International Journal of Gerontology 7 (2013) 116–121

Contents lists available at SciVerse ScienceDirect

International Journal of Gerontology

journal homepage: www.ijge-online.com

Original Article

Gender Difference in Statin Intervention on Blood Lipid Control among Patients with Coronary Heart Disease☆

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ARTICLE INFO

Article history:
Received 18 February 2013
Received in revised form
25 February 2013
Accepted 27 February 2013
Available online 28 April 2013

Keywords:
dyslipidemia,
low-density lipoprotein cholesterol (LDL-C),
statin

SUMMARY

Background: The aim of this study was to clarify the current status in the effective control of dyslipidemia in Taiwanese women and men with coronary heart disease (CHD).
Materials and methods: A total 1584 patients with CHD (1188 men, aged 64.8 ± 11.6 years and 396 women, aged 69.0 ± 9.8 years) from 3486 patients who had atherosclerotic vascular disease and complete lipids measured values [total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C)] were used for analysis.
Results: The waist, height, weight, and creatinine levels were higher in men than in women. The systolic blood pressure, TC, HDL-C, LDL-C, fasting blood glucose, and platelet were lower in men than in women. Men were more likely to achieve the target goal than women in TC < 160 mg/dL, LDL-C < 100 mg/dL, and TG < 150 mg/dL as well as to achieve HDL-C goal.
Conclusion: A significant gap was found between the guidelines and clinical practice in statin intervention among these CHD patients, particularly for women. The strategy in control of dyslipidemia should consider gender difference.

1. Introduction

Low-density lipoprotein cholesterol (LDL-C) reduction by statin therapy has shown benefits in decreasing morbid and mortal cardiovascular events in both the secondary and primary prevention trials of coronary heart disease (CHD)[1–5]. However, subgroup analysis did not consistently show benefits in women compared with men in secondary prevention trials. In addition, usually the percent of female participants ranged from 20% to 30% in statin trials. The Heart Protection Study showed further benefit could be achieved by lowering the LDL-C level to below 100 mg/dL in high-risk patients[5]. In the Translating Research Into Action for Diabetes (TRIAD) study, women were significantly more likely than men to have LDL-C ≥ 130 mg/dL[6]. Women were found to relatively receive a less aggressive approach to cardiovascular risk factors and, mostly, to a less intense cholesterol management than men[7]. Therefore, the focus on cardiovascular risk management in women is rising. Nevertheless, all these lipid-lowering trials (LLTs) were mainly conducted in Europe and American and data from Asians were fragmented.

The gender gap between guidelines and clinical practice remained elusive in Taiwan. To clarify the issue, we explored gender-related differences in the rates of achieving the target LDL-C levels suggested by National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)[8] in patients with coronary heart disease from the Taiwanese Lipid Registry Study (TLRS).

☆ We certify that all our affiliations with or financial involvement in, within the past 5 years and foreseeable future, any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript are completely disclosed.

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1873-9598/$ – see front matter
http://dx.doi.org/10.1016/j.ijge.2013.03.002

2. Materials and methods

2.1. Study population

Taiwanese Secondary Prevention for patients with AtheRosCLErotic disease (T-SPARCLE) Registry was initiated by Taiwan society of lipids and atherosclerosis in 2011 for investigating the control of dyslipidemia and the association between dyslipidemia and future cardiovascular events. Twelve hospitals (8 medical centers and 6 regional hospitals) were invited to participate in this registry (T-SPARCLE). The enrollment criteria were as follows[9]: (1) patients with atherosclerotic vascular diseases, including coronary atherosclerosis as diagnosed by cardiac catheterization examination, history of myocardial infarction as evidenced by electrocardiography (ECG) or hospitalization, angina diagnosed by ischemic ECG changes, or positive response to stress test; (2) patients with cerebral vascular disease, cerebral infarction, and intracerebral hemorrhage, excluding those with intracerebral hemorrhage caused by other diseases (such as cancer); and patients with transient ischemic attack (TIA) whose carotid artery duplex showed atheromatous change with more than 70% stenosis. Peripheral atherosclerosis with symptoms of ischemia and confirmed by Doppler ultrasound or angiography.

There were 4361 participants meeting the enrollment criteria. Finally, a total of 3486 patients (2386 men and 1100 women) with complete lipids measure values [total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C)] were included in this analysis. Data of demographic characteristics, medical history, and drug history were collected. Hypertension (HTN) was defined as: (1) known history of hypertension; (2) taking antihypertensive drugs at referral; and (3) systolic blood pressure (BP) $\geq$140 mmHg or diastolic BP $\geq$ 90 mmHg by medical chart review. Those patients with an established diagnosis of diabetes mellitus (DM) or those on glucose lowering drugs or fasting glucose $\geq$ 126 mg/dL were labeled as DM. Fasting glucose level between 100 mg/dL and 126 mg/dL was defined as impaired glucose tolerance (IGT). The 1584 patients with CHD were included in our analysis. Lipid-lowering agents were prescribed following the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines[8]. As the potency of statins was different[10], statin equivalent doses were calculated as given in Appendix 1. All patients had given written informed consent for this study, and this study had been proved by Joint Institute Review Board, Taiwan.

2.2. Statistical methods

Data are expressed as mean $\pm$ SD or percentage. Student *t* test was applied to the continuous data, and Chi-square tests of categorical data were used to compare the differences between groups. Multivariate logistic regression analysis were used to examine the odds of optimal lipid value attainment [TC $<$ 160 mg/dL, TG $<$ 150 mg/dL, LDL-C $<$ 100 mg/dL, and HDL-C (men: $\geq$40 mg/dL and women: $\geq$50 mg/dL)]. Age, gender, body mass index (BMI), history of HTN, history of DM or IGT, smoking status, and status of alcohol consumption were included in the model to assess their impact on goal attainment. The participants without optimal lipid value attainment were considered as the reference group. All analyses were performed with SAS statistical software version 9.2 (SAS Institute, Carey, NC, USA).

3. Results

The demographic data of 1188 men (aged 64.8 $\pm$ 11.6 years) and 396 women (69.0 $\pm$ 9.8 years) are shown in Table 1. Most of the participants were men (75%). More than 90% of women were older than 55 years. Men were significantly younger and had higher waist, height, weight, and creatinine levels than women. The BMI and TG levels were not different between men and women. Men had significantly lower systolic blood pressure (SBP), TC, HDL-C, LDL-C, and fasting blood glucose than women. The percentages of history of HTN, diabetes, or IGT were lower in men than in women. Men were much more likely to smoke and drink alcohol than women. The percentages of statin use in men and women were 68.5% and 65.4%, respectively. Women were significantly more likely to take pravastatin than men. The percentage of fibrate use in men and women was not different ($p = 0.56$).

Table 1
Demographic data of men and women with myocardial infarction or coronary artery disease.

	Men ($n = 1188$)	Women ($n = 396$)	p
Age (y)	64.8 $\pm$ 11.6	69.0 $\pm$ 9.8	<0.0001
Waist (cm)	95.3 $\pm$ 9.6	90.8 $\pm$ 10.7	<0.0001
Height (cm)	166.2 $\pm$ 6.0	153.5 $\pm$ 5.8	<0.0001
Weight (kg)	72.7 $\pm$ 11.2	62.4 $\pm$ 10.7	<0.0001
BMI (kg/m^2)	26.3 $\pm$ 3.5	26.5 $\pm$ 4.3	0.41
SBP (mmHg)	131.3 $\pm$ 17.6	135.9 $\pm$ 18.9	<0.0001
TC (mg/dL)	167.8 $\pm$ 39.2	178.9 $\pm$ 43.5	<0.0001
HDL-C (mg/dL)	43.1 $\pm$ 12.6	50.4 $\pm$ 16.7	<0.0001
LDL-C (mg/dL)	97.4 $\pm$ 33.4	101.5 $\pm$ 36.0	0.04
TG (mg/dL)	141.0 $\pm$ 98.3	144.1 $\pm$ 101.4	0.59
Creatinine (mg/dL)	1.22 $\pm$ 0.78	1.03 $\pm$ 0.85	0.0001
FBG (mg/dL)	118.3 $\pm$ 40.8	123.1 $\pm$ 42.5	0.05
HbA1C, %	7.0 $\pm$ 1.4	7.2 $\pm$ 1.4	0.05
Current Smoking	217 (18.3)	14 (3.5)	0.006
History of HTN	827 (69.6)	327 (82.6)	<0.0001
History of DM or IGT	458 (38.6)	216 (54.6)	<0.0001
History of ischemic stroke	39 (3.3)	15 (3.8)	0.64
History of nonischemic stroke	22 (1.9)	12 (3.1)	0.16
History of TIA	23 (2.0)	11 (2.8)	0.32
Alcohol consumption	233 (19.6)	14 (3.5)	<0.0001
Lipid-lowering agents			
Statin, yes	873 (73.4)	288 (72.7)	0.09
Atorvastatin	300 (25.3)	107 (27.0)	0.49
Rosuvastatin	373 (31.4)	110 (27.78)	0.18
Simvastatin	68 (5.7)	20 (5.0)	0.61
Fluvastatin	81 (6.82)	22 (5.56)	0.38
Pravastatin	51 (4.29)	29 (7.32)	0.02
Statin, no	315 (26.5)	108 (27.3)	0.77
Statin equivalent dose	2.08 $\pm$ 2.00	1.98 $\pm$ 1.92	0.39
Fibrate	66 (5.56)	19 (4.80)	0.56
Ezetimibe or cholestyramine	111 (9.3)	31 (7.8)	0.36
Niacin or acipimox	2 (0.17)	1 (0.25)	0.74

Data are presented as yes (%) unless otherwise stated.
BMI = body mass index; DM = diabetes mellitus; FBG = fasting blood glucose; HbA1c = hemoglobin A1c; HDL-C = high density lipoprotein cholesterol; HTN = hypertension; IGT = impaired glucose tolerance; LDL-C = low density lipoprotein cholesterol; SBP = systolic blood pressure; TC = total cholesterol; TG = triglyceride; TIA = transient ischemic stroke.

The men taking statin were more likely than women to achieve the goal of TC (<160 mg/dL), HDL-C ($\geq$40 mg/dL in men compared to $\geq$50 mg/dL in women) and LDL-C (<100 mg/dL) (Table 2). Such trends did not exist with other lipid-lowering agents.

To further clarify the factors associated with effective control of dyslipidemia, the logistic regression model was performed (Table 3). Men were more likely to achieve the target goal than women in TC $<$ 160 mg/dL [adjusted odds ratio (OR): 2.31, $p < 0.0001$], in HDL-C ($\geq$ 40 mg/dL in men compared to $\geq$50 mg/dL in women; adjusted OR:1.64, $p = 0.0002$), in LDL-C $<$ 100 mg/dL (adjusted OR: 1.41, $p = 0.009$) and in TG $<$ 150 mg/dL (adjusted OR: 1.38, $p = 0.03$). Regarding age, increased age had odds to have optimal lipid control. As men had a higher percentage of attaining the goal than women, we separately investigated the determinants of goal attainment between men and women. Patients taking statin led to a statistically significant benefit in attaining TC $<$ 160 mg/dL

Table 2
The percentage of goal attainment in patients taking lipid-lowering agents.

	TC < 160 mg/dL			HDL-C ≥ 40/50 mg/dL[a]			LDL-C < 100 mg/dL			TG < 150 mg/dL		
	Men	Women	*p*	Men	Women	*p*	Men	Women	*p*	Men	Women	*p*
Statin (men = 873; women = 288)	446 (51.1)	99 (34.4)	<0.0001	497 (56.9)	133 (46.2)	0.002	549 (62.9)	161 (55.9)	0.04	605 (69.3)	192 (66.7)	0.40
Fibrate (men = 66; women = 19)	20 (30.3)	8 (42.1)	0.33	21 (31.8)	3 (15.8)	0.17	38 (57.6)	10 (52.6)	0.70	16 (24.2)	5 (26.3)	0.85
Ezetimibe and cholestyramine (men = 76; women = 19)	29 (38.2)	6 (31.6)	0.58	46 (60.5)	12 (63.2)	0.83	40 (52.6)	7 (36.8)	0.22	45 (59.2)	14 (73.7)	0.24
Niacin and acipimox (men = 2;women = 1)	0	0	–	1 (50)	0	0.39	2 (100)	1 (100)		0	0	

Data are presented as (%).
HDL-C = high density lipoprotein cholesterol; LDL-C = low density lipoprotein cholesterol; TC = total cholesterol; TG = triglyceride.
[a] HDL-C: in men ≥40 mg/dL; in women ≥50 mg/dL.

(adjusted OR: 1.75, $p < 0.0001$), LDL-C < 100 mg/dL (adjusted OR: 1.44, $p = 0.002$) and TG < 150 mg/dL (adjusted OR:1.42, $p = 0.005$), compared to those not taking statin. For men, those taking statin were more likely to achieve TC < 160 mg/dL (adjusted OR: 1.89, $p < 0.0001$), LDL-C <100 mg/dL (adjusted OR: 1.52, $p = 0.002$), and TG < 150 mg/dL (adjusted OR: 1.60, $p = 0.002$), but no similar trends were found in women. The effect of statin on achieving the TC, LDL-C, and TG goals was also statistically significant in patients with DM or IGT.

By contrast, an increased BMI was associated with a decrease in OR of TG and HDL (HDL > 40 mg/dL in men and HDL > 50 mg/dL in women) goal attainment. An increased age led to an increase in OR of attaining TC, LDL-C, HDL-C, and TG goals. Participants who were current smokers and with DM or IGT had decreased ORs of TG goal attainment. As the potencies of statins were different, we use statin equivalent doses instead of statin use (yes vs. no) in logistic regression models (Table 4). Compared to women, men were more likely to achieve the target goal than women in TC < 160 mg/dL (adjusted OR: 2.27, $p < 0.0001$), in HDL-C (≥ 40 mg/dL in men or ≥50 mg/dL in women; adjusted OR: 1.64, $p = 0.0002$), in LDL-C < 100 mg/dL (adjusted OR: 1.40, $p = 0.01$) and in TG < 150 mg/dL (adjusted OR: 1.38, $p = 0.03$). As a whole, patients taking statin had a statistically significant benefit in attaining TC < 160 mg/dL (adjusted OR: 1.54, $p = 0.0001$), LDL-C < 100 mg/dL (adjusted OR: 1.37, $p = 0.005$) and TG < 150 mg/dL (adjusted OR: 1.45, $p = 0.002$). For men, those taking statin were more likely to achieve TC (adjusted OR: 1.75, $p < 0.0001$), HDL-C (≥ 40 mg/dL in men or ≥50 mg/dL in women; adjusted OR: 1.33, $p = 0.04$), LDL-C < 100 mg/dL (adjusted OR: 1.46, $p = 0.004$), and TG goals (adjusted OR: 1.69, $p = 0.002$), but no similar trends were found in women. The effects of statin on achieving the TC, HDL-C, and LDL-C goals were statistically significant in patients with DM or IGT. An increased BMI was associated with a decrease in ORs of TG and HDL (HDL > 40 mg/dL in men and HDL > 50 mg/dL in women) goal attainments. Patients who were current smokers and with DM or IGT had decreased ORs of TG goal attainments.

4. Discussion

The results of the present study indicated a significant gender disparity in attaining the TC, LDL-C, HDL-C, and TG goals in Taiwanese patients with CHD. In the Heart and Estrogen/Progestin Replacement Study (HERS), only a small proportion of women (9.5%) reached the LDL-C levels below 100 mg/dL[11]. The southeastern US health plan indicated that only 17% of women had an LDL-C < 100 mg/dL, and 7% attained an LDL-C < 100 mg/dL, HDL-C > 50 mg/dL, and TG > 150 mg/dL[12]. The results of the European Action on Secondary Prevention through Intervention to Reduce Event (EUROASPIRE) III showed that despite similarities in medication exposure, women are less likely than men to achieve LDL-C target goal (LDL-C < 2.5 mmol/L, 97 mg/dL) after a coronary event[13]. The Lipid Treatment Assessment Project (L-TAP) 2 indicated that in 9955 of patients (45.3% women) evaluated, women had a significantly lower overall LDL-C success rate than men[7]. Similar results have been demonstrated in China[14,15]. The findings of the present study are consistent with those of all the above mentioned studies.

In our study, men taking statin were more likely to achieve the LDL-C goal than women taking statin, despite the exposures of statin equivalent dose between men and women being comparable. This result might be partially explained by the effect of estrogen on lipid metabolism. In our study, the average age of women was 69 years, and approximately 91.9% of women were postmenopausal. Higher endogenous estrogen levels were reported to be associated with increased LDL receptors and reduced activity of 3-hydroxy 3-methylglutaryl coenzyme A reductase (HMG-CoAR)[16,17]. When the estrogen levels in postmenopausal women reduced, the effect of statins was attenuated in reducing the LDL-C level via the mechanisms involving LDL receptors and metabolism. In this sense, we should pay more attention to women with CHD, particularly postmenopausal women, and give more aggressive LDL-C-lowering treatment than men.

In the Maryland-based health maintenance organization study, there was no difference between the proportion of men (71.4%) and women (63.3%) prescribed lipid-lowering therapy. As a result, more men (51.0%) than women (36.7%) reached the LDL-C of <2.59 mmol/L (<100 mg/dL)[18]. A report from China showed that in patients with high cardiovascular risk, the rate of statin therapy was much higher (82.2%); however, the LDL-C attainment (<2.6 mmol/L, 100 mg/dL) rate was relatively lower in men (45.5%) and women (28.5%)[15]. In our study, statin was prescribed to men (73.4%) and women (72.7%), but the LDL-C target attainment rate was 51.1% for men and 34.4% for women. Together, these data indicated that the gap between the rate of goal attainment and statin therapy was still widening, particularly in women.

Higher goal attainment rates could be achieved with higher doses of statin[19]. In the present study, moderate doses of statin were given. Even though men took statin doses comparable with women, the men taking statin were more likely to attain the lipid goal than the women in the present study. It has been shown that in patients with CHD and risk equivalents, fewer women than men achieved the lipid goal partly owing to the inadequate dose of statin[20]. This might be due to the incorrect perception of both women and their physicians regarding the cardiovascular risk in women. A previous study showed that physicians perceived women to be at a lower risk than men, even if they had a similar calculated CHD risk[21], and this led to the undertreatment of women with dyslipidemia. However, in Taiwan, the undertreatment of dyslipidemia is not seen for women alone. A previous Taiwanese study conducted in a medical center showed that only 31% of patients with cardiovascular disease reached the LDL-C target[22]. Although medical expenses in Taiwan are mainly covered by the

Table 3
Contributions of statin use and other covariates in gender difference in optimal lipid goal attainment among patients with coronary artery disease.

	Achieving TC < 160 mg/dL					
	All (n = 1584)	p	Men (n = 1188)	p	Women (n = 396)	p
	AOR (95% CI)		AOR (95% CI)		AOR (95% CI)	
Age (y)	1.02 (1.01,1.03)*	0.003	1.02 (1.01,1.03)*	0.002	1.01 (0.99,1.03)	0.46
BMI (kg/m^2)	0.99 (0.96,1.02)	0.40	0.99 (0.96,1.03)	0.66	0.98 (0.93,1.03)	0.40
Smoking status	0.94 (0.74,1.18)	0.58	0.93 (0.73,1.18)	0.53	0.93 (0.36,2.40)	0.88
History of DM or IGT	1.47 (1.19,1.81)*	0.0003	1.50 (1.18,1.90)*	0.001	1.36 (0.88,2.12)	0.17
History of HTN	1.08 (0.85,1.36)	0.55	1.09 (0.84,1.42)	0.51	0.99 (0.56,1.77)	0.98
Alcohol consumption	0.84 (0.63,1.12)	0.23	0.90 (0.67,1.22)	0.51	0.15 (0.02,1.16)	0.07
Statin	1.75 (1.38,2.23)*	<0.0001	1.89 (1.44,2.49)*	<0.0001	1.46 (0.89,2.39)	0.13
Gender	2.31 (1.76,3.03)*	<0.0001				
	Achieving HDL > 40 mg/dL in men and HDL > 50 mg/dL in women					
	All (n = 1584)	p	Men (n = 1188)	p	Women (n = 396)	p
	AOR (95% CI)		AOR (95% CI)		AOR (95% CI)	
Age (y)	1.02 (1.01,1.03)*	<0.0001	1.02 (1.01,1.03)*	<0.0001	1.01 (0.99,1.03)	0.40
BMI (kg/m^2)	0.95 (0.93,0.98)*	0.001	0.93 (0.90,0.96)*	<0.0001	1.00 (0.95,1.05)	0.98
Smoking status	0.82 (0.65,1.03)	0.09	0.83 (0.65,1.06)	0.13	0.94 (0.38,2.31)	0.89
History of DM or IGT	0.70 (0.57,0.86)*	0.0008	0.80 (0.63,1.02)	0.07	0.48 (0.32,0.72)*	0.0004
History of HTN	1.03 (0.82,1.31)	0.79	1.02 (0.78,1.33)	0.88	1.16 (0.67,2.00)	0.60
Alcohol consumption	1.13 (0.84,1.51)	0.42	1.17 (0.87,1.59)	0.30	1.03 (0.35,3.09)	0.95
Statin	1.17 (0.93,1.48)	0.18	1.27 (0.97,1.68)	0.09	0.93 (0.59,1.47)	0.77
Gender	1.64 (1.26,2.13)*	0.0002				
	Achieving LDL-C < 100 mg/dL					
	All (n = 1584)	p	Men (n = 1188)	p	Women (n = 396)	p
	AOR (95% CI)		AOR (95% CI)		AOR (95% CI)	
Age (y)	1.02 (1.01,1.03)*	0.002	1.01 (1.00,1.03)*	0.01	1.03 (1.01,1.05)*	0.02
BMI (kg/m^2)	0.98 (0.96,1.01)	0.22	0.98 (0.95,1.02)	0.28	0.99 (0.94,1.03)	0.53
Smoking status	0.99 (0.79,1.25)	0.95	0.94 (0.74,1.20)	0.62	1.62 (0.63,4.15)	0.31
History of DM or IGT	1.27 (1.03,1.57)*	0.03	1.23 (0.96,1.57)	0.10	1.34 (0.89,2.04)	0.17
History of HTN	0.94 (0.74,1.19)	0.58	0.98 (0.75,1.28)	0.89	0.77 (0.44,1.34)	0.35
Alcohol consumption	0.99 (0.74,1.32)	0.95	1.10 (0.81,1.49)	0.54	0.21 (0.06,0.78)*	0.02
Statin	1.44 (1.14,1.81)*	0.002	1.52 (1.16,1.99)*	0.002	1.28 (0.81,2.01)	0.30
Gender	1.41 (1.09,1.84)*	0.009				
	Achieving TG < 150 mg/dL					
	All (n = 1584)	p	Men (n = 1188)	p	Women (n = 396)	p
	AOR (95% CI)		AOR (95% CI)		AOR (95% CI)	
Age (y)	1.03 (1.02,1.04)*	<0.0001	1.04 (1.02,1.05)*	<0.0001	1.01 (0.99,1.03)	0.43
BMI (kg/m^2)	0.93 (0.90,0.96)*	<0.0001	0.91 (0.87,0.94)*	<0.0001	0.98 (0.93,1.02)	0.31
Smoking status	0.69 (0.54,0.89)*	0.004	0.70 (0.54,0.91)*	0.008	0.76 (0.31,1.88)	0.56
History of DM or IGT	0.80 (0.64,1.00)*	0.04	0.79 (0.61,1.03)	0.08	0.81 (0.52,1.24)	0.33
History of HTN	0.93 (0.72,1.20)	0.57	0.97 (0.73,1.30)	0.85	0.81 (0.45,1.45)	0.48
Alcohol consumption	0.93 (0.69,1.27)	0.66	0.95 (0.69,1.30)	0.74	1.20 (0.37,3.98)	0.76
Statin	1.42 (1.11,1.82)*	0.005	1.60 (1.19,2.14)*	0.002	1.08 (0.68,1.74)	0.74
Gender	1.38 (1.04,1.84)*	0.03				

Data (smoking status, history of DM or IGT, history of HTN, alcohol consumption, statin) are presented as (yes vs. no).
*:$p < 0.05$.
AOR = adjusted odds ratio; BMI = body mass index; DM = diabetes mellitus; HDL-C = high density lipoprotein cholesterol; HTN = hypertension; IGT = impaired glucose tolerance; LDL-C = low density lipoprotein cholesterol; TC = total cholesterol; TG = triglyceride.

National Health Insurance (NHI), the policy of insurance payment and the statement of NHI payment for drugs used for dyslipidemia may influence the physician's behavior. One such example is the global budget system of NHI, in which physicians may choose not to titrate statin aggressively to a high dose. Another point of consideration is whether physicians are hesitant to prescribe statin or give more intensive statin therapy because of the concern about statin safety. A recent guideline from the American Heart Association recommended statin therapy to achieve the same LDL-C goals in women as in men[23]. Improving awareness of achieving lipid goal in women among physicians is an important step to rectify the undertreatment in women.

According to lipid treatment guidelines, the patients with chronic diseases such as HTN and DM have more strict lipid-lowering treatment goals. The present study also showed that cardiovascular comorbidities and risk factors were associated with reaching lipid-lowering treatment goals. However, even the prevalence rate of HTN and DM or IGT was higher in women and men with DM or IGT were more likely to attain the TC goal than women. We also found that men with higher BMI are difficult to achieve the

Table 4
Contributions of statin equivalent dose and other covariates in gender difference in optimal lipid goal attainment among patients with coronary artery disease.

	Achieving TC < 160 mg/dL					
	All (n = 1584)	p	Men (n = 1188)	p	Women (n = 396)	p
	AOR (95% CI)		AOR (95% CI)		AOR (95% CI)	
Age (y)	1.01 (1.01,1.02)*	0.004	1.02 (1.01,103)*	0.003	1.01 (0.99,1.03)	0.45
BMI (kg/m^2)	0.99 (0.96,1.02)	0.34	0.99 (0.96,1.03)	0.61	0.98 (0.93,1.03)	0.42
Smoking status	0.94 (0.75,1.19)	0.60	0.92 (0.73,1.17)	0.51	0.97 (0.38,2.49)	0.95
History of DM or IGT	1.47 (1.19,1.81)*	0.0004	1.49 (1.17,1.90)*	0.001	1.35 (0.87,2.10)	0.18
History of HTN	1.06 (0.84,1.35)	0.61	1.08 (0.84,1.41)	0.54	0.98 (0.55,1.75)	0.95
Alcohol consumption	0.83 (0.62,1.11)	0.20	0.89 (0.66,1.21)	0.47	0.16 (0.02,1.21)	0.08
Statin equivalent dose	1.54 (1.24,1.93)*	0.0001	1.75 (1.35,2.27)*	<0.0001	1.12 (0.71,1.75)	0.63
Gender	2.27 (1.73,2.97)*	<0.0001				
	Achieving HDL > 40 mg/dL in men and HDL > 50 mg/Dl in women					
	All (n = 1584)	p	Men (n = 1188)	p	Women (n = 396)	p
	AOR (95% CI)		AOR (95% CI)		AOR (95% CI)	
Age (y)	1.02 (1.01,1.03)*	<0.0001	1.02 (1.01,1.03)*	<0.0001	1.01 (0.99,1.03)	0.39
BMI (kg/m^2)	0.95 (0.93,0.98)*	0.0009	0.93 (0.90,0.96)*	<0.0001	1.00 (0.95,1.05)	0.98
Smoking status	0.82 (0.65,1.03)	0.09	0.82 (0.64,1.05)	0.11	0.94 (0.38,2.32)	0.90
History of DM or IGT	0.70 (0.57,0.86)*	0.0008	0.80 (0.63,1.02)	0.07	0.48 (0.31,0.72)*	0.0004
History of HTN	1.03 (0.82,1.31)	0.78	1.03 (0.79,1.33)	0.86	1.15 (0.67,1.99)	0.61
Alcohol consumption	1.12 (0.84,1.50)	0.43	1.17 (0.86,1.58)	0.31	1.06 (0.35,3.17)	0.92
Statin equivalent dose	1.19 (1.96,1.49)	0.12	1.33 (1.02,1.72)*	0.03	0.87 (0.57,1.34)	0.53
Gender	1.64 (1.26,2.12)*	0.0002				
	Achieving LDL-C < 100 mg/dL					
	All (n = 1584)	p	Men (n = 1188)	p	Women (n = 396)	p
	AOR (95% CI)		AOR (95% CI)		AOR (95% CI)	
Age (y)	1.02 (1.01,1.03)*	0.002	1.01 (1.00,1.03)*	0.02	1.03 (1.01,1.05)*	0.02
BMI(kg/m^2)	0.98 (0.95,1.01)	0.19	0.98 (0.95,1.02)	0.26	0.98 (0.94,1.03)	0.51
Smoking status	0.99 (0.79,1.25)	0.95	0.94 (0.74,1.20)	0.60	1.64 (0.64,4.19)	0.30
History of DM or IGT	1.27 (1.03,1.57)*	0.03	1.23 (0.96,1.57)	0.10	1.34 (0.88,2.03)	0.17
History of HTN	0.93 (0.74,1.18)	0.56	0.98 (0.75,1.27)	0.86	0.77 (0.44,1.34)	0.35
Alcohol consumption	0.99 (0.74,1.32)	0.92	1.09 (0.81,1.48)	0.57	0.21 (0.06,0.79)*	0.02
Statin equivalent dose	1.37 (1.10,1.70)*	0.005	1.46 (1.13,1.89)*	0.004	1.20 (0.78,1.84)	0.41
Gender	1.40 (1.08,1.82)*	0.01				
	Achieving TG < 150 mg/dL					
	All (n = 1584)	p	Men (n = 1188)	p	Women (n = 396)	p
	AOR (95% CI)		AOR (95% CI)		AOR (95% CI)	
Age (y)	1.03 (1.02,1.04)*	<0.0001	1.04 (1.02,1.05)*	<0.0001	1.01 (0.99,1.03)	0.43
BMI (kg/m^2)	0.93 (0.90,0.96)*	<0.0001	0.91 (0.87,0.94)*	<0.0001	0.98 (0.93,1.03)	0.33
Smoking status	0.69 (0.54,0.89)*	0.004	0.69 (0.53,0.90)*	0.006	0.78 (0.32,1.90)	0.58
History of DM or IGT	0.80 (0.64,0.99)*	0.04	0.79 (0.61,1.03)	0.08	0.81 (0.52,1.24)	0.33
History of HTN	0.93 (0.72,1.21)	0.60	0.98 (0.735,1.31)	0.89	0.81 (0.45,1.45)	0.47
Alcohol consumption	0.93 (0.68,1.26)	0.63	0.94 (0.68,1.30)	0.71	1.23 (0.37,4.06)	0.74
Statin equivalent dose	1.45 (1.15,1.83)*	0.002	1.69 (1.28,2.24)*	0.0002	0.99 (0.63,1.54)	0.95
Gender	1.38 (1.04,1.83)*	0.03				

Data (smoking status, history of DM or IGT, history of HTN, alcohol consumption) are presented as (yes vs. no).
*: $p < 0.05$.
AOR = adjusted odds ratio; BMI = body mass index; DM = diabetes mellitus; HDL-C = high density lipoprotein cholesterol; HTN = hypertension; IGT = impaired glucose tolerance; LDL-C = low density lipoprotein cholesterol; TC = total cholesterol; TG = triglyceride.

HDL-C goal. Reaching these lipid-lowering goals will be a greater challenge for the high-risk patients, especially for the women, who were more likely to have comorbidities as shown in the present study. This may contribute to the gender disparity in the lipid-lowering goal.

There are several limitations in the present study. First, our study was a cross-sectional study and the results may not reflect beyond the study population. However, our study provided the benchmark data of lipid goal attainment rate. Second, indeed, the registry data we use, although it provided comprehensive data on many variables, it should be mentioned that there may be some factors such as patient's preferences, attitudes, physical activity, dietary habits, adherence to lipid-lowering agents, education levels, and using oral contraceptives influencing goal attainment. The poorer socioeconomic factor had been reported to affect goal attainment[14]. However, health insurance in Taiwan covered by NHI may attenuate the effect of socioeconomic factors. These unobserved characteristics and behaviors may be potential sources of residual confounding. Further research is needed to these potential effects. Third, the number of women enrolled in our study was less

than the number of men, and the women were older than men. Selection bias may lead to difference in gender-related goal attainment because women enrolled in our study may have more severe dyslipidemia than men. In addition, it is difficult to estimate the extent of selection bias effect on gender disparity in achieving goal attainment rates. A follow-up study that focuses on these points needs to be conducted.

Our results have significant implications for clinical practice. Most of the factors in our study are modifiable. Physicians should attempt to narrow the gender-related lipid-lowering treatment gap by paying more attention to women, especially postmenopausal women and those with high LDL-C levels, providing an optimal treatment strategy to women.

Appendix 1

The calculation of statin equivalent doses according to dose efficacy of statin-based therapies for LDL-C reduction.

Equivalent dose of statin	Lovastatin	Pravastatin	Simvastatin	Fluvastatin	Atorvstatin	Rosuvastatin
1 dose	20	20	10	40	5	2.5
2 dose	40	40	20	80	10	5
4 dose	80	80	40		20	10
8 dose			80		40	20

Data are presented as mg.[10]

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