



## Vegetarians have a lower fasting insulin level and higher insulin sensitivity than matched omnivores: A cross-sectional study

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### KEYWORDS

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BMI

**Abstract** *Background and aims:* Potential associations of vegetarian diet patterns with fasting insulin (FI) and insulin sensitivity remain unclear. We aimed to investigate whether vegetarian diets were associated with FI and insulin sensitivity in a cross-sectional study in Chinese vegetarians and matched omnivores and then to test whether it is independent of body mass index (BMI).

*Methods and results:* This study included 279 vegetarians (73 vegans, 206 lacto-ovo-vegetarians) and 279 age- and sex-matched omnivores. Fasting blood glucose (FG) and FI concentrations were measured, and  $\beta$ -cell function (HOMA- $\beta$ ) and insulin resistance index (HOMA-IR) were used to evaluate insulin sensitivity. All blood glucose and insulin sensitivity indices were naturally log-transformed, and multiple-linear regression was used to determine the association between vegetarian diet patterns and insulin sensitivity after adjusting for confounders including BMI, visceral fat area, physical activity, sedentary time, income, alcohol consumption, and daily dietary intakes of macronutrients. Compared to omnivores, both vegan diet [ $\beta = -0.25$ , 95% CI: (-0.38, -0.14)] and lacto-ovo-vegetarian diet [ $\beta = -0.10$ , 95% CI: (-0.18, -0.01)] were negatively associated with HOMA-IR after adjusting for BMI. Vegan diet remained negatively associated with FI [ $\beta = -0.16$ , 95% CI: (-0.30, -0.01)] and HOMA-IR [ $\beta = -0.17$ , 95% CI: (-0.32, -0.03)] after adjusting for all confounders.

*Conclusion:* Vegetarian diet, especially vegan diet, is negatively associated with FI and IR, independent of BMI.

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*List of abbreviations:* BMI, body mass index; WHR, waist-to-hip ratio; DM, diabetes mellitus; FG, fasting blood glucose; FI, fasting insulin; HOMA, homeostasis model assessment; HOMA-IR, homeostasis model assessment-insulin resistance index; HOMA- $\beta$ , homeostasis model assessment- $\beta$  cell function; BCD,  $\beta$  cell dysfunction; IR, insulin resistance; FFQ, food frequency questionnaire; Ln(FG), fasting blood glucose in natural log-scale; Ln(FI), fasting insulin in natural log-scale; Ln(HOMA-IR), homeostasis model assessment-insulin resistance index in natural log-scale; Ln(HOMA- $\beta$ ), homeostasis model assessment- $\beta$  cell function in natural log-scale; Ref, reference; CI, confidence interval.

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## Introduction

Type 2 diabetes mellitus (DM) has become a serious global health issue [1,2]. The International Diabetes Federation estimated in 2013 that there were 382 million people with diabetes worldwide, and this was predicted to increase to 471 million by 2035 [1,2]. Approximately 80% of people with diabetes currently live in low- and middle-income countries [1,2]. In China, a rapid increase in the prevalence of diabetes has been reported, recently estimated to affect 11.6% of the Chinese adult population [1,3]. Obesity and overweight are recognized to be important risk factors for diabetes and critical points of intervention for the control of diabetes [4–6]. An energy-restricted vegetarian diet has recently been reported to be effective for weight loss in subjects with diabetes, which decreases subcutaneous fat and visceral fat, along with intramuscular fat, which plays an important role in metabolic disorders and IR [7]. Periodic short-term energy restriction modulates  $\beta$ -cell regeneration and promotes normal insulin secretion and glucose homeostasis, with a potential role in treating both type 1 and type 2 diabetes [8] and suggesting that diet is a key element in diabetes control and treatment.

Vegetarian diets include several dietary patterns such as vegan and lacto-ovo-vegetarian diets. These contain a range of natural products and food forms of benefit for both the carbohydrate and lipid abnormalities found in diabetes [9–12]. It has been suggested that vegetarian diet may have a potential protective effect on the prevention and treatment of diabetes and its complications [9,13–19]. In addition, metabolic syndrome, blood lipids, and glucose metabolic profiles were reported to be lower and in better status in people who adopt vegetarian diet than those eating other diets [20–23]. However, whether the higher insulin sensitivity status in vegetarians is accounted for by weight loss remains unclear and controversial. In addition, the association between vegetarian diet duration and insulin sensitivity among various vegetarian diet patterns also requires further study.

In previous studies focused on vegetarian diet and IR, vegetarians were rarely classified by different vegetarian diet patterns for comparative analysis. Moreover, the duration of vegetarian diet and visceral fat area have rarely been considered in cross-sectional studies. Studies focused on the differences in insulin and insulin sensitivity among various vegetarian diet patterns and omnivores are required.

According to the results of previous studies, we assume that vegetarians may have a better glucose metabolic profile than omnivores, which may not be fully accounted for by obesity. This study aimed to test fasting blood glucose (FG), fasting blood insulin,  $\beta$ -cell function (HOMA- $\beta$ ), and insulin resistance index (HOMA-IR) status in subjects with different vegetarian diet patterns and compare the data with results in omnivores matched by gender and age. Then, we aimed to verify whether reported associations between vegetarian diet patterns and insulin sensitivity are accounted for by difference in BMI.

## Methods

### Population

A total of 558 subjects were recruited in this study, including 279 vegetarians and 279 omnivores, all of whom reported no history of diabetes or metabolic diseases. Vegetarians were recruited through vegetarian restaurants, vegetarian social organization activities, social media, official WeChat account, and Internet advertisements. Omnivores were matched for the same sex and age ( $\pm 1$  year) with vegetarians and were commonly relatives or friends of the matched vegetarians. The recruitment criteria included 1) following a vegetarian diet for at least 1 year; 2) being a resident of Shanghai for more than 6 months; 3) age between 18 and 60 years; and 4) being able to understand the contents of questionnaires. Subjects with severe nutritional malabsorption or systemic diseases such as cancer, heart failure, uremia, and liver cirrhosis or acute illness such as acute myocardial infarction were excluded. Female subjects who had been pregnant or breastfeeding in the previous year were excluded. After providing written informed consent, subjects participated in the study conducted at Xinhua Hospital between March 2016 and May 2016.

### Dietary and baseline assessments

Face-to-face interviews were conducted by trained dietitians to collect dietary information about vegetarian status (vegan or lacto-ovo-vegetarian), vegetarian duration, and additional baseline information. Subjects were defined as vegetarians if they had followed a vegetarian diet at all meals daily and persistently for at least 1 year; otherwise, they were considered as omnivores. Those who did not consume any animal product were defined as “vegans,” while those who consumed eggs and/or dairy products were “lacto-ovo-vegetarians.” Among the 279 vegetarians, there were 73 vegans (26.4%) and 206 lacto-ovo-vegetarians (73.6%). Daily macronutrient intakes for all subjects were assessed using a 24 h dietary recall method, supplemented with a semi-quantitative food frequency questionnaire (FFQ). The FFQ and baseline questionnaire were designed and modified according to vegetarian dietary habits based on a 2002 Chinese nutrition and health investigation questionnaire [24]. Oral descriptions, food images, and food models were provided by dietitians in the 24 h dietary recall method to help subjects recall and estimate their dietary intakes. Data collected using FFQs were inputted using Epi-Data software version 3.1 and preprocessed using software Microsoft Excel 2010. Daily nutrient intakes were calculated from the 24 h dietary recall data using Nutrition Calculator v2.5 software developed by National Institute of Nutrition and Food Safety of the Chinese Center for Disease Control and Prevention and Beijing Dwin Technology Co. Ltd.

### Laboratory tests

Blood samples were collected according to a standard method after 10–12 h of fasting and were sent to the Clinical Laboratory Center of Shanghai Xinhua Hospital for laboratory tests of FG and fasting insulin (FI) concentrations.

### Glucose metabolic profile and insulin sensitivity indices

Insulin sensitivity and  $\beta$ -cell function were assessed by the homeostasis model assessment (HOMA) and determined according to an established method [25], in which FI (mU/L) and fasting blood glucose (FG, mmol/L) used

$$\begin{aligned} \text{HOMA-IR} &= \text{FI} \times \text{FG}/22.5, \\ \beta\text{-cell function (\%)} &= 20 \times \text{FI}/(\text{FG} - 3.5), \end{aligned} \quad [21,26,27]$$

Lower HOMA-IR indicates higher insulin sensitivity. IR was defined as HOMA-IR > 2.60 [25,28].

### Physical activity and obesity assessment

Data of frequency, average duration, and the most common forms of exercise were collected using a baseline questionnaire [24], and daily physical activity was calculated to an approximate value by multiplying frequency with average duration. Working intensity was recorded; body weight and height were measured while subjects were minimally clothed without shoes using digital scales. Visceral fat area was examined using a calibrated Inbody 720 bio-impedance device (Biospace, Co., Ltd., Seoul, Korea). Waist circumference was measured at the umbilical level using a tape measure. According to the cut-off values recommended by BMI standards for the Chinese, obesity was defined as BMI  $\geq 28$  kg/m<sup>2</sup> and central obesity was defined as WHR  $\geq 0.85$  in this study.

### Covariates

BMI, vegetarian diet duration; income; alcohol consumption; daily dietary intakes including energy, fat, protein, carbohydrate, and fiber; physical activity; sedentary time; and visceral fat area.

### Statistical analysis

Data analysis was performed using Stata software version 14.0 (StataCorp, College Station, TX, USA). Continuous variables were presented as means  $\pm$  standard deviations (SDs) if they were normally distributed; otherwise, median (interquartile ranges) were used (e.g., age; physical activity; sedentary

time; visceral fat area; BMI; waist-to-hip ratio; daily dietary intakes including energy, protein, fat, carbohydrate, and fiber; and alcohol consumption). Categorical variables (e.g., sex, marital status, physical examination frequency, ethnicity, education level, working intensity, income, obesity, central obesity, vegetarian duration, alcohol use, IR, and  $\beta$ -cell dysfunction) were presented as proportions. To compare the differences between the vegetarian group and the omnivore group, paired *t* tests were performed for normally distributed continuous data, Wilcoxon matched-pair signed-rank tests were performed for non-normally distributed continuous or ordinal variables, and McNemar tests were performed for matched categorical variables. To compare the differences between the vegan group and the lacto-ovo-vegetarian group, Wilcoxon rank-sum tests were used for non-normally distributed continuous or ordinal variables, and  $\chi^2$  tests were used for categorical variables.

Multivariable adjusted  $\beta$  coefficients [95% confidence intervals (CIs)] and *P* values for the associations of vegetarian diet patterns [omnivore (reference), lacto-ovo-vegetarian, and vegan] with blood glucose metabolic profile (FG, FI, HOMA- $\beta$ , and HOMA-IR) in natural log-scale were estimated by linear regression. *P* values for linear trend were calculated with dietary patterns coded as 0, 1, and 2, for the three groups, respectively. The meanings of different models in the linear regression were as follows: Model 1, unadjusted regression; Model 2, regression with BMI controlled; Model 3, regression with BMI, vegetarian duration, income, alcohol consumption, and daily dietary intakes (energy, fat, protein, carbohydrate, and fiber) controlled; Model 4, regression with physical activity and sedentary time controlled building upon model 3; Model 5, regression with visceral fat area controlled building upon model 4.

All *P* values were calculated by two-sided tests, and the significance level for each test was set at *P* < 0.05.

## Results

### Characteristics of subjects

The mean ages of vegetarians and omnivores were 33 years and 32 years, respectively, and the mean vegetarian duration of vegetarians was 4 years. Vegetarians had lower body mass index (BMI) and lower waist-to-hip ratio values than omnivores (*P* < 0.05), and there was also a 10.4% lower proportion of obesity and a 14.3% lower proportion of central obesity in vegetarians (*P* < 0.05). Compared to omnivores, vegetarians reported higher income and higher daily intakes of carbohydrate and fiber but lower daily intakes of energy, protein, and fat. Additionally, the proportion of alcohol users and alcohol consumption were both lower in vegetarians than in omnivores (all *P* values < 0.05, Table 1). The proportion of subjects with IR was also lower in vegetarians at 1.4% than in omnivores at 4.7% (*P* < 0.05), but no difference was observed between the vegan group and the lacto-ovo-vegetarian group.

### Glucose metabolic profile and insulin sensitivity indices

Multilinear regression results showed that vegan diet was negatively associated with Ln (FG) ( $\beta = 0.03$ , 95% CI:  $-0.05$  to  $-0.01$ ), Ln (FI) ( $\beta = -0.23$ , 95% CI:  $-0.34$  to  $-0.11$ ), and Ln (HOMA-IR) ( $\beta = -0.25$ , 95% CI:  $-0.38$  to  $-0.14$ ) after adjusting for BMI, respectively, and lacto-ovo-vegetarian diet was negatively associated with Ln (FG) ( $\beta = -0.03$ ,

95% CI:  $-0.04$  to  $-0.02$ ) and Ln (HOMA-IR) ( $\beta = -0.10$ , 95% CI:  $-0.18$  to  $-0.01$ ) after controlling for BMI (Table 2). Furthermore, a vegan diet remained negatively associated with Ln (FI) ( $\beta = -0.18$ , 95% CI:  $-0.32$  to  $-0.04$ ) and Ln (HOMA-IR) ( $\beta = -0.21$ , 95% CI:  $-0.36$  to  $-0.06$ ) after adjusting for BMI, vegetarian duration, daily dietary intakes, and income per month in model 3. Physical activity and sedentary time were also controlled in model 4. To

**Table 1** Characteristics of vegetarians and omnivores.

|  | Vegan<br>(n = 73)    | Lacto-ovo-vegetarian<br>(n = 206) | Vegetarian<br>(n = 279)           | Omnivore<br>(n = 279) |
|--|----------------------|-----------------------------------|-----------------------------------|-----------------------|
| Female, %                                  | 74.0                 | 85.4                              | 82.4                              | 82.4                  |
| Age (y)                                    | 34 (29, 44)          | 32.5 (28, 39)                     | 33 (28, 41)                       | 32 (27, 40)           |
| Nonsmoker, %                               | 84.9                 | 92.7                              | 90.7                              | 92.5                  |
| Marital status, %                          |                      |                                   |                                   |                       |
| Unmarried                                  | 46.5                 | 47.6                              | 46.9                              | 41.9                  |
| Married                                    | 46.5                 | 49.0                              | 48.4                              | 54.8                  |
| Divorced or widowed                        | 7.0                  | 3.4                               | 4.0                               | 3.2                   |
| Physical examination frequency (y/time), % |                      |                                   |                                   |                       |
| $\leq 1$                                   | 40.3                 | 43.7                              | 42.8                              | 47.8                  |
| 2  | 11.1                 | 12.6                              | 12.2                              | 15.1                  |
| $> 2$                                      | 48.6                 | 43.7                              | 45.0                              | 37.1                  |
| Ethnicity, %                               |                      |                                   |                                   |                       |
| Han  | 97.3                 | 94.7                              | 95.3                              | 93.9                  |
| Else                                       | 2.7                  | 5.3                               | 4.7                               | 6.1                   |
| Education level, %                         |                      |                                   |                                   |                       |
| Elementary and Secondary                   | 21.9                 | 13.7                              | 15.8                              | 17.0                  |
| Vocational                                 | 19.2                 | 15.6                              | 16.5                              | 18.1                  |
| University and above                       | 58.9                 | 70.7                              | 67.7                              | 64.9                  |
| Working intensity, %                       |                      |                                   |                                   |                       |
| Light                                      | 84.9                 | 88.8                              | 87.8                              | 88.5                  |
| Middle                                     | 12.3                 | 6.8                               | 8.2                               | 6.8                   |
| Heavy                                      | 2.7                  | 4.4                               | 3.9                               | 4.7                   |
| Income (Yuan/month/person), %              |                      |                                   |                                   |                       |
| $< 3000$                                   | 17.8                 | 20.0                              | 19.5 <sup>a</sup>                 | 25.6                  |
| 3000–8000                                  | 38.4                 | 45.9                              | 43.9 <sup>a</sup>                 | 45.0                  |
| 8000–15,000                                | 28.8                 | 21.9                              | 23.7 <sup>a</sup>                 | 21.2                  |
| $> 15,000$                                 | 15.0                 | 12.2                              | 12.9 <sup>a</sup>                 | 8.3                   |
| Physical activity (min/wk)                 | 60 (0, 150)          | 60 (0, 180)                       | 60 (0, 180)                       | 60 (0, 120)           |
| Sedentary time (h/d)                       | 8 (5, 11.0)          | 8 (6, 10.0)                       | 8 (5, 10.0)                       | 8 (6, 10.1)           |
| Visceral fat area (cm <sup>2</sup> )       | 51.4 (40.7, 74.8)    | 52.8 (37.8, 72.7)                 | 52.7 (38.1, 74.0) <sup>a</sup>    | 64.6 (48.2, 89.0)     |
| Body mass index (kg/m <sup>2</sup> ), %    | 20.2 (18.8, 22.6)    | 20.6 (19.3, 23.6)                 | 20.5 (19.2, 22.6) <sup>a</sup>    | 21.9 (20.0, 24.0)     |
| $< 24$                                     | 91.8                 | 88.4                              | 89.2 <sup>a</sup>                 | 74.6                  |
| 24–28                                      | 6.8                  | 9.7                               | 9.0 <sup>a</sup>                  | 20.4                  |
| $\geq 28$                                  | 1.4                  | 1.9                               | 1.8 <sup>a</sup>                  | 5.0                   |
| Waist-to-hip ratio                         | 0.81 (0.79, 0.84)    | 0.82 (0.78, 0.85)                 | 0.82 (0.76, 0.83) <sup>a</sup>    | 0.83 (0.80, 0.88)     |
| Central obesity, %                         | 20.6                 | 21.8                              | 21.5 <sup>a</sup>                 | 35.8                  |
| Vegetarian duration (y)                    | 4 (2, 7)             | 4 (3, 6)                          | 4 (3, 6)                          | –                     |
| 1–4  | 56.2                 | 60.2                              | 59.1                              | –                     |
| 5–9  | 27.4                 | 29.1                              | 28.7                              | –                     |
| $\geq 10$                                  | 16.4                 | 10.7                              | 12.2                              | –                     |
| Dietary intake                             |                      |                                   |                                   |                       |
| Energy (Kcal/d)                            | 1431 (1136, 1825)    | 1471 (1128, 1793)                 | 1461 (1128, 1803) <sup>a</sup>    | 1678 (1378, 2090)     |
| Protein (g/d)                              | 46.9 (34.2, 58.1)    | 42.7 (32.7, 55.1)                 | 43.5 (33.1, 56.9) <sup>a</sup>    | 64.6 (49.1, 85.8)     |
| Fat (g/d)                                  | 36.2 (25.3, 48.0)    | 39.7 (29.7, 50.8)                 | 39.1 (28.8, 50.6) <sup>a</sup>    | 59.6 (44.4, 81.1)     |
| Carbohydrate (g/d)                         | 217.5 (163.4, 282.4) | 220.0 (166.7, 288.5)              | 217.9 (164.7, 281.9) <sup>a</sup> | 210.9 (157.2, 265.2)  |
| Fiber (g/d)                                | 15.6 (11.2, 20.3)    | 12.65 (8.5, 17.7) <sup>b</sup>    | 13.6 (9.2, 18.9) <sup>a</sup>     | 10.6 (7.5, 15)        |
| Alcohol user, %                            | 98.6                 | 93.7                              | 95.0                              | 81.7                  |
| Alcohol consumption (g/month)              | 420                  | 40 (30, 92)                       | 53 (30, 96) <sup>a</sup>          | 54 (12.0, 180)        |
| Insulin resistance (IR), %                 | 1.4                  | 1.5                               | 1.4 <sup>a</sup>                  | 4.7                   |

Data are expressed as percentage for categorical variables or median (interquartile range) for continuous variables due to their non-normal distribution. McNemar tests and Wilcoxon matched-pair sign rank tests were used for comparisons between the vegetarian group and the omnivore group.  $\chi^2$  tests and Wilcoxon rank-sum tests were used for comparisons between the vegan group and the lacto-ovo-vegetarian group.

<sup>a</sup> Statistical significance when comparing vegetarian and omnivore groups.

<sup>b</sup> Statistical significance when comparing vegan and lacto-ovo-vegetarian groups.

detect the influence of visceral fat on insulin sensitivity, visceral fat area was controlled in model 5 building upon model 4. Vegan diet remained negatively associated with Ln (FI) ( $\beta = -0.16$ , 95% CI:  $-0.30$  to  $-0.01$ ) and Ln (HOMA-IR) ( $\beta = -0.17$ , 95% CI:  $-0.32$  to  $-0.03$ ) after adjusting for all confounders in model 5, while lacto-ovo-vegetarian diet was no longer associated with Ln (FI) or Ln (HOMA-IR) after further adjustment.

**Discussion**

We showed that vegans had a lower level of fasting blood glucose, FI, and IR index than omnivores. In addition, a vegan diet was negatively associated with IR index independently from BMI and other confounding factors. As the first cross-sectional study among vegetarian population in mainland China, our study provides new evidence for the potential merits of different vegetarian dietary patterns.

Overweight and obesity are recognized as independent risk factors for type 2 diabetes, and evidence indicates that insulin sensitivity can be improved with weight loss interventions [29,30]. However, vegan and lacto-ovo-vegetarian diets were associated with lower IR index, even after adjusting for BMI and visceral fat area. This suggests that vegetarian diets may have a direct influence on insulin sensitivity unrelated to BMI. In a previous study, we have shown that vegetarians in Shanghai report consuming a balanced dietary energy supply of carbohydrates, fat, and

protein, with adequate consumption of whole grains, tubers, vegetables, and fruits according to the dietary recommended intakes of China [31]. Vegetarians were also found to consume more legumes and nuts with less fat and cholesterol but with some health-benefit minerals and vitamins than omnivores [31]. A plant-based diet with a variety of foods rich in phytochemicals and anti-oxidants, which may have a direct effect on alleviating inflammation and oxidative stress, may account for the higher insulin sensitivity in vegetarians, especially vegans. A recent prospective study reported that higher consumption of phytochemical-rich foods may have protective effects against the development of IR [32]. A combined dose of several natural antioxidants including vitamin C, green tea polyphenols, and grape seed extract proanthocyanidin may reduce obesity, cause improved insulin sensitivity, and be beneficial for obese patients and those with diabetes [33]. In addition, several studies have focused on phytochemicals such as soy isoflavone, extract of ginkgo leaves, allicin, bitter melon extract, and platyconic acid, concluding that these phytochemicals can decrease blood glucose and improve insulin sensitivity [33–39]. Increased plant consumption is a potential reason for improved insulin sensitivity in those consuming a vegan diet.

We found no association between vegetarian duration and blood glucose or insulin sensitivity among vegetarians. A research from Taiwan reported that long-term vegetarians have a lower IR index than omnivores and a

**Table 2** Associations between vegetarian diet patterns and glucose metabolic indexes.

|             |         | Omnivore | Lacto-ovo-vegetarian | P for lacto-ovo-vegetarian | Vegan                | P for vegan | P for linear trend |
|-------------|---------|----------|----------------------|----------------------------|----------------------|-------------|--------------------|
| Ln (FG)     | Model 1 | 0 (Ref.) | -0.04 (-0.05, -0.02) | <0.01                      | -0.04 (-0.06, -0.02) | <0.01       | <0.01              |
|             | Model 2 |          | -0.03 (-0.04, -0.02) | <0.01                      | -0.03 (-0.05, -0.01) | <0.01       | <0.01              |
|             | Model 3 |          | -0.03 (-0.04, -0.01) | <0.01                      | -0.03 (-0.05, -0.00) | 0.03        | <0.01              |
|             | Model 4 |          | -0.02 (-0.04, -0.01) | 0.01                       | -0.03 (-0.05, -0.00) | 0.04        | 0.03               |
|             | Model 5 |          | -0.01 (-0.03, 0.00)  | 0.12                       | -0.02 (-0.04, 0.00)  | 0.12        | 0.10               |
| Ln(FI)      | Model 1 | 0 (Ref.) | -0.14 (-0.23, -0.05) | <0.01                      | -0.33 (-0.45, -0.21) | <0.01       | <0.01              |
|             | Model 2 |          | -0.07 (-0.15, 0.02)  | 0.11                       | -0.23 (-0.34, -0.11) | <0.01       | <0.01              |
|             | Model 3 |          | -0.03 (-0.14, 0.08)  | 0.58                       | -0.18 (-0.32, -0.04) | 0.01        | 0.02               |
|             | Model 4 |          | -0.02 (-0.13, 0.09)  | 0.68                       | -0.17 (-0.31, -0.03) | 0.02        | 0.03               |
|             | Model 5 |          | -0.00 (-0.11, 0.11)  | 0.94                       | -0.16 (-0.30, -0.01) | 0.03        | 0.04               |
| Ln(HOMA-IR) | Model 1 | 0 (Ref.) | -0.18 (-0.27, -0.09) | <0.01                      | -0.37 (-0.50, -0.24) | <0.01       | <0.01              |
|             | Model 2 |          | -0.10 (-0.18, -0.01) | 0.03                       | -0.25 (-0.38, -0.14) | <0.01       | <0.01              |
|             | Model 3 |          | -0.06 (-0.17, 0.06)  | 0.34                       | -0.21 (-0.36, -0.06) | <0.01       | <0.01              |
|             | Model 4 |          | -0.05 (-0.16, 0.07)  | 0.42                       | -0.20 (-0.35, -0.04) | 0.01        | 0.01               |
|             | Model 5 |          | -0.02 (-0.13, 0.10)  | 0.76                       | -0.17 (-0.32, -0.03) | 0.02        | 0.03               |
| Ln(HOMA-β)  | Model 1 | 0 (Ref.) | 0.02 (-0.07, 0.11)   | 0.70                       | -0.15 (-0.28, -0.02) | 0.02        | 0.10               |
|             | Model 2 |          | 0.06 (-0.03, 0.15)   | 0.17                       | -0.09 (-0.21, 0.04)  | 0.19        | 0.62               |
|             | Model 3 |          | 0.07 (-0.05, 0.19)   | 0.22                       | -0.06 (-0.22, 0.09)  | 0.43        | 0.56               |
|             | Model 4 |          | 0.08 (-0.04, 0.20)   | 0.20                       | -0.06 (-0.21, 0.10)  | 0.48        | 0.61               |
|             | Model 5 |          | 0.06 (-0.06, 0.17)   | 0.33                       | -0.07 (-0.23, 0.08)  | 0.39        | 0.45               |

BMI = body mass index; FG = fasting blood glucose; FI = fasting insulin; HOMA-IR = homeostasis model assessment-insulin resistance index; HOMA-β = homeostasis model assessment-β cell function. Data were multivariable adjusted β coefficients [95% confidence intervals] using the omnivore group as control. P values for linear trend were calculated by coding dietary patterns (omnivore, lacto-ovo-vegetarian, and vegan) in the order of 0, 1, and 2, respectively.

Model 1, unadjusted regression;

Model 2, regression with BMI controlled;

Model 3, regression with BMI, vegetarian duration, income, alcohol consumption, and daily dietary intakes (energy, fat, protein, carbohydrate, and fiber) controlled;

Model 4, regression with physical activity and sedentary time controlled building upon model 3;

Model 5, regression with visceral fat area controlled building upon model 4.

long vegetarian duration ( $\geq 10$  years) may have protective effects against diabetes, metabolic disorders, and cardiovascular diseases [20]. This study only compared long-term vegetarians with omnivores but did not consider vegetarian duration into adjustment or detect the association of vegetarian duration and IR index among vegetarian patterns. We analyzed the association between vegetarian duration and IR index both between vegetarians and omnivores and within vegetarians; however, no association was detected. Therefore, it is lack of evidence to determine whether vegetarian duration over a year is protective against IR. This is potentially due to the effects on insulin sensitivity plateauing in less than a year after adopting a vegetarian or vegan diet. A few intervention studies suggest that short-term vegetarian diet interventions of less than one year can decrease IR [20,21,26]; hence, we consider that there is a possibility that a longer vegetarian duration (more than 1 year) may not contribute to consistent IR index decline but stabilize the organism's insulin sensitivity to a certain level that is evidently lower than that in omnivores. Nevertheless, further evidence is in need to verify a definite association between vegetarian diet duration and insulin sensitivity.

The cross-sectional nature of this study is a limitation and only capable of providing explorative evidence into the health influences of vegetarian diets. Additionally, the subjects in our study were younger and healthier and had more concern about their physical conditions in that the median ages of vegetarians and omnivores were at 33 years and 32 years and with over 60% of subjects having received higher education. The age and health of participants may make the results less applicable to other populations as our previous study showed that the average age of vegetarians in Shanghai is 65 years [31]. The small vegetarian population in China introduced practical limitations, thereby preventing the conducting of random sampling, while the relatively small sample size of vegans will need to be enlarged in future studies.

This is the first study in mainland China indicating that vegetarians, especially vegans, may be in a healthier insulin sensitivity status than omnivores, which is not completely accounted for by the difference of BMI.

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XS designed the research; WC and QT assisted the research design and field survey; BW, LX, XC, and YW conducted the research; XC performed the statistical analysis; PX provided advice and verification for statistical analysis; XC and XS wrote the manuscript; XS had primary responsibility for the final content. All authors contributed to the discussion of analyses, critically reviewed the manuscript, and approved the final manuscript. We thank the dietitians from nutrition department of Xinhua Hospital and nutrition department of Shanghai Jiao Tong University, School of Medicine, for assistance with the field investigation and measurements. This study has no competing interest and is supported by the Danone Institute Dietary Nutrition Research and

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