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Taiwanese Female Vegetarians Have Lower Lipoprotein-Associated Phospholipase A2 Compared with Omnivores

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Purpose: Many studies supported that vegetarians have a lower risk of cardiac diseases and mortality, partly due to better blood pressure and serum cholesterol profiles. However, the inflammatory markers, especially lipoprotein-associated phospholipase A2 (Lp-PLA2), have not been well-studied. This study aimed to compare inflammatory markers and conventional risk factors between vegetarians and omnivores. **Materials and Methods:** One hundred and seventy-three vegetarians and 190 omnivores were studied. Fasting blood samples were obtained to compare levels of glucose, total cholesterol, triacylglycerol, high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol, homocysteine, Lp-PLA2 activity, and high-sensitivity C-reactive protein (hs-CRP). **Results:** Vegetarians had higher serum levels of the following markers: hs-CRP (1.8 ± 3.4 vs. 1.2 1.8 mg/L, respectively; $p = 0.05$), homocysteine (9.39 ± 3.22 vs. 7.62 ± 2.41 μmol/L, respectively; $p < 0.01$), and triacylglycerol (96.91 ± 59.56 vs. 84.66 ± 43.24 mg/dL, respectively; $p < 0.05$). Vegetarians also had lower levels of Lp-PLA2 (18.32 ± 7.19 10-3 μmol/min/mL vs. 20.22 8.13 10-3 μmol/min/mL; $p < 0.05$), total cholesterol (180.62 ± 36.55 mg/dL vs. 192.73 ± 36.57 mg/dL; $p < 0.01$), LDL cholesterol (118.15 ± 32.8 vs. 126.41 ± 34.28 mg/dL; $p < 0.05$), and HDL cholesterol (55.59 ± 13.30 vs. 62.09 ± 14.52 mg/dL, $p < 0.01$). Multivariate analyses demonstrated that a vegetarian diet increases the chances for high serum hs-CRP and low Lp-PLA2 activity. **Conclusion:** In addition to lower total cholesterol, LDL-cholesterol, and HDL-cholesterol, Taiwanese female vegetarians have lower serum Lp-PLA2 activity but higher levels of hs-CRP, homocysteine, and triacylglyerol. It might be due to geographic differences of vegetarian diets, and further studies are needed.

Key Words: Vegetarian diet, risk factors, lipoprotein associated phospholipase A2, C-reactive protein, inflammation

INTRODUCTION

Many studies have shown that people on vegetarian diets have lower risks of ischemic heart disease mortality[1-4] and even lower overall mortality rates.[1,3] A vegetari-

an diet lowers blood pressure, serum total, and low density lipoprotein (LDL) cholesterol levels, and also improves endothelial function and insulin sensitivity, and thus reduces the risk of atherosclerosis.[5-11]

There are still some conflicting facts about the benefits of a vegetarian diet. For example, serum homocysteine has been reported to be higher in vegetarians than in omnivores.[7,12] Homocysteine stimulates vascular smooth muscle cells to proliferate and synthesize collagen; it also affects endothelial cell function and adversely affects anticoagulation, which may result in atherosclerosis.[13]

Chronic inflammation is an essential feature of the atherosclerotic process. High-sensitivity C-reactive protein (hs-CRP), a very important inflammatory marker, has been reported to be a strong independent risk factor for atherosclerosis and a cardiovascular prognosis.[14,15] Some studies[16] showed lower hs-CRP in vegetarians than omnivores. Other studies[7,17] failed to demonstrate that.

Lipoprotein-associated phospholipase A2 (Lp-PLA2), an enzyme mainly produced by monocytes/macrophages, generates potent proinflammatory products. In one study, elevated levels of Lp-PLA2 appeared to predict future coronary events in apparently healthy middle-aged men with moderately elevated total cholesterol levels, independent of hs-CRP.[18] This suggests that the cardiovascular outcome predictive effect of Lp-PLA2 and CRP may be additive.[18]

The status of Lp-PLA2-associated inflammation in vegetarians has not been studied. Thus, we designed a cross-section study enrolling a larger number of subjects, to compare the differences in inflammation markers in addition to conventional risk factors between vegetarians and omnivores by examining hs-CRP and Lp-PLA2 levels. To eliminate any gender bias on inflammation status, we enrolled only females in this study.

MATERIALS AND METHODS

All of the subjects were adult females (more than 20 years old) who had undergone a general health examination at the Buddhist Dalin Tzu-Chi General Hospital, Chia-Yi, Taiwan, from Jan 1, 2006 to Dec 31, 2006. All of the subjects filled out questionnaires regarding their dietary preferences and past medical history. Exclusion criteria include a history of smoking, diabetes, dyslipidemia, hypertension, cerebrovascular disease, chronic gingivitis, connective tissue disease such as systemic lupus erythematosus or rheuma-

toid arthritis, diagnosis of a coronary artery disease, or a fever or another infectious disease within 3 weeks prior to the start of the study. Those who fit the above criteria but not on a regular vegetarian diet at least one year before inclusion were enrolled into the omnivore group. Patients who had been on an ovo-lactovegetarian diet for at least 1 year before inclusion were enrolled into the vegetarian group.

Informed consent forms were obtained from all subjects and the study protocol was approved by the research committee and the institutional review board (IRB) of The Buddhist Dalin Tzu-Chi General Hospital (B09404004).

After an overnight fast for at least 12 hours, venous blood samples were obtained from all subjects. Each patient age, weight, height, heart rate, and blood pressure were recorded before blood withdrawal on the day of study inclusion. The fasting blood samples were tested for Lp-PLA2, hs-CRP, glucose, cholesterol, triacylglycerol, high density lipoprotein (HDL) cholesterol, LDL cholesterol, uric acid and homocysteine levels, and white blood cell (WBC) counts were recorded. Frozen serum samples were used for analyzing Lp-PLA2, hs-CRP, and homocysteine. Serum Lp-PLA2 activity was analyzed by dynamic assay with a platelet-activating factor acetylhydrolase assay kit in a unit of μmol/min/mL (Cayman Chemical Company, Ann Arbor, MI, USA). Samples were centrifuged with a Micron centrifugal filter device (YM-30, Millipore, Billerica, MA, USA) under a centrifugal force of 14,000 g and temperature controlled at 4°C, to reach a cut-off molecular weight of 30,000 Daltons. hs-CRP was measured with an enzyme-linked immunosorbent assay (ELISA) based on purified protein and polyclonal anti-C-reactive protein antibodies with a unit of mg/L (Cobas Integra 800 system, Roche Diagnostics GmbH, Mannheim, Germany). Homocysteine levels were measured using an immunoassay method in a unit of μmol/L (FPIA assay, AXSYM system, Abbott Laboratories, Chicago, IL, USA).

Statistical analysis

For basic comparisons, the two groups characteristics were primarily examined by independent t-tests. Furthermore, based on the two hypotheses specified for the effects of a vegetarian diet on the inflammation factors of Lp-PLA2 and CRP, we applied linear regressions to the influencing factors for exposure to a vegetarian diet. B values with 95% confidence intervals were estimated for the effects of predicting factors. Separately, Lp-PLA2 and CRP were treated as dependent variables in univariate and multivariate analy-

ses. In multivariate analyses, age and body mass index (BMI) were considered as potential confounders. However, in the case of secondary or intermediate associations within the causal relationship between dietary habit and these two inflammation markers, variables of basic characteristics that were not clearly independent influencing factors were excluded from the final model of multivariate analyses. SPSS 13.0 for Windows (SPSS Inc, Chicago, IL, USA) was utilized to perform all the statistical analyses and the significance level (a value) was set at 0.05.

RESULTS

A total of 363 subjects (190 omnivores, 173 vegetarians) were involved in the analysis. Their average age was 51.9 years old (SD: 9.9 years old), and all were female. Table 1 presents the basic characteristics of each group by independent t-tests. Remarkable discrepancies for age, levels of Lp-PLA2, glucose, cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, and homocysteine were detected between the two groups (p values < 0.05 or 0.01). However, basic comparisons showed no significant differences for BMI, blood pressure, heart rate, uric acid, WBC, and platelet

counts. It was noteworthy that the level of CRP reached borderline statistical significance between these two groups ($p = 0.05$). As to the results of linear regressions on Lp-PLA2, vegetarianism had significant effects on changes on Lp-PLA2 levels on univariate analyses (Table 2). In multivariate analyses, after adjusting for age and BMI as potential confounders, vegetarianism remained a significant factor influencing the Lp-PLA2 level [B value: - 1.79, 95% confidence interval (CI): - 3.58, - 0.01; $p < 0.05$]. A vegetarian diet decreased Lp-PLA2 levels remarkably (Table 3). Meanwhile, because of the overall low levels of CRP among healthy subjects, the estimated changes influenced by predicting factors were tiny. Thus, we applied three digits after the decimal point. In univariate (Table 4) or multivariate (Table 5) analyses, significant positive correlation to CRP levels with vegetarianism and BMI were detected (B values for vegetarianism and BMI, separately: 0.058 and 0.010, 95% CIs: 0.001, 0.114 and 0.001, 0.018; both p values < 0.05).

DISCUSSION

Our current study demonstrated that as a new inflammation marker, serum Lp-PLA2 activity is lower in apparently

Table 1. Basic Characteristics of Both Groups

Variable	Omnivores (n = 190)	Vegetarians (n = 173)	p value*
Age SD (yrs)	49.94 ± 9.77	54.00 ± 9.70	< 0.01[†]
BMI SD (kg/m^2)	23.28 ± 3.47	22.87 ± 2.94	0.22
SBP SD (mmHg)	120.61 ± 18.07	122.29 ± 18.10	0.38
DBP SD (mmHg)	71.34 ± 10.22	72.02 ± 11.71	0.56
HR SD (times/min)	74.22 ± 9.91	74.69 ± 10.41	0.66
Lp-PLA2 SD (10^{-3} μmol/min/mL)	20.22 ± 8.13	18.32 ± 7.19	< 0.05[†]
Glucose SD (mg/dL)	87.45 ± 9.63	84.79 ± 8.06	< 0.01[†]
UA SD (mg/dL)	4.84 ± 1.22	4.66 ± 1.18	0.23
Cholesterol SD (mg/dL)	192.73 ± 36.57	180.62 ± 36.55	< 0.01[†]
TG SD (mg/dL)	84.66 ± 43.24	96.91 ± 59.56	< 0.05[†]
HDL-C SD (mg/dL)	62.09 ± 14.52	55.59 ± 13.30	< 0.01[†]
LDL-C SD (mg/dL)	126.41 ± 34.28	118.15 ± 32.80	< 0.05[†]
hs-CRP SD (mg/L)	1.2 ± 1.8	1.8 ± 3.4	0.05
WBC SD (1,000/μL)	6.15 ± 1.51	6.02 ± 1.36	0.39
Plt SD (1,000/μL)	247.79 ± 52.99	254.73 ± 68.69	0.29
Homocysteine SD (μmol/L)	7.62 ± 2.41	9.39 ± 3.22	< 0.01[†]

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; Lp-PLA2, lipoprotein-associated phospholipase A2; UA, uric acid; TG, triglyceride, HDL-C, high density lipoprotein cholesterol, LDL-C, low density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; WBC, white blood cell; Plt, platelet counts.
*Independent t-tests were performed.
[†]Statistically significant.

Table 2. Univariate Analyses for Influencing Factors on Lp-PLA2 (n = 363)

Variable	B value	95 % Confidence interval	p value
Vegetarian			
No	Ref.	-	
Yes	- 0.19	- 3.63, - 0.16	< 0.05*
Age (yr)	0.03	- 0.12, 0.06	0.47
BMI (kg/m^2)	0.07	- 0.20, 0.34	0.61
SBP (mmHg)	0.05	- 0.01, 0.09	0.06
DBP (mmHg)	0.10	0.02, 0.18	< 0.05*
HR (times/min)	0.05	- 0.04, 0.13	0.31
Glucose (mg/dL)	0.11	0.01, 0.20	< 0.05*
UA (mg/dL)	0.04	- 0.69, 0.76	0.92
Cholesterol (mg/dL)	0.02	- 0.01, 0.04	0.08
TG (mg/dL)	- 0.01	- 0.02, 0.02	0.95
HDL (mg/dL)	0.01	- 0.06, 0.06	0.91
LDL (mg/dL)	0.03	0.00, 0.05	0.05
hs-CRP (mg/L)	0.98	- 3.15, 5.11	0.64
WBC (1,000/μL)	0.48	- 0.11, 1.06	0.11
Plt (1,000/μL)	- 0.01	- 0.02, 0.01	0.25
Homocysteine (μmol/L)	- 0.16	- 0.49, 0.17	0.34

Lp-PLA2, lipoprotein-associated phospholipase A2; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; UA, uric acid; TG, triglyceride; HDL, high density lipoprotein; LDL, low density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; WBC, white blood cell; Plt, platelet counts.
*Statistically significant.

Table 3. Multivariate Analyses for Influencing Factors on Lp-PLA2 (n = 363)

Variable	B value	95% Confidence interval	p value
Vegetarian			
No	Ref.	-	
Yes	- 1.79	- 3.58, - 0.01	< 0.05*
Age (yr)	- 0.02	- 0.11, 0.07	0.68
BMI (kg/m^2)	0.06	- 0.21, 0.34	0.65

Lp-PLA2, lipoprotein-associated phospholipase A2; BMI, body mass index.
*Statistically significant.

healthy Taiwanese vegetarians than in omnivores. Elevated Lp-PLA2 has been proven to be an independent risk factor for inflammation, was additive to hs-CPR as a predictor of cardiovascular events[18,19] and a risk factor for a new or recurrent ischemic stroke.[20,21] This provided the basis that Taiwanese vegetarian diets might have protective effects on cardiovascular disease and ischemic stroke via the mechanism of lower Lp-PLA2 levels in vegetarians.

However, our results also demonstrated a lower serum hs-CRP level in omnivores than in vegetarians. This result is different from Szeto report,[16] which showed a lower serum hs-CRP in apparently healthy Hong Kong vegetarians than in omnivores. It is different from our previous study, too.[7] Our previous study showed a borderline lower serum hs-CRP in vegetarians but there are many study limitations in it. As we know, gender and smoking influenced the serum hs-CRP level significantly.[22,23] In our previous study, there are more males and smokers in the omnivore group that can influence the statistical power of difference of hs-CRP between both groups. Actually, it failed to demonstrate a significant difference if male and female samples were analyzed separately. Also, the case number of our previous study is small. So, we conducted the present study with more subjects and only female nonsmokers were enrolled. We believe that our present study is better controlled and more reliable than our previous one. There are several possible explanations for lower Lp-PLA2 and higher hs-CRP in Taiwanese female vegetarians. Firstly, there are

Table 4. Univariate Analyses for Influencing Factors on hs-CRP (n = 363)

Variable	B value	95 % Confidence interval	p value
Vegetarian			
No	Ref.	-	
Yes	0.057	0.001, 0.112	< 0.05*
Age (yr)	0.002	- 0.001, 0.005	0.187
BMI (kg/m^2)	0.010	0.001, 0.018	< 0.05*
SBP (mmHg)	0.000	- 0.001, 0.002	0.690
DBP (mmHg)	0.001	- 0.002, 0.003	0.657
HR (times/min)	0.002	0.000, 0.005	0.098
Glucose (mg/dL)	0.002	- 0.001, 0.005	0.286
UA (mg/dL)	0.023	0.001, 0.046	< 0.05*
Cholesterol (mg/dL)	0.000	- 0.001, 0.001	0.647
TG (mg/dL)	0.001	0.000, 0.001	< 0.01*
HDL-C (mg/dL)	- 0.002	- 0.004, 0.000	0.052
LDL-C (mg/dL)	0.000	- 0.001, 0.001	0.991
Lp-PLA2 (10^{-3} μmol/min/mL)	0.001	- 0.002, 0.004	0.641
WBC (1,000/μL)	0.023	0.004, 0.042	< 0.05*
Plt (1,000/μL)	0.000	0.000, 0.001	0.125
Homocysteine (μmol/L)	0.007	- 0.002, 0.016	0.150

hs-CRP, high-sensitivity C-reactive protein; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; UA, uric acid; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; Lp-PLA2, lipoprotein-associated phospholipase A2; WBC, white blood cell; Plt, platelet counts.
*Statistically significant.

Table 5. Multivariate Analyses for Influencing Factors on hs-CRP (n = 363)

Variable	B value	95% Confidence interval	p value
Vegetarian			
No	Ref.	-	
Yes	0.058	0.001, 0.114	< 0.05*
Age (yr)	0.001	- 0.002, 0.004	0.698
BMI (kg/m^2)	0.010	0.001, 0.018	< 0.05*

hs-CRP, high-sensitivity C-reactive protein; BMI, body mass index.
*Statistically significant.

large variations of hs-CRP levels which makes statistical analysis difficult (as evidenced by standard deviation greater than mean in both our current study and Szeto report). Secondly, Lp-PLA2 appeared to be a specific marker of vascular inflammation, whereas hs-CRP is a circulating marker influenced by chronic systemic inflammation and obesity.[24-26] Thirdly, it might be due to the geographic differences in vegetarian diets. Most western vegetarians include fresh vegetables and fruits as their main source of nutrition and energy, based on health benefits of the foods. In contrast, most Taiwanese vegetarians choose a vegetarian diet because of their Buddhist religion, which teaches a policy of "no killing" Buddhists in Taiwan have a dietary pattern similar to that of most Taiwanese in terms of meal pat-

terns and cooking methods, except that they do not include any meat, fish, or poultry in their meals. The Taiwanese vegetarian diet includes a large intake of soybean products, which are the major substitute for animal products.[27] In comparison to western vegetarians, Taiwanese vegetarians consume fewer fresh vegetables and usually cook their vegetables in oil. They also consume many deep-fried and refined soybean and grain products, which probably contain many more oxidative groups, and more oil and even trans fatty acids since trans fatty acids are mainly produced during oil hardening in food processing.[28] Studies have confirmed that a diet and a cooking pattern that includes processed, fried, and refined foods, such as meats, grains, and beans, are associated with an elevation of inflammation markers,

such as hs-CRP, adhesion molecules, and impaired endothelial function.[29,30] Consuming foods containing more trans fatty acids will also result in higher serum inflammation markers, adhesion molecules, and impaired endothelial function.[31] Further study with detailed food item questionnaires might serve to elucidate the exact mechanism.

As the Atherosclerosis Risk in Communities (ARIC) Study showed, there was no correlation between Lp-PLA2 and hs-CRP.[19] According to the comments of Zalewski and Macphee,[24] circulating Lp-PLA2 levels are dependent on the level of its carrier, LDL cholesterol, and CRP and Lp-PLA2 do not correlate because they probably reflect disparate inflammatory pathways.

Ridker, et al.[15] demonstrated that hs-CRP was the strongest univariate predictor of future cardiovascular events (relative risk, 4.4), followed by the ratio of total cholesterol to HDL-C, total cholesterol, LDL cholesterol, and homocysteine (relative risk, 2) in a prospective case-control study of 28,263 healthy postmenopausal women followed for more than 3 years. Our study demonstrated that Taiwanese vegetarians have lower Lp-PLA2, total cholesterol, HDL cholesterol, and LDL cholesterol, but higher hs-CRP, homocysteine, and triacylglycerol. Since each of these risk factors carries different relative risk ratios, the net effect on cardiovascular protection is difficult to estimate. Long-term follow-up on this group of subjects is warranted and interventions to modify these risk profiles should be studied.

ACKNOWLEDGEMENTS

REFERENCES

1. Burr ML, Sweetnam PM. Vegetarianism, dietary fiber, and mortality. Am J Clin Nutr 1982;36:873-7.
2. Phillips RL, Lemon FR, Beeson WL, Kuzma JW. Coronary heart disease mortality among Seventh-Day Adventists with differing dietary habits: a preliminary report. Am J Clin Nutr 1978;31: S191-8.
3. Key TJ, Appleby PN, Davey GK, Allen NE, Spencer EA, Travis RC. Mortality in British vegetarians: review and preliminary results from EPIC-Oxford. Am J Clin Nutr 2003;78:533S-8S.
4. Key TJ, Fraser GE, Thorogood M, Appleby PN, Baral V, Reeves G, et al. Mortality in vegetarians and nonvegetarians: detailed findings from a collaborative analysis of 5 prospective studies. Am J Clin Nutr 1999;70:516S-24S.
5. Fraser GE. Associations between diet and cancer, ischemic heart disease, and all-cause mortality in non-Hispanic white California Seventh-day Adventists. Am J Clin Nutr 1999;70:532S-8S.
6. Knuiman JT, West CE. The concentration of cholesterol in serum and in various serum lipoproteins in macrobiotic, vegetarian and non-vegetarian men and boys. Atherosclerosis 1982;43:71-82.
7. Chen CW, Lin YL, Lin TK, Lin CT, Chen BC, Lin CL. Total cardiovascular risk profile of Taiwanese vegetarians. Eur J Clin Nutr 2008;62:138-44.
8. Ko YC. Blood pressure in Buddhist vegetarians. Nutr Rep Int 1983;28:1375-83.
9. Lin CL, Fang TC, Gueng MK. Vascular dilatory functions of ovo-lactovegetarians compared with omnivores. Atherosclerosis 2001;158:247-51.
10. Kuo CS, Lai NS, Ho LT, Lin CL. Insulin sensitivity in Chinese ovo-lactovegetarians compared with omnivores. Eur J Clin Nutr 2004;58:312-6.
11. Hung CJ, Huang PC, Li YH, Lu SC, Ho LT, Chou HF. Taiwanese vegetarians have higher insulin sensitivity than omnivores. Br J Nutr 2006;95:129-35.
12. Krajcovicová -Kudláčková M, Blazíček P, Kopcová J, Béderová A, Babinská K. Homocysteine levels in vegetarians versus omnivores. Ann Nutr Metab 2000;44:135-8.
13. Harpel PC. Homocysteine, atherogenesis and thrombosis. Fibrinolysis & Proteolysis 1997;11:77-80.
14. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1997;336:973-9.
15. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342:836-43.
16. Szeto YT, Kwok TC, Benzie IF. Effects of a long-term vegetarian diet on biomarkers of antioxidant status and cardiovascular disease risk. Nutrition 2004;20:863-6.
17. Mezzano D, Muñoz X, Martínez C, Cuevas A, Panes O, Aranda E, et al. Vegetarians and cardiovascular risk factors: hemostasis, inflammatory markers and plasma homocysteine. Thromb Haemost 1999;81:913-7.
18. Koenig W, Khuseyinova N, Löwel H, Trischler G, Meisinger C. Lipoprotein-associated phospholipase A2 adds to risk prediction of incident coronary events by C-reactive protein in apparently healthy middle-aged men from the general population: results from the 14-year follow-up of a large cohort from southern Germany. Circulation 2004;110:1903-8.
19. Ballantyne CM, Hoogeveen RC, Bang H, Coresh J, Folsom AR, Heiss G, et al. Liporotein-associated phospholipase A2, high-sensitivity C-reactive protein, and risk for incident coronary heart disease in middle-aged men and women in the Atherosclerosis Risk

in Communities (ARIC) study. Circulation 2004;109:837-42.

20. Oei HH, van der Meer IM, Hofman A, Koudstaal PJ, Stijnen T, Breteler MM, et al. Lipoprotein-associated phospholipase A2 activity is associated with risk of coronary heart disease and ischemic stroke: the Rotterdam Study. Circulation 2005;111:570-5.

21. Elkind MS, Tai W, Coates K, Paik MC, Sacco RL. High-sensitivity C-reactive protein, lipoprotein-associated phospholipase A2, and outcome after ischemic stroke. Arch Intern Med 2006;166: 2073-80.

22. Zedler BK, Kinser R, Oey J, Nelson B, Roethig HJ, Walk RA, et al. Biomarkers of exposure and potential harm in adult smokers of 3-7 mg tar yield (Federal Trade Commission) cigarettes and in adulted non-smokers. Biomarkers 2006;11:201-20.

23. Lakoski SG, Cushman M, Criqui M, Rundek T, Blumenthal RS, D'Agostino RB Jr, et al. Gender and C-reactive protein: data from the Multiethnic Study of Atherosclerosis (MESA) cohort. Am Heart J 2006;152:593-8.

24. Zalewski A, Macphee C. Role of lipoprotein-associated phospholipase A2 in atherosclerosis. Biology, epidemiology, and possible therapeutic target. Arterioscler Thromb Vasc Biol 2005;25:923-31.

25. Garza CA, Montori VM, McConnell JP, Somers VK, Kullo IJ, Lopez-Jimenez F. Association between lipoprotein-associated phospholipase A2 and cardiovascular disease: a systematic review. Mayo Clin Proc 2007;82:159-65.

26. Packard CJ, O'Reilly DS, Caslake MJ, McMahon AD, Ford I, Cooney J, et al. Lipoprotein-associated phospholipase A2 as an independent predictor of coronary heart disease. West of Scotland Coronary Prevention Study Group. N Engl J Med 2000;343:1148-55.

27. Pan WH, Chin CJ, Sheu CT, Lee MH. Hemostatic factors and blood lipids in young Buddhist vegetarians and omnivores. Am J Clin Nutr 1993;58:354-9.

28. Lee HY, Woo J, Chen ZY, Leung SF, Peng XH. Serum fatty acid, lipid profile and dietary intake of Hong Kong Chinese omnivores and vegetarians. Eur J Clin Nutr 2000;54:768-73.

29. Nettleton JA, Steffen LM, Mayer-Davis EJ, Jenny NS, Jiang R, Herrington DM, et al. Dietary patterns are associated with biochemical markers of inflammation and endothelial activation in the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Clin Nutr 2006;83:1369-79.

30. Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, et al. Major dietary patterns are related to plasma concentration of markers of inflammation and endothelial dysfunction. Am J Clin Nutr 2004;80:1029-35.

31. Lopez-Garcia E, Schulze MB, Meigs JB, Manson JE, Rifai N, Stampfer MJ, et al. Consumption of trans fatty acid is related to plasma biomarkers of inflammation and endothelial dysfunction. J Nutr 2005;135:562-6.