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Cashew Nut Consumption Increases HDL Cholesterol and Reduces Systolic Blood Pressure in Asian Indians with Type 2 Diabetes: A 12-Week Randomized Controlled Trial

Viswanathan Mohan,[1] Rajagopal Gayathri,[2] Lindsay M Jaacks,[3] Nagarajan Lakshmipriya,[2] Ranjit Mohan Anjana,[1] Donna Spiegelman,[3,4] Raman Ganesh Jeevan,[2] Kandappa K Balasubramaniam,[2] Shanmugam Shobana,[2] Mathialagan Jayanthan,[2] Viswanathan Gopinath,[2] Selvakumar Divya,[2] Vasudevan Kavitha,[2] Parthasarathy Vijayalakshmi,[2] Mookambika Ramya Bai R,[2] Ranjit Unnikrishnan,[1] Vasudevan Sudha,[2] Kamala Krishnaswamy,[2] Jordi Salas-Salvadó,[6] and Walter C Willett[4,5]

Departments of [1]Diabetology and [2]Foods, Nutrition & Dietetics Research, Madras Diabetes Research Foundation, Chennai, Tamil Nadu, India; Departments of [3]Global Health and Population, [4]Nutrition, and [5]Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA and [6]Human Nutrition Unit, Hospital Universitari Sant Joan de Reus, Biochemistry and Biotechnology Department, IISPV, Universitat Rovira i Virgili, Reus, Spain, and CIBERobn Physiopathology of Obesity and Nutrition, Instituto de Salud Carlos III, Madrid, Spain

Abstract

Background: There is increasing evidence that nut consumption decreases the risk of cardiovascular disease. However, there are few data on the health effects of cashew nuts among adults with type 2 diabetes (T2DM).

Objective: The study aimed to investigate the effects of cashew nut supplementation on glycemia, body weight, blood pressure, and lipid profile in Asian Indians with T2DM.

Methods: In a parallel-arm, randomized controlled trial, 300 adults with T2DM [mean ± SD age: 51 ± 9.3 y; body mass index (BMI; in kg/m^2): 26.0 ± 3.4; 55% male] were randomly assigned to receive advice to follow a standard diabetic diet (control) or similar advice plus 30 g cashew nuts/d (intervention) for 12 wk. The macronutrient composition of the prescribed diabetic diet was 60–65% energy from carbohydrates, 15–25% from fat, and the rest from protein. Differences between groups in changes in anthropometric and biochemical variables were analyzed using linear models with robust variance estimation under an assumed independence working correlation.

Results: Participants in the intervention group had a greater decrease in systolic blood pressure from baseline to 12 wk than did controls (–4.9 ± 13.7 compared with –1.7 ± 11.6 mm Hg; $P = 0.04$) and a greater increase in plasma HDL cholesterol compared with controls (+1.7 ± 5.6 compared with +0.1 ± 4.6 mg/dL; $P = 0.01$). There were no differences between the groups with respect to changes in body weight, BMI, blood lipid, and glycemic variables. Plasma oleic acid concentrations and self-reported dietary intake of nuts, oleic acid, and monounsaturated fatty acids suggested excellent compliance with the nut consumption.

Conclusion: Cashew nut supplementation in Asian Indians with T2DM reduced systolic blood pressure and increased HDL cholesterol concentrations with no deleterious effects on body weight, glycemia, or other lipid variables. This study was registered at the clinical trial registry of India as CTRI/2017/07/009022. *J Nutr* 2018;148:63–69.

Keywords: cashew nut, type 2 diabetes, high-density lipoprotein cholesterol, body weight

Introduction

Populations of Asian Indian ethnicity are characterized by a high lifetime risk of cardiovascular disease (CVD) and type 2 diabetes (T2DM) (1). Asian Indians are prone to a unique pattern of dyslipidemia characterized by low HDL cholesterol and high TGs and LDL cholesterol (2). Nearly 80% of Asian Indian adults have dyslipidemia, largely driven by low HDL cholesterol concentrations (3). Among those with T2DM, 86% of males and 98% of females have been shown to have dyslipidemia (4). Although the link between low HDL cholesterol and CVD is established (5), current evidence suggests that raising HDL cholesterol using pharmacologic approaches is challenging and may not directly translate into reduced CVD risk (6).

Current Indian diets are high in carbohydrates (predominantly derived from refined grains such as polished rice and refined wheat), which account for 64% of total energy intake (7). Indian diets are low in MUFAs, which provide just 7–8%

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of total energy (8) compared to the recommended intake of 15–20% (9), as well as omega-3 PUFAs, which provide just 0.24% of total energy compared to the recommended intake of 0.5–2% (9, 10). Consumption of nuts, a rich source of MUFAs, has historically been low in India (8 g/d in 1975–79 and 17 g/d in 1996–97) (11). There is growing evidence that replacement of refined grains with healthy fats such as MUFAs may have beneficial effects on HDL cholesterol (12) and that daily intake of ~60 g of nuts may also improve diabetes control through reduction in fasting blood glucose and glycosylated hemoglobin A1c (13). Moreover, a recent meta-analysis of clinical trials indicates that nuts, despite their higher fat and energy content, have no significant effects on body weight when substituted in a healthy diet (14). This is important as weight control is crucial for prevention of diabetes and diabetes-related complications (15).

Previous studies have focused on the beneficial health effects of nuts, including pistachios, walnuts, and almonds, on insulin resistance and other CVD risk factors (16–19). Only one study has evaluated the effects of cashew nuts on CVD risk factors. Subjects with metabolic syndrome were randomly assigned to receive 66–115 g cashew nuts/d or a control diet for 8 wk; no significant effects were observed for the lipid variables evaluated (20). This could be due to the fact that baseline lipid concentrations (LDL cholesterol) were already low, the small sample size ($n = 64$), the short duration of the intervention, ethnicity, or other factors.

To date, though widely used in Indian cuisines, cashew nuts have not been evaluated for their potential effects on CVD risk factors among Asian Indians, particularly those with T2DM. The aim of this parallel-arm, randomized controlled trial was to test the effect of cashew nut supplementation on glycemia (primary outcome) and body weight, blood pressure and lipid profiles (secondary outcomes) in Asian Indian adults with T2DM. The primary hypothesis was that diets supplemented with 30 g unsalted cashew nuts/d would result in improvements in glycemic status among Asian Indians with T2DM.

Methods

Study participants. Participants in this parallel-arm, randomized controlled trial were identified from the medical records of a tertiary care center for diabetes in Chennai, India, based on prespecified inclusion and exclusion criteria. Inclusion criteria were: age 30–65 y, physician-diagnosed T2DM, duration of T2DM <10 y, and currently receiving oral hypoglycemic drugs. Exclusion criteria were: cashew nut allergy, currently receiving insulin therapy, glycated hemoglobin (HbA1c) >10%, LDL cholesterol >190 mg/dL, total cholesterol >240 mg/dL, TGs >300 mg/dL, and any known diabetes complications.

Eligible participants identified via this medical record review ($n = 500$) were then contacted and briefed by research dieticians about the study and its objectives (**Figure 1**). Individuals expressing an interest in participating were given 30 g cashew nuts/d for 1 wk (run-in period) free of cost in order to ensure compliance. Individuals who completed the run-in period and expressed their willingness to comply and take part in the study were randomized to either intervention ($n = 150$) or control ($n = 150$) groups and completed the baseline visit 2 wk after the run-in period.

Written informed consent was obtained from all participants. The study received approval from the Institutional Ethics Committee of the Madras Diabetes Research Foundation and was conducted in accordance with guidelines in the Declaration of Helsinki. The study was registered at the clinical trial registry of India as CTRI/2017/07/009022.

Dietary intervention. Participants assigned to the intervention group were provided with 30 g unsalted, raw, broken cashew nuts/d free of charge on a weekly basis for 12 wk. This quantity was based on previous studies that have used similar amounts: the PREvención con DIeta MEDiterránea (PREDIMED) study used 30 g mixed nuts/d (18) and Tapsell et al. (21) in their randomized trial used 30 g walnuts/d. The cashew nuts constituted ~11–13% of prescribed diabetic diet calories (~182 kcal/30 g cashew nut) (22). Participants were advised to consume the cashew nuts either as a mid-morning or evening snack, and to maintain their prescribed standard diabetic diet, exercise, and medication as usual. The cashew nut group (intervention) participants were further instructed not to use the cashew nuts as a cooking ingredient or to roast or fry them, and not to consume any nuts other than the allotted quantity of cashew nuts. They were further taught to substitute the calories from 30 g cashew nuts with equivalent calories from carbohydrates in their meals. Participants assigned to the control group were advised to follow their prescribed standard diabetic diet, exercise, and medications as usual. Control participants were also advised not to consume any other type of nuts.

For both groups, all dietary advice was individualized and provided by dietitians, as is standard practice for the tertiary care center for diabetes in Chennai, India, where this study was conducted. The Asian Indian diabetic diet (1400–1600 kcal/d) upon which advice was based is typically composed of 60–65% energy from carbohydrates, 15–25% from fat, and the remaining calories from protein (23). A review with dietitians took place every 4 wk throughout the duration of the study. In-person monthly interviews were carried out by trained dietitians to collect 24-h dietary recalls (1 weekday and 1 weekend). A total of 6 dietary recalls were performed over 12 wk, including a single 24-h recall at baseline for the participants in both groups. The average of the 5 recalls collected during the intervention (second recall at the end of the fourth week, third and fourth recalls between 5 and 8 wk, fifth and sixth recalls between 9 and 12 wk) was compared with the single recall collected at baseline in order to improve the precision and accuracy of the estimates of dietary intake during the intervention period.

Participant compliance. Participant compliance was assessed using *1*) self-reported dietary intake by 24-h dietary recall administered by trained dietitians in a face-to-face interview (the average of 5 recalls collected during the 12-wk intervention was compared to baseline); and *2*) a plasma biomarker of the predominant MUFA, oleic acid (the concentrations at 12 wk compared to baseline) (24). Participants assigned to the intervention group were also asked *3*) to return the empty sachets of cashew nuts every week. In an attempt to avoid any sharing of the 30 g cashew nut supplement with family members, an additional 200-g cashew nut sachet was supplied to each participant in the intervention group during weekly visits. We did not have a prespecified compliance cutoff nor did we remove noncompliant participants from the analysis; this information was primarily collected in order to facilitate the interpretation and translation of study results.

Nutrient intake (total calories and percentage of calories from SFAs, MUFAs, PUFAs, *trans* fatty acids, oleic acid, total fat, carbohydrates, protein, and cholesterol) was estimated from the 24-h dietary recalls using the nutrient database EpiNu (25). Plasma oleic acid was determined by the method described by Glaser et al. (26) as reference method and that of Folch et al. (27) for oleic acid methyl ester

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Supplemental Table 1 is available from the "Supplementary Data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn.
Address correspondence to VM (e-mail: drmohans@diabetes.ind.in).
Abbreviations used: CVD, cardiovascular disease; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; T2DM, type 2 diabetes.

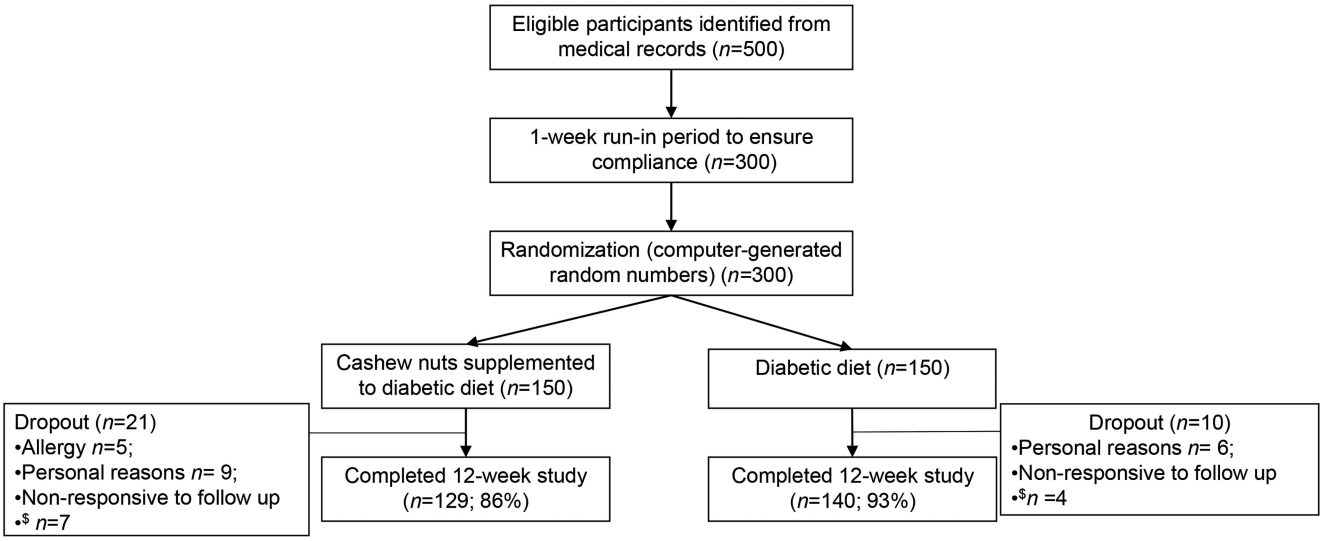

FIGURE 1 Study flow diagram for randomized controlled trial of a cashew nut supplement (30 g/d) among adults with type 2 diabetes consuming a standard prescribed diabetic diet (control). $ Nonresponsive to follow-up despite repeated attempts to reach participants in both groups by telephone after baseline visit, and hence, considered dropouts.

preparation with minor modifications—the final volume of the sample made up for GC analysis was 1 mL compared with 50 μL referred by the method, and the centrifuge was used at 1350 × *g* in contrast to 900 × *g* for a comparable time. Oleic acid methyl ester was quantified with flame ionization detection on a Shimadzu GC-2010 plus gas chromatograph using an Agilent DB-Wax column (30 m, 0.250 mm diameter, film 0.25 μm). Data were acquired using Lab Solutions software version 5.52. The qualitative and quantitative processing of the integrated peaks was achieved with a mixture of standard fatty acids (Lot No. 24305 and Catalogue No. 35077, Restek). The intra- and inter-day CV were 3.3% and 3%, respectively. Plasma oleic acid methyl ester was quantified using standard oleic acid (Batch No. BCBQ2570V and Product No. 75090, Sigma Aldrich) for comparison.

Outcome assessment. Glycemic and lipid profiles were assessed in a laboratory certified by the National Accreditation Board for Testing and Calibration Laboratories and the College of American Pathologists on a Hitachi 912 Autoanalyzer. Fasting (≥8 h) venous whole blood samples were collected at baseline and at the end of the study (12 wk) into tubes containing EDTA as an anticoagulant. Plasma glucose was estimated using the glucose oxidase-peroxidase method (Roche Diagnostics). HbA1c was estimated by HPLC (Variant; Bio-Rad) and serum insulin by electrochemiluminescence assay (Roche Diagnostics). Insulin resistance was calculated using the homoeostasis model assessment (28). A Beckman Coulter AU 2700/480 Autoanalyzer was used to measure serum cholesterol (cholesterol esterase oxidase-peroxidase-amidopyrine method), serum TG (glycerol phosphate oxidase-peroxidase-amidopyrine method), and HDL cholesterol by direct method with polyethylene glycol-pretreated enzymes. LDL and VLDL cholesterol were calculated using the Friedewald formula (29). The coefficients of variation for the biochemical assays ranged from 3.1% to 7.6% (30).

Body weight (kilograms) (Omron HBF 212), height (centimeters), and waist circumference (centimeters) were measured at baseline and at the end of the study (12 wk) according to standard protocols. BMI was calculated as weight divided by squared height (kg/m^2). Blood pressure was measured at baseline and end of study (12 wk) using an electronic monitor (Omron HEM 7120). Participants were seated comfortably with back straight and feet flat on the floor. Blood pressure was assessed twice on each occasion at 5-min intervals and the average reading was taken (31).

Statistical analysis. Differences in baseline characteristics between the intervention and control groups were tested using chi-square tests and independent sample 2-sided *t* tests. Between-group differences in the change in dietary intake and the health measurements between baseline and 12 wk were analyzed using linear models with robust variance estimation under an assumed independence working correlation. This is equivalent to a 2-sample (independent group) *t* test with the exception of the variance estimation in that we used robust variance estimation to account for nonnormality of the data. Missing outcome data were not imputed, and thus this was a partial intent-to-treat analysis. As a sensitivity analysis, we compared mean change in HDL cholesterol between intervention participants with low- compared with high-HDL cholesterol at baseline (for women, HDL cholesterol <50 compared with ≥50 mg/dL; for men, HDL cholesterol <40 compared with ≥40 mg/dL) using a *t* test, and also calculated the Pearson correlation coefficient between changes in plasma oleic acid concentration and changes in HDL cholesterol, stratified by intervention compared with control group. A 2-tailed *P* value <0.05 was considered statistically significant. Statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc.).

Results

Of the 300 participants enrolled, 269 (89.7%) completed the end-of-study visit at 12 wk (Figure 1). Results herein are reported for the 269 participants who completed the study. The study participants' age was 50.8 ± 9.5 y (mean ± SD) and 53.9% ($n = 145$) were men. There was a higher percentage of men in the intervention group compared to the control group ($P = 0.04$; Table 1).

As a measure of compliance in the intervention group participants, 83% returned the empty sachets for the entire study period while 10% of the participants returned empty sachets for 2–4 wk. Plasma oleic acid concentrations increased significantly ($P = 0.001$) from baseline in the intervention group compared to the control group (Table 2). Consistent with this, there was a significantly greater increase in self-reported intake of nuts, MUFAs, and oleic acid (as percentage of energy) in the intervention group (Table 2) compared to the control group. However, the correlation between changes in plasma oleic acid concentrations and changes in HDL cholesterol (**Supplemental Table 1**) were nonsignificant.

TABLE 1 Baseline characteristics of participants with type 2 diabetes who completed the study, randomly assigned to either a cashew nut supplement group (30 g/d) or a control group ($n = 269$)[1]

Characteristics	Cashew nut supplement group ($n = 129$)	Control group ($n = 140$)	P value[2]
Age, y	51.3 ± 8.8	50.4 ± 10.1	0.43
Male, % (n)	60.5 (78)	47.9 (67)	0.04
Duration of diabetes, y	6.0 ± 3.9	5.6 ± 4.5	0.51
Current smoker, % yes (n)	3.1 (4)	2.1 (3)	0.62
Consume alcohol, % yes (n)	9.3 (12)	6.4 (9)	0.38
Oral hypoglycemic agent(s), % yes (n)	74.4 (96)	70.7 (98)	0.42
Medication for hypertension, % yes (n)	14.8 (19)	12.1 (17)	0.51
Medication for dyslipidemia, % yes (n)	15.5 (20)	9.3 (13)	0.12

[1] Values are means ± SDs or percentage (n).
[2] P-value from chi-square test (binary variables) or independent sample 2-sided t test (continuous variables) comparing cashew nut supplement group and control group characteristics at baseline.

Participants in the intervention group had a 1.9-fold greater reduction in systolic blood pressure (SBP) compared to participants in the control group (**Table 3**). Participants in the intervention group also had a 16-fold greater increase in HDL cholesterol compared to participants in the control group. When participants were stratified by their baseline HDL cholesterol status, we observed a mean (SD) change of +2.2 (5.7) mg/dL among participants in the low–HDL cholesterol category ($n = 98$) in the intervention group compared to a mean (SD) change of 0.0 (4.9) mg/dL among participants in the intervention group with high HDL cholesterol ($n = 31$) at baseline ($P = 0.04$). When models were adjusted for differences between groups in baseline sex, the results for SBP were slightly attenuated ($P = 0.05$), but all other results were consistent. There were no significant changes in other serum lipid variables, fasting plasma glucose, fasting insulin, HbA1c, body weight, BMI, or waist circumference between the 2 groups.

Discussion

To our knowledge, this is the first randomized controlled trial to assess the effect of cashew nut supplementation on blood pressure, serum lipids, body weight, and glycemia in Asian Indian adults with T2DM. The key findings of the study include a significant increase in HDL cholesterol concentrations and a significant decrease in SBP in the intervention group supplemented with 30 g cashew nuts/d over 12 wk compared to the control (standard of care) group. Moreover, despite a significantly greater reported increase in caloric intake among the intervention participants, there was not a significant increase in body weight, BMI, or waist circumference.

There is a misconception in India that eating nuts increases body weight due to their high fat content and energy density (32). This study showed that consumption of moderate amounts of cashew nuts did not increase body weight, BMI, waist circumference, serum cholesterol or LDL cholesterol. This supports the findings from earlier studies on pistachios, walnuts and almonds (16–19, 33, 34). A meta-analysis of clinical trials of the effects of tree nuts, including almonds, walnuts, and pistachios, on adiposity showed that nut-rich diets did not increase body weight, BMI, waist circumference, or serum cholesterol compared with different control diets. Hence, it was suggested to include nuts as part of healthy diets for prevention of obesity-related chronic diseases including CVD (14). Furthermore, trials of nuts alone or nuts as part of the Mediterranean diet or as Dietary Approaches to Stop Hypertension (DASH) trial patterns have shown neutral or weight-loss effects (17, 35–37). Petersen et al. (20) investigated the effects of walnuts, unsalted cashew nuts, and a "no nuts diet" on selected markers of the metabolic syndrome. They showed that following a walnut or cashew nut diet for 8 wk was not associated with weight gain. There are several possible mechanisms that could explain the observation that increased nut consumption had a neutral effect on body weight. Nuts including cashews are high in readily oxidizable MUFAs and PUFAs, which may increase their thermogenic effect (14). Studies have also suggested that incomplete mastication of nuts leads to loss of calories in the stool (38, 39). Mori et al. (40) showed that including nuts in breakfast could improve

TABLE 2 Markers of dietary compliance (by self-reported average 24-h dietary recalls) of participants with type 2 diabetes who completed the study, randomly assigned to either a cashew nut supplement group (30 g/d) or a control group ($n = 269$)[1]

	Cashew nut supplement group			Control group			Between-group difference in within-group changes (95% CI)[2]	P value[2]
	Baseline ($n = 129$)	12 wk ($n = 129$)	Change ($n = 129$)	Baseline ($n = 140$)	12 wk ($n = 140$)	Change ($n = 140$)		
Plasma oleic acid, μmol/L	303 ± 338	451 ± 529	90.8 ± 432	703 ± 569	526 ± 493	−190 ± 765	280 (107, 453)	0.001
Nuts and oil seed, g/d	13.0 ± 14.6	48.7 ± 33.9	35.7 ± 37.2	12.6 ± 15.7	11.3 ± 9.5	−1.1 ± 17.8	36.8 (29.8, 43.7)	<0.0001
Cashew nut, g/d	1.1 ± 1.7	31.9 ± 3.5	30.7 ± 4.0	0.5 ± 0.8	0.9 ± 5.1	0.5 ± 5.5	30.2 (29.0, 31.4)	<0.0001
MUFAs,[3] %E	7.7 ± 2.3	9.3 ± 2.1	1.6 ± 2.9	8.0 ± 2.5	7.0 ± 1.3	−1.1 ± 2.6	2.7 (2.0, 3.3)	<0.0001
PUFAs,[3] %E	10.4 ± 3.1	9.5 ± 7.3	−0.7 ± 3.9	10.2 ± 3.4	10.6 ± 3.4	0.5 ± 4	−1.0 (−1.9, 0.04)	0.03
TFAs,[3] %E	0.1 ± 0.1	0 ± 0.1	0 ± 0.1	0.1 ± 0.2	0 ± 0.1	0 ± 0.1	0 (−0.04, 0.03)	0.92
SFAs,[3] %E	9.0 ± 3.2	7.9 ± 2.3	−0.7 ± 4.4	9.2 ± 3.5	7.6 ± 2.6	−1.3 ± 5	0.4 (−0.4, 1.3)	0.42
Cholesterol, mg/d	83.3 ± 125.4	45.2 ± 48.0	−38.7 ± 114.4	97.1 ± 161.5	49.9 ± 72.1	−47.8 ± 177.7	0.07 (−27.6, 45.7)	0.63
Oleic acid,[3] %E	7.2 ± 2.2	8.6 ± 1.8	1.4 ± 2.8	7.5 ± 2.4	6.5 ± 1.3	−1.0 ± 2.5	2.3 (1.7, 3.0)	<0.0001
Energy, kcal/d	1536 ± 467	1598 ± 415	68.4 ± 489	1532 ± 508	1451 ± 355	−77.9 ± 464	146.3 (30.8, 261.8)	0.01
Carbohydrate,[3] %E	59.1 ± 6.4	57.9 ± 4.2	−1.2 ± 7.0	58.1 ± 8.5	61.4 ± 4.3	3.3 ± 8.8	−4.5 (−6.5, 2.6)	<0.0001
Protein,[3] %E	12.8 ± 2.7	11.8 ± 1.1	−1.0 ± 2.7	13.4 ± 3.1	11.7 ± 1.4	−1.7 ± 3.3	0.7 (−0.04, 1.4)	0.06
Fat,[3] %E	28.7 ± 5.5	30.4 ± 4.0	1.7 ± 6.4	28.9 ± 6.8	27.0 ± 4.0	−1.9 ± 7.2	3.7 (2, 5.3)	<0.0001

[1] Values are means ± SDs. TFA, *trans* fatty acid; %E, percentage of energy.
[2] From linear models with robust variance estimation under an assumed independence working correlation.
[3] Values may not add up to 100% due to rounding.

TABLE 3 Anthropometric and biochemical characteristics of participants with type 2 diabetes who completed the study, randomly assigned to either a cashew nut supplement group (30 g/d) or a control group ($n = 269$)[1]

	Cashew nut supplement group			Control group			Between-group difference in within-group changes (95% CI)[2]	*P* value[2]
	Baseline ($n = 129$)	12 wk ($n = 129$)	Change ($n = 129$)	Baseline ($n = 140$)	12 wk ($n = 140$)	Change ($n = 140$)		
Weight, kg	67.6 ± 9.1	67.9 ± 9.0	0.2 ± 1.1	67.3 ± 11.5	67.2 ± 11.5	−0.1 ± 1.7	0.32 (−0.02, 0.65)	0.07
BMI, kg/m^2	25.6 ± 2.8	25.7 ± 2.7	0.1 ± 0.4	26.2 ± 3.9	26.2 ± 3.9	0.0 ± 0.6	0.12 (−0.01, 0.25)	0.07
WC, cm	91.0 ± 8	91.2 ± 7.9	0.1 ± 2.3	90.7 ± 9.3	90.9 ± 9.3	0.3 ± 2.6	−0.12 (−0.71, 0.46)	0.69
SBP, mm Hg	125.5 ± 15.1	121 ± 14.0	−4.9 ± 13.7	123.6 ± 15.9	122 ± 15.1	−1.7 ± 11.6	−3.15 (−6.17, −0.12)	0.04
DBP, mm Hg	82.3 ± 9.1	81.2 ± 8.8	−1.0 ± 7.9	80.9 ± 9.3	81.4 ± 8.3	0.5 ± 7.3	−1.55 (−3.37, 0.27)	0.09
Fasting glucose,[3] mg/dL	136.4 ± 43	139 ± 50.8	2.8 ± 41.3	146.6 ± 54.9	146 ± 47.0	−0.5 ± 45.1	3.28 (−7.00, 13.57)	0.53
HbA1c,[3] %	7.3 ± 1.2	7.4 ± 1.4	0.1 ± 0.9	7.8 ± 1.5	7.8 ± 1.4	0.0 ± 0.9	0.10 (−0.13, 0.32)	0.40
Insulin,[3] μIU/mL	13.6 ± 6.7	14.1 ± 7.8	0.5 ± 6.6	15.2 ± 9.5	15.8 ± 12.6	0.5 ± 7.4	−0.06 (−1.73, 1.61)	0.95
HOMA-IR	4.6 ± 3.2	5.0 ± 3.6	0.4 ± 3.2	5.7 ± 4.6	5.7 ± 5.1	0.0 ± 3.8	0.33 (−0.51, 1.17)	0.44
TG,[3] mg/dL	143.0 ± 69.7	147 ± 70.5	4.3 ± 51.1	146.9 ± 62.9	147 ± 68.8	0.4 ± 62.2	3.87 (−9.64, 17.38)	0.57
TChol,[3] mg/dL	161.5 ± 32.8	165 ± 34.9	3.3 ± 25.9	171.7 ± 35.5	170 ± 35.8	−1.9 ± 25.6	5.17 (−0.98, 11.31)	0.10
HDL cholesterol,[3] mg/dL	38.4 ± 8.1	40.1 ± 7.9	1.7 ± 5.6	40.1 ± 7.9	40.2 ± 7.4	0.1 ± 4.6	1.58 (0.35, 2.80)	0.01
LDL cholesterol,[3] mg/dL	94.6 ± 29	95.8 ± 29.9	0.9 ± 25.1	102.2 ± 31.1	99.2 ± 30.7	−3.0 ± 21.6	3.87 (−1.75, 9.49)	0.18
VLDL cholesterol,[3] mg/dL	28.0 ± 12.6	28.4 ± 11.7	0.7 ± 9.5	29.4 ± 12.6	29.5 ± 13.7	0.1 ± 12.5	0.60 (−2.04, 3.25)	0.66
TChol:HDL cholesterol ratio	4.4 ± 1.2	4.2 ± 0.9	−0.2 ± 1.0	4.4 ± 1.1	4.3 ± 1.1	−0.1 ± 0.8	−0.09 (−0.31, 0.13)	0.41

[1] Values are means ± SDs. DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; TChol, total cholesterol; TChol:HDL ratio, total cholesterol to high-density lipoprotein cholesterol ratio; WC, waist circumference.
[2] From linear models with robust variance estimation under an assumed independence working correlation.
[3] HbA1c and fasting glucose are plasma analytes, whereas others (insulin, HDL cholesterol, LDL cholesterol, VLDL cholesterol, TG, TChol/HDL cholesterol ratio) are serum analytes.

satiety acutely and reduce second meal consumption in adults with impaired glucose tolerance. Future studies should evaluate satiety as one potential mechanism underlying the observed lack of weight gain among individuals consuming cashew nuts.

Substituting ~15% of calories from pistachios (2–3 ounces/d) for other sources of fat in the diet showed a significant increase in HDL cholesterol and no change in total cholesterol, LDL cholesterol, or TGs among adults with mild hypercholesterolemia (41). In another parallel-arm, randomized controlled trial, 30 g walnuts consumed as part of a modified low-fat diet was associated with a significant increase in HDL cholesterol among adults with T2DM (21). Trials testing the effects of almonds and pistachios have also found a significant increase in HDL cholesterol in mildly and moderately hypercholesterolemic subjects (41, 42). In the present study, it was observed that supplementation of 30 g cashew nuts/d for 12 wk among adults with T2DM resulted in a significant increase in HDL cholesterol (on average, 1.58 mg/dL) but no significant changes in TGs, total cholesterol, or LDL cholesterol. Considering that the seminal Framingham Heart Study found that HDL cholesterol was the most important predictor of heart disease among older men and women (43), and that nearly three-fourths of Asian Indians have low HDL cholesterol concentrations (4), our results have important clinical implications. Indeed, just a 1% increase in HDL cholesterol has been associated with a 3% reduction in heart disease risk in previous studies (44). The mechanism by which cashew nuts favorably influence HDL cholesterol concentrations remains unclear. Mensink et al. (45) reported that MUFA-rich diets increased the level of apoA-I, and apoA-I has been demonstrated to increase cholesterol efflux in THP-1-derived macrophages (46). The increase in HDL cholesterol concentrations could also be due to the fatty acid composition of the intervention diet with subsequent decrease in carbohydrate intake as a percentage of energy. Kris-Etherton et al. (47) reported that substituting MUFAs for saturated fatty acids or carbohydrates tends to increase HDL cholesterol concentrations. Cashew nuts are rich in fat, predominantly MUFAs (~60% of total fat) (22). This is reflected in the significantly higher MUFA intake reported by the intervention group compared to the control group in the present study.

Our study showed a significantly greater decrease in SBP in the intervention group compared to the control group. These results are consistent with a large randomized controlled trial conducted in the United States showing that partial replacement of carbohydrate with MUFAs (10% calories from carbohydrate replaced with 8% calories from MUFAs) reduces blood pressure (48). A randomized controlled trial by Schutte et al. (49) found that consuming unsalted cashew nuts (20% of energy) for 8 wk improved the baroreflex sensitivity, a key mechanism for maintaining healthy blood pressure, compared to walnut consumption among participants with metabolic syndrome. Moreover, in addition to fatty acids, several other nutritive components of nuts may explain their benefits on metabolic and cardiovascular outcomes. In particular, cashew nuts are high in the amino acid arginine: 30 g cashew nuts provides 2.9 g arginine (50). Given that arginine is a precursor for nitric oxide, an endogenous vasodilator (51), this may explain some of the observed beneficial effect on SBP in this study. Indeed, a meta-analysis of 13 randomized controlled trials testing the effects of oral L-arginine supplements (ranging in dose from 6 to 63 g/d) on endothelial function found significant overall improvements in flow-mediated dilation (52), thus lending support to the hypothesized protective cardiovascular effects of arginine in cashew nuts.

A recent systematic review (53) reported that studies with MUFA intake >12% of energy conferred a significant reduction in HbA1c. In our study, despite the 30 g cashew nut/d supplementation, the total MUFA concentrations in the intervention group (9% of total daily calories) was still far below the recommendations of 15–20% total daily calories. Whether positive effects on glycemia could be produced by consumption of higher amounts of cashew nuts as part of a healthy diet needs further investigation. A study by Lovejoy et al. (54) showed that almond supplementation (57–113 g/d) in a high-fat diet (37%

calories from fat) resulted in greater reductions in HbA1c when compared to similar almond supplementation in a low-fat diet (25% calories from fat). Thus, the null effect on HbA1c in our study could be due to the lower dose of cashew nuts (30 g/d) or the lower total fat content of the diet (~30%); further research on the impact of nut supplementation on glycemia is warranted.

The present study has several strengths. First, the participants' overall compliance to the study was good, with a dropout rate of only ~10%. Second, dietary compliance was measured both by nutrient biomarker (plasma oleic acid) and self-reported dietary intake of oleic acid, MUFAs, and nuts. These were significantly higher in the intervention group compared to the control group, suggesting good adherence. This could explain the positive changes in HDL cholesterol in the intervention group. Well-trained dietitians collected the data through face-to-face interviews. However, the study also has a few limitations. Although we advised the participants to adhere to the study protocol and not to make major lifestyle and dietary changes, in a community-based trial such as this, family and environmental influences such as festivals and marriage feasts might have had some impact on the results. These effects would be likely to occur in both groups, biasing results towards the null. The 24-h dietary recall collected during the study to assess participants' adherence could have suffered from recall bias or might not have reflected typical intake. Because Indian diets are usually low in oleic acid (8), we used plasma concentrations of oleic acid as a proxy of its intake in our study. However, we acknowledge that plasma levels of oleic acid depend not only on the intake but also on the endogenous synthesis; therefore, this cannot be considered a good marker of consumption. The levels of fatty acids in adipocytes or erythrocytes are considered more accurate and reliable markers of intake in the medium and long term than plasma levels. Despite this, the plasma concentrations of fatty acids have been used in large studies as a measure of compliance (55). The lack of a significant correlation between plasma levels of oleic acid and changes in HDL cholesterol is not surprising because, as pointed out above, plasma concentrations of oleic acid reflect individual differences in endogenous synthesis and metabolism, and are only weakly correlated with dietary intake of this fatty acid (56). Thus, other nutrient biomarkers should be explored in the future as markers of individual compliance to nut supplement trials; on a group basis, changes in plasma oleic acid can be a useful qualitative indicator of compliance.

One might argue whether the results obtained would have been different if higher quantities of nuts had been used. For this reason, it will be interesting in the future to analyze if the effects of nut consumption on glycemia, lipids, and other risk factors of CVD are dose dependent. Finally, due to budget constraints, we were not able to assess apo proteins such as apoA-I. Future studies should expand the panel of biomarkers assessed in order to further elucidate potential biological mechanisms underlying observed associations.

In conclusion, this study reports that in Asian Indians with T2DM, regular consumption of 30 g cashew nuts decreased SBP and increased HDL cholesterol concentrations with no undesirable effects on body weight, glycemia, or other lipid variables. Supplementation of Indian diets with cashew nuts could help to improve the Asian Indian phenotype of dyslipidemia with low HDL concentrations, which is an important CVD risk factor contributing to premature CVD in this population.

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