Dietary phytochemical index associated with cardiovascular risk factor in patients with type 1 diabetes mellitus

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Abstract

Background

Dietary phytochemical index (DPI) is useful and inexpensive method to identify the role of phytochemicals on cardiovascular disease (CVD) risk factors. This study aimed to assess the relationship between DPI and CVD risk factors in patients with type1 diabetes mellitus (T1DM).

Methods

A total of 261 participants aged 18–35 years with T1DM were enrolled in this cross-sectional study to assess the relationship between DPI and CVD risk factors. Anthropometric measurements, blood lipids, glucose, and antioxidant level were measured. Food intakes were determined using a food frequency questionnaire to calculate DPI. Logistic regression was used.

Results

The mean age of participants was 25 years. After adjustment for potential confounders, participants in the highest tertile of DPI had 88% lower chance of hyperglycemia (P for trend = 0.020), 81% lower chance of low high-density lipoprotein cholesterol (HDL-C) (P for trend = 0.030) and 98% lower chance of high low-density lipoprotein cholesterol to HDL-C ratio (P for tend = 0.040). There were no relationships between DPI and other CVD risk factors.

Conclusions

Although higher intake of phytochemical-rich foods had a beneficial effect on some risk factors of CVD, more studies more studies are warranted to corroborate the present findings.

Introduction

Diabetes mellitus (DM) is one of the most important cause of death worldwide, especially in developed countries [1]. It is associated with the risk of hypertension (HTN), hypercholesterolemia, and cardiovascular diseases (CVD) [2]. Seven to 12 percent of patients who suffer from diabetes have type 1 DM (T1DM) [3]. Genetic and environmental triggers including toxins, viral infections, and some dietary factors may affect incidence of T1DM [3]. Unfortunately, there are currently no preventive measures for the prevention of T1DM, so the reduction of its complications must be focused [3].

Oxidative stress (OS) as an imbalance between oxidants and anti-oxidants in the favor of the oxidants, leading to a disruption of redox signaling and control and/or molecular damage [4]. OS plays an important role in the major diabetic complications, including retinopathy, nephropathy, neuropathy and

accelerated coronary artery disease [5, 6]. Insulin deficiency, in turn leads to chronic hyperglycemia [7] and an increase level of lipid and protein peroxidation products, oxidative DNA damage markers, and lower activity of antioxidant enzymes, subsequently [8]. Some evidence showed that antioxidant capacity impairs in T1DM due to lower consumption of antioxidant components or lower levels of antioxidant substances [9–11].

Phytochemicals are mainly found in plant foods such as fruits, vegetables, cereals, soy and tea [12], which is inversely associated with chronic diseases including DM, CVD, and some cancers [13]. The beneficial effects of phytochemicals can be attributed to their antioxidant and anti-inflammatory properties, their effect on cell cycle regulation, hormones, vascular endothelium and immune cells [14]. Dietary phytochemical index (DPI) is a quantitative index defined as percentage of energy intake that are derived from phytochemicals rich foods in order to identify the role of phytochemicals on health [15].

Previous studies investigated the association of DPI with chronic diseases risk factors. Most of these studies conducted on healthy individuals, except of 2 case-control studies on women with breast cancer [16] and individuals with pre-diabetes [17]. The result of these studies showed inverse association between DPI and waist circumference (WC) [18–20], body mass index (BMI) [21], HTN [19, 22], glucose intolerance [17, 23], chance of pre-diabetes [17], dyslipidemia [19, 24], and blood biomarkers of OS [21].

Few studies investigated the relationship between DPI and health outcomes and none of them were performed in patients with T1DM, who have complex conditions such as impaired glucose and lipid disturbances [25]. We hypothesis that DPI may have a beneficial relationship with the CVD risks; therefore, the aim of this study was to determine the relationship between DPI with CVD risk factors including blood glucose, lipid profile, antioxidant levels, blood pressure and anthropometric measurements in patients with T1DM.

Materials And Methods

Study design

The present study is part of a cross-sectional study, which investigated the association between dietary patterns with CVD risk factors and OS in patients with T1DM with the approval of Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.REC.1394.1595), and written informed consent was obtained from all the participants. The study was conducted on 273 patients with T1DM from the Iranian diabetes society and Endocrine and Metabolism Research Institute of Tehran University of Medical Sciences in Tehran, Iran. According to the exclusion criteria (individuals who had reported energy intake outside the range of 500–3,500 kcal/day in women and 800–4,200 kcal/day in men) 261 patients were finally analyzed for the non-biochemical assessments and due to financial limitation, 81 patients recruited for biochemical examination using simple random sampling method. Inclusion criteria were patients who were diagnosed with T1DM for at least six months, aged between 18–35 and hemoglobin A1c (HbA1c) $\leq$ 8%. Participants were not enrolled into the study if they had BMI $\geq$ 40 kg/m², drugs intake

other than insulin to lower blood glucose (such as metformin), diagnosed CVD, cancer, kidney or liver disease, use of contraceptives, hormones and recombinant drugs, thyroid control drugs, taking weight reducing agents, anti-depressants and anti-anxiety drugs, use of any smoking (cigarette, hookah, tobacco pipe) and pregnancy or lactation.

Demographic and general characteristics

Information about age, sex, duration of DM, educational level, daily insulin dose, type of insulin and dietary supplements intake were collected by questionnaires.

Dietary intake assessment

Individual's typical dietary intake, during the last year, was evaluated using a semi-quantitative food frequency questionnaire (FFQ) with 147 food items [26], interviewed by a trained dietitian. The validity and reproducibility of the FFQ were determined previously for fruits, vegetables, and energy intake [26,27]. In this FFQ, there is a list of food items with a standard serving size that Iranian people commonly consume [28]. Individuals were asked to report their usual frequency and amount of consumption of food items listed by day, week, and month over the previous year. The values listed for each food item were converted to gram using US Department of Agriculture (USDA) serving sizes whenever possible; if this was not possible, household measures were chosen and were then converted to grams. Energy and nutrient contents of food items were obtained from USDA food composition tables (FCTs) because Iranian FCTs are incomplete. The Iranian FCT was used for traditional food items that are not listed in the USDA FCT. Analyzing the energy and nutrients of each food item was done with the Nutritionist IV software version 3.5.1 [29], that modified for Iranian food [30].

DPI is calculated based on the division of energy content of foods rich in phytochemicals on the total daily energy intake $\times 100$, based on McCarty formula ($DPI = \frac{\text{Dietary energy derived from phytochemical-rich foods (kcal)}}{\text{Total daily energy intake (kcal)}} \times 100$) [15]. To calculate the DPI, all the phytochemical-rich foods including fruits, vegetables (except potatoes), whole grains, legumes, fruit and vegetable juice, soy products, nuts, seeds, olive and olive oil were gathered from the FFQ [21].

Clinical assessment

The weight was measured by a nutritionist using a digital scale (GAIA 359 PLUS. Jawon Medical Co. Ltd., Gyeongsan, Korea), to the nearest 100 g, with minimal dress and no shoes. Height was measured to the nearest 0.5 cm with a tape while the patient standing without shoes. The BMI was calculated by dividing the weight (kg) by height (square meter). WC was measured using an elastic tape measuring midpoint

between the iliac crest and lowest rib [31]. Blood pressure was measured from the right hand of the participants to the nearest 2 mmHg, after at least 10 minutes rest, while sitting on a chair with a mercury sphygmomanometer. Overweight and obesity defined as $BMI = 25-29.9 \text{ kg/m}^2$ and $BMI \geq 30 \text{ kg/m}^2$, respectively [32], central obesity as $WC \geq 80 \text{ cm}$ in women and $\geq 94 \text{ cm}$ in men [33]. HTN was defined as blood pressure $\geq 140/90 \text{ mmHg}$ [34].

Physical activity assessment

Physical activity of participants, during the previous week, was measured using the short form of International Physical Activity Questionnaire (IPAQ) [35]. The average time that a person would normally spend on different activities each day was asked. Then, to measure the value of metabolic equivalent task (MET)-hour/week, the sum of frequency and duration of activities multiplied by the MET of activity. The reliability and validity of IPAQ across 12 countries was assessed previously [36].

Laboratory measurements

After a 12–14 hour fasting at night, a trained nurse collected 5 mL of venous blood from the participants. Blood samples were collected in 2 separate tubes. One of the tubes was for separating serum and another tube containing ethylenediaminetetraacetic acid was used to separate the plasma. In order to separate the plasma samples from cells, the blood was centrifuged in 3,000 rounds for 10 minutes. Then the remaining blood was washed three times with sodium chloride solution 0.9 g/L. Separation of cell membranes was performed by centrifugation for 5 minutes at 4°C. Then hemolytic cells were used to determine the activity of antioxidant enzymes. The serum was separated from the blood by centrifugation for 10 minutes at 4°C. After that, all the blood samples were stored at -79°C. Blood glucose measurements were performed on the day of the test. This study was conducted with observance of the Declaration of Helsinki and the National Ethical Guidelines in Biomedical Research in Iran.

Measurements of serum glucose and lipids were performed, using Pars Azmoon kit (Pars Azmoon, Tehran, Iran). The measurement of triglyceride (TG) levels was conducted by colorimetric and photometry. Fasting blood glucose (FBG) and total cholesterol (TC) measurement were conducted by enzymatic colorimetric and single point with photometric method. The measurement of total antioxidant capacity (TAC) and activity of glutathione peroxidase (GPx) and superoxide dismutase (SOD) were measured by commercial kits following the manufacturer's protocol (ZellBio GmbH, Lonsee, Germany). The intra- and inter-assay coefficients of variation for SOD, GPx, and TAC were 5.8% and 7.2%, 3.5% and 4.7%, and 3.4% and 4.2%, respectively. The following formula was used for calculating low-density lipoprotein cholesterol (LDL-C) [37]: $LDL-C = TC - \text{high-density lipoprotein cholesterol (HDL-C)} - TG/5.0 \text{ (mg/dL)}$.

Hypertriglyceridemia was defined as serum $TG \geq 150 \text{ mg/dL}$ (1.7 mmol/L) [33,34], low HDL-C as serum $HDL-C < 40 \text{ mg/dL}$ (1.0 mmol/L) for men and $< 50 \text{ mg/dL}$ (1.3 mmol/L) for women [33,34], high LDL-C as serum $LDL-C \geq 100$ (2.6 mg/dL) [34], hypercholesterolemia as $TC > 200 \text{ mg/dL}$ [38], high HbA1c as

HbA1c ≥ 7 [34], hyperglycemia as FBG ≥ 100 mg/dL [33] and high LDL-C/HDL-C ratio as LDL-C/HDL-C > 3 in women and > 3.5 in men [39].

Statistical analysis

Statistical analysis was performed using SPSS software for Windows (version 23; SPSS Inc., Chicago, IL, USA; 2015) [40]. Individuals who had reported energy intake outside the range of 500–3,500 kcal/day in women and 800–4,200 kcal/day in men were excluded from the study [41]. In this order 3 men and 9 women were excluded from the data analysis and the final analysis was done on 261 participants. At first, energy-adjusted DPI was determined by residual method [42], then according to DPI, participants were categorized into tertiles. Normality of data distribution was tested using graph and Kolmogorov-Smirnov test. Comparison of the general and nutritional characteristics of the participants between the tertiles of energy-adjusted DPI was done using analysis of variance (ANOVA) or χ^2 test depending on the type of variables. Means $\pm$ SD of CVD risk factors across tertiles of DPI were compared by ANOVA test for crude model and analysis of covariance for adjusted models which adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/hour/week), BMI (kg/m²), diabetes duration (year), total daily insulin dose, education and dietary supplement intake. Further adjustment for intake of saturated fatty acids (SFA), mono-unsaturated fatty acids (MUFA), poly-unsaturated fatty acids (PUFA) and trans fatty acids was done for lipids levels. In addition, dietary intake of sodium and potassium was adjusted for systolic blood pressure (SBP) and diastolic blood pressure (DBP). Logistic regression test was used in crude and adjusted model to determine the odds ratio (OR) of cardiovascular risk factors and their 95% confidence interval (CI) in each tertile of DPI, which adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/hour/week), BMI (kg/m²), diabetes duration (year), total insulin dose (unit/day), education, dietary supplement intake. These potential confounders were identified to be related with DPI according to the present study and previous literatures [18,19,21,22,24]. In all analyzes, the first tertile of DPI was considered as a reference and OR of the cardiovascular risk factor in the other tertiles was calculated towards it. Furthermore, to determine the overall trends of OR across increasing tertiles of DPI, the median of each tertile was used instead of the number of tertiles. *P*-value lower than 0.05 was considered significant.

Results

Characteristics of participants across tertiles of DPI

The mean $\pm$ SD age of participants was 25 ± 5.4 years and 62.1% of the participants were women. DPI in the first, second and third tertiles of energy-adjusted DPI was < 31.75 , $31.75\text{--}40.06$, and > 40.06 , respectively for females and < 27.73 , $27.73\text{--}36.05$, and > 36.05 , respectively for males. The characteristics of participants across tertiles of DPI are shown in Table 1. Participants in the lower tertile of DPI were significantly younger (*P*-trend = 0.02). Other characteristics including gender, education, short-acting insulin intake, long-acting insulin intake, dietary supplement intake, daily insulin dose, BMI, weight, WC, diabetes duration, energy intake and physical activity were not significantly different across DPI

tertiles (P -trend > 0.05). The relative contributions of different phytochemical-rich food groups of DPI are shown in Fig. 1. The percentage of daily intake of energy from fruits and vegetables were higher than the other sources of phytochemical rich foods.

CVD risk factors across tertiles of DPI

Table 2 presents the mean $\pm$ SD of CVD risk factors across tertiles of DPI. In the crude model, there was not any significant association between CVD risk factors and DPI (P -trend > 0.05) (Model 1). After adjustment for age, sex, total energy intake, physical activity, BMI, diabetes duration, insulin dose, education and dietary supplement intake, participants in the higher tertile of DPI had significantly lower LDL-C to HDL-C ratio compared with those in the lower tertile (P -trend = 0.03) (Model 2). In addition, after further adjustment for intake of SFA, MUFA, PUFA and trans fatty acids participants in the higher tertile of DPI, had significantly lower LDL-C (P -trend = 0.03) and LDL-C to HDL-c ratio (P -trend = 0.03) compared with those in the lower tertile (Model 3). After further adjustment for dietary intake of sodium and potassium, significant relation was observed between DPI and SBP (P -trend = 0.04) (Model 3) (Fig. 2). No significant association was found between GPx, SOD, TAC and DPI. By increasing the tertiles of DPI, levels of FBG decreased, while TAC increased, however these findings were not statistically significant (P -trend > 0.05).

The OR and 95% CI of CVD risk factors are shown in Table 3. In crude model, no significant association was found between CVD risk factors and DPI (P -trend > 0.05), except for hyperglycemia that compared with participants in the lowest tertile, those in the highest tertile of DPI, had 85% lower chance of hyperglycemia (OR, 0.15; 95% CI, 0.03–0.77). After adjustment for age, sex, total energy intake, physical activity, BMI, diabetes duration, total insulin dose, education and dietary supplement intake, compared with participants in the lowest tertile, those in the highest tertile of DPI, had 88% lower chance of hyperglycemia (OR, 0.12; 95% CI, 0.02–0.82), 81% lower chance of low HDL-C level (OR, 0.19; 95% CI, 0.04–0.86) and 98% lower chance of high LDL-C/HDL-C ratio (OR, 0.02; 95% CI, 0.001–0.89). In Fig 3, the ORs of CVD risk factors across DPI tertiles are presented for statistically significant findings. No relationship was found between DPI and overweight or obesity, central obesity and HTN (P -trend > 0.05). Although the chance of high LDL-C decreased across the DPI tertile in both crude and adjusted model, it was not significant (P -trend > 0.05). All participants had DBP lower than 90 mmHg, so we were not able to calculate the OR for high DBP. Furthermore, just few participants (7 from 261) had hypertriglyceridemia, so logistic regression was not performed to assess the chance of hypertriglyceridemia. Because of the sparsity of data, wide 95% CI for high SBP was observed (Table 3).

Discussion

Based on our knowledge, there is no previous study which investigated the association between CVD risk factors in patients with T1DM and DPI. Results from this cross-sectional study revealed that compared with participants in the lowest tertile of DPI, those in the highest tertile, had 88% lower chance of high FBG, 81% lower chance of low HDL-C level and 98% lower chance of high LDL-C to HDL-C ratio.

In line with our findings, a longitudinal study reported significant inverse association between FBG level and DPI at baseline of study but not after 3-years of follow-up [23]. Furthermore, a case-control study has found that participants in the upper quartiles of DPI had lower odds of pre-diabetes [17]. Several studies reported significant association between intake of different phytochemicals and better FBG levels in healthy subjects [43, 44] and patients with type 2 DM [45–49]. However, some studies have not found significant relationship between FBG level and DPI in healthy individuals [19, 20]. There are several mechanisms that phytochemicals influence carbohydrate metabolism and improve FBG [50], such as inhibition of carbohydrate digestion and intestinal glucose absorption, stimulation of insulin secretion from pancreatic β -cells, stimulation of hepatic glycolysis and glycogenesis, anti-inflammatory and antioxidant properties, effect on intracellular signaling pathway and gene expression [50–53].

Our study revealed that higher intake of phytochemical rich food is associated with lower mean LDL-C and higher chance of high HDL-C levels. Golzarand et al. [24] observed that after 3 years of follow-up, the levels of TC, TG, HDL-C, and non-high-density lipoprotein cholesterol (non-HDL-C) in the highest quartile of DPI, significantly decreased in healthy men but not in women. Furthermore, our findings about HDL-C is in line with the study of Bahadoran et al. [19] that found higher mean serum HDL-C in the higher DPI tertile in healthy adults. However, in another study no association was reported between HDL-C level and DPI in healthy adults [20]. Different findings might be explained by the discrepancy in characteristics of participants, study design and study sample size.

Our study showed that higher intake of phytochemical rich food is significantly associated with lower chance of high LDL-C/HDL-C ratio, which is a predictor of CVD risk [54]. There are some studies that investigated the effect of phytochemicals intake on LDL-C/HDL-C ratio. A randomized clinical study on subjects with hypercholesterolemia, showed that intake of insoluble polyphenols could reduce the LDL-C/HDL-C ratio [55]. Another intervention study indicated that consumption of red wine polyphenols resulted in 7% reduction in LDL-C/HDL-C ratio compared to the baseline values in men who are at high risk of CVD [56]. Phytochemicals may improve lipid profile [57]. One of the best examples of a phytochemical-rich diet is Mediterranean diet. However, adding specific phytochemicals such as phytosterols and proanthocyanidins to Mediterranean diet increased the effect of diet on decreasing TC, LDL-C, and non-HDL-C and increasing HDL-C compared with Mediterranean diet alone [58, 59]. Peroxisome proliferator-activated receptors (PPARs) are compounds that play an important role in lipid metabolism. Some phytochemicals as natural PPARs ligands could activate PPARs and affect lipid metabolism, increase fatty acid uptake, utilization, and catabolism by affecting on fatty acid transport [60]. Furthermore, PPARs lead to lower plasma levels of cholesterol, triacylglycerol and higher HDL-C level [61].

Our findings showed that mean SBP decreased across increasing DPI tertiles, which is similar to the result of a study in healthy participants [19]. However, in logistic regression no association was found between SBP and DPI. On the contrary, some studies reported that participants with higher intake of phytochemical-rich diet had lower risk for occurrence of HTN in 3 years follow-up. However, no significant difference was observed in mean SBP and DBP across DPI quartiles [20, 22]. Previous studies indicated

that consumption of phytochemical rich food, such as fruits and vegetables [62, 63], legumes [64, 65] and olive [66, 67], is inversely associated with HTN. Two met-analysis reported that consumption of different sources of phytochemicals including soy isoflavones and berries polyphenols significantly reduced SBP but not DBP [68, 69]. However, another study on participants with HTN observed that a combination of isolated phytochemicals and botanical extracts just decreased DBP but not SBP [70]. The dietary approaches to stop hypertension (DASH), which is rich in fruits, vegetables and low-fat dairy foods, reduces blood pressure [71]. DASH diet provides an abundance of phytochemicals that may contribute to blood pressure lowering properties of this type of diet [72]. OS is an important factor in pathogenesis of HTN, that phytochemicals with antioxidant properties could reduce the risk of HTN [73, 74]. Flavonoids by modulating endothelial nitric oxide synthase activity, could increase endothelial-derived nitric oxide which is a vasodilator factor that enhances endothelial function [75].

In the present study, no association was found between antioxidant biomarkers and DPI. In line with our result, a previous cross-sectional study observed that DPI was not significantly related to total antioxidant statue in overweight adults [21]. In a cross- sectional study on healthy adolescents, higher intake of phytochemicals such as retinol, α -tocopherol, lycopene and the carotenoids was associated with higher serum levels of the mentioned antioxidant compounds, except lycopene [76]. The result of an experimental study showed no significant effect of phytosterol supplementation on plasma TAC in patients with metabolic syndrome [77]. Moreover, flavonoids supplement in patients with T1DM significantly decreased GPx activity, while other parameters of antioxidant capacity such as glutathione, activity of catalase and SOD remained unchanged [78]. These discrepancies could be explained by measuring different antioxidant biomarkers and various phytochemical supplementation.

This study has some limitations. The cross-sectional design is the major limitation of this study, which prevents to observe the cause and effect of the relationship. The other limitation is inherent limitations of DPI. In this index phytochemical rich food without energy content like spices, green and black tea were not considered. In addition, not considering the type of consumed phytochemicals is another limitation, because two diets with the same DPI but different source of phytochemicals could have different potential benefits. Although the various confounders were carefully controlled, it is possible to miss other residual confounders.

However, the strength of this study is investigating on dietary intake of patients with T1DM who are at high risk of several diabetic complications. Moreover, a validated and reliable FFQ was used which was completed by a trained dietitian.

Conclusion

In conclusion, the findings of this study demonstrated that higher intake of phytochemical rich food, measured by DPI score was associated with lower chance of some CVD risk factors including dyslipidemia and high FBG in T1DM patients. More studies more studies are warranted to corroborate the present findings.

List Of Abbreviations

BMI: Body mass index

CI: Confidence interval

CVD: Cardiovascular disease

DBP: Diastolic blood pressure

DPI: Dietary phytochemical index

DM: Diabetes mellitus

FBG: Fasting blood glucose

FCT: Food composition tables

FFQ: Food frequency questionnaire

GPx: Glutathione peroxidase

HbA1c: Hemoglobin A1c

HDL-C: High-density lipoprotein cholesterol

HTN: Hypertension

IPAQ: International Physical Activity Questionnaire

LDL-C: Lipoprotein cholesterol

MET: Metabolic equivalent task

MUFA: Mono-unsaturated fatty acids

OR: Odds ratio

OS: Oxidative stress

PUFA: Poly-unsaturated fatty acids

SBP: Systolic blood pressure

SFA: Saturated fatty acids

T1DM: Type1 diabetes mellitus

TAC: Total antioxidant capacity

TG: Triglyceride

TC: Total cholesterol

USDA: US Department of Agriculture

WC: Waist circumference

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.REC.1394.1595) and written informed consent was obtained from all the participants. This study was conducted with observance of the Declaration of Helsinki and the National Ethical Guidelines in Biomedical Research in Iran.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare no potential conflicts of interests.

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Authors' contributions

All authors have read and approved the final manuscript. Overall G.S., F.S. and M.Q. supervised the project and approved the final version of the manuscript to be submitted; S.D. and G.S. designed the research; S.D., Z.S., A.B., E.N., and A.R., collected data sampling; S.D., M.A., and M.Q., analyzed and interpreted the data; F.S. A.R, critically reviewed the manuscript; and S.D. and G.S., drafted the initial manuscript.

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References

1. Lefèbvre P, Pierson A. The global challenge of diabetes. *World Hosp Health Serv* 2004;40:37–40, 42.
2. International Diabetes Federation. *Diabetes and Cardiovascular Disease*. Brussels: International Diabetes Federation; 2016.
3. Garralda-Del-Villar M, Carlos-Chillerón S, Diaz-Gutierrez J, Ruiz-Canela M, Gea A, Martínez-González MA, Bes-Rastrollo M, Ruiz-Estigarribia L, Kales SN, Fernández-Montero A. Healthy lifestyle and incidence of metabolic syndrome in the SUN cohort. *Nutrients* 2018;11:65.
4. Sies H, Jones D. Oxidative stress. In: Fink G, editor. *Encyclopedia of Stress*. 2nd ed. New York (NY): Academic Press; 2007. p.45–48.
5. Rösen P, Nawroth PP, King G, Möller W, Tritschler HJ, Packer L. The role of oxidative stress in the onset and progression of diabetes and its complications: a summary of a Congress Series sponsored by UNESCO-MCBN, the American Diabetes Association and the German Diabetes Society. *Diabetes Metab Res Rev* 2001;17:189–212.
6. Phillips M, Cataneo RN, Cheema T, Greenberg J. Increased breath biomarkers of oxidative stress in diabetes mellitus. *Clin Chim Acta* 2004;344:189–94.
7. Bastaki S. Diabetes mellitus and its treatment. *Int J Diabetes Metab* 2005;13:111–34.
8. Ayepola OR, Brooks NL, Oguntibeju OO. Oxidative stress and diabetic complications: the role of antioxidant vitamins and flavonoids. In: Oguntibeju O, editor. *Antioxidant-Antidiabetic Agents and Human Health*. Rijeka: IntechOpen; 2014.
9. Varvarovská J, Racek J, Stozický F, Souček J, Trefil L, Pomahacová R. Parameters of oxidative stress in children with type 1 diabetes mellitus and their relatives. *J Diabetes Complications* 2003;17:7–10.
10. Asayama K, Uchida N, Nakane T, Hayashibe H, Dobashi K, Amemiya S, Kato K, Nakazawa S. Antioxidants in the serum of children with insulin-dependent diabetes mellitus. *Free Radic Biol Med* 1993;15:597–602.
11. Domínguez C, Ruiz E, Gussinye M, Carrascosa A. Oxidative stress at onset and in early stages of type 1 diabetes in children and adolescents. *Diabetes Care* 1998;21:1736–42.
12. Dillard CJ, German JB. Phytochemicals: nutraceuticals and human health. *J Sci Food Agric* 2000;80:1744–56.
13. Firdous SM. Phytochemicals for treatment of diabetes. *EXCLI J* 2014;13:451–3.
14. Han X, Shen T, Lou H. Dietary polyphenols and their biological significance. *Int J Mol Sci* 2007;8:950–88.
15. McCarty MF. Proposal for a dietary “phytochemical index”. *Med Hypotheses* 2004;63:813–7.
16. Bahadoran Z, Karimi Z, Houshiar-rad A, Mirzayi HR, Rashidkhani B. Dietary phytochemical index and the risk of breast cancer: a case control study in a population of Iranian women. *Asian Pac J Cancer*

Prev 2013;14:2747–51.

17. Abshirini M, Mahaki B, Bagheri F, Siassi F, Koohdani F, Sotoudeh G. Higher intake of phytochemical-rich foods is inversely related to prediabetes: a case-control study. *Int J Prev Med* 2018;9:64.
18. Mirmiran P, Bahadoran Z, Golzarand M, Shiva N, Azizi F. Association between dietary phytochemical index and 3-year changes in weight, waist circumference and body adiposity index in adults: Tehran Lipid and Glucose study. *Nutr Metab (Lond)* 2012;9:108.
19. Bahadoran Z, Golzarand M, Mirmiran P, Saadati N, Azizi F. The association of dietary phytochemical index and cardiometabolic risk factors in adults: Tehran Lipid and Glucose Study. *J Hum Nutr Diet* 2013;26 Suppl 1:145–53.
20. Bahadoran Z, Golzarand M, Mirmiran P, Amouzgar A, Azizi F. Association between dietary phytochemical index and occurrence of metabolic syndrome and its risk factors (among Tehranian adults): Tehran Lipid and Glucose Study. *Iranian J Endocrinol Metab* 2012;14:343–51.
21. Vincent HK, Bourguignon CM, Taylor AG. Relationship of the dietary phytochemical index to weight gain, oxidative stress and inflammation in overweight young adults. *J Hum Nutr Diet* 2010;23:20–9.
22. Golzarand M, Bahadoran Z, Mirmiran P, Sadeghian-Sharif S, Azizi F. Dietary phytochemical index is inversely associated with the occurrence of hypertension in adults: a 3-year follow-up (the Tehran Lipid and Glucose Study). *Eur J Clin Nutr* 2015;69:392–8.
23. Bahadoran Z, Mirmiran P, Tohidi M, Azizi F. Dietary phytochemical index and the risk of insulin resistance and β -cell dysfunction: a prospective approach in Tehran Lipid and Glucose Study. *Int J Food Sci Nutr* 2015;66:950–5.
24. Golzarand M, Mirmiran P, Bahadoran Z, Alamdari S, Azizi F. Dietary phytochemical index and subsequent changes of lipid profile: a 3-year follow-up in Tehran Lipid and Glucose Study in Iran. *ARYA Atheroscler* 2014;10:203–10.
25. Vergès B. Lipid disorders in type 1 diabetes. *Diabetes Metab* 2009;35:353–60.
26. Esfahani FH, Asghari G, Mirmiran P, Azizi F. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran Lipid and Glucose Study. *J Epidemiol* 2010;20:150–8.
27. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran Lipid and Glucose Study. *Public Health Nutr* 2010;13:654–62.
28. Ghaffarpour M, Houshiar-Rad A, Kianfar H. The manual for household measures, cooking yields factors and edible portion of foods. Tehran: Nashre Olume Keshavarzy; 1999.
29. Hearst Corporation, First DataBank. Nutritionist IV: Diet Analysis. San Bruno (CA): First DataBank; 1995.
30. Azar M, Sarkisian E. Food Composition Table of Iran. Tehran: National Nutrition and Food Research Institute, Shahid Beheshti University; 1978.
31. World Health Organization. Obesity: Preventing and Managing the Global Epidemic. Geneva: World Health Organization; 2000.

32. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. National Institutes of Health. *Obes Res* 1998;6 Suppl 2:51S-209S.
33. Alberti G, Zimmet P, Shaw J, Grundy SM. The IDF Consensus Worldwide Definition of the Metabolic Syndrome. Brussels: International Diabetes Federation; 2006.
34. American Diabetes Association. Standards of medical care in diabetes—2017 abridged for primary care providers. *Clin Diabetes* 2017;35:5–26.
35. Moghaddam MHB, Aghdam FB, Jafarabadi MA, Allahverdipour H, Nikookheslat SD, Safarpour S. The Iranian version of International Physical Activity Questionnaire (IPAQ) in Iran: content and construct validity, factor structure, internal consistency and stability. *World Appl Sci* 2012;18:1073–80.
36. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;35:1381–95.
37. Nigam PK. Calculated low density lipoprotein-cholesterol: Friedewald's formula versus other modified formulas: calculated LDL-cholesterol. *Int J Life Sci Med Res* 2014;4:25–31.
38. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith SC Jr, Watson K, Wilson PW; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. *J Am Coll Cardiol* 2014;63:2889–934.
39. Millán J, Pintó X, Muñoz A, Zúñiga M, Rubiés-Prat J, Pallardo LF, Masana L, Mangas A, Hernández-Mijares A, González-Santos P, Ascaso JF, Pedro-Botet J. Lipoprotein ratios: physiological significance and clinical usefulness in cardiovascular prevention. *Vasc Health Risk Manag* 2009;5:757–65.
40. IBM Corp. I. IBM SPSS Statistics for Windows, Version 23.0. Armonk (NY): IBM Corp.; 2015.
41. Willett W. *Nutritional Epidemiology*. Oxford University Press; 2012.
42. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr* 1997;65:1220S-1228S.
43. Urquiaga I, D'Acuña S, Pérez D, Dicenta S, Echeverría G, Rigotti A, Leighton F. Wine grape pomace flour improves blood pressure, fasting glucose and protein damage in humans: a randomized controlled trial. *Biol Res* 2015;48:49.
44. Almoosawi S, Fyfe L, Ho C, Al-Dujaili E. The effect of polyphenol-rich dark chocolate on fasting capillary whole blood glucose, total cholesterol, blood pressure and glucocorticoids in healthy overweight and obese subjects. *Br J Nutr* 2010;103:842–50.
45. Lu T, Sheng H, Wu J, Cheng Y, Zhu J, Chen Y. Cinnamon extract improves fasting blood glucose and glycosylated hemoglobin level in Chinese patients with type 2 diabetes. *Nutr Res* 2012;32:408–12.
46. Yin J, Xing H, Ye J. Efficacy of berberine in patients with type 2 diabetes mellitus. *Metabolism* 2008;57:712–7.

47. Zhang H, Wei J, Xue R, Wu JD, Zhao W, Wang ZZ, Wang SK, Zhou ZX, Song DQ, Wang YM, Pan HN, Kong WJ, Jiang JD. Berberine lowers blood glucose in type 2 diabetes mellitus patients through increasing insulin receptor expression. *Metabolism* 2010;59:285–92.
48. Movahed A, Nabipour I, Lieben Louis X, Thandapilly SJ, Yu L, Kalantarhormozi M, Rekabpour SJ, Netticadan T. Antihyperglycemic effects of short term resveratrol supplementation in type 2 diabetic patients. *Evid Based Complement Alternat Med* 2013;2013:851267.
49. Rahimi HR, Mohammadpour AH, Dastani M, Jaafari MR, Abnous K, Ghayour Mobarhan M, Kazemi Oskuee R. The effect of nano-curcumin on HbA1c, fasting blood glucose, and lipid profile in diabetic subjects: a randomized clinical trial. *Avicenna J Phytomed* 2016;6:567–77.
50. Hanhineva K, Törrönen R, Bondia-Pons I, Pekkinen J, Kolehmainen M, Mykkänen H, Poutanen K. Impact of dietary polyphenols on carbohydrate metabolism. *Int J Mol Sci* 2010;11:1365–402.
51. Vinayagam R, Xiao J, Xu B. An insight into anti-diabetic properties of dietary phytochemicals. *Phytochem Rev* 2017;16:535–53.
52. Kim Y, Keogh JB, Clifton PM. Polyphenols and glycemic control. *Nutrients* 2016;8:17.
53. Bahadoran Z, Mirmiran P, Azizi F. Dietary polyphenols as potential nutraceuticals in management of diabetes: a review. *J Diabetes Metab Disord* 2013;12:43.
54. Buchwald H, Boen JR, Nguyen PA, Williams SE, Matts JP. Plasma lipids and cardiovascular risk: a POSCH report. Program on the Surgical Control of the Hyperlipidemias. *Atherosclerosis* 2001;154:221–7.
55. Ruiz-Roso B, Quintela JC, de la Fuente E, Haya J, Pérez-Olleros L. Insoluble carob fiber rich in polyphenols lowers total and LDL cholesterol in hypercholesterolemic subjects. *Plant Foods Hum Nutr* 2010;65:50–6.
56. Chiva-Blanch G, Urpi-Sarda M, Ros E, Valderas-Martinez P, Casas R, Arranz S, Guillén M, Lamuela-Raventós RM, Llorach R, Andres-Lacueva C, Estruch R. Effects of red wine polyphenols and alcohol on glucose metabolism and the lipid profile: a randomized clinical trial. *Clin Nutr* 2013;32:200–6.
57. Cicero AF, Colletti A. Role of phytochemicals in the management of metabolic syndrome. *Phytomedicine* 2016;23:1134–44.
58. Lerman RH, Minich DM, Darland G, Lamb JJ, Schiltz B, Babish JG, Bland JS, Tripp ML. Enhancement of a modified Mediterranean-style, low glycemic load diet with specific phytochemicals improves cardiometabolic risk factors in subjects with metabolic syndrome and hypercholesterolemia in a randomized trial. *Nutr Metab (Lond)* 2008;5:29.
59. Jones JL, Fernandez ML, McIntosh MS, Najm W, Calle MC, Kalynych C, Vukich C, Barona J, Ackermann D, Kim JE, Kumar V, Lott M, Volek JS, Lerman RH. A Mediterranean-style low-glycemic-load diet improves variables of metabolic syndrome in women, and addition of a phytochemical-rich medical food enhances benefits on lipoprotein metabolism. *J Clin Lipidol* 2011;5:188–96.
60. Ko JK, Lee SS, Martin H. Phytochemicals as modulators of PPARs and RXRs. *PPAR Res* 2010;2010:407650.

61. Ehrmann J Jr, Vavrusová N, Collan Y, Kolár Z. Peroxisome proliferator-activated receptors (PPARs) in health and disease. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2002;146:11–4.
62. Utsugi MT, Ohkubo T, Kikuya M, Kurimoto A, Sato RI, Suzuki K, Metoki H, Hara A, Tsubono Y, Imai Y. Fruit and vegetable consumption and the risk of hypertension determined by self measurement of blood pressure at home: the Ohasama study. *Hypertens Res* 2008;31:1435–43.
63. Wu L, Sun D, He Y. Fruit and vegetables consumption and incident hypertension: dose-response meta-analysis of prospective cohort studies. *J Hum Hypertens* 2016;30:573–80.
64. Jayalath VH, de Souza RJ, Sievenpiper JL, Ha V, Chiavaroli L, Mirrahimi A, Di Buono M, Bernstein AM, Leiter LA, Kris-Etherton PM, Vuksan V, Beyene J, Kendall CW, Jenkins DJ. Effect of dietary pulses on blood pressure: a systematic review and meta-analysis of controlled feeding trials. *Am J Hypertens* 2014;27:56–64.
65. Lee YP, Puddey IB, Hodgson JM. Protein, fibre and blood pressure: potential benefit of legumes. *Clin Exp Pharmacol Physiol* 2008;35:473–6.
66. Moreno-Luna R, Muñoz-Hernandez R, Miranda ML, Costa AF, Jimenez-Jimenez L, Vallejo-Vaz AJ, Muriana FJ, Villar J, Stiefel P. Olive oil polyphenols decrease blood pressure and improve endothelial function in young women with mild hypertension. *Am J Hypertens* 2012;25:1299–304.
67. Martín-Peláez S, Castañer O, Konstantinidou V, Subirana I, Muñoz-Aguayo D, Blanchart G, Gaixas S, de la Torre R, Farré M, Sáez GT, Nyssönen K, Zunft HJ, Covas MI, Fitó M. Effect of olive oil phenolic compounds on the expression of blood pressure-related genes in healthy individuals. *Eur J Nutr* 2017;56:663–70.
68. Taku K, Lin N, Cai D, Hu J, Zhao X, Zhang Y, Wang P, Melby MK, Hooper L, Kurzer MS, Mizuno S, Ishimi Y, Watanabe S. Effects of soy isoflavone extract supplements on blood pressure in adult humans: systematic review and meta-analysis of randomized placebo-controlled trials. *J Hypertens* 2010;28:1971–82.
69. Huang H, Chen G, Liao D, Zhu Y, Xue X. Effects of berries consumption on cardiovascular risk factors: A meta-analysis with trial sequential analysis of randomized controlled trials. *Sci Rep* 2016;6:23625.
70. Biesinger S, Michaels HA, Quadros AS, Qian Y, Rabovsky AB, Badger RS, Jalili T. A combination of isolated phytochemicals and botanical extracts lowers diastolic blood pressure in a randomized controlled trial of hypertensive subjects. *Eur J Clin Nutr* 2016;70:10–6.
71. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997;336:1117–24.
72. Most MM. Estimated phytochemical content of the dietary approaches to stop hypertension (DASH) diet is higher than in the Control Study Diet. *J Am Diet Assoc* 2004;104:1725–7.
73. Moline J, Bukharovich IF, Wolff MS, Phillips R. Dietary flavonoids and hypertension: is there a link? *Med Hypotheses* 2000;55:306–9.
74. Perez-Vizcaino F, Duarte J, Jimenez R, Santos-Buelga C, Osuna A. Antihypertensive effects of the flavonoid quercetin. *Pharmacol Rep* 2009;61:67–75.

75. Cassidy A, O'Reilly ÉJ, Kay C, Sampson L, Franz M, Forman JP, Curhan G, Rimm EB. Habitual intake of flavonoid subclasses and incident hypertension in adults. *Am J Clin Nutr* 2011;93:338–47.

76. Neuhouwer ML, Rock CL, Eldridge AL, Kristal AR, Patterson RE, Cooper DA, Neumark-Sztainer D, Cheskin LJ, Thornquist MD. Serum concentrations of retinol, alpha-tocopherol and the carotenoids are influenced by diet, race and obesity in a sample of healthy adolescents. *J Nutr* 2001;131:2184–91.

77. Sialvera TE, Koutelidakis AE, Richter DJ, Yfanti G, Kapsokefalou M, Micha R, Goumas G, Diamantopoulos E, Zampelas A. Phytosterol supplementation does not affect plasma antioxidant capacity in patients with metabolic syndrome. *Int J Food Sci Nutr* 2013;64:21–7.

78. Manuel y Keenoy B, Vertommen J, De Leeuw I. The effect of flavonoid treatment on the glycation and antioxidant status in type 1 diabetic patients. *Diabetes Nutr Metab* 1999;12:256–63

Tables

Table 1. Characteristics of participants across tertiles of the sex-specific energy-adjusted DPI in type 1 diabetic patients

Variables		DPI tertiles				<i>P</i> -trend
		T1 (n = 87)	T2 (n = 87)	T3 (n = 87)	Total (n = 261)	
Gender						
Men		33 (33.3)	33 (33.3)	33 (33.3)	99	1.000 ¹⁾
Women		54 (33.3)	54 (33.3)	54 (33.3)	162	
Age (yrs)		24.3 ± 5.1	24.7 ± 5.4	26.0 ± 5.4	25.0 ± 5.4	0.022 ²⁾
Weight (kg)		66.3 ± 12.3	65.9 ± 11.8	65.5 ± 11.6	65.9 ± 11.8	0.638 ²⁾
Waist circumference (cm)		86.0 ± 10.2	84.8 ± 10.3	85.7 ± 9.8	85.5 ± 10.1	0.828 ²⁾
BMI (kg/m ²)		23.4 ± 3.2	23.5 ± 3.5	23.5 ± 3.1	23.4 ± 3.3	0.857 ²⁾
Diabetes duration (yrs)		11.2 ± 6.0	12.6 ± 6.6	12.6 ± 6.7	12.1 ± 6.4	0.168 ²⁾
Insulin dose (unit/day)		48.5 ± 15.4	48.8 ± 16.7	47.0 ± 20.5	48.1 ± 17.6	0.590 ²⁾
Short-acting insulin intake						
Novo rapid		18 (34.3)	20 (32.8)	19 (32.8)	57	0.908 ¹⁾
Regular/mix		69 (31.6)	66 (35.1)	66 (33.3)	201	
Long-acting insulin intake						
Lantus/levemir		18 (31.0)	21 (36.2)	19 (32.8)	58	0.814 ¹⁾
NPH/mix		68 (34.8)	63 (32.4)	66 (32.8)	197	
Dietary supplement intake						
Yes		31 (34.8)	32 (36.0)	26 (29.2)	89	0.564 ¹⁾
No		56 (32.7)	54 (31.6)	61 (35.7)	171	
Education						
Diploma and lower		27 (39.7)	22 (32.4)	19 (27.9)	68	0.382 ¹⁾
Academic		60(31.3)	64 (33.3)	68 (35.4)	192	
Physical activity (MET-hour/week)		26.2 ± 27.5	23.8 ± 26.5	27.3 ± 31.2	25.8 ± 28.4	0.804 ²⁾
Energy intake (kcal/day)		2,287.1 ± 632.9	2,476.6 ± 680.3	2,368.7 ± 732.4	2,377.5 ± 684.9	0.433 ²⁾
Dietary phytochemical index		23.6 ± 5.0	34.3 ± 3.2	45.8 ± 6.6	34.6 ± 10.4	< 0.001

Data are shown as the mean ± SD or number (%).

DPI, dietary phytochemical index; BMI, body mass index; NPH Neutral Protamine Hagedorn, no description; MET, metabolic equivalent.

¹⁾ *P*-value is for χ^2 test, used for categorical data.

²⁾ *P*-trend is for analysis of variance test, used to compare continuous variables, calculated by linear regression test.

Table 2. Cardiovascular risk factors across tertiles of the sex-specific energy-adjusted DPI in type 1 diabetic patient (n = 81)

	DPI tertiles			<i>P</i> -value	<i>P</i> -trend ³⁾
	T1 (n = 29)	T2 (n = 25)	T3 (n = 27)		
uric acid (mg/dL) ¹⁾					
1	23.4 ± 3.2	23.5 ± 3.5	23.5 ± 3.1	0.983	0.857
2	23.4 ± 3.2	23.5 ± 3.2	23.4 ± 3.2	0.945	0.983
waist circumference (cm) ¹⁾					
1	86.0 ± 10.2	84.8 ± 10.3	85.7 ± 9.8	0.725	0.828
2	86.0 ± 6.5	84.7 ± 6.5	85.8 ± 6.5	0.422	0.848
systolic blood pressure (mmhg) ¹⁾					
1	117.3 ± 12.6	110.9 ± 11.5	108.8 ± 14.0	0.308	0.135
2	111.8 ± 11.3	110.8 ± 11.3	109.0 ± 11.4	0.301	0.126
3 ²⁾	112.6 ± 12.6	110.7 ± 11.2	108.4 ± 12.4	0.144	0.041
diastolic blood pressure (mmhg) ¹⁾					
1	73.1 ± 6.0	74.0 ± 6.3	73.5 ± 6.7	0.611	0.626
2	73.1 ± 6.5	73.9 ± 6.5	73.6 ± 6.5	0.735	0.633
3 ²⁾	74.0 ± 7.1	73.8 ± 6.3	72.9 ± 7.0	0.585	0.364
fasting blood glucose (mg/dL)					
1	175.1 ± 5.9	163.3 ± 5.5	143.0 ± 5.7	0.225	0.112
2	168.7 ± 5.5	167.9 ± 5.5	145.2 ± 5.7	0.421	0.238
fasting insulin (μU/mL)					
1	7.0 ± 0.8	7.0 ± 0.8	7.0 ± 0.8	0.839	0.571
2	7.0 ± 0.8	7.0 ± 0.8	7.0 ± 0.8	0.966	0.876
total cholesterol (mg/dL)					
1	171.7 ± 26.8	167.7 ± 37.0	169.8 ± 30.1	0.898	0.819
2	170.1 ± 32.6	171.1 ± 33.4	168.3 ± 32.6	0.941	0.927
3	174.0 ± 30.3	172.2 ± 31.1	163.1 ± 31.4	0.456	0.266
triglyceride (mg/dL)					
1	81.5 ± 1.6	63.5 ± 1.5	78.5 ± 1.4	0.075	0.703
2	79.8 ± 5.8	61.9 ± 5.4	82.0 ± 5.6	0.038	0.856
3	82.4 ± 5.8	63.5 ± 5.4	77.4 ± 5.7	0.079	0.487
HbA1c (mg/dL)					
1	51.8 ± 9.8	55.1 ± 9.3	53.8 ± 9.4	0.429	0.425
2	50.9 ± 9.4	55.5 ± 9.6	54.4 ± 9.3	0.223	0.232
3	51.8 ± 9.9	55.9 ± 10.2	53.1 ± 10.3	0.203	0.551

mg/dL)					
1	101.9 ± 5.7	92.3 ± 5.3	94.1 ± 5.5	0.344	0.327
2	101.9 ± 5.7	95.9 ± 5.3	91.0 ± 5.5	0.329	0.134
3	104.5 ± 5.7	95.1 ± 5.3	89.1 ± 5.5	0.130	0.033
HDL-C					
1	2.1 ± 0.7	1.8 ± 0.7	1.8 ± 0.5	0.157	0.124
2	2.1 ± 0.6	1.9 ± 0.6	1.7 ± 0.6	0.085	0.027
3	2.1 ± 0.6	1.8 ± 0.6	1.8 ± 0.6	0.137	0.029
ide dismutase activity (IU/mL)					
1	35.2 ± 1.2	34.5 ± 1.1	34.6 ± 1.1	0.871	0.671
2	35.4 ± 5.4	34.2 ± 5.3	34.5 ± 5.3	0.556	0.419
one peroxidase activity (IU/mL)					
1	144.7 ± 3.4	125.2 ± 3.5	135.2 ± 3.4	0.911	0.835
2	142.6 ± 6.7	126.2 ± 6.6	136.1 ± 6.5	0.906	0.902
antioxidant capacity (mmol/L)					
1	362.5 ± 62.0	376.8 ± 65.9	379.9 ± 47.4	0.510	0.274
2	357.6 ± 57.0	380.5 ± 59.1	381.5 ± 57.4	0.246	0.132

Data are shown as mean ± SD.

Model 1 = crude, analysis of variance test was used. Model 2 = adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/min/week), BMI (kg/m²), diabetes duration (year), total daily insulin dose (unit/day), education and dietary supplement intake. Model 3 = adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/min/week), BMI (kg/m²), diabetes duration (year), total daily insulin dose (unit/day), education, dietary supplement intake, saturated fatty acid (g/day), mono-unsaturated fatty acid (g/day), poly-unsaturated fatty acid (g/day) and trans fatty acid (g/day), analysis of covariance test was used. DPI, dietary phytochemical index; BMI, body mass index; HbA1c, hemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; MET, metabolic equivalent.

¹⁾ T1 = 87, T2 = 87, T3 = 87. ²⁾ Adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/min/week), BMI (kg/m²), diabetes duration (year), total daily insulin dose, education, dietary supplement intake, dietary intake of sodium (mg) and potassium (mg). ³⁾ P-trend calculated by linear regression.

Table 3. Odds ratio and 95% confidence intervals for cardiovascular risk factors across tertiles of sex-specific energy-adjusted DPI in type 1 diabetic patients

	Models	DPI tertile			<i>P</i> -trend ²⁾
		T1 (n = 29)	T2 (n = 25)	T3 (n = 27)	
Hyperglycemia (> 100 mg/dL)	Model 1	1.0	0.38 (0.06–2.33)	0.15 (0.03–0.77)	0.016
	<i>P</i> -value		0.326	0.022	
	Model 2	1.0	0.39 (0.05–3.14)	0.12 (0.02–0.82)	0.020
	<i>P</i> -value		0.485	0.031	
LDL-C (< 40 mg/dL in men and < 50 mg/dL in women)	Model 1	1.0	0.52 (0.16–1.69)	0.47 (0.14–1.52)	0.195
	<i>P</i> -value		0.303	0.274	
	Model 2	1.0	0.24 (0.05–1.09)	0.19 (0.04–0.86)	0.033
	<i>P</i> -value		0.064	0.039	
LDL-C (> 100 mg/dL)	Model 1	1.0	0.60 (0.20–1.80)	0.54 (0.18–1.58)	0.254
	<i>P</i> -value		0.487	0.333	
	Model 2	1.0	0.95 (0.26–3.46)	0.40 (0.11–1.44)	0.167
	<i>P</i> -value		0.905	0.201	
Hypercholesterolemia (> 200 mg/dL)	Model 1	1.0	2.17 (0.46–10.16)	1.08 (0.20–5.89)	0.928
	<i>P</i> -value		0.324	0.998	
	Model 2	1.0	4.59 (0.72–29.28)	1.20 (0.20–7.29)	0.882
	<i>P</i> -value		0.114	0.832	
LDL-C/HDL-C (> 3.5 in men, > 3 in women)	Model 1	1.0	0.33 (0.06–1.83)	0.48 (0.11–2.15)	0.299
	<i>P</i> -value		0.222	0.302	
	Model 2	1.0	0.08 (0.004–1.77)	0.02 (0.001–0.89)	0.041
	<i>P</i> -value		0.109	0.414	
HbA1c (> 7%) ¹⁾	Model 1	1.0	1.00 (0.55–1.81)	1.00 (0.55–1.81)	1.000
	<i>P</i> -value		1.000	1.000	
	Model 2	1.0	1.10 (0.59–2.03)	1.12 (0.60–2.08)	0.722
	<i>P</i> -value		0.898	0.729	

light or obesity (BMI > 24.9 kg/m ²) ¹⁾	Model	1.0	1.06 (0.55–	0.79 (0.41–	0.498
	1		2.01)	1.55)	
	<i>P</i> -value		0.973	0.554	
	Model	1.0	1.06 (0.54–	0.73 (0.37–	0.383
abdominal obesity (waist circumference > 94 cm in men >80 cm in women) ¹⁾	2		2.08)	1.48)	
	<i>P</i> -value		0.989	0.458	
	Model	1.0	0.79 (0.43–	0.83 (0.45–	0.542
	1		1.44)	1.51)	
diastolic blood pressure (systolic blood pressure > 140 mmHg) ¹⁾	<i>P</i> -value		0.433	0.501	
	Model	1.0	0.49 (0.15–	0.47 (0.14–	0.201
	2		1.61)	1.55)	
	<i>P</i> -value		0.210	0.244	
systolic blood pressure (systolic blood pressure > 140 mmHg) ¹⁾	Model	1.0	2.02 (0.18–	4.14 (0.45–	0.174
	1		22.73)	37.85)	
	<i>P</i> -value		0.658	0.203	
	Model		1.59 (0.09–	4.15 (0.36–	0.205
	2		28.31)	48.06)	
	<i>P</i> -value		0.887	0.342	

Logistic regression model was used.

Model 1 = crude. Model 2 = adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/min/week), BMI (kg/m²), diabetes duration (year), total insulin dose (unit/day), education and dietary supplement intake.

DPI, dietary phytochemical index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HbA1c, hemoglobin A1c; BMI, body mass index; MET, metabolic equivalent.

¹⁾ T1 = 87, T2 = 87, T3 = 87.

²⁾ *P*-trend calculated by logistic regression test.

Figures

Figure 1

Contributions of different phytochemical-rich food groups to energy-adjusted dietary phytochemical index.

Figure 2

Multivariate-adjusted means of cardiovascular risk factors across tertiles of dietary phytochemical index determined by general linear model with adjustment for age, sex, total energy intake (kcal/day), physical activity (metabolic equivalent task/hour/week), body mass index (kg/m²), diabetes duration (year), insulin dose (unit/day), education and dietary supplement intake. LDL-C and LDL-C/HDL-C were further adjusted for intake of saturated fatty acids, mono-unsaturated fatty acids, poly-unsaturated fatty acids, and trans fatty acid. SBP further adjusted for dietary intake of sodium (mg) and potassium (mg). LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure.

Figure 3

OR of cardiovascular risk factors in each tertile of dietary phytochemical index determined by multivariable logistic regression model with adjustment for age, sex, total energy intake (kcal/day), physical activity (metabolic equivalent task/hour/week), body mass index (kg/m²), diabetes duration (year), total insulin dose (unit/day), education and dietary supplement intake. OR, odds ratio; CI, confidence interval; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.