Journal of the American College of Cardiology
© 2005 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 46, No. 10, 2005
ISSN 0735-1097/05/$30.00

CORRESPONDENCE

Research Correspondence

Vascular Dysfunction in Chinese Vegetarians: An Apparent Paradox?

To the Editor: It is commonly believed that vegetarian diets are cardioprotective. But a recent analysis of three major epidemiologic studies of vegetarians in the United Kingdom failed to show significant reduction in cardiovascular mortality, when compared with omnivores of similar lifestyles (1).

Chinese vegetarians have high prevalence of vitamin B_{12} deficiency, because of low intakes of dairy products and fortified cereal products, and higher serum triglyceride concentrations and salt intakes, when compared with omnivores (2). In contrast, the omnivores in Hong Kong have high intakes of fish and seafood, which might have cardioprotective effects from omega-3 fatty acids (3).

Therefore, a community-based case-control study was performed to examine vascular health of vegetarians by measuring the risk factors: carotid intima-media thickness (IMT) and flow-mediated dilation (FMD) of brachial artery, both key surrogate atherosclerosis markers predictive of cardiovascular events and stroke.

Community-dwelling vegetarian subjects, ages 18 to 70 years, were recruited from local vegetarian and religious societies. The subjects had been vegetarian for five years or more, were non-smoking, had no known major diseases, and were not receiving regular medication, including B vitamins.

For each vegetarian subject, one age- and gender-matched omnivore control subject was selected from participants in a Hong Kong community-based study of atherosclerosis in Southeastern Chinese (4). The same exclusion criteria were applied.

Fifteen milliliters of fasting blood was taken, kept in an ice-box, and delivered to a hospital laboratory within 1 h. Serum was analyzed for total cholesterol, triglyceride, creatinine, and glucose concentrations. Plasma was kept frozen at −70°C and analyzed later for total plasma homocysteine (enzymatic immunoassay, Abbott IMX analyzer; GMI, Ramsey, Minnesota) (5), folate, and vitamin B_{12} (solid-phase no-boil dual count radioimmunoassay). Sitting blood pressure was measured with an electronic sphygmomanometer. The mean of systolic and diastolic blood pressures was used for data analysis.

A locally validated food frequency questionnaire was administered to estimate dietary intakes over the previous one week (6).

Carotid IMT scans were performed by operators following a standardized scanning protocol for the right and left carotid arteries (3). The measurement procedures of brachial artery FMD have been documented previously (4). All scans were recorded on super-VHS videotape and subsequently analyzed by the same blinded investigator.

Vascular risk factors, dietary nutrient intakes, carotid IMT, and brachial FMD (mean ± SD) of vegetarian and age/gender-matched omnivore control subjects were compared by paired *t* test.

Known traditional cardiovascular risk factors, including age, gender, mean blood pressure, and serum cholesterol and triglyceride concentrations, were used to adjust for differences between vegetarian and omnivore groups in IMT and FMD in a multivariate analysis model.

Forty-nine vegetarian subjects (49% male) were examined. The mean duration of vegetarianism was 16.0 ± 8.4 years (range 6 to 40 years). Two subjects were vegans. The comparison of vascular risk factors of vegetarians and omnivores is shown in Table 1.

The nutrient intakes of vegetarians and omnivore control subjects were comparable, except that vegetarians had significantly lower intake of protein (59.1 ± 33.8 g/day vs. 82.0 ± 35.6 g/day in control subjects), saturated fatty acid (11.2 ± 5.8 g/day vs. 14.9 ± 6.0 g/day), and cholesterol (106 ± 116 mg/day vs. 275 ± 151 mg/day), after Bonferroni correction for multiple comparisons (all $p < 0.001$).

When compared with age- and gender-matched omnivore control subjects, vegetarians had significantly greater mean carotid IMT (0.67 ± 0.09 mm vs. 0.56 ± 0.11 mm, 95% confidence interval [CI] 0.07 to 0.13 mm, $p < .0001$) and less brachial FMD (6.4 ± 1.8% vs. 10.0 ± 2.6%, 95% CI −4.4% to −2.7%, $p < 0.0001$) (Fig. 1).

Among all subjects, age, gender, triglyceride, blood pressures, plasma homocysteine, and vitamin B_{12} concentrations were significantly correlated with IMT and FMD (all $p < 0.02$). There was no correlation between FMD or IMT and protein intake. On

Table 1. Characteristics of Vegetarian and Age- and Gender-Matched Omnivore Control Subjects*

	Vegetarian (n = 49)	Control (n = 49)	95% CI of Difference
Age (yrs)	45.3 ± 10.0	44.9 ± 11.4	−0.3 to 1.2
Body mass index (kg/m^2)	22.6 ± 2.7	22.5 ± 3.0	−1.0 to 1.1
Waist-hip ratio	0.82 ± 0.07	0.84 ± 0.07	−0.05 to 0.01
Mean blood pressure (mm Hg)	99.0 ± 13.2†	93.7 ± 9.6	1.1 to 9.7
Total cholesterol (mmol/l)	4.6 ± 0.8‡	5.3 ± 1.0	−1.1 to −0.5
LDL-cholesterol (mmol/l)	2.4 ± 0.6‡	3.4 ± 1.0	−1.3 to −0.7
Triglyceride (mmol/l)	1.4 ± 1.4†	0.9 ± 0.4	0.1 to 0.9
Glucose (mmol/l)	4.8 ± 0.6†	5.5 ± 1.9	−1.2 to 0.1
Creatinine (μmol/l)	78.4 ± 15.7†	71.1 ± 19.2	1.4 to 13.2
Homocysteine (μmol/l)	12.9 ± 7.8‡	9.2 ± 2.6	1.6 to 6.0
Folate (nmol/l)	45.0 ± 21.7†	35.7 ± 16.1	2.3 to 16.2
Vitamin B_{12} (pmol/l)	189 ± 165‡	327 ± 137	−196 to −79

*Values expressed as mean ± SD; †$p < 0.05$; ‡$p < .005$, paired *t* test.
CI = confidence interval; Control = control subject; LDL = low-density lipoprotein.

JACC Vol. 46, No. 10, 2005
November 15, 2005:1957–64

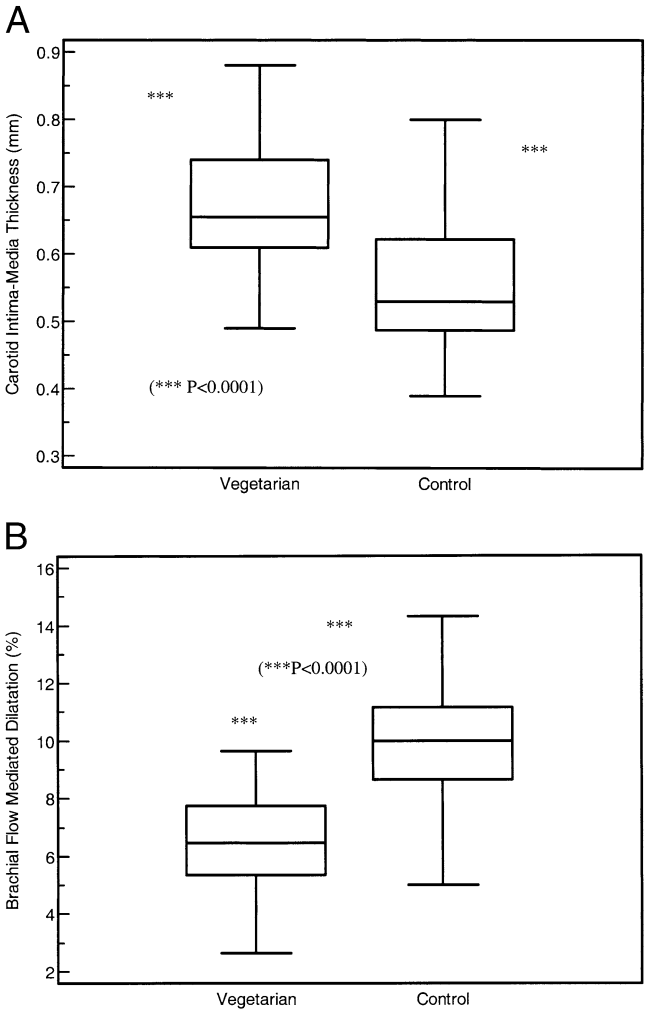

Figure 1. Comparison of the carotid intima-media thickness **(A)** and brachial flow-mediated dilatation **(B)** (box and whisker plot) in vegetarians and age/gender-matched omnivore control subjects.

multivariate analyses, age (beta = 0.304), gender (beta = 0.169), and vegetarian group (beta = 0.464) were independently associated with IMT [$r = 0.64$, $p < 0.0001$], whereas triglyceride (beta = −0.202) and vegetarian group (beta = 0.588) were correlated with FMD [$r = 0.67$, $p < 0.0001$]. When plasma homocysteine or vitamin B_{12} concentration was added into the model, the vegetarian group remained significantly associated with IMT and FMD.

This study showed that vegetarians had greater carotid intima-media thickening and less effective endothelial function than the age- and gender-matched omnivore control subjects, raising concern, for the first time, about the vascular health of vegetarians.

The mean blood pressures and serum creatinine of this group of Chinese vegetarians were significantly higher than those of control subjects. This might be attributed to the high sodium contents of the local vegetarian diets, which include processed protein food substitutes, vegetarian oyster sauce, and tomato paste. In addition, vegetarians had higher triglyceride concentrations than the omnivores, probably because of the high carbohydrate contents, which also increase insulin resistance.

Vegetarians had significantly lower plasma vitamin B_{12} and higher homocysteine concentrations, which might also be associated with greater carotid IMT and decreased brachial artery FMD. This suggests that vitamin B_{12} deficiency in vegetarians might have adverse effects on their vascular health. A vitamin B_{12} supplementation intervention study in improving vascular function in vegetarians is awaited with much interest.

In summary, contrary to common belief, vegetarians, at least in the Chinese, might have accelerated atherosclerosis and abnormal arterial endothelial function, compared with omnivore control subjects. The increased risk could only be partially explained by their higher blood pressure, triglyceride, homocysteine, and lower vitamin B_{12} concentrations.

Timothy Kwok, MD
Ping Chook, MD
Lucia Tam, MPh
Mu Qiao, PhD
Jean L. F. Woo, MD
David S. Celermajer, PhD
***Kam S. Woo, MD, FACC**

*Department of Medicine and Therapeutics
Prince of Wales Hospital, Shatin
Hong Kong SAR
E-mail: ramsangwoo@cuhk.edu.hk

doi:10.1016/j.jacc.2005.07.054

Please note: This project was partially supported by the Hong Kong Institute of Heart Health Promotion of the Hong Kong College of Cardiology and a Direct Grant of the Chinese University of Hong Kong.

REFERENCES

1. Key TJ, Appleby PN, Davey GK, Allen NE, Specncer EA, Travis RC. Mortality in British vegetarians: review and preliminary results from EPIC-Oxford. Am J Clin Nutr 2003;78 Suppl:533S–8S.
2. Woo J, Kwok T, Ho SC, Sham A, Lau E. Nutritional status of elderly Chinese vegetarians. Age Ageing 1998;27:455–61.
3. Woo J, Woo KS, Leung SS, et al. The Mediterranean score of dietary habits in Chinese populations in four different geographical areas. Eur J Clin Nutr 2001;55:215–20.
4. Woo KS, Chook P, Raitakari OT, McQuillan B, Feng JZ, Celermajer DS. Westernization of Chinese adults and increased subclinical atherosclerosis. Arterioscler Thromb Vas Biol 1999;19:2487–93.
5. Woo KS, Chook P, Lolin YI, et al. Hyperhomocysteinemia is a risk factor for arterial endothelial dysfunction in humans. Circulation 1997;96:2542–4.
6. Woo J, Leung SSF, Ho SC, Sham A, Lam TH, Janus ED. A food frequency questionnaire for use in the Chinese population in Hong Kong: description and examination of validity. Nutr Res 1997;17: 1633–41.