


Figure 2. Survival function for revascularization, according to (A) dinner satiety, (B) tobacco use, (C) heavy drinking and (D) exercise, in the two groups during the 7-year follow-up period.

accelerate the progression of the original lesion and promote the emergence of new lesions.

The evening is an important period for physical rest and self-healing, in which sympathetic nerve activity decreases and parasympathetic nerve activity increases, resulting in the normal secretion and regulation of a variety of circulatory endocrine factors and hormones (13,14). Anxiety and irregular sleep disrupt this balance to a certain extent, and eventually impair various balance and repair mechanisms. The results from the current study revealed that anxiety and irregular sleep did not significantly differ between the two groups ($P>0.05$); however, the incidence of anxiety and irregular sleep in the two groups was ~50% (Table I). This observation demonstrates that anxiety and irregular sleep are relatively common phenomena in patients with CHD, indicating that anxiety and irregular sleep may be precipitating factors for developing vascular lesions (15-17).

The present study found that the dinner satiety rate in the re-revascularization group (84.21%) was significantly higher compared with that in the non-revascularization group (57.89%). A previous study (18) demonstrated that dinner satiety can affect sleep, and that high food consumption during dinner is followed by a series of adverse consequences. A high fat intake can elevate serum leptin levels and decrease leptin receptor levels, leading to the leptin resistance phenomenon (19). Leptin resistance not only affects the transfer of satiety signals, but also activates the sympathetic nervous system and affects the stability of vascular endothelial cells through the endothelin (ET-1) receptor, a downstream effector of nicotinamide adenine dinucleotide phosphate oxidase (20,21). Leptin resistance also promotes endothelial inflammatory factor activity, which may lead to the development of atherosclerosis and promote adenosine diphosphate-induced platelet aggregation to form thromboses, thereby causing acute coronary events (22). Impaired dinner

Table III. Seven-year clinical follow-up.

Follow-up data	Cases, n (%)
Missed follow-up	6 (4.65)
Mortality	2 (1.55)
Cardiac mortality	4 (3.10)
Refusal	3 (2.33)
Re-revascularization (n=38)	
Lesions aggravated	10 (26)
In-stent restenosis	10 (26)
New lesions	7 (19)
Entrance and exit stenosis of stent	11 (29)

Re-revascularization, repeat revascularization.

Table IV. Multivariate logistic regression analysis of the prognostic factors for patients with PCI.

Prognostic factor	OR	95% CI	P-value
Dinner satiety	3.32	1.06-10.48	0.040
Tobacco use	11.71	3.95-34.71	<0.001
Heavy drinking	3.74	1.27-10.98	0.017
Regular sleep	1.50	0.51-4.39	0.461
Anxiety	1.57	0.56-4.44	0.395
Exercise	0.14	0.02-0.65	0.013

PCI, percutaneous coronary intervention; CI, confidence interval; OR, odds ratio.

satiety is also one of the main causes of excess weight and obesity, which are major risk factors for CHD in the Chinese population (23,24). In addition, smoking is a well-known independent risk factor for CHD. The current study demonstrated that tobacco use in the re-revascularization group (65.79%) was significantly higher when compared with the non-revascularization group (17.11%). Smoking can damage vascular endothelial function and stability, promote myocardial hypoxia and cause coronary artery spasm (25). Furthermore, smoking can induce a variety of factors, such as thromboxane A₂, CD40 and prostacyclin, that cause atherosclerosis-accelerated plaque formation, which subsequently induces plaque rupture and thrombosis (26,27). In a previous study, heavy drinking was found to be a risk factor for cardiovascular disease (28); the study found that alcohol consumption had a U-shaped curve association with cardiovascular disease, particularly the incidence of MI and CHD (29,30). Heavy drinking affects the normal function of the body's clotting system and the vascular endothelium. In addition, increased alcohol consumption can activate oxidative stress and alter the activities of several inflammatory cytokines, including ET-1, tumor necrosis factor- α , interleukin-6 and nitric oxide, subsequently leading to plaque formation and blood clots in the blood vessels (31-33). Patients with CHD require exercise; however, the present study found

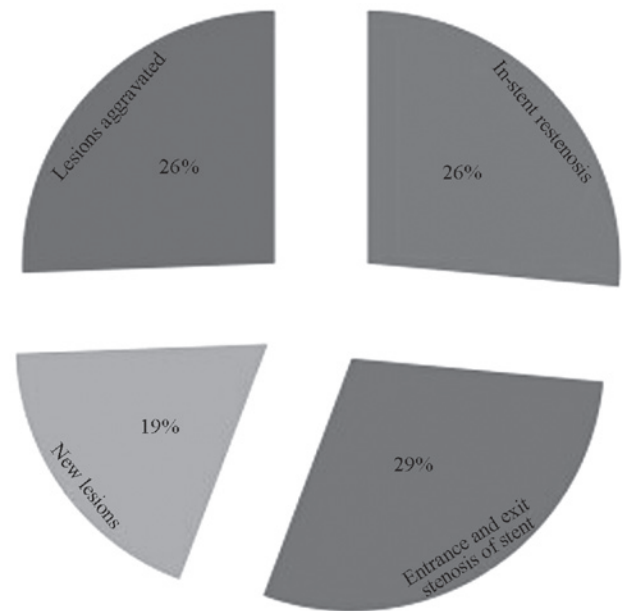


Figure 3. Lesion sites and characteristics.

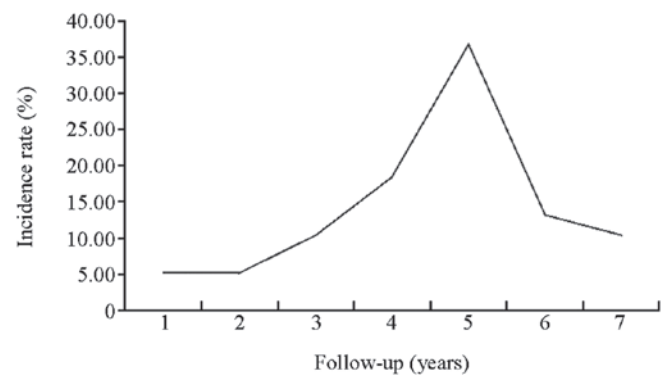


Figure 4. Incidence of revascularization over the 7-year follow-up period.

that just 5.26% of patients in the re-revascularization group and 27.63% of patients in the non-revascularization group exercised regularly. Previous studies have shown that adequate exercise improves blood circulation, prevents thrombosis and embolism, improves the internal functioning of the body, improves sleep, relieves anxiety and restores normal nerve and humoral regulation (34-36).

In the current study, 55% of patients exhibited revascularization and showed poor daily lifestyle habits during the 3-5 years of the 7-year follow-up. The highest frequency of events occurred in the fifth year of follow-up. Based on the analysis of these results, the following hypothesis can be concluded: Among patients with CHD who undergo stent implantation and do not improve on their lifestyle choices, 55% of individuals are likely to require revascularization in the subsequent 3-5-year period.

The present study had several important limitations. The major limitation was the relatively small number of patients. The study was a retrospective, randomized, single-blind study, rather than a double-blind study. In addition, the type of stent implanted was left to the discretion of the surgeon; thus, different types of stents were used in different clinical circumstances and

the procedure was not standardized. Finally, few of the patients who did not require revascularization received angiographic follow-up.

In conclusion, despite major breakthroughs in the prevention and treatment of CHD, this disease remains the most common cause of mortality in the Asian Pacific region (37). PCI with stent placement is the gold standard for treating patients with CHD; however, re-revascularization is a recurring problem following PCI. Currently, there is a large amount of data with regard to in-stent restenosis; however, in numerous stent patients, deterioration of the original lesions and new lesion sites have been found to occur subsequent to the administration of sufficient treatment. In the present study, daily lifestyle factors were demonstrated to significantly affect the prognosis of patients with stents. Therefore, future large-scale clinical trials are required with the aim of offering more specific treatment guidance.

References

- He J, Gu D, Wu X, *et al*: Major causes of death among men and women in China. *N Engl J Med* 353: 1124-1134, 2005.
- Biondi Zoccai G, Abbate A, D'Ascenzo F, *et al*: Percutaneous coronary intervention in nonagenarians: pros and cons. *J Geriatr Cardiol* 10: 82-90, 2013.
- Bangalore S, Gupta N, Guo Y and Feit F: Trend in the use of drug eluting stents in the United States: insight from over 8.1 million coronary interventions. *Int J Cardiol* 175: 108-119, 2014.
- Giacoppo D, Baber U and Mehran R: Current developments in dual antiplatelet therapy after stenting. *Minerva Cardioangiol* 62: 261-276, 2014.
- Nöthlings U, Ford ES, Kröger J and Boeing H: Lifestyle factors and mortality among adults with diabetes: Findings from the European Prospective Investigation into Cancer and Nutrition-Potsdam study. *J Diabetes* 2: 112-117, 2010.
- Hu FB, Liu Y and Willett WC: Preventing chronic diseases by promoting healthy diet and lifestyle: public policy implications for China. *Obes Rev* 12: 552-559, 2011.
- Reddy P, Rankins D, Timoshanko A and Dunbar JA: Life! in Australia: translating prevention research into a large-scale intervention. *Br J Diabetes Vasc Dis* 11: 193-197, 2011.
- Krueger PM and Chang VW: Being poor and coping with stress: health behaviors and the risk of death. *Am J Public Health* 98: 889-896, 2008.
- Menotti A, Puddu PE, Lanti M, Maiani G, Catasta G and Fidanza AA: Lifestyle habits and mortality from all and specific causes of death: 40-year follow-up in the Italian Rural Areas of the Seven Countries Study. *J Nutr Health Aging* 18: 314-321, 2014.
- Smith SC Jr, Dove JT, Jacobs AK, *et al*: American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Committee to Revise the 1993 Guidelines for Percutaneous Transluminal Coronary Angioplasty: ACC/AHA guidelines of percutaneous coronary interventions (revision of the 1993 PTCA guidelines) - executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty). *J Am Coll Cardiol* 37: 2215-2239, 2001.
- Hamilton M: A rating scale for depression. *J Neurol Neurosurg Psychiatry* 23: 56-62, 1960.
- Eisenstein EL, Anstrom KJ, Kong DF, *et al*: Clopidogrel use and long-term clinical outcomes after drug-eluting stent implantation. *JAMA* 297: 159-168, 2007.
- Leproult R and Van Cauter E: Role of sleep and sleep loss in hormonal release and metabolism. *Endocr Dev* 17: 11-21, 2010.
- Copinschi G: Metabolic and endocrine effects of sleep deprivation. *Essent Psychopharmacol* 6: 341-347, 2005.
- Lespérance F, Frasure-Smith N, Thérioux P and Irwin M: The association between major depression and levels of soluble intercellular adhesion molecule 1, interleukin-6 and C-reactive protein in patients with recent acute coronary syndromes. *Am J Psychiatry* 161: 271-277, 2004.
- Sherwood A, Hinderliter AL, Watkins LL, Waugh RA and Blumenthal JA: Impaired endothelial function in coronary heart disease patients with depressive symptomatology. *J Am Coll Cardiol* 46: 656-659, 2005.
- Pizzi C, Manzoli L, Mancini S and Costa GM: Analysis of potential predictors of depression among coronary heart disease risk factors including heart rate variability, markers of inflammation and endothelial function. *Eur Heart J* 29: 1110-1117, 2008.
- Lucassen EA, Zhao X, Rother KI, *et al*: Sleep Extension Study Group: Evening chronotype is associated with changes in eating behavior, more sleep apnea, and increased stress hormones in short sleeping obese individuals. *PLoS One* 8: e56519, 2013.
- Ku IA, Farzaneh-Far R, Vittinghoff E, Zhang MH, Na B and Whooley MA: Association of low leptin with cardiovascular events and mortality in patients with stable coronary artery disease: the Heart and Soul Study. *Atherosclerosis* 217: 503-508, 2011.
- Rajendran K, Devarajan N, Ganesan M and Ragunathan M: Obesity, Inflammation and Acute Myocardial Infarction-Expression of leptin, IL-6 and high sensitivity-CRP in Chennai based population. *Thromb J* 10: 13, 2012.
- Knudson JD, Payne GA, Borbouse L and Tune JD: Leptin and mechanisms of endothelial dysfunction and cardiovascular disease. *Curr Hypertens Rep* 10: 434-439, 2008.
- Elbatarny HS and Maurice DH: Leptin-mediated activation of human platelets: involvement of a leptin receptor and phosphodiesterase 3A-containing cellular signaling complex. *Am J Physiol Endocrinol Metab* 289: E695-E702, 2005.
- Hou X, Lu J, Weng J, *et al*: Chinese National Diabetes and Metabolic Disorders Study Group: Impact of waist circumference and body mass index on risk of cardiometabolic disorder and cardiovascular disease in Chinese adults: a national diabetes and metabolic disorders survey. *PLoS One* 8: e57319, 2013.
- Bays H and Dujovne C: Pharmacotherapy of obesity: currently marketed and upcoming agents. *Am J Cardiovasc Drugs* 2: 245-253, 2002.
- Gu D, Kelly TN, Wu X, *et al*: Mortality attributable to smoking in China. *N Engl J Med* 360: 150-159, 2009.
- Barua RS and Ambrose JA: Mechanisms of coronary thrombosis in cigarette smoke exposure. *Arterioscler Thromb Vasc Biol* 33: 1460-1467, 2013.
- Bliden KP, Dichiara J, Lawal L, *et al*: The association of cigarette smoking with enhanced platelet inhibition by clopidogrel. *J Am Coll Cardiol* 52: 531-533, 2008.
- Klatsky AL, Armstrong MA and Friedman GD: Alcohol and mortality. *Ann Intern Med* 117: 646-654, 1992.
- Emberson JR, Shaper AG, Wannamethee SG, Morris RW and Whincup PH: Alcohol intake in middle age and risk of cardiovascular disease and mortality: accounting for intake variation over time. *Am J Epidemiol* 161: 856-863, 2005.
- Goldberg DM, Hahn SE and Parkes JG: Beyond alcohol: beverage consumption and cardiovascular mortality. *Clin Chim Acta* 237: 155-187, 1995.
- Albert CM, Manson JE, Cook NR, Ajani UA, Gaziano JM and Hennekens CH: Moderate alcohol consumption and the risk of sudden cardiac death among US male physicians. *Circulation* 100: 944-950, 1999.
- Guan Z, Lui CY, Morkin E and Bahl JJ: Oxidative stress and apoptosis in cardiomyocyte induced by high-dose alcohol. *J Cardiovasc Pharmacol* 44: 696-702, 2004.
- O'Keefe JH, Bybee KA and Lavie CJ: Alcohol and cardiovascular health: the razor-sharp double-edged sword. *J Am Coll Cardiol* 50: 1009-1014, 2007.
- Luk TH, Dai YL, Siu CW, *et al*: Effect of exercise training on vascular endothelial function in patients with stable coronary artery disease: a randomized controlled trial. *Eur J Prev Cardiol* 19: 830-839, 2012.
- Hedbäck B, Perk J, Hörnblad M and Ohlsson U: Cardiac rehabilitation after coronary artery bypass surgery: 10-year results on mortality, morbidity and readmissions to hospital. *J Cardiovasc Risk* 8: 153-158, 2001.
- Yu CM, Lau CP, Chau J, McGhee S, Kong SL, Cheung BM and Li LS: A short course of cardiac rehabilitation program is highly cost effective in improving long-term quality of life in patients with recent myocardial infarction or percutaneous coronary intervention. *Arch Phys Med Rehabil* 85: 1915-1922, 2004.
- Meng Khoo C and Tai ES: Trends in the incidence and mortality of coronary heart disease in asian pacific region: The Singapore experience. *J Atheroscler Thromb* 21 (Suppl 1): S2-S8, 2014.