Original Research

Almond Consumption and Cardiovascular Risk Factors in Adults with Prediabetes

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Objective: The authors tested the hypothesis that in adults with prediabetes, an almond-enriched American Diabetes Association (ADA) diet improves measures of insulin sensitivity and other cardiovascular risk factors compared with an ADA nut-free diet.

Methods: Design: Randomized parallel-group trial. Setting: Outpatient dietary counseling and blood analysis. Subjects: Sixty-five adult participants with prediabetes. Intervention: Sixteen weeks of dietary modification featuring an ADA diet containing 20% of energy from almonds (approximately 2 oz per day). Measures of Outcome: Outcomes included fasting glucose, insulin, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, TC:HDL-C, and HbA1c, which were measured at weeks 0, 8, and 16. Body weight, body mass index (BMI), waist circumference, blood pressure, and nutrient intake were measured at weeks 0, 4, 8, 12, and 16.

Results: The almond-enriched intervention group exhibited greater reductions in insulin (−1.78 μU/ml vs. +1.47 μU/ml, $p = 0.002$), homeostasis model analysis for insulin resistance (−0.48 vs. +0.30, $p = 0.007$), and homeostasis model analysis for beta-cell function (−13.2 vs. +22.3, $p = 0.001$) compared with the nut-free control group. Clinically significant declines in LDL-C were found in the almond-enriched intervention group (−12.4 mg/dl vs. −0.4 mg/dl) as compared with the nut-free control group. No changes were observed in BMI (−0.4 vs. −0.7 kg/m^2, $p = 0.191$), systolic blood pressure (−4.4 mm Hg vs. −3.5 mm Hg, $p = 0.773$), or for the other measured cardiovascular risk factors.

Conclusions: An ADA diet consisting of 20% of calories as almonds over a 16-week period is effective in improving markers of insulin sensitivity and yields clinically significant improvements in LDL-C in adults with prediabetes.

INTRODUCTION

Prediabetes currently affects up to 13% of the U.S. adult population and 16% of U.S. teens [1], which translates to 54 million individuals [2]. Prediabetes is a precursor to type 2 diabetes mellitus (T2DM), which is present in approximately 8% of the U.S. population. Fifty percent of patients with prediabetes will progress to T2DM unless there is aggressive intervention (i.e., diet modification and exercise to facilitate moderate weight loss or use of medications that improve glucotoxicity without elevating endogenous insulin) [3].

The American Diabetes Association (ADA) guidelines address the need for medical nutrition therapy and public health interventions for patients with prediabetes to decrease the risk of developing T2DM and cardiovascular disease (CVD) [4]. Population-based prospective cohort studies [5,6] have demonstrated that lifestyle modification including diet can reduce the progression of prediabetes to T2DM, which has stimulated enthusiasm for evaluating novel nutrition approaches among patients with prediabetes. Such approaches have the potential to also improve the cluster of diabetogenic and atherogenic abnormalities including insulin resistance, dyslipidemia, and hypertension. Thus, health care professionals are seeking feasible and innovative patient-oriented strategies in the context of beneficial nutritional therapies.

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Almonds contain high levels of fiber, arginine, magnesium, polyphenolic compounds, vitamin E, and monounsaturated fatty acids (MUFA), specifically oleic acid. Population-based prospective cohort studies have shown an association between frequent nut consumption and reduced risk of T2DM and CVD [7–9]. These findings have generated proposed mechanisms for these associations including improved insulin sensitivity, increased antioxidant activity, and reduced concentrations of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C). Prior *in vivo* studies have shown that MUFA enhances the intestinal secretion of glucagon-like peptide-1 (GLP-1) [10–12], an incretin hormone that improves the regulation of postprandial glucose disposal and insulin secretion [13]. In addition, Wang et al. [14] have shown that lipid infusions containing primarily polyunsaturated fats (PUFA) trigger a gut-brain-liver axis that increases insulin sensitivity in the liver. Intermediary roles for gut hormones, including incretins, remain possible in this circuit and offer a conceptual basis for antidiabetes diets.

We sought to explore a possible role for daily almond consumption in persons with prediabetes as a simple, cost-effective nutrition intervention to preserve beta-cell function and improve insulin sensitivity and other CVD risk factors. We therefore conducted a randomized trial of an almond-enriched diet in the context of ADA diet guidelines to test the hypothesis that in individuals with prediabetes, an almond-enriched ADA diet improves measures of insulin sensitivity and other CVD risk factors compared with an ADA nut-free diet.

MATERIALS AND METHODS

We conducted a parallel-group randomized trial at the University of Medicine and Dentistry of New Jersey (UMDNJ), Newark, New Jersey, testing the hypothesis that an almond-enriched ADA diet would be more effective than a nut-free ADA diet on improving measures of insulin sensitivity in individuals with prediabetes. The total study time period for each participant was 16 weeks.

Eligibility Criteria

Research participants were recruited from a pool of adult employees at UMDNJ, from patients attending the UMDNJ-Newark–based Endocrine and Diabetes Clinics, and from community-based health fairs. Inclusion criteria included the presence of prediabetes according to the 2005 ADA diagnostic guidelines (fasting blood glucose between 100 and 125 mg/dl or casual blood glucose $\geq$ 140–199 mg/dl), body mass index (BMI) 20–35 kg/m^2, and willingness to discontinue vitamin E supplement usage. Persons with a self-reported allergy to almonds, history of irritable bowel disease or diverticulitis, use of corticosteroids or immunosuppressant medications, or presence of liver disease, renal disease, and/or severe dyslipidemia (triglyceride [TG] $>$ 400 mg/dl or TC $>$ 300 mg/dl) were excluded. The study protocol was approved by the UMDNJ-Newark campus Institutional Review Board, and all participants gave written informed consent.

Participants were randomized without stratification using computer-generated random integer generator software (www.random.org) to consume almonds (almond enriched, intervention) or to avoid nuts (nut-free, control). The principal investigator enrolled the participants and generated the allocation sequence, which was concealed until the interventions were assigned.

Intervention Design

During the week 0 visit, daily energy needs for ADA diet meal plans were computed based on resting energy expenditure (REE) measurements obtained from a handheld self-calibrating indirect calorimeter device (MedGem, model 100, Microlife USA, Inc., Dunedin, FL). The 510K class II medical device measures oxygen consumption (VO2) and assesses REE in 5 to 10 minutes using the Weir equation [15] and a constant RQ value of 0.85. All but 5 participants were evaluated for REE after an overnight fast (12–14 hours) but were tested at least 4 hours after a meal. Participants sat in a quiet room for a 15-minute rest period and during testing. The study dietitian prescribed an individualized ADA diet according to the REE results and the participant's self-reported activity level. Participants with a BMI $>$ 25 kg/m^2 (all but 14 participants) were prescribed energy intake deficits of 250–500 kcal in accordance with the ADA's guidelines to achieve modest weight loss in persons with prediabetes [4]. No meals were provided, and alcoholic beverages were limited to 2 per day for men and 1 per day for women.

Participants consumed either an ADA diet with 20% of energy from almonds and avoided other tree nuts and peanuts (intervention) or consumed an ADA diet without tree nuts and peanuts (control). The amount of almonds was determined based on published data reporting favorable changes in insulin, glucose, and lipid levels in subjects with impaired glucose tolerance consuming a diet containing 20% of energy from MUFA [16]. The prescribed ADA diets contained 15%–20% protein, $<$10% saturated fat, 60%–70% carbohydrate and MUFA, and cholesterol $<$ 300 mg/d.

A 3-day food and activity record (2 weekdays and 1 weekend day) was requested from participants 1 week prior to the start of the study. At week 0, each participant met with the study dietitian for a 1-hour counseling session to receive their individualized ADA diet. The intervention group received instruction on how to select 80% of their energy needs using the ADA Food Exchange System. Monthly supplies of prepackaged raw or dry roasted almonds were provided at

clinic visits for the intervention participants. The clinic supplied the entire almond portion of the diet to the intervention participants, who were instructed to use only the prepackaged study almonds. Both groups received instruction to consume the same number of servings of carbohydrate exchanges for a given calorie level. In light of the 20% energy contribution from the almonds, control group participants were prescribed compensatory servings from the meat and fat exchange lists. In addition, each participant received 20-minute counseling sessions for reinforcement of their ADA diet at weeks 4, 8, and 12 (total of 120 minutes per participant).

Dietary Adherence

To evaluate adherence, a 3-day food/activity record was completed by each participant at weeks 4, 8, 12, and 16. The study dietitian reviewed the records according to the prescribed number of ADA food exchanges and provided reinforcement. The records were analyzed using the U.S. Department of Agriculture's database Web site (http://www.mypyramidtracker.gov/). Dietary adherence was operationally defined as consuming within 75% of the prescribed diet, which is the approximate midpoint of the within- and between-subject variation in energy expenditure as measured by doubly-labeled water versus self-reported dietary intake [17]. Poor dietary adherence prompted additional individualized follow-up phone calls for reinforcement.

Outcomes

Outcomes included fasting glucose, insulin, TC, LDL-C, high-density lipoprotein cholesterol (HDL-C), TG, TC:HDL-C, and HbA1c. We also examined change in body weight, BMI, waist circumference (WC), and blood pressure (BP). Plasma α-tocopherol concentrations were evaluated as a biological marker to assess almond consumption compliance. In addition, self-reported dietary intake was examined in the context of changes from baseline to the second 8 weeks of the study.

Anthropometrics and Laboratory Assessment

Height was measured to the nearest centimeter using a stadiometer at week 0. Weight and BP were obtained at each clinic visit. Weight was measured using an internally calibrated segmental body composition scale/analyzer (model BC-418 MA, Tanita, Arlington Heights, IL) and recorded to the nearest 0.01 lb. BMI was calculated as weight (kg)/height (m^2). BP was measured using a calibrated automated digital monitor (Omron HEM-711). WC was measured to the nearest 0.1 cm, midway between the last rib and the ileac crest.

Venous blood samples were collected at the New Jersey Medical School General Clinical Research Center after a 12- to 14-hour fast at weeks 0, 8, and 16. Blood was disregarded in 5 participants at a single time point and for 1 participant at 2 time points due to blood draw protocol violations and/or acute medical conditions known to affect biological measures. Serum glucose, insulin, TC, LDL-C, HDL-C, TG, and HbA1c were measured by the UMDNJ University Hospital Clinical Laboratory according to Clinical Laboratory Improvement Amendment methods and standardized enzymatic procedures. Serum insulin levels were measured using direct enzyme-linked immunoassay methods by LabCorp, Inc. and ICAM Research Laboratory, UMDNJ. Plasma α-tocopherol concentrations were measured by LabCorp, Inc. using high-performance liquid chromatography with fluorometric detection.

Insulin resistance was assessed using homeostasis model analysis (HOMA) based on fasting glucose and insulin levels [18]. HOMA for insulin resistance (HOMA-IR) and beta-cell function (HOMA-B) were calculated using the formula [insulin(pM) × glucose(mM)]/22.5 and [20 × insulin(pM)]/[glucose(mM) − 3.5], respectively.

Sample Size

To achieve 80% power using a 5% significance level to detect a 20% difference in HOMA-IR, a total of 44 participants was required. Eighty-two individuals met inclusion criteria and 17 declined to participate; thus, 65 participants were enrolled into the trial.

Analysis

Sample size and power calculations were performed using SAS version 9.1 (SAS Institute, Cary, NC). Data were entered into an SPSS version 12.0 (SPSS Inc., Chicago, IL) database, and statistical analysis was performed using SPSS and SAS. Bivariate statistical analysis using the chi-square test for differences in proportions and 2-sided independent *t* tests were performed on baseline characteristics using a probability value of 0.05. To assess the significance of changes in anthropometric and metabolic variables, a mixed-model repeated-measures analysis of covariance was used with diet, week, and diet × week interaction as fixed effects, adjusting for baseline measurements of the outcome variable. A natural log transformation was performed on outcome variables for the modeling analysis when indicated to improve normality, and the results were exponentiated for reporting purposes. An appropriate within-subject covariance structure was determined for each of the outcome variables, and an unstructured, compound symmetric or first-order autoregressive covariance structure was applied. Additional analyses for glucose, insulin, HOMA-IR, and HOMA-B models were performed and adjusted for weight by adding the baseline weight as a covariate. An intent-to-treat analysis was performed, and all percentage change values presented are calculated from least-squares means (LSM) estimated from mixed models. Week 0, 8, and 16 measurements were included in the analysis, with the

Table 1. Baseline Characteristics by Intervention and Control Arms[a]

Characteristic	Intervention (n = 32)	Control (n = 33)
Age (y)	53 ± 9	54 ± 11
Gender		
Female	22 (69)	26 (79)
Male	10 (31)	7 (21)
Race		
Caucasian	12 (38)	13 (40)
Hispanic	4 (12)	5 (15)
African American	14 (44)	9 (27)
Asian	2 (6)	6 (18)
Weight (kg)	82.9 ± 14.4	80.5 ± 14.4
Body mass index (kg/m^2)	30 ± 5	29 ± 5
Waist circumference (cm)	95 ± 13	96 ± 12
Resting energy expenditure (kcal)	1708 ± 364	1635 ± 375
Plasma lipids, mg/dl[b]		
Total cholesterol	202 ± 36	199 ± 42
LDL cholesterol	117 ± 32	118 ± 38
HDL cholesterol	63 ± 16	59 ± 12
Triglycerides	113 ± 58	124 ± 75
Total cholesterol:HDL cholesterol	3.40 ± 0.93	3.49 ± 1.10
HbA1c (%)	5.8 ± 0.6	6.1 ± 0.5
Fasting blood glucose, mg/dl[b]	101 ± 13	104 ± 14
Fasting insulin, μU/ml	11.4 ± 9.4	9.0 ± 5.6
HOMA-IR	2.9 ± 2.5	2.4 ± 1.7
HOMA-B	112 ± 82	83 ± 60
Systolic blood pressure (mm Hg)	132 ± 12	129 ± 16
Diastolic blood pressure (mm Hg)	78 ± 9	75 ± 10

[a] Data are means ± SD or *n* (%) unless otherwise indicated. On average, ~5% of the data were missing or disregarded for any particular biological variable.
[b] To obtain mmol/L values for low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol, multiply values by 0.0259; for triglycerides, multiply values by 0.0113; and for glucose; multiply values by 0.0555.

exception of weight, BMI, WC, and BP that included additional measurements from weeks 4 and 12. The assumption used in the intent-to-treat model with regard to the aforementioned disregarded samples and missing data and unmeasured endpoints for the dropouts was that they were missing at random.

RESULTS

Study recruitment occurred from January 2006 to January 2007, and the last participant completed the study in April 2007.

Sixty-five individuals met all inclusion criteria and enrolled (intervention arm, n = 32; control arm, n = 33). During the study, 11 participants withdrew (intervention arm, n = 7; control arm, n = 4), primarily due to work and personal schedule conflicts.

Participants randomized into the intervention and control arms were similar in terms of baseline characteristics (Table 1).

The intent-to-treat analyses are presented based on percentage change in LSM (Table 2). Both groups experienced declines in weight, BMI, and WC during the study, but there were no significant differences between groups in these measurements at any time point ($p = 0.191$ to $p = 0.557$). Fasting blood glucose levels decreased ~2 mg/dl (~2%) in both groups ($p = 0.978$). However, almond consumption was associated with a greater reduction in fasting insulin (−1.78 μU/ml [−23.3%] vs. +1.47 μU/ml [+19.2%], $p = 0.002$), HOMA-IR (−0.48 [−24.9%] vs. +0.30 [+15.5%], $p = 0.007$) and HOMA-B (−13.2 [−17.8%] vs. +22.3 [+30.0%], $p = 0.001$). The magnitudes of change in insulin, HOMA-IR, and HOMA-B were virtually unaffected after adjusting for weight. The intervention group experienced a 2.11-μU/ml (27.6%) reduction in fasting insulin by week 8 and overall reduction of 1.78 μU/ml (23.3%) at week 16, in contrast to the control group, who showed a 0.06-μU/ml (0.8%) increase by week 8 and overall increase of 1.47 μU/ml (19.2%) at week 16 (Fig. 1).

Two participants in each group were taking lipid-lowering medications. There was no significant change in TC, HDL-C, or TG between the almond-enriched intervention and the nut-free control group. While failing to meet the prespecified cutoff for statistical significance, a clinically significant decline in LDL-C was found in the almond-enriched intervention group (−12.4 mg/dl vs. −0.4 mg/dl, $p = 0.052$) as compared with the nut-free control group. No significant changes were observed in HbA1c, systolic BP, or diastolic BP between the almond-enriched intervention and the nut-free control group.

The mean intake of almonds for participants in the intervention group was 60 g per day. There was a 0.27-mg/L (2%) decrease in the mean plasma α-tocopherol level in the nut-free control group ($p = 0.65$) at week 8 in contrast to a 1.74-mg/L (17%) increase observed in the almond-enriched intervention ($p < 0.01$).

Approximately 80% of participants met the operational definition of dietary adherence in both groups. There was no difference in self-reported mean dietary intakes from week 4 to 8 (first 8 weeks) and week 12 to 16 (second 8 weeks); therefore, the 2 sets of 3-day food records were collapsed (Table 3). Using paired data to evaluate within-group changes from baseline to the second 8 weeks of the study, a 5% decrease in energy from carbohydrate was observed in the intervention group in the context of a 5% increase in total fat, 5% increase in MUFA, 1% increase in PUFA, 5-g/d increase in fiber, and 10-mg α-tocopherol equivalent (TE) increase in

Table 2. Anthropometric and Metabolic Parameters by Intervention and Control Arms at Week 16[a]

Parameter	Intervention LSM [CI]	Control LSM [CI]	Change (% Change)		
			Intervention	Control	*p* Value[b]
Weight (kg)[c]	80.4 [77.0, 83.9]	79.6 [76.1, 83.1]	−1.1 (−1.4)	−2.0 (−2.4)	0.232
BMI (kg/m^2)[c]	29.3 [28.1, 30.5]	29.0 [27.8, 30.1]	−0.4 (−1.3)	−0.7 (−2.4)	0.191
Waist circumference (cm)[d]	91.5 [88.3, 94.7]	92.2 [89.1, 95.4]	−3.9 (−4.1)	−3.2 (−3.3)	0.557
TC (mg/dl)[d]	191 [178, 205]	205 [192, 218]	−8.7 (−4.4)	+5.0 (+2.5)	0.088
LDL-C (mg/dl)[e]	104 [93, 116]	116 [105, 127]	−12.4 (−10.6)	−0.4 (−0.4)	0.052
HDL-C (mg/dl)[e,f]	62 [58, 67]	61 [57, 66]	+3.1 (+5.3)	+2.1 (+3.6)	0.669
TC:HDL-C[d]	3.12 [2.83, 3.41]	3.43 [3.14, 3.71]	−0.33 (−9.5)	−0.03 (−0.9)	0.055
Triglycerides (mg/dl)[e,f]	92 [78, 110]	106 [90, 126]	−10.7 (−10.4)	+3.3 (+3.2)	0.123
HbA1c (%)[e]	5.9 [5.8, 6.1]	5.8 [5.6, 6.0]	−0.03 (−0.6)	−0.18 (−3.0)	0.070
Fasting glucose (mg/dl)[e]	100 [95, 105]	100 [96, 105]	−2.5 (−2.5)	−2.4 (−2.4)	0.978
Fasting insulin (μU/ml)[e,f]	5.85 [4.57, 7.49]	9.10 [7.25, 11.43]	−1.78 (−23.3)	+1.47 (+19.2)	0.002
HOMA-IR[e,f]	1.44 [1.10, 1.88]	2.21 [1.72, 2.83]	−0.48 (−24.9)	+0.30 (+15.5)	0.007
HOMA-B[e,f]	61.1 [47.9, 78.0]	96.6 [77.1, 121.0]	−13.2 (−17.8)	+22.3 (+30.0)	0.001
Systolic blood pressure (mm Hg)[e]	126 [121, 131]	127 [122, 132]	−4.4 (−3.3)	−3.5 (−2.7)	0.773
Diastolic blood pressure (mm Hg)[e]	75 [71, 78]	74 [70, 77]	−1.5 (−1.9)	−2.6 (−3.4)	0.645

[a] Items in brackets are 95% confidence intervals (CIs). All outcome variables in this intent-to-treat analysis were adjusted for their baseline values in the models. All baseline values were estimated from the model.

[b] Between-group differences (diet × week interaction) at week 16.

[c] *p* values for treatment differences for percentage change are based on mixed models with a unstructured covariance with all time points included in the model.

[d] *p* values for treatment differences for percentage change are based on mixed models with an autoregressive covariance structure with all time points included in the model.

[e] *p* values for treatment differences for percentage change are based on mixed models with a compound symmetric covariance structure with all time points included in the model.

[f] Least-squares means are based on log transformation values for the modeling analysis and then exponentiated back to the original scale for reporting purposes.

TC = total cholesterol; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; HOMA-IR = homeostasis model analysis for insulin resistance; HOMA-B = homeostasis model analysis for beta-cell function.

vitamin E ($p = 0.01$ to $p < 0.001$), whereas a 3% increase in protein was observed in the control group ($p = 0.002$) in the context of a 2% decrease in MUFA ($p = 0.103$) and 1% decrease in PUFA ($p = 0.090$). Between-group differences were found for change in carbohydrate, total fat, MUFA, PUFA, fiber, and vitamin E from baseline to the second 8 weeks of the study ($p < 0.01$ to $p < 0.001$).

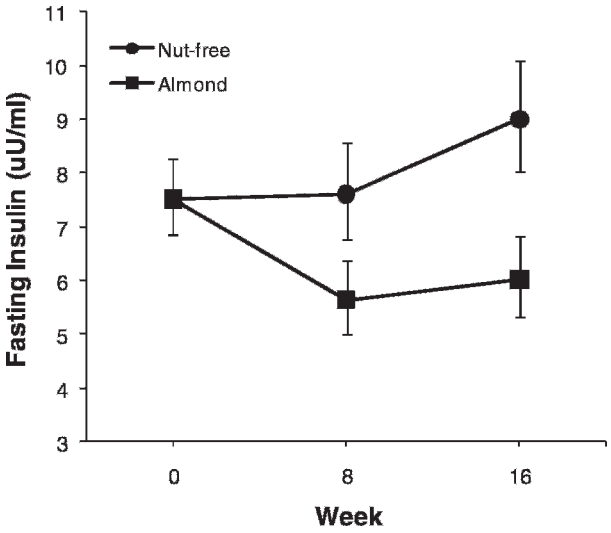

Fig. 1. Change in fasting insulin in the intervention (almond) and control (nut-free) groups. Data are least-squares means and SEM.

DISCUSSION

The present trial was designed to evaluate the effect of an almond-enriched ADA diet on measures of insulin sensitivity and CVD risk factors in adults with prediabetes over a 16-week period. We studied the intervention's effect under free-living conditions with few eligibility requirements, thus maximizing the finding's applicability to patients in the United States who have a diagnosis of prediabetes. Dietary adherence to the prescribed ADA meal patterns was very good, as judged by self-reported diaries.

There were no significant differences in weight, BMI, WC, HbA1c, or BP between the groups at any measured time point. The prescribed ADA meal patterns for the intervention and control groups produced a greater reduction in WC, 4.1% and 3.3%, respectively, compared with the ~1.4% and 2.4% reduction in weight and BMI. The mean weight loss in the intervention group was 1.1 kg and 2.0 kg in the control group, which is less than the predicted weight loss of approximately 5 kg over the 16-week trial. This discrepancy between predicted and actual weight loss may be due to participants'

Table 3. Self-reported Mean Dietary Intakes (± SD) at Baseline and during the Study[a]

	Intervention[b]				Control[c]				
	Baseline	First 8 Weeks	Second 8 Weeks	% Change[d]	Baseline	First 8 Weeks	Second 8 Weeks	% Change[d]	*p* Value
Energy (kcal/d)	1743 (427)	1662 (327)	1677 (338)	−4	1682 (494)	1535 (398)	1609 (404)	−3	0.48
Carbohydrate (%)	47 (9)	41 (7)	42 (6)	−9	48 (6)	48 (7)	48 (7)	0	<0.01
Protein (%)	19 (4)	18 (3)	19 (3)	0	18 (4)	19 (3)	21 (3)	+17	0.10
Total fat (%)	34 (8)	39 (7)	39 (6)	+15	33 (7)	30 (5)	30 (6)	−9	0.001
SFA (%)	10 (3)	9 (2)	9 (2)	−10	10 (3)	9 (2)	10 (3)	0	0.83
MUFA (%)	13 (5)	18 (3)	18 (3)	+38	12 (3)	11 (3)	11 (3)	−17	<0.001
PUFA (%)	7 (2)	9 (2)	8 (2)	+14	7 (3)	7 (2)	6 (2)	−14	<0.01
Total dietary fiber (g/d)	18 (8)	22 (5)	23 (7)	+28	17 (8)	19 (9)	18 (7)	+6	<0.01
Cholesterol (mg/d)	256 (143)	203 (106)	206 (101)	−20	262 (156)	213 (110)	287 (166)	+11	0.65
Vitamin E (mg TE)	7 (4)	17 (4)	17 (4)	+143	7 (4)	6 (3)	6 (3)	−14	<0.001

[a] *p* values are for between-group percentage changes from baseline to the second 8 weeks of the study (independent *t* tests).

[b] Almonds as 20% energy contributed approximately 9% MUFA, 4% PUFA, 1% SFA, 3% carbohydrate, and 3% protein to the diet.

[c] Participants in the control group were prescribed compensatory servings from the meat and fat exchange lists in light of the lack of almonds.

[d] Percentage change from baseline to the second 8 weeks of the study.

SFA = saturated fatty acids; MUFA = monounsaturated fatty acids; PUFA = polyunsaturated fatty acids.

overestimation of their physical activity level at the initial counseling session. This overestimation would have yielded a higher calculation of daily energy, thus negating the effects of the prescribed daily energy deficit.

Our finding that the almond intervention was associated with lower fasting insulin levels as compared with the control group after adjusting for weight is encouraging in the context of emerging research on lipid infusions and gut hormones, more specifically, the gut-brain-liver axis that increases insulin sensitivity in the liver [14]. The HOMA prediction models provide a quantitative assessment of the contribution of insulin resistance and beta-cell function from fasting glucose and insulin concentrations [18]. Insulin secretion is pulsatile; hence, using the mean of 3 fasting insulin samples taken at 5-minutes intervals is better than using a single sample to improve the intrasubject CVs [18]. The use of a single insulin sample in participants with T2DM has been shown to yield CVs of 10.3% for HOMA-IR and 7.7% for HOMA-B compared with 5.8% and 4.4%, respectively, when 3 samples are taken [19]. This study found a 40.4% difference in the magnitude of change in HOMA-IR between the groups (intervention: −24.9%; control, +15.5%) in the context of a 47.8% difference in the magnitude of change in HOMA-B (intervention, −17.8%; control, +30.0%). In light of a potential confounding effect of weight loss on insulin, HOMA-IR, and HOMA-B, we added weight change to the mixed models and found no significant interaction ($p > 0.05$). A potential weakness of using HOMA modeling in this study exists because of our single fasting insulin sample and our sample size. Thus, our findings must be interpreted with caution as these conditions may possibly contribute to the heightened risk of a type I error. We have previously observed an improvement in insulin sensitivity among overweight and obese adults consuming almonds using a formula-based low-calorie diet approach [20] and have suggested that the high oleic acid content in the almonds may improve beta-cell efficiency through enhanced intestinal secretion of GLP-1 [12]. Jenkins et al. [21] recently evaluated the effect of almonds on insulin secretion using 24-hour urinary C-peptide output as a marker of 24-hour insulin secretion in 27 nondiabetic hyperlipidemic participants. This team of investigators found significant reductions in 24-hour insulin secretion in participants who were fed full-dose (73 ± 3 g/d) and half-dose almond supplements by comparison with the control whole-wheat muffin supplement. Fasting insulin is a marker of insulin resistance, and elevated fasting and postprandial insulin levels in association with impaired carbohydrate intolerance have been associated with increased CVD risk [21]. Macronutrient approaches that enhance the beta-cell secretory response are desirable for improving the regulation of postprandial glucose disposal and insulin sensitivity [13], which may be efficacious for individuals with prediabetes. Therefore, we concur with this investigative team's commentary that the use of nuts to improve factors associated with abnormal carbohydrate metabolism and reducing plasma insulin levels may benefit CVD risk beyond cholesterol lowering.

Although we instructed the participants in both groups to consume an equivalent amount of carbohydrate (50% of energy), the participants in the almond-enriched intervention derived 41% to 42% of their energy intake from carbohydrate compared with 48% in the control group. This 6% to 7% difference in carbohydrate intake between the 2 groups may have potentially influenced the fasting plasma glucose levels and our markers of insulin resistance.

In light of the heightened risk of CVD among persons with prediabetes, an evaluation of fasting blood lipids was

warranted. A meta-analysis of 60 controlled trials evaluating carbohydrates and dietary fatty acids found that substituting carbohydrates with dietary fat will reduce TG levels and increase HDL-C levels, whereas replacing saturated fatty acids by or with MUFAs reduces LDL-C levels [22]. Although we observed a 4% reduction in energy from carbohydrate and 5% increase in MUFA in the intervention group, there was no significant difference in HDL-C and TG levels over time or between the groups. These findings are similar to that of a recent meta-analysis of 5 randomized trials featuring almonds [23]. However, in contrast to additional findings of the almond trial meta-analysis, we did not find a significant lowering of TC over time or between the groups. We observed a clinically significant 10.6% decrease in LDL-C in the intervention group over time ($p < 0.01$) in contrast to a 0.4% decline in the control group ($p = 0.92$). Recent studies suggest that inhibition of the reverse cholesterol transporter ABCA1 might impair pancreatic beta-cell function through the accumulation of intracellular LDL-C levels [24]. Our findings marginally support the almond trial meta-analysis' null findings for the effect of high-dose almonds (≥50 g/d) on LDL-C as we closely approached statistical significance between our 2 groups ($p = 0.052$). Our results would have likely become statistically significant if we had a larger study population because LDL-C was not the trial's primary endpoint. The TC:HDL-C ratio has recently emerged as a good or better indicator of predicting CVD risk than LDL-C or apolipoprotein fractions in large cohort studies [25,26] and has been included in a recent pooled analysis of 25 intervention trials evaluating nut consumption and blood lipid levels [27]. We found a clinically significant 9.5% reduction in TC:HDL-C in the intervention group as compared with less than a 1% reduction in the control group ($p = 0.055$).

Although the control group participants with a BMI ≥ 25 received equivalent recommendations on negative energy balance to facilitate modest weight loss, the lipid profile, insulin, and HOMA models did not show improvement as compared with the intervention group. It is possible that error existed in the control group's self-reported dietary intakes, specifically the quality of protein and fat selections, thus contributing to the lack of improvement observed from the prescribed ADA diet.

The adult recommended dietary allowance (RDA) for vitamin E is 15 mg/day TE. Self-reported intake for the intervention and control group at baseline was equivalent at 7 ± 4 mg TE. The almonds were primarily responsible for the increase to 17 ± 4 mg TE at week 4 in the intervention group, which remained above the RDA for the study duration. In contrast, the control group's vitamin E intake remained below the RDA level throughout the trial.

The intervention group experienced a 17% increase in plasma α-tocopherol by week 8 compared with virtually no change in the control group. A whole food that is capable of delivering the RDA of vitamin E using a reasonable portion size may confer protection from CVD risk among adults with prediabetes. Jenkins et al. found a 14% reduction in LDL-C oxidation in hyperlipidemic adults who consumed 22% of their daily energy from almonds over a 1-month period [28]. Evidence for the finding that almonds reduce LDL-C oxidation was demonstrated by their effect on 2 biomarkers of lipid peroxidation: serum malondialdehyde and urinary isoprostanes.

The Heart Outcomes Prevention Evaluation [29] featured a pharmacological dose of vitamin E (400 IU) and found a higher risk of heart failure among older patients with vascular disease or diabetes, which suggests that in specific cases, isolated vitamin components of naturally occurring foods do not recapitulate the beneficial effects of whole foods. In addition, the Arterial Disease Multiple Intervention Trial provided evidence for potential vitamin E–warfarin interactions (e.g., increased von Willebrand factor) in patients with peripheral arterial disease [30].

This study is not without limitations. As previously mentioned, our single fasting insulin sample and our sample size are study limitations. In addition, it is possible that error may have existed in the participant's self-reported dietary intakes. Lastly, although participants were instructed to consume equivalent amounts of energy from carbohydrates, there was difference in self-reported carbohydrate intake between the 2 groups.

CONCLUSION

Health care professionals who provide counseling to patients with prediabetes can recommend inclusion of almonds into ADA meal patterns and monitor metabolic parameters to ensure patient safety and efficacy. For patients with prediabetes who are unable to incorporate almonds into their diet due to food intolerances, allergies, or economic factors, the use of α-tocopherol–rich foods should be encouraged to achieve the RDA without the use of supplements, which will confer benefits from other important nutrients and bioactive substances. The present study found that almond enrichment of ADA meal patterns of adults with prediabetes is a feasible option and has a potential role in diminishing factors linked to insulin sensitivity and CVD risk. Tightly controlled metabolic feeding studies and postprandial studies are warranted in the future to evaluate the effects of almonds in the context of carbohydrate-containing meals and snacks to assess their influence on postprandial glucose levels and additional markers of CVD risk in persons with prediabetes.

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