Article

Association of ALDH2 Genotypes and Alcohol Intake with Dietary Patterns: The Bunkyo Health Study

Mari Sugimoto 1, Hiroki Tabata 2, Hideyoshi Kaga 3, Yuki Someya 2, Saori Kakehi 1,2, Abulaiti Abudurezake 2, Hitoshi Naito 3, Naoki Ito 3, Huicong Shi 1, Hikaru Otsuka 1, Futaba Umemura 1, Yasuyo Yoshizawa 4, Ryuzo Kawamori 1,2,3,4, Hirotaka Watada 2,3 and Yoshifumi Tamura 1,2,3,4,*

1 Department of Sports Medicine and Sportology, Graduate School of Medicine, Juntendo University, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan
2 Sportology Center, Graduate School of Medicine, Juntendo University, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan
3 Metabolism and Endocrinology, Graduate School of Medicine, Juntendo University, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan
4 Center for Healthy Life Expectancy, Graduate School of Medicine, Juntendo University, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan
5 Faculty of International Liberal Arts, Juntendo University, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan
* Correspondence: ys-tamur@juntendo.ac.jp; Tel.: +81-3-5802-1579

Abstract: Dietary habits are associated with various diseases and assessed by dietary patterns (DPs). Since the ALDH2 genotype is correlated with alcohol and several food preferences, this genotype is probably associated with DPs. In this cross-sectional study of 1612 elderly adults, we investigated the effects of the ALDH2 genotype on DPs and the mediating role of alcohol intake. We identified the ALDH2 genotype and conducted a dietary history survey, then used principal component analysis to determine DPs for each gender. We performed multiple regression analysis to determine the independent contribution of the ALDH2 genotype and alcohol intake to DP scores. We identified three DPs: the “Japanese side dish type” (DP1), the “Japanese dish with alcohol type” (DP2), and the “Western dish with alcohol type” (DP3). In men, the single nucleotide polymorphism ALDH2 rs671 was significantly associated with all DP scores. When alcohol intake was added as a covariate, ALDH2 rs671 was still significantly correlated with the DP2 score but not with the DP1 or DP3 score, and alcohol intake was significantly correlated with all DP scores. In women, ALDH2 rs671 was significantly associated with the DP2 and DP3 scores; however, after adding alcohol intake as a covariate, these associations disappeared, and alcohol intake significantly correlated with all DP scores. In conclusion, the ALDH2 genotype was associated with several DPs in elderly adults, but most associations were mediated by alcohol intake.

Keywords: dietary patterns; ALDH2 genotype; alcohol intake

1. Introduction

Dietary habits are associated with the development of various diseases and are assessed by dietary patterns (DPs) [1–6]. DPs are statistically evaluated by dietary survey data on the quantities, proportions, varieties, and combinations of different foods, drinks, and nutrients in diets, and the frequency with which they are habitually consumed [1,5,6]. Since people obtain nutrition from multiple foods, it would be beneficial to consider how the risk of disease development is affected by interactions between nutrients and their synergistic effects. In fact, DPs may be more predictive of disease risk than single nutrients or foods [2–4]. Additionally, in clinical intervention trials, changes in DPs appeared to be more effective than single-nutrient interventions [7,8]. Thus, clarifying DPs may facilitate the individualized risk prediction of disease development and help optimize dietary interventions.
Previous reports showed that the single nucleotide polymorphism aldehyde dehydrogenase 2 gene (ALDH2) rs671 is associated with alcohol intake [9–11]. Ethanol is oxidized by alcohol dehydrogenase to acetaldehyde, which is subsequently oxidized by ALDH2 to acetic acid. The ALDH2 rs671 G allele encodes Glu at amino acid 504, resulting in the enzymatically active form, and the ALDH2 rs671 A allele encodes Lys at amino acid 504, yielding the enzymatically inactive form [12]. Approximately 99% of Caucasians are ALDH2 rs671 G homozygotes [13], compared to only about 55% of Japanese individuals. Individuals with ALDH2 rs671 A/A metabolize toxic acetaldehyde more slowly, resulting in side effects such as flushing, nausea, and vomiting after alcohol intake; therefore, alcohol intake usually depends on the ALDH2 genotype [9–11]. Volumes of alcohol intake in Japanese men who were ALDH2 rs671 G/G, G/A, or A/A carriers were found to be ~28 g/day, ~13 g/day, and 1 g/day, respectively [10].

ALDH2 rs671 is also associated with individual dietary habits [5,14–19]. The A allele of ALDH2 rs671 is associated with increased coffee, tea, milk, yogurt, and sweet food intake, and with decreased fish, natto, tofu, and alcohol intake [9,14,15,18,19]. Given these numerous correlations between ALDH2 rs671 and food and beverage intake, ALDH2 rs671 may also be associated with DPs, although this remains unproven. On the other hand, several previous studies have reported that many DPs are characterized by alcohol intake [20–26]. Therefore, even if the ALDH2 genotype is associated with DPs, alcohol intake may be an intermediate factor. Given that the ALDH2 rs671 G allele is associated with increased blood glucose, blood pressure, and high-density lipoprotein cholesterol [27–29], clarifying the relationships between the ALDH2 genotype, alcohol consumption, and DPs may be beneficial for preventing diseases related to these clinical parameters.

Against this background, the purpose of this study was to examine the association between DPs and ALDH2 gene polymorphisms in community-dwelling Japanese elderly adults who participated in the Bunkyo Health Study [30]. We hypothesized that the ALDH2 rs671 would be associated with DPs and that even if the ALDH2 genotype was associated with DPs, this association would be intermediated by alcohol intake.

2. Method

2.1. Study Design and Participants

This cross-sectional study used the baseline data of the Bunkyo Health Study [30]. Briefly, we recruited individuals aged 65–84 years living in Bunkyo-ku, an urban area in Tokyo, Japan, at the Sportology Center of Juntendo University from 15 October 2015 to 1 October 2018. Exclusion criteria consisted of pacemaker or defibrillator placement and diabetes requiring insulin therapy. After an overnight fast, participants underwent body composition measurement by bioelectrical impedance analysis (InBody770, InBody Japan, Tokyo, Japan) and fasting blood sampling, followed by a 75 g oral glucose tolerance test.

As shown in Figure 1, we excluded nine of the 1629 participants enrolled in the Bunkyo Health Study, due to missing data (body composition \( n = 5 \), systolic blood pressure \( n = 3 \), hemoglobin A1c \( n = 1 \)). Furthermore, of the remaining 1620 participants, eight who met the exclusion criteria of the nutrition survey [31] (<600 kcal/day or ≥4000 kcal/day) were excluded. Finally, 1612 participants (male: 677, female: 935) were included in this analysis.

The study protocol was approved by the ethics committee of Juntendo University in November 2015 (Nos. 2015078, 2016138, 2016131, 2017121, and 2019085). This research was conducted in accordance with the principles outlined in the Declaration of Helsinki. All participants provided written informed consent and were informed that they had the right to withdraw from the trial at any time.
Figure 1. Flowchart of the participants.

2.2. Dietary Assessment

Dietary and nutrient intake were assessed using the brief-type self-administered diet history questionnaire (BDHQ) [32,33]. The BDHQ is a questionnaire printed on four A4-size pages and takes about 15 min to complete. The BDHQ asks about the frequency of dietary behaviors and consumption of 58 foods and beverages over the past month, including the frequency of daily consumption of 46 foods and nonalcoholic beverage items, rice, and miso soup, the frequency of consumption of five alcoholic beverages and the amount of each alcoholic beverage consumed per drinking occasion, and the frequency of daily consumption of five seasonings (salt, oil, sugar, soy sauce, and noodle soup) used in cooking and the general diet. Average daily food and nutrient intakes were estimated using an ad hoc computer algorithm for the BDHQ, based on the Standard Tables of Food Composition in Japan [34]. Food and nutrient intakes were energy-adjusted using the nutrient density method [35].

2.3. DPs

To identify DPs, we conducted a principal component analysis for each gender based on the energy-adjusted intake of 52 food and beverage items. In this analysis, we excluded the following six items as previously described: sugar added to coffee and black tea; salt, oil, and sugar used during cooking; table salt (and salt-containing seasonings); and soup consumed with noodles because they are considered cooking methods or seasonings/condiments [20,24,25]. We retained three factors for both men and women, considering eigenvalues, scree tests, and factor interpretability. The factor scores for each DP and for each individual were calculated by summing the intakes of the food items weighted by their factor loadings.
2.4. Genotyping

Genomic DNA was extracted from peripheral blood cells using a DNA extraction kit (DNeasy Blood and Tissue Kit; Qiagen, Fenlo, The Netherlands). We used the Illumina Infinium Asian Screening Array-24 v1.0 BeadChip (Illumina, San Diego, CA, USA) for ALDH2 rs671 genotyping. Microarray scans were analyzed and genotyped with GenomeStudio (version 2013; Illumina, San Diego, CA, USA).

2.5. Other Measurements

Physical activity level was evaluated using the International Physical Activity Questionnaire (IPAQ) [36,37]. Brachial systolic and diastolic blood pressures were measured in the supine position after 10 min of rest. For biochemical tests, blood samples were collected in the morning after an overnight fast. All blood samples were tested at a contracted clinical laboratory (SRL, Tokyo, Japan).

Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or the current use of antihypertensive medications. Diabetes mellitus was defined as hemoglobin A1c ≥6.5% plus either fasting blood glucose ≥126 mg/dL or 2 h blood glucose level ≥200 mg/dL after a 75 g oral glucose tolerance test or current use of diabetes medications. Dyslipidemia was defined as low-density lipoprotein (LDL) cholesterol ≥140 mg/dL, high-density lipoprotein (HDL) cholesterol <40 mg/dL, triglycerides ≥150 mg/dL, or current use of lipid-lowering agents.

2.6. Statistical Analyses

The Kolmogorov–Smirnov normality test was performed to evaluate the distribution of data. The participants were divided into two groups (ALDH2 rs671 G/G carriers and ALDH2 rs671 G/A or A/A carriers). Differences between genotypes and participant characteristics were compared by the unpaired t-test (for normally distributed variables), Mann–Whitney U-test (for non-normally distributed variables), and chi-squared test (for categorical variables). Normally and non-normally distributed variables are presented as means ± SD and medians (interquartile range), respectively, and categorical variables are presented as frequencies (percentages). Multiple regression analysis was performed to determine the independent contribution of the ALDH2 rs671 G allele and alcohol intake (g/1000 kcal/day) to each DP. To adjust for potential covariates, we also added age, body mass index (BMI), years of education, smoking history, and physical activity as explanatory variables.

The Statistical Package for the Social Sciences v. 28.0 for Windows (SPSS, Chicago, IL, USA) was employed to analyze the data. All statistical tests were two-sided, with a 5% significance level.

3. Result

The median age of the subjects was 73 (68–77) years for both sexes, and the median BMI of men and women was 23.3 (21.7–25.1) and 22.0 (20.0–24.2), respectively. Three DPs were identified by principal component analysis in both men and women (Table 1). The first DP was named “Japanese side dish type” (DP1) because it was characterized by a high intake of fish, vegetables, potatoes, soy products, mushrooms, and fruits, and a low intake of rice. The second DP was characterized by a high intake of alcoholic beverages, seafood, and soy products, and a low intake of bread and confectioneries, and thus it was named “Japanese dish with alcohol type” (DP2). The third DP was the “Western dish with alcohol type” (DP3), characterized by a high intake of ham, pasta, mayonnaise, and alcoholic beverages, and a low intake of rice and miso soup. In men, these three main DPs accounted for 9.1%, 5.1%, and 4.1% of the variance in food intake, respectively, and together explained 18.3% of food intake variability. In women, they accounted for 8.4%, 4.9%, and 4.2% of the variance in food intake, respectively, and together explained 17.5% of food intake variability.
Table 1. Factor loading matrix for major dietary patterns identified by principal component analysis.

| Food Groups                                      | Men DP1 | Women DP1 | Men DP3 | Women DP3 | Men DP2 | Women DP2 | Men DP3 | Women DP3 |
|--------------------------------------------------|---------|-----------|---------|-----------|---------|-----------|---------|-----------|
| Law fat milk                                     | 0.193   | 0.188     |         |           | −0.155  |           |         |           |
| Milk/yogurt                                      | 0.183   | 0.179     | 0.194   |           |         |           |         |           |
| Chicken                                          | 0.197   | 0.264     |         |           |         |           |         |           |
| Ham/ sausage/ bacon                               |         | 0.338     |         |           |         |           |         |           |
| Liver                                            | 0.292   | 0.163     |         |           |         |           |         |           |
| Squid/ octopus/ shrimps/ shellfish               | 0.279   | 0.290     | −0.215  |           |         |           |         |           |
| Dried/ salted fish                               | 0.192   | 0.417     |         |           | 0.204   |           |         |           |
| Oily fish                                        | 0.212   | 0.318     | 0.241   | 0.162     |         |           |         |           |
| Lean fish                                        | 0.220   | 0.288     | 0.262   |           |         |           |         |           |
| Egg                                              | 0.193   | 0.162     | 0.219   |           |         |           |         |           |
| Tofu/ Deep-fried tofu                            | 0.360   | 0.215     | 0.442   | 0.167     |         |           |         |           |
| Natto †                                          | 0.330   | 0.256     | 0.357   | 0.158     | −0.162  |           |         |           |
| Potatoes                                         | 0.396   | 0.326     |         |           |         |           |         |           |
| Pickled green leaves vegetable                   | 0.277   | 0.279     |         |           |         |           |         |           |
| Other pickled vegetables                         | 0.225   | 0.181     |         |           | 0.207   |           |         |           |
| Lettuces/ cabbage (raw)                          | 0.517   | −0.189    | 0.303   | 0.533     | 0.293   |           |         |           |
| Green leaves vegetable                           | 0.594   |           | 0.589   |           |         |           |         |           |
| Cabbage/ Chinese cabbage                         | 0.548   |           | 0.594   |           |         |           |         |           |
| Carrots/ pumpkin                                 | 0.650   |           | 0.629   |           |         |           |         |           |
| Japanese radish/ turnip                          | 0.553   |           | 0.492   |           |         |           |         |           |
| Other root vegetables                            | 0.627   |           | 0.605   |           |         |           |         |           |
| Tomatoes                                         | 0.485   | −0.173    | 0.225   | 0.437     | 0.187   |           |         |           |
| Mushrooms                                        | 0.603   |           | 0.594   |           |         |           |         |           |
| Seaweeds                                         | 0.470   | 0.273     | −0.215  | 0.516     | 0.182   |           |         |           |
| Western-type confectioneries                     | −0.477  |           | −0.187  | −0.438    |         |           |         |           |
| Japanese confectioneries                         | −0.312  | −0.150    | −0.161  | −0.312    |         |           |         |           |
| Rice crackers/ rice cake/ okonomiyaki ‡          | −0.335  | −0.157    | −0.227  | −0.285    |         |           |         |           |
| Ice cream                                        | −0.197  | −0.225    | −0.187  | −0.223    | 0.202   |           |         |           |
| Citrus fruit                                     | 0.353   | −0.232    | 0.156   | −0.197    |         |           |         |           |
| Persimmons/ strawberry/ kiwifruit                | 0.330   | −0.225    | 0.243   | −0.194    |         |           |         |           |
| Other fruit                                      | 0.361   | −0.316    | −0.195  | 0.294     | −0.307  |           |         |           |
| Mayonnaise/ dressing                             | 0.190   | −0.346    | 0.320   | −0.177    | −0.387  | 0.396     |         |           |
| Bread                                            | −0.550  |           | −0.183  |           | 0.268   |           |         |           |
| Buckwheat noodles                                |         |           |         |           |         | 0.302     |         |           |
| Japanese noodles                                 | 0.221   |           | −0.183  |           | 0.268   |           |         |           |
| Chinese noodles                                  | −0.221  |           | −0.183  |           | 0.268   |           |         |           |
| Pasta                                            | 0.168   |           |         |           |         | 0.302     |         |           |
| Green tea                                        | 0.168   | −0.300    |         |           | −0.285  |           |         |           |
| Black tea/ oolong tea                            | −0.294  |           | −0.172  | 0.163     |         |           |         |           |
| Coffee                                           | −0.223  |           | −0.176  | 0.245     |         |           |         |           |
| Cola drink/ soft drink                           | −0.193  | −0.168    | −0.185  |           |         |           |         |           |
| 100% fruit and vegetable juice                   | 0.192   | −0.652    | −0.374  | 0.192     |         |           |         |           |
| Rice                                             | −0.333  | −0.482    | −0.374  | 0.245     | −0.480  |           |         |           |
| Miso soup                                        | 0.225   | 0.246     | 0.506   | 0.236     |         |           |         |           |
| Sake                                             | −0.218  | 0.349     | 0.437   | 0.301     |         |           |         |           |
| Beer                                             | −0.227  | 0.375     | 0.374   | 0.485     | 0.299   |           |         |           |
| Shochu                                           | −0.238  | 0.324     | 0.539   | 0.276     |         |           |         |           |
| Whisky                                           | −0.218  | 0.234     | 0.406   | 0.245     |         |           |         |           |
| Wine                                             | 0.172   |           | 0.349   |           |         | 0.437     | 0.301   |           |

Factor loadings less than ±0.15 are represented by a dash for simplicity. † Fermented soybeans. ‡ Savory pancake with various ingredients (meat, fish, and vegetable).
As shown in Table 2, 371 (55%) male subjects had ALDH2 rs671 G/G, 254 (37%) had G/A, and 52 (8%) had A/A. In women, the distribution was 520 (56%), 355 (38%), and 60 (6%), respectively. These genotype frequencies were similar to those previously reported for Japanese men and women [10]. Due to the small number of participants with ALDH2 rs671 A/A, we divided these individuals into two groups: ALDH2 rs671 G/G carriers and ALDH2 rs671 G/A or A/A carriers.

Table 2. Anthropometric characteristics of participants by ALDH2 genotype.

| Number of Subjects | ALDH2 rs671 (G/G) | ALDH2 rs671 (G/A or A/A) | p Value | ALDH2 rs671 (G/G) | ALDH2 rs671 (G/A or A/A) | p Value |
|--------------------|------------------|-------------------------|---------|------------------|-------------------------|---------|
| Age (years)        | 371 (55%)        | 306 (45%)               | 0.503   | 520 (56%)        | 415 (44%)               | 0.213   |
| BMI (kg/m²)        | 72 (68–77)       | 73 (69–77)              | 0.003   | 72 (68–77)       | 73 (69–77)              | 0.004   |
| Physical activity (MET h/week) | 23.0 (21.9–25.2) | 23.2 (21.6–25.1) | 0.282   | 22.0 (19.9–24.2) | 22.0 (19.9–24.2) | 0.089   |
| Education (years)  | 5.5 (4.0–6.4)    | 5.3 (4.0–6.3)           | 0.123   | 12 (12–14)       | 12 (12–14)              | 0.332   |
| Smoking history (%)| 263 (71%)        | 230 (75%)               | 0.213   | 70 (17%)         | 70 (17%)                | 0.741   |
| Systolic BP (mmHg) | 137.0            | 133.0                   | 0.005   | 136.0            | 136.0                   | 0.282   |
| Diastolic BP (mmHg)| 86.0 (80.0–93.0) | 85.0 (80.0–91.0)        | 0.033   | 85.0 (80.0–90.0) | 85.0 (80.0–90.0)        | 0.004   |
| Fasting plasma glucose (mg/dL) | 100.0 (93.0–111.0) | 98.0 (92.0–107.0)        | 0.047   | 100.0 (93.0–111.0) | 98.0 (92.0–107.0)        | 0.004   |
| HbA1c (%)          | 5.7 (5.4–6.1)    | 5.8 (5.5–6.1)           | 0.141   | 5.7 (5.5–6.0)    | 5.7 (5.5–6.0)           | 0.652   |
| Triglycerides (mg/dL) | 80.0 (67.0–124.0) | 93.5 (68.0–126.0)       | 0.692   | 80.0 (62.0–110.0) | 85.0 (64.0–116.0)        | 0.064   |
| HDL-C (mg/dL)      | 80.0 (49.0–68.0) | 56.0 (47.0–66.0)        | 0.011   | 67.5 (58.0–79.0) | 66.0 (57.0–77.0)         | 0.042   |
| LDL-C (mg/dL)      | 100.0 (88.0–128.0) | 117.0 (96.8–140.0)     | <0.001  | 124.0            | 128.0                   | 0.036   |
| AST (IU/L)         | 22 (19–27)       | 21 (18–25)              | 0.003   | 22 (19–25)       | 22 (19–25)              | 0.049   |
| ALT (IU/L)         | 18 (14–24)       | 17 (14–21)              | 0.019   | 16 (13–21)       | 16 (13–20)              | 0.060   |
| γ-GTP (IU/L)       | 30 (20–47)       | 24 (18–37)              | <0.001  | 19 (15–28)       | 18 (14–24)              | 0.005   |

BMI: body mass index; MET: metabolic equivalents; BP: blood pressure; HbA1c: hemoglobin A1c; HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γ-GTP: γ-glutamyl transpeptidase. Data are expressed as means ± SD or medians (interquartile range). Data were analyzed using unpaired t-test (for distributed variables), Mann–Whitney U test (for non-normally distributed variables), or χ² test (for categorical variables).

The anthropometric data of the participants with ALDH2 rs671 G/G and ALDH2 rs671 G/A or A/A are shown in Table 2. Men with ALDH2 rs671 G/G had a significantly lower Brinkman index than men with ALDH2 rs671 G/A or A/A. In addition, men with ALDH2 rs671 G/G had significantly higher systolic blood pressure, diastolic blood pressure, fasting blood glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and γ-glutamyl transpeptidase (γ-GTP) than the men with ALDH2 rs671 G/A or A/A. On the other hand, men with ALDH2 rs671 G/G had significantly higher LDL cholesterol than men with ALDH2 rs671 G/A or A/A. Women with ALDH2 rs671 G/G had significantly higher fasting blood glucose and γ-GTP than women with ALDH2 rs671 G/A or A/A. In terms of nutrients, women with ALDH2 rs671 G/G had significantly higher intakes of fat, carbohydrates, total dietary fiber, salt, and sugar (sucrose), and significantly higher intakes of alcohol and animal protein than men with ALDH2 rs671 G/G or A/A. In terms of foods, men with ALDH2 rs671 G/G had significantly lower intakes of fat, carbohydrates, total dietary fiber, salt, and sugar (sucrose), and significantly higher intakes of beverages than men with ALDH2 rs671 G/A or A/A. In women, DP2 and DP3 scores were significantly higher in individuals with ALDH2 rs671 G/G than in those with ALDH2 rs671 G/A or A/A. Regarding nutrients, women with ALDH2 rs671 G/G had...
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significantly lower intakes of fat, carbohydrates, and sucrose and significantly higher intakes of alcohol and animal protein than women with ALDH2 rs671 G/A or A/A. In terms of food groups, only confectionery intake was significantly lower in women with ALDH2 rs671 G/G compared to women with ALDH2 rs671 G/A or A/A. These data suggest that in women, DP2 and DP3, and not DP1, were associated with the ALDH2 rs671 genotype.

Table 3. Dietary pattern scores and nutrient and food group intake by ALDH2 genotype in all participants.

| Number of Subjects | ALDH2 rs671 G/G | ALDH2 rs671 G/A or A/A | p Value | ALDH2 rs671 G/G | ALDH2 rs671 G/A or A/A | p Value |
|--------------------|----------------|------------------------|---------|----------------|------------------------|---------|
| DP1 score          | −0.16          | 0.10                   | <0.001  | −0.13          | −0.04                   | 0.652   |
|                    | (−0.74 to 0.48) | (−0.60 to 0.81)        |         | (−0.69 to 0.55) | (−0.69 to 0.56)        |         |
| DP2 score          | 0.25 ± 0.93    | −0.31 ± 1.00           | <0.001  | 0.04           | −0.32                   | <0.001  |
|                    | (0.49 ± 0.02)  | (−1.00 to 0.83)        |         | (−0.04 ± 1.00) | (−0.77 to 0.15)        |         |
| Total energy intake (kcal) | 2087 (1722–2538) | 2012 (1635–2422) | 0.176   | 1978 (1469–2153) | 1744 (1197–2153) | 0.686   |
| Protein intake (% energy) | 54.3 (40.5–53.0) | 52.3 (46.2–56.9)     | <0.001  | 52.3 (46.2–59.9) | 57.5 (51.7–63.3)      | <0.001  |
| Carbohydrate intake (% energy) | 49.2 ± 6.4     | 49.2 ± 7.8             | <0.001  | 51.3 ± 7.5       | <0.001                 |         |
| Other vegetables (g/1000 kcal) | 80.7 (57.1–112.4) | 90.5 (62.4–122.6) | 0.076   | 119.1 (88.9–154.5) | 119.0 (88.5–156.9) | 0.052   |
| Confectioneries (g/1000 kcal) | 14.9 ± 7.2     | 23.0 ± 13.53           | <0.001  | 24.4 ± 12.0 (27.0 ± 14.4) | 0.021   |
| Grains (g/1000 kcal) | 171.5          | 187.4                  | 0.003   | 155.5           | 0.266                   |         |
| Potatoes (g/1000 kcal) | 134.1–220.5    | 147.0–233.2            | <0.001  | 114.9–198.2     | 0.159                   |         |
| Sweets and sweeteners (g/1000 kcal) | 2.1 (1.2–3.3) | 2.5 (1.5–4.3)          | <0.001  | 2.8 (1.7–4.2)   | 0.539                   |         |
| Beans (g/1000 kcal) | 30.0 (15.8–50.2) | 30.4 (16.9–48.9)     | 0.012   | 40.3 (23.4–58.1) | 0.970                   |         |
| Green and yellow vegetables (g/1000 kcal) | 55.4 (32.6–82.7) | 65.0 (41.7–94.8) | 0.004   | 76.6 (53.5–112.8) | 0.471                   |         |
| Other vegetables (g/1000 kcal) | 80.7 (57.1–112.4) | 90.5 (62.4–122.6) | 0.076   | 119.1 (88.9–154.5) | 0.958                   |         |
| Fruits (g/1000 kcal) | 55.0 (32.4–89.9) | 73.7 (39.3–113.9)    | <0.001  | 85.1 (51.4–123.4) | 0.050                   |         |
| Fish and shellfish (g/1000 kcal) | 44.5 (33.0–63.5) | 41.5 (27.8–62.0)    | 0.086   | 52.5 (36.4–75.0) | 0.423                   |         |
| Meats (g/1000 kcal) | 34.1 (25.7–45.9) | 36.8 (25.8–48.0)     | 0.347   | 41.3 (28.7–54.7) | 0.390                   |         |
| Eggs (g/1000 kcal) | 17.9 (10.5–30.5) | 18.6 (9.7–32.2)      | 0.824   | 23.7 (12.6–39.9) | 0.993                   |         |
| Dairy products (g/1000 kcal) | 81.7 (45.3–111.0) | 86.2 (45.0–123.6) | 0.180   | 93.2 (58.7–129.9) | 0.850                   |         |
| Fats and oils (g/1000 kcal) | 5.5 (3.9–7.0) | 5.3 (4.1–7.0)          | 0.822   | 5.2 (3.7–6.7)   | 0.079                   |         |
| Confectioneries (g/1000 kcal) | 14.9 (7.2–29.0) | 23.0 (12.3–35.6)     | <0.001  | 24.4 (12.0–27.5) | 0.021                   |         |
| Beverages (g/1000 kcal) | 420.7          | 371.0                  | 0.003   | 389.4           | 0.584                   |         |
| Seasonings (g/1000 kcal) | 125.3 (90.0–169.6) | 127.4 (96.6–168.7) | 0.228   | 106.5 (75.2–152.4) | 0.733                   |         |

DP: dietary pattern, SFA: saturated fatty acid, MUFA: monounsaturated fatty acid, PUFA: polyunsaturated fatty acid. Data are expressed as means ± SD or medians (interquartile range). Data were analyzed using unpaired t-test (for distributed variables) or Mann-Whitney U test (for non-normally distributed variables).

Next, to determine whether alcohol intake is an intermediate factor between the ALDH2 genotype and DPs, we performed multiple regression analyses (Tables 4 and 5). In men (Table 4), ALDH2 rs671 was significantly correlated with the DP1 (β = 0.109, p = 0.004) and DP3 (β = −0.226, p < 0.001) scores in model 1. However, when we added alcohol intake as a covariate (model 2), alcohol intake was significantly correlated with these DP1; β = −0.349, p < 0.001; DP3; β = 0.499, p < 0.001 scores, while ALDH2 rs671 was not (DP1; β = −0.027, p = 0.483; DP3; β = −0.032, p = 0.361). ALDH2 rs671 was also significantly correlated with the DP2 (β = −0.276, p < 0.001) score in model 1, and both ALDH2 rs671
and alcohol intake were significantly correlated with the DP2 (\textit{ALDH2} rs671; $\beta = -0.092$, $p = 0.011$, alcohol intake; $\beta = 0.475$, $p < 0.001$) score in model 2. In women (Table 5), \textit{ALDH2} rs671 was not associated with the DP1 ($\beta = 0.007$, $p = 0.818$) score in model 1, while in model 2, alcohol intake was significantly correlated with the DP1 ($\beta = -0.150$, $p < 0.001$) score. \textit{ALDH2} rs671 was significantly correlated with the DP2 ($\beta = -0.236$, $p < 0.001$) and DP3 ($\beta = -0.107$, $p < 0.001$) scores in model 1; however, these correlations were not observed in model 2 (DP2; $\beta = -0.011$, $p = 0.630$, DP3; $\beta = 0.017$, $p = 0.588$), and only alcohol intake was significantly correlated with these DP (DP2; $\beta = 0.746$, $p < 0.001$, DP3; $\beta = 0.408$, $p < 0.001$) scores. In addition, age and years of education were significantly correlated with all DP in men (age: DP1; $\beta = 0.129$, $p < 0.001$, DP3; $\beta = -0.080$, $p = 0.015$, years of education: DP1; $\beta = 0.106$, $p = 0.003$, DP2; $\beta = -0.131$, $p < 0.001$, DP3; $\beta = 0.146$, $p < 0.001$) and in women (age: DP1; $\beta = 0.077$, $p = 0.026$, DP2; $\beta = 0.079$, $p < 0.001$, DP3; $\beta = -0.114$, $p < 0.001$, years of education: DP1; $\beta = 0.121$, $p < 0.001$, DP2; $\beta = -0.097$, $p < 0.001$, DP3; $\beta = 0.120$, $p < 0.001$) scores in model 2 in both men and women, excluding the relationship between age and the DP2 score in men ($\beta = 0.046$, $p = 0.174$).

Table 4. Effect of \textit{ALDH2} genotype and alcohol consumption on dietary pattern scores in men.

| Dependent Variable | Independent Variable | B    | Std. Error | $\beta$ | $p$    |
|-------------------|----------------------|------|------------|---------|--------|
| DP1               | Age (years)          | 0.031| 0.007      | 0.163   | <0.001 |
| Model 1           | BMI (kg/m$^2$)       | 0.013| 0.014      | 0.035   | 0.354  |
| (R$^2 = 0.067$)   | Physical activity (MET h/week) | 0.009| 0.002      | 0.163   | <0.001 |
|                   | Education (years)    | 0.009| 0.015      | 0.098   | 0.011  |
|                   | Smoking history (n/%)| -0.132| 0.084   | -0.059  | 0.116  |
|                   | \textit{ALDH2} rs671 (G/G or G/A and A/A) | 0.219| 0.075      | 0.109   | 0.004  |
| DP1               | Age (years)          | 0.024| 0.007      | 0.129   | <0.001 |
| Model 2           | BMI (kg/m$^2$)       | 0.007| 0.013      | 0.019   | 0.600  |
| (R$^2 = 0.167$)   | Physical activity (MET h/week) | 0.009| 0.002      | 0.156   | <0.001 |
|                   | Education (years)    | 0.043| 0.015      | 0.106   | 0.003  |
|                   | Smoking history (n/%)| -0.020| 0.080   | -0.009  | 0.807  |
|                   | \textit{ALDH2} rs671 (G/G or G/A and A/A) | -0.054| 0.077  | -0.027  | 0.483  |
|                   | Alchool (g/day)      | -0.027| 0.003    | -0.349  | <0.001 |
| DP2               | Age (years)          | 0.000| 0.007      | 0.000   | 0.990  |
| Model 1           | BMI (kg/m$^2$)       | 0.004| 0.013      | 0.012   | 0.754  |
| (R$^2 = 0.089$)   | Physical activity (MET h/week) | 0.002| 0.002      | 0.038   | 0.309  |
|                   | Education (years)    | -0.048| 0.015   | -0.120  | 0.002  |
|                   | Smoking history (n/%)| 0.135| 0.083      | 0.060   | 0.103  |
|                   | \textit{ALDH2} rs671 (G/G or G/A and A/A) | -0.555| 0.074   | -0.276  | <0.001 |
|                   | Alchool (g/day)      | 0.037| 0.003      | 0.475   | <0.001 |
| DP3               | Age (years)          | -0.024| 0.007    | -0.129  | <0.001 |
| Model 1           | BMI (kg/m$^2$)       | -0.007| 0.013    | -0.019  | 0.610  |
| (R$^2 = 0.091$)   | Physical activity (MET h/week) | 0.002| 0.002      | 0.047   | 0.151  |
|                   | Education (years)    | 0.063| 0.015      | 0.157   | <0.001 |
|                   | Smoking history (n/%)| 0.102| 0.083      | 0.045   | 0.220  |
|                   | \textit{ALDH2} rs671 (G/G or G/A and A/A) | -0.454| 0.074   | -0.226  | <0.001 |
|                   | Alchool (g/day)      | 0.039| 0.003      | 0.499   | <0.001 |

DP: dietary pattern, BMI: body mass index, MET: metabolic equivalents. B: partial regression coefficients, Std. Error: standard error of partial regression coefficients B, $\beta$: standardized partial regression coefficients $\beta$. 
Table 5. Effect of ALDH2 genotype and alcohol consumption on dietary pattern scores in women.

| Dependent Variable | Independent Variable | B     | Std. Error | β     | p     |
|--------------------|----------------------|-------|------------|-------|-------|
| DP1                | Age (years)          | 0.016 | 0.006      | 0.087 | 0.012 |
| Model 1            | BMI (kg/m²)          | −0.012| 0.010      | −0.037| 0.264 |
| (R² = 0.024)       | Physical activity (MET h/week) | 0.005 | 0.003      | 0.059 | 0.073 |
|                    | Education (years)    | 0.057 | 0.016      | 0.124 | <0.001|
|                    | Smoking history (n/%)| −0.210| 0.086      | −0.080| 0.015 |
|                    | ALDH2 rs671 (G/G or G/A and A/A) | 0.015 | 0.065      | 0.007 | 0.818 |
| DP1                | Age (years)          | 0.014 | 0.006      | 0.077 | 0.026 |
| Model 2            | BMI (kg/m²)          | −0.011| 0.010      | −0.035| 0.277 |
| (R² = 0.042)       | Physical activity (MET h/week) | 0.005 | 0.003      | 0.064 | 0.046 |
|                    | Education (years)    | 0.055 | 0.016      | 0.121 | <0.001|
|                    | Smoking history (n/%)| −0.132| 0.087      | −0.050| 0.131 |
|                    | ALDH2 rs671 (G/G or G/A and A/A) | −0.076| 0.068      | −0.038| 0.264 |
|                    | Alcohol (g/day)      | −0.022| 0.005      | −0.150| <0.001|
| DP2                | Age (years)          | 0.005 | 0.006      | 0.028 | 0.403 |
| Model 1            | BMI (kg/m²)          | 0.013 | 0.010      | 0.042 | 0.185 |
| (R² = 0.093)       | Physical activity (MET h/week) | −0.001| 0.002      | −0.018| 0.576 |
|                    | Education (years)    | −0.052| 0.015      | −0.113| <0.001|
|                    | Smoking history (n/%)| 0.384 | 0.083      | 0.145 | <0.001|
|                    | ALDH2 rs671 (G/G or G/A and A/A) | −0.475| 0.063      | −0.236| <0.001|
| DP2                | Age (years)          | 0.011 | 0.004      | 0.079 | <0.001|
| Model 2            | BMI (kg/m²)          | 0.011 | 0.007      | 0.035 | 0.102 |
| (R² = 0.575)       | Physical activity (MET h/week) | −0.004| 0.002      | −0.047| 0.028 |
|                    | Education (years)    | −0.044| 0.010      | −0.097| <0.001|
|                    | Smoking history (n/%)| −0.007| 0.058      | −0.003| 0.907 |
|                    | ALDH2 rs671 (G/G or G/A and A/A) | −0.022| 0.045      | −0.011| 0.630 |
|                    | Alcohol (g/day)      | 0.111 | 0.003      | 0.746 | <0.001|
| DP3                | Age (years)          | −0.026| 0.006      | −0.142| <0.001|
| Model 1            | BMI (kg/m²)          | 0.012 | 0.010      | 0.037 | 0.251 |
| (R² = 0.068)       | Physical activity (MET h/week) | 0.004| 0.003      | 0.052 | 0.102 |
|                    | Education (years)    | 0.055 | 0.015      | 0.111 | <0.001|
|                    | Smoking history (n/%)| 0.333 | 0.084      | 0.126 | <0.001|
|                    | ALDH2 rs671 (G/G or G/A and A/A) | −0.215| 0.064      | −0.107| <0.001|
| DP3                | Age (years)          | −0.021| 0.006      | −0.114| <0.001|
| Model 2            | BMI (kg/m²)          | 0.010 | 0.009      | 0.033 | 0.260 |
| (R² = 0.212)       | Physical activity (MET h/week) | 0.003| 0.002      | 0.036 | 0.222 |
|                    | Education (years)    | 0.055 | 0.014      | 0.120 | <0.001|
|                    | Smoking history (n/%)| 0.119 | 0.079      | 0.045 | 0.133 |
|                    | ALDH2 rs671 (G/G or G/A and A/A) | 0.033| 0.062      | 0.017 | 0.588 |
|                    | Alcohol (g/day)      | 0.061 | 0.005      | 0.408 | <0.001|

DP: dietary pattern, BMI: body mass index, MET: metabolic equivalents. B: partial regression coefficients B, Std. Error: standard error of partial regression coefficients B, β: standardized partial regression coefficients β.

4. Discussion

We investigated the effects of ALDH2 rs671 genotype and alcohol intake on DPs in elderly community-dwelling subjects. We identified three major DPs in both men and women based on principal component analysis: the “Japanese side dish type” (DP1), the “Japanese dish with alcohol type” (DP2), and the “Western dish with alcohol type” (DP3). In men, ALDH2 rs671 was significantly associated with all DP scores. When alcohol intake was added as a covariate, ALDH2 rs671 was still significantly correlated with the DP2 score, but not with the DP1 or DP3 score, and alcohol intake was significantly correlated with all DP scores. In women, ALDH2 rs671 was significantly associated with the DP2 and DP3 scores; when alcohol intake was added as a covariate, however, those associations disappeared, and alcohol intake was significantly correlated with all DP scores.

The three major DPs identified in this study are consistent with those found in previous reports. The first DP defined in this study, the “Japanese side dish type” (DP1), is similar to the first DP described in many previous studies of Japanese people [5,20,22,23,25,38–40], which named it the “prudent type”, “healthy type”, or “side dish type”. In this study, DP2, the “Japanese dish with alcohol type”, and DP3, the “Western dish with alcohol type”...
type”, were characterized by alcohol intake. Concerningly, it has been shown that several DPs in young and middle-aged adults are characterized by alcohol intake. For example, previous reports identified DPs characterized by the intake of fish, seafood, and alcoholic beverages [20,25,26], or noodles and alcoholic beverages [21,22,41]; however, it remains unclear whether DPs are also characterized by alcohol intake in elderly people, who drink less than young people. This study is the first to show that alcohol intake is closely related to DPs even in elderly people.

While previous studies have demonstrated associations between the ALDH2 genotype and several food preferences [14,15,18,19], this study is the first to reveal correlations between the ALDH2 genotype and DPs. However, when adjusted for alcohol intake, most of these associations disappeared, and conversely, alcohol intake was significantly associated with each DP. Thus, the association between the ALDH2 genotype and DPs seems to be strongly mediated by alcohol intake, and this is theoretically reasonable since the ALDH2 genotype is strongly associated with alcohol consumption [10].

Several previous studies have shown that many DPs are characterized by alcohol consumption and that there is an inverse correlation between the intake of carbohydrates and alcohol [42]. In fact, people with higher alcohol intake were shown to have a lower intake of carbohydrates, protein, and fat [42–44]. In addition, the consumption of sweet foods was found to be increased during alcohol abstinence in people with alcohol dependence [45] or alcohol use disorders [46]. Two mechanisms have been suggested to explain the inverse relationship between carbohydrate intake and alcohol consumption. The first is that carbohydrates induce insulin secretion, which increases the activity of the serotonin system in the brain, thereby suppressing the preference for alcohol intake. The second is that the hedonic response to both alcohol and sweet consumption is mediated by the brain’s opioid system, and the consumption of one attenuates that of the other due to competition for receptors [47]. These results indicate that DPs may be more readily altered by alcohol intake than by ALDH2 gene polymorphisms, which would have important clinical implications when considering alcohol-restricted dietary interventions. For example, DPs may change during such interventions, which could affect outcomes such as blood glucose levels and body weight [48].

On the other hand, this study showed that in men, the ALDH2 genotype was significantly associated with DP2 independently of alcohol intake. In general, eating habits become more diverse as individuals enter their teens and 20s, stabilize in their 30s and 40s, and are maintained thereafter [49]. Alcohol consumption is more strongly influenced by the ALDH2 genotype in younger age groups [50]. Therefore, it is hypothesized that eating habits are formed between the 20s and 40s when alcohol intake is high, and then alcohol intake decreases with age; however, dietary habits in this study were not significantly affected by decreased alcohol intake. This may be why the ALDH2 genotype was associated with DP2 independently of alcohol intake.

There are several limitations to the present study. First, the three DPs identified in this study comprised about 20% of DPs calculated for this population, and it is unclear whether ALDH2 genotype and alcohol intake contribute to the other DPs. However, the explained variance ratio depends on the number of food items, and the smaller the number of food items analyzed, the larger the explained variance ratio [51]. Similar to this study, previous studies that identified DPs involving around 50 food items found that the cumulative explained variance ratio of three major DPs was around 20% [20,24,25]. In this study, DPs were calculated based on 52 food items; therefore, the cumulative explained variance ratio is considered reasonable and acceptable. Second, because of regional variations in the Japanese diet [52–54], it is unclear whether the analyzed DPs can be generalized to other regions. In particular, previous studies have suggested that elderly people in urban areas of Japan are more likely to consume alcohol than those in other areas of the country [55]. Third, the subjects in this study were elderly city-dwelling Japanese with a high educational background who may have had high health literacy [56]. Therefore, further studies are required to generalize these results.
5. Conclusions

In conclusion, the ALDH2 genotype was associated with a variety of DPs in community-dwelling elderly people. However, most associations were mediated by alcohol intake as an intermediate factor.

Author Contributions: H.K., Y.S., S.K., R.K., H.W. and Y.T. contributed to drafting the Bunkyo Health Study. M.S., H.T. and H.K. contributed substantially to the data analysis. H.K. and Y.T. were responsible for the overall conception and design of this manuscript. M.S., H.K., H.T., S.K., A.A., H.N., N.I., H.S., H.O., F.U. and Y.Y. contributed to the data interpretation. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Medical Research Ethics Committee of the Juntendo University (2019085 and November 2015).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Some or all datasets generated and/or analyzed during the current study are not publicly available; however, they can be obtained from the corresponding author upon a reasonable request.

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References
1. LB, J.A.; Heymsfield, S.; Mayer-Davis, E.; Sabaté, J.; Snetselaar, L.; Van Horn, L. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: PartD_Ch8_DietaryPatterns_. Available online: https://www.dietaryguidelines.gov/sites/default/files/2020-07/PartD_Ch8_DietaryPatterns_first-print.pdf (accessed on 10 May 2022).
2. Hu, F.B. Dietary pattern analysis: A new direction in nutritional epidemiology. Curr. Opin. Lipidol. 2002, 13, 3–9. [CrossRef] [PubMed]
3. Jacobs, D.R.; Steffen, L.M. Nutrients, foods, and dietary patterns as exposures in research: A framework for food synergy. Am. J. Clin. Nutr. 2003, 78, 508S–513S. [CrossRef] [PubMed]
4. Jacques, P.F.; Tucker, K.L. Are dietary patterns useful for understanding the role of diet in chronic disease? Am. J. Clin. Nutr. 2001, 73, 1–2. [CrossRef] [PubMed]
5. Murakami, K.; Shinozaki, N.; Fujiwara, A.; Yuan, X.; Hashimoto, A.; Fujihashi, H.; Wang, H.-C.; Livingstone, M.B.E.; Sasaki, S. A Systematic Review of Principal Component Analysis-Derived Dietary Patterns in Japanese Adults: Are Major Dietary Patterns Reproducible Within a Country? Adv. Nutr. 2019, 10, 237–249. [CrossRef]
6. Zhao, J.; Li, Z.; Gao, Q.; Zhao, H.; Chen, S.; Huang, L.; Wang, W.; Wang, T. A review of statistical methods for dietary pattern analysis. Nutr. J. 2021, 20, 37. [CrossRef] [PubMed]
7. Whelton, P.K.; Appel, L.; Charleston, J.; Dalcin, A.T.; Ewart, C.; Fried, L.; Kaidy, D.; Klag, M.J.; Kumanyika, S.; Steffen, L.; et al. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels. Results of the Trials of Hypertension Prevention, Phase I. JAMA 1992, 267, 1213–1220. [CrossRef]
8. Appel, L.J.; Moore, T.J.; Obarzanek, E.; Vollmer, W.M.; Svetkey, L.P.; Sacks, F.M.; Bray, G.A.; Vogt, T.M.; Cutler, J.A.; Windhauser, M.M.; et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N. Engl. J. Med. 1997, 336, 1117–1124. [CrossRef]
9. Enomoto, N.; Takase, S.; Yasuhara, M.; Takada, A. Acetaldehyde Metabolism in Different Aldehyde Dehydrogenase-2 Genotypes. Alcohol. Clin. Exp. Res. 1991, 15, 141–144. [CrossRef] [PubMed]
10. Takeshita, T.; Morimoto, K.; Mao, X.; Hashimoto, T.; Furuyama, Y. Characterization of the three genotypes of low Km aldehyde dehydrogenase in a Japanese population. Hum. Genet. 1994, 94, 217–223. [CrossRef]
11. Hendershot, C.S.; Neighbors, C.; George, W.H.; McCarthy, D.M.; Wall, T.L.; Liang, T.; Larimer, M.E. ALDH2, ADH1B and Alcohol Expectancies: Integrating Genetic and Learning Perspectives. Psychol. Addict. Behav. 2009, 23, 452–463. [CrossRef]
12. Eng, M.V.; Lyczak, S.E.; Wall, T.L. ALDH2, ADH1B, and ADH1C genotypes in Asians: A literature review. Alcohol. Res. Health 2007, 30, 22–27. [PubMed]
13. Goedde, H.W.; Agarwal, D.P.; Fritz, G.; Meier-Tackmann, D.; Singh, S.; Beckmann, G.; Bhattacharjee, K.; Chen, L.Z.; Fang, B.; Lisker, R.; et al. Distribution of ADH2 and ALDH2 genotypes in different populations. *Hum. Genet.* 1992, 88, 344–346. [CrossRef] [PubMed]

14. Kawafune, K.; Hachiya, T.; Nogawa, S.; Takahashi, S.; Jia, H.; Saito, K.; Kato, H. Strong association between the 12q24 locus and sweet taste preference in the Japanese population revealed by genome-wide meta-analysis. *J. Hum. Genet.* 2020, 65, 939–947. [CrossRef] [PubMed]

15. Matoba, N.; Akiyama, M.; Ishigaki, K.; Kanai, M.; Takahashi, A.; Momozawa, Y.; Ikegawa, S.; Ikeda, M.; Iwata, N.; Hirata, M.; et al. GWAS of 165,084 Japanese individuals identified nine loci associated with dietary habits. *Nat. Hum. Behav.* 2020, 4, 308–316. [CrossRef]

16. Nakamura, Y.; Narita, A.; Sutoh, Y.; Imaeda, N.;goto, C.; Matsu, K.; Takashima, N.; Kadota, A.; Miura, K.; Nakatochi, M.; et al. A genome-wide association study on meat consumption in a Japanese population: The Japan Multi-Institutional Collaborative Cohort study. *J. Nutr. Sci.* 2021, 10, e61. [CrossRef] [PubMed]

17. Suzuki, H.; Nakamura, Y.; Matsuo, K.; Imaeda, N.; goto, C.; Matsu, K.; Shimizu, A.; Takashima, N.; Matsu, K.; Miura, K.; et al. A genome-wide association study in Japanese identified one variant associated with a preference for a Japanese dietary pattern. *Eur. J. Clin. Nutr.* 2021, 75, 937–945. [CrossRef]

18. Suzuki, T.; Nakamura, Y.; Doi, Y.; Narita, A.; Shimizu, A.; Imaeda, N.; goto, C.; Matsu, K.; Kadota, A.; Miura, K.; et al. A genome-wide association study on confection consumption in a Japanese population: The Japan Multi-Institutional Collaborative Cohort Study. *Br. J. Nutr.* 2021, 126, 1843–1851. [CrossRef]

19. Suzuki, T.; Nakamura, Y.; Matsuo, K.; Oze, I.; Doi, Y.; Narita, A.; Shimizu, A.; Imaeda, N.; goto, C.; Matsu, K.; et al. A genome-wide association study on fish consumption in a Japanese population-the Japan Multi-Institutional Collaborative Cohort study. *Eur. J. Clin. Nutr.* 2021, 75, 480–488. [CrossRef]

20. Konishi, K. Associations between healthy Japanese dietary patterns and depression in Japanese women. *Public Health Nutr.* 2021, 24, 1753–1765. [CrossRef]

21. Okada, E.; Takahashi, K.; Takimoto, H.; Takabayashi, S.; Kishi, T.; Kobayashi, T.; Nakamura, K.; Ukawa, S.; Nakamura, M.; Sasaki, S.; et al. Dietary patterns among Japanese adults: Findings from the National Health and Nutrition Survey, 2012. *Asia Pac. J. Clin. Nutr.* 2018, 27, 1120–1130.

22. Sugawara, N.; Yatsuy-Furukuri, N.; Satoh, S.; Saito, M.; Furukori, H.; Nakagami, T.; Ishiooka, M.; Kaneko, S. Dietary patterns are associated with obesity in Japanese patients with schizophrenia. *Bmc Psychiatry* 2014, 14, 184. [CrossRef] [PubMed]

23. Sugawara, N.; Yatsuy-Furukuri, N.; Umeda, T.; Tsuchimine, S.; Kani, A.; Tsuruga, K.; Iwabe, K.; Okubo, N.; Takahashi, I.; Kaneko, S. Relationship between Dietary Patterns and Cognitive Function in a Community-Dwelling Population in Japan. *Asia-Pac. J. Public Health* 2015, 27, NP2651–NP2660. [CrossRef] [PubMed]

24. Tanisawa, K.; Ito, T.; Kawakami, R.; Usui, C.; Kawamura, T.; Suzuki, K.; Sakamoto, S.; Ishii, K.; Muraoka, I.; Oka, K.; et al. Association Between Dietary Patterns and Different Metabolic Phenotypes in Japanese Adults: WASEDA’S Health Study. *Front. Nutr.* 2022, 9. [CrossRef]

25. Ito, T.; Kawakami, R.; Tanisawa, K.; Miyawaki, R.; Ishii, K.; Torii, S.; Suzuki, K.; Sakamoto, S.; Muraoka, I.; Oka, K.; et al. Dietary patterns and abdominal obesity in middle-aged and elderly Japanese adults: Waseda Alumni’s Sports, Exercise, Daily Activity, Sedentariness and Health Study (WASEDA’s Health Study). *Nutrition* 2019, 58, 149–155. [CrossRef] [PubMed]

26. Tanisawa, K.; Ito, T.; Kawakami, R.; Usui, C.; Kawamura, T.; Suzuki, K.; Sakamoto, S.; Ishii, K.; Muraoka, I.; Oka, K.; et al. Association between alcohol dietary pattern and prevalence of dyslipidaemia: WASEDA’S Health Study. *Br. J. Nutr.* 2021, 127, 1712–1722. [CrossRef]

27. Takeno, K.; Tamura, Y.; Kakehi, S.; Kaga, H.; Kawamori, R.; Watada, H. ALDH2 rs671 Is Associated With Elevated FPG, Reduced Glucose Clearance and Hepatic Insulin Resistance in Japanese Men. *J. Clin. Endocrinol. Metab.* 2021, 106, e3573–e3581. [CrossRef]

28. Kato, N.; Takeuchi, F.; Tabara, Y.; Kelly, T.N.; Go, M.J.; Sim, X.; Tay, W.T.; Chen, C.-H.; Zhang, Y.; Yamamoto, K.; et al. Meta-analysis of genome-wide association studies identifies common variants associated with blood pressure variation in east Asians. *Nat. Genet.* 2011, 43, 531–538. [CrossRef]

29. Takeuchi, F.; Isono, M.; Nabika, T.; Katsuya, T.; Sugiyama, T.; Yamaguchi, S.; Kobayashi, S.; Oghara, T.; Yamori, Y.; Fujioka, A.; et al. Confirmation of ALDH2 as a Major Locus of Drinking Behavior and of Its Variants Regulating Multiple Metabolic Phenotypes in a Japanese Population. *Circ. J.* 2011, 75, 911–918. [CrossRef]

30. Someya, Y.; Tamura, Y.; Kaga, H.; Nojiri, S.; Shimada, K.; Daida, H.; Ishijima, M.; Kaneko, K.; Aoki, S.; Miida, T.; et al. Skeletal muscle function and need for long-term care of urban elderly people in Japan (the Bunkyo Health Study): A prospective cohort study. *BMJ Open* 2019, 9, e031584. [CrossRef]

31. Sasaki, S. BDHQ under/over Reporting: Exclusion Criteria. Available online: http://www.nutrepi.m.u-tokyo.ac.jp/dhq/Q&A.pdf (accessed on 25 May 2022).

32. Kobayashi, S.; Honda, S.; Murakami, K.; Sasaki, S.; Okubo, H.; Hirota, N.; Notsu, A.; Fukui, M.; Date, C. Both Comprehensive and Brief Self-Administered Diet History Questionnaires Satisfactorily Rank Nutrient Intakes in Japanese Adults. *J. Epidemiol.* 2012, 22, 151–159. [CrossRef]

33. Kobayashi, S.; Murakami, K.; Sasaki, S.; Okubo, H.; Hirota, N.; Notsu, A.; Fukui, M.; Date, C. Comparison of relative validity of food group intakes estimated by comprehensive and brief-type self-administered diet history questionnaires against 16 d dietary records in Japanese adults. *Public Health Nutr.* 2011, 14, 1200–1211. [CrossRef] [PubMed]

34. Hosoya, N. *Standard Tables of Food Composition in Japan*; Printed Bureau of Ministry of Finance: Tokyo, Japan, 2005. (In Japanese)
