Effect of improving dietary quality on carotid intima media thickness in subjects with type 1 and type 2 diabetes: a 12-mo randomized controlled trial¹,²

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ABSTRACT

Background: People with diabetes are at a heightened risk of cardiovascular disease compared with the general population. To our knowledge, randomized controlled trials investigating the effect of improving dietary quality on carotid intima media thickness, a marker of subclinical atherosclerosis and predictor of cardiovascular disease, have not been conducted in populations with diabetes.

Objective: We aimed to determine whether increasing fruit (+1 serving; 150 g/d), vegetable (+2 servings; 150 g/d), and dairy (+1 serving; 200–250 g/d) intakes slows 12-mo common carotid artery intima media thickness (CCA IMT) progression, compared with a control group continuing to consume their usual diet, in people with type 1 and type 2 diabetes.

Design: A 12-mo randomized controlled trial was conducted. The primary outcome was mean CCA IMT, measured at baseline and 12 mo, with B-mode ultrasound. Participants in the intervention group received counseling from a dietitian at baseline and 1, 3, 6, and 9 mo, and compliance was measured with a food-frequency questionnaire at baseline, 3 mo, and 12 mo. The control group continued consuming their usual diet.

Results: In total, 118 participants completed the study. Vegetable (46 g/d; 95% CI: 14, 77 g/d; P < 0.001) and fruit (179 g/d; 95% CI: 119, 239 g/d; P < 0.001) intakes were increased at 3 mo in the intervention group compared with the control group. This increase was not maintained at 12 mo, but intake increased overall in the cohort (fruit, 48 g/d; vegetables, 14 g/d). An increase in dairy consumption was not achieved, but yogurt intake was higher in the intervention group at 3 mo (38 g; 95% CI: 12, 65 g; P < 0.001); this was not maintained at 12 mo. At 12 mo, CCA IMT regressed (mean ± SD: −0.01 ± 0.04 mm; P < 0.001), with a greater effect in the treatment group (mean ± SD: −0.02 ± 0.04 mm compared with −0.004 ± 0.04 mm; P = 0.009).

Conclusion: Improving dietary quality in people with well-controlled type 1 and type 2 diabetes may slow CCA IMT progression. This trial was registered at https://www.anzctr.org.au as ACTRN12613000251729.


Keywords: carotid intima media thickness, diabetes, dietary quality, fruit, vegetables, dairy, randomized controlled trial

INTRODUCTION

In 2013, 8.3% of the world’s population had type 1 or type 2 diabetes, and the incidence is projected to increase by 55% to 8.8% by 2035 (1). Individuals with type 1 and type 2 diabetes are 2–3 times more likely to develop cardiovascular disease (CVD)³ than the general population (2, 3). In Australia, in 2010, ~30% of all deaths in people with type 1 and type 2 diabetes were due to CVD (4).

Epidemiologic studies show that better dietary quality is associated with lower rates of CVD in people with type 1 and type 2 diabetes (5, 6). Primary and secondary prevention trials have shown that improving dietary quality is associated with a reduction in cardiovascular events (7, 8). We have previously shown that people with type 1 and type 2 diabetes have similar dietary quality to age-, sex-, and BMI-matched nondiabetic subjects (9).

Carotid intima media thickness (IMT), measured by using B-mode ultrasound, is an early marker of atherosclerosis (10). In a systematic review of 21 epidemiologic studies, type 2 diabetes was associated with a 0.134-mm (95% CI: 0.123, 0.144 mm) greater carotid IMT, in comparison with healthy subjects, which increases the risk of myocardial infarction and stroke by 38% and 37%, respectively (11). In participants with type 1 diabetes for a mean of 5.5 y, carotid IMT was comparable to healthy subjects 10 y older (12). The annual progression rate of carotid IMT is also greater in people with diabetes. In a 3-y prospective study (13) of people with type 2 diabetes, carotid IMT progression was 0.040 mm/y compared with 0.0147 mm/y in people with diabetes.

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²Supplemental Tables 1–4 are available from the “Supplemental data” link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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³Abbreviations used: CCA IMT, common carotid artery intima media thickness; CRP, C-reactive protein; CVD, cardiovascular disease; HbA1c, glycated hemoglobin; IMT, intima media thickness; MMP-7, matrix metalloproteinase 7.

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without diabetes (14). Epidemiologic evidence shows that greater intake of fruit, whole grains, and soluble fiber and lower consumption of saturated fat in favor of polyunsaturated fat are associated with lower carotid IMT (15). Few randomized controlled trials have investigated the effect of improving dietary quality on carotid IMT, but data from trials in populations without diabetes show that the Mediterranean diet may slow carotid IMT progression (16, 17) or, in some cases, cause regression (18).

The aim of this study is to determine whether increasing fruit (+1 serving/d), vegetable (+2 servings/d), and dairy (+1 serving/d) intakes slows common carotid artery IMT (CCA IMT) progression over 12 mo, compared with a control group continuing to consume their usual diet, in people with type 1 and type 2 diabetes. It is hypothesized that the dietary intervention will slow the progression of CCA IMT by 10% over the 1-y period compared with the control group.

METHODS

Study design

A 12-mo randomized controlled trial was conducted to determine the effect of improving dietary quality on CCA IMT, compared with a control group continuing to consume their habitual diet, in a cohort of people with type 1 and type 2 diabetes. Ethics approval was obtained from the University of South Australian Human Research Ethics Committee, and the trial was registered with the Australian New Zealand Clinical Trials Registry as ACTRN12613000251729.

Subjects

Subjects (>18 y of age with diagnosed type 1 or type 2 diabetes for any duration managed with diet, oral hypoglycemic agents, and/or insulin) were recruited from August 2012 through December 2013 from a database of volunteers, public advertisements, and a recruitment company (Intuito Market Research). Exclusion criteria were unstable CVD requiring active treatment, heart failure, renal impairment (estimated glomerular filtration rate <30 mL/min), liver disease, cancer, or allergic/intolerant/dislike of fruit, vegetables, or dairy.

Dietary intervention

In a parallel design, participants were randomly allocated to either the intervention group (improved diet quality) or the control group (continue usual intake) by using an online-generated balanced random-number allocation sequence (www.randomization.com), stratified by diabetes type and sex, by a person independent of the study.

The intervention group attended a group or individual session conducted by a dietitian at baseline. Nutritional counseling to increase consumption of fruit (+1 serving/d), vegetables (+2 servings/d), and dairy (+1 serving/d), regardless of usual intake, was provided (see Supplemental Table 1). Participants in the intervention group had nutrition counseling at 1, 3, 6, and 9 mo. The control group was not told in detail about the dietary intervention, only that dietary quality was to be improved.

Compliance with the dietary intervention

At 1, 3, 6, 9, and 12 mo, participants met with the dietitian and completed a checklist to determine on how many days of the week they complied with the intervention. A random spot urine sample was provided by the participants at the 3 monthly appointments for measurement of potassium. A food-frequency questionnaire was administered at 3 and 12 mo to determine whether food and nutrient intake was changed from baseline.

Measurements

The main outcome measure was CCA IMT, and this was performed at baseline and 12 mo. Anthropometric measures, blood pressure, blood lipids, fasting glucose, C-reactive protein (CRP), and spot urinary sodium and potassium excretion were measured every 3 mo. Matrix metalloproteinase 7 (MMP-7) was measured at baseline and 12 mo as a biomarker of vascular remodeling. All measurements were completed after an overnight fast, and the operator completing the vascular measurements was blinded to the participant’s randomization.

Anthropometric measurements

Height was measured by using a stadiometer (SECA) to the nearest 0.1 cm while barefoot/flat footwear. Weight was measured to the nearest 0.05 kg with calibrated electronic scales (SECA) while the participants were barefoot/light footwear and wearing light clothing.

Peripheral blood pressure

Clinic blood pressure was measured with an automated sphygmomanometer (SureSigns VS3; Philips) once the participant had been seated for 5 min. A normal sleeve (16 × 52 cm) was used for an arm circumference of 24–32 cm and a large sleeve (16 × 70 cm) for an arm circumference of 32–42 cm. A minimum of 4 consecutive readings were taken at 1-min intervals. The first reading was discarded and the following 3 consistent measurements (i.e., systolic blood pressure within a range of 10 mm Hg) were used.

CCA IMT

The measurements of the carotid artery were taken by using B-mode ultrasound by one operator, with an intraobserver CV of 4.4% (n = 34). Participants were supine with their head positioned at 45 degrees away from the side of the neck being measured. A high-resolution ultrasound machine with a 12-MHz transducer was used (Medison MySono U6; Samsung). A 1-cm region of the IMT on the far wall of the distal common carotid artery on both sides was measured with automatic edge detection software (Medison MySono U6 Auto IMT; Samsung), as recommended in the Mannheim Carotid Intima-Media Thickness Consensus Paper (2004-2006-2011) (19). Areas of plaque, defined as a 50% greater IMT than the surrounding IMT or IMT >1.5 mm, were not imaged. Three 3-s clips were captured, and the mean of 10 measurements taken from each of these clips was averaged for a mean and mean maximum CCA IMT value at baseline and 12 mo.
Biological measurements

Spot urine sample

A spot urine sample was provided by participants when they attended the University of South Australia. Analysis of urinary sodium, potassium, creatinine, and albumin was done by SA Pathology. The albumin-to-creatinine ratio was calculated from one spot urine sample at baseline to determine the presence of microalbuminuria.

Fasting blood sample

A fasting venous blood sample was taken at each time point by a trained phlebotomist. Total cholesterol, HDL cholesterol, triglycerides, CRP, and glucose were measured with a Konelab 20XTi automatic analyzer (Thermo Electron Corporation) with reagents from ThermoFisher Scientific. LDL cholesterol was calculated by using the Friedewald formula: [(total cholesterol − HDL cholesterol) − (triglycerides x 0.45)] (20). Serum MMP-7 was measured in duplicate by ELISA (Quantikine Human Total MMP-7; R&D Systems) according to the manufacturer’s instructions. The interassay CV was 5.6%.

Glycated hemoglobin

The participants were asked to provide the pathology report from their most recent glycated hemoglobin (HbA1c) measurement, or the result was sourced from their general practitioner or the pathology company.

Dietary intake

Dietary intake was measured by using the electronic version of the Dietary Questionnaire for Epidemiologic Studies version 2 food-frequency questionnaire, as previously described (21).

Statistical analysis

Data are presented as means ± SDs or medians (IQRs), depending on the distribution. Data were checked for normality by using Shapiro-Wilk and Kolmogorov-Smirnov values. Independent samples t tests were used to determine between-group differences at baseline for continuous variables, and χ² tests were used for categorical variables. Mixed-effect modeling was used to determine between-group changes over time, and post hoc analyses were adjusted for multiple comparisons by using the Bonferroni method. Twelve-month change in antihypertensive medication, lipid-lowering medication, oral hypoglycemic agents, and insulin was calculated with the following formula: mean (percentage dose change from baseline for each medication) ÷ number of different medications (22). Independent samples t tests were used to determine whether there was a difference in medication change between the groups at 12 mo. Univariate correlations were used to determine correlates of 12-mo CCA IMT change. A power analysis was done, and based on a 10% reduction in CCA IMT progression compared with the control group, 37 people were required in each group for 80% power, P < 0.05. All analysis was performed with SPSS (version 19; SPSS Inc.). Statistical significance was set at P < 0.05.

RESULTS

Cohort characteristics

In total, 146 participants were randomly allocated (intervention group, n = 73; control group, n = 73) (Figure 1). There were no significant differences between the baseline characteristics of the intervention and control groups (Table 1). A total of 118 participants completed the 12-mo study (intervention group, n = 58; control group, n = 60). Baseline characteristics of the completers and the participants who withdrew with regard to weight, peripheral blood pressure, and mean and mean maximum CCA IMT were not different.
Carotid IMT

Mean CCA IMT regressed over time (\(P = 0.001\)) with a significant time-by-treatment effect (\(P = 0.009\)) (Table 2). There was no significant time effect (\(P = 0.07\)), but a time-by-treatment (\(P = 0.013\)) effect existed for mean maximum CCA IMT. There was no interaction by sex (\(P = 0.83\)), diabetes type (\(P = 0.62\)), presence of microalbuminuria (\(P = 0.40\)), smoking status (\(P = 0.44\)), baseline HbA1c (\(P = 0.40\)), baseline MMP-7 concentration (\(P = 0.31\)), or prescription of antihypertensive (\(P = 0.83\)) or lipid-lowering medication (\(P = 0.33\)). There was no statistically significant difference in the percentage medication dose change over the 12-mo study period by randomization for antihypertensive (83% of participants’ dose was unchanged) or lipid-lowering medication (85% of participants’ dose was unchanged), oral hypoglycemic agents (78% of participants’ dose was unchanged), or insulin use (82% of participants’ dose was unchanged).

Predictors of CCA IMT progression

The 12-mo change in mean CCA IMT and mean maximum CCA IMT was 0.01 ± 0.04 mm and 0.008 ± 0.05 mm,

### TABLE 2

CCA IMT measurements at baseline and 12 mo by treatment group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intervention group (n = 58)</th>
<th>Control group (n = 60)</th>
<th>Time effect(^1)</th>
<th>Time × treatment effect(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline 12 mo</td>
<td>Baseline 12 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean CCA IMT, mm</td>
<td>0.73 ± 0.13(^3)</td>
<td>0.71 ± 0.12</td>
<td>0.001</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>0.70 ± 0.13</td>
<td>0.69 ± 0.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>0.71 ± 0.13</td>
<td>0.70 ± 0.13</td>
<td>0.008</td>
<td>0.13</td>
</tr>
<tr>
<td>Left</td>
<td>0.74 ± 0.15</td>
<td>0.73 ± 0.13</td>
<td>0.018</td>
<td>0.04</td>
</tr>
<tr>
<td>Mean maximum CCA IMT, mm</td>
<td>0.79 ± 0.14</td>
<td>0.80 ± 0.13</td>
<td>0.07</td>
<td>0.013</td>
</tr>
<tr>
<td>Right</td>
<td>0.78 ± 0.14</td>
<td>0.78 ± 0.14</td>
<td>0.24</td>
<td>0.19</td>
</tr>
<tr>
<td>Left</td>
<td>0.83 ± 0.16</td>
<td>0.82 ± 0.14</td>
<td>0.16</td>
<td>0.04</td>
</tr>
</tbody>
</table>

\(^1\)Mean ± SD (all such values).

\(^2\)Mixed-effect modeling.

\(^3\)CCA IMT, common carotid artery intima media thickness.
respectively, in the whole cohort. In univariate analysis, involving data from the whole cohort, HbA1c (r = 0.20; P = 0.03) and baseline mean CCA IMT (r = −0.19; P = 0.04) were correlated with mean CCA IMT change, and baseline HbA1c (r = 0.18; P = 0.05) and mean maximum CCA IMT (r = −0.23; P = 0.01) were correlated with the 12-mo change in CCA IMT.

Intake at baseline or change in fruit, vegetable, and dairy intakes at 3 and 12 mo did not predict mean or mean maximum CCA IMT change. Change in peripheral blood pressure; total, LDL, or HDL cholesterol; glucose; CRP; or HbA1c at 12 mo was not correlated with mean or mean maximum CCA IMT change. Change in triglycerides at 12 mo was correlated with the change in mean maximum CCA IMT change (r = 0.25; P = 0.007).

Anthropometric measures, peripheral blood pressure, and biochemistry

Anthropometric measures, peripheral blood pressure, and biochemistry data by treatment group for all time points are provided in Table 3. During the study period, there was no statistically significant change in weight. A significant time and time-by-treatment effect existed for diastolic blood pressure (P < 0.05), but there was no significant change in pulse pressure, mean arterial pressure, or heart rate. CRP was measured in 95 participants, and there was no statistically significant time or time-by-treatment effect. Fasting glucose, HbA1c, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides remained unchanged throughout the study.

MMP-7

In a subsample of the cohort (n = 80; intervention n = 40, control n = 40), MMP-7 was measured at baseline and 12 mo. There was no change in MMP-7 concentration over the intervention period (Table 3). After age adjustment, there was no significant correlation between MMP-7 and mean or mean maximum CCA IMT at baseline. However, MMP-7 concentration at baseline did predict 12-mo mean maximum CCA IMT progression (r = 0.24; P = 0.03).

Compliance

Food-frequency questionnaire

Reported nutrient intake and consumption of the major food groups by treatment group are reported in Supplemental Tables 2 and 3. There was a statistically significant time-by-treatment effect for intake of vegetables (P = 0.001), fruit (P = 0.0001), and dairy (P = 0.002). There was a time-by-treatment effect for fiber (P = 0.0001), potassium (P = 0.0001), magnesium (P = 0.004), and calcium (P = 0.01). Carbohydrate (time × treatment, P = 0.01) and sugar (time × treatment, P = 0.0001) intakes also increased in the intervention group. This increase was accounted for by the increase in fruit consumption. A time effect existed for consumption of extra foods (P = 0.01), particularly sweet foods (P = 0.001), such that the whole cohort reduced their consumption.

Post hoc testing showed that total vegetable consumption was significantly higher in the intervention group at 3 mo (46 g; 95% CI: 14, 77 g; P = 0.005), but there was no statistically significant difference at 12 mo. Baseline vegetable intake was not different. At 3 mo (179 g; 95% CI: 119, 239 g; P = 0.0001), fruit intake was higher in the intervention group, but there was no statistically significant difference at baseline or 12 mo. Total dairy intake was higher in the control group at 12 mo (97 g; 95% CI: 26, 169 g; P = 0.008), but there was no statistically significant difference at the other time points. There was a significant time-by-treatment effect for yogurt intake, and this was a result of higher consumption in the intervention group at 3 mo (38 g; 95% CI: 12, 65 g; P = 0.005). At no other times points was yogurt consumption significantly different between the intervention and control groups. Milk consumption was higher in the control group at 12 mo (94 g; 95% CI: 31, 157 g; P = 0.004).

Compliance questionnaire

Participants reported that the extra serving of fruit and dairy was consumed on a median of 5.5 d/wk throughout the study. The 2 extra servings of vegetables were consumed 5.5 d/wk until 9 mo and 7 d/wk at 12 mo.

Urinary excretion

The sodium-to-potassium ratio and potassium-to-creatine ratio remained unchanged throughout the intervention period in both the treatment and control groups (see Supplemental Table 4). There was a significant time effect for sodium, potassium, creatinine, and the sodium-to-potassium ratio, but no time-by-treatment effects were observed.

DISCUSSION

In this cohort with type 1 and type 2 diabetes, improving dietary quality by increasing consumption of fruit, vegetables, and dairy resulted in a statistically significant difference in 12-mo mean CCA IMT change between the groups (P = 0.009 for time × treatment), with greater CCA IMT regression observed in the treatment group (−0.02 ± 0.04 mm compared with −0.004 ± 0.04 mm). Diastolic blood pressure was reduced by −3 mm Hg in the treatment group at 12 mo (P = 0.02 for time × treatment), which is expected to decrease cardiovascular events and all-cause mortality by −8% and 16%, respectively, at a population level (23).

A recent meta-analysis of randomized controlled trials (n = 7) showed that intensive lifestyle modification reduced carotid IMT progression (standardized mean difference: −0.21; 95% CI: −0.36, −0.05; P = 0.01) (24). This is approximately equivalent to a 0.02-mm reduction in carotid IMT with lifestyle modification; the trials ranged from 6 mo to 6.5 y in length. Only one of the included studies had a diet-only intervention, and it was shown that a Mediterranean-style diet high in fruit and vegetables with reduced red meat and monounsaturated and polyunsaturated fat in favor of saturated fat significantly reduced CCA IMT progression compared with the control diet (0.038 mm compared with 0.068 mm; P = 0.018) after 3 y in elderly men with hyperlipidemia (25). In the PREvención con Díeta MEDiterránea (PREDIMED) trial (Barcelona-North cohort), after a mean follow-up time of 2.4 y, internal carotid artery IMRT regressed (−0.084 mm; 95% CI: −0.158, −0.010 mm) in the participants allocated to the Mediterranean diet plus nuts, and progression occurred in the control group (internal carotid artery: 0.052 mm; 95% CI: −0.014, 0.118 mm), P = 0.024
TABLE 3
Change in weight, blood pressure, and biochemistry by treatment group over the 12-mo intervention period

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (n = 58)</th>
<th>Control group (n = 60)</th>
<th>Time effect&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Time × treatment effect&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline 3 mo 6 mo 9 mo 12 mo</td>
<td>Baseline 3 mo 6 mo 9 mo 12 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>97.2 ± 16.8&lt;sup&gt;1&lt;/sup&gt; 96.2 ± 17.1 96.5 ± 15.9 96.9 ± 15.8 97.2 ± 16.7</td>
<td>95.3 ± 23.3 95.6 ± 23.7 95.6 ± 23.4 94.7 ± 23.7 95.0 ± 23.7</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>127 ± 13 126 ± 14 126 ± 12 125 ± 11 126 ± 13</td>
<td>128 ± 15 129 ± 14 127 ± 14 125 ± 14 128 ± 14</td>
<td>0.19</td>
<td>0.83</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>73 ± 11 71 ± 10 70 ± 10 72 ± 11 70 ± 9</td>
<td>71 ± 10 72 ± 10 71 ± 9 70 ± 10 72 ± 11</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>91 ± 10 89 ± 10 88 ± 9 89 ± 9 88 ± 8</td>
<td>90 ± 10 90 ± 10 89 ± 9 88 ± 10 90 ± 11</td>
<td>0.08</td>
<td>0.22</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>54 ± 12 54 ± 12 56 ± 13 53 ± 13 56 ± 14</td>
<td>57 ± 14 58 ± 14 56 ± 13 56 ± 12 56 ± 13</td>
<td>0.28</td>
<td>0.26</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>72 ± 12 71 ± 11 72 ± 12 71 ± 11 72 ± 12</td>
<td>73 ± 14 72 ± 12 71 ± 12 73 ± 15 71 ± 12</td>
<td>0.50</td>
<td>0.82</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>3.9 ± 1.1 3.7 ± 1.0 3.9 ± 1.0 3.9 ± 0.9 3.8 ± 0.9</td>
<td>3.6 ± 1.0 3.6 ± 0.8 3.8 ± 1.0 3.7 ± 0.9 3.7 ± 0.9</td>
<td>0.14</td>
<td>0.87</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.2 ± 0.3 1.2 ± 0.3 1.2 ± 0.3 1.3 ± 0.3 1.2 ± 0.3</td>
<td>1.3 ± 0.3 1.2 ± 0.3 1.3 ± 0.4 1.3 ± 0.4 1.3 ± 0.3</td>
<td>0.14</td>
<td>0.96</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>2.2 ± 1.0 2.0 ± 0.8 2.1 ± 0.9 2.1 ± 0.7 2.1 ± 0.8</td>
<td>1.8 ± 0.7 1.8 ± 0.7 1.9 ± 0.8 1.9 ± 0.7 1.9 ± 0.8</td>
<td>0.89</td>
<td>0.83</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.0 ± 0.6 1.1 ± 0.6 1.1 ± 0.5 1.1 ± 0.6 1.1 ± 0.6</td>
<td>1.1 ± 1.2 1.2 ± 1.0 1.3 ± 1.4 1.2 ± 1.2 1.2 ± 1.1</td>
<td>0.57</td>
<td>0.99</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>7.3 ± 3.1 7.1 ± 2.8 6.9 ± 2.6 7.2 ± 2.9 7.1 ± 2.9</td>
<td>7.4 ± 2.9 7.5 ± 2.7 7.6 ± 3.3 7.5 ± 3.3 7.3 ± 2.5</td>
<td>0.95</td>
<td>0.76</td>
</tr>
<tr>
<td>hsCRP, mg/L</td>
<td>2.3 ± 2.2 2.4 ± 2.2 2.4 ± 1.9 2.3 ± 2.0 2.3 ± 2.1</td>
<td>2.8 ± 2.7 2.6 ± 2.7 3.0 ± 2.8 2.3 ± 2.3 2.4 ± 2.4</td>
<td>0.11</td>
<td>0.83</td>
</tr>
<tr>
<td>HbA1c %</td>
<td>7.0 ± 1.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>53 ± 13</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>MMP-7, ng/mL</td>
<td>3.38 ± 1.37</td>
<td>3.42 ± 1.34</td>
<td>3.44 ± 1.49</td>
<td>3.51 ± 1.55</td>
</tr>
</tbody>
</table>

<sup>1</sup>bpm, beats per minute; HbA1c, glycated hemoglobin; hsCRP, high-sensitivity C-reactive protein; MMP-7, matrix metalloproteinase 7.

<sup>2</sup>Mean ± SD (all such values).
In our cohort overall, CCA IMT regression was observed at 12 mo (−0.01 ± 0.04 mm), and a greater amount of regression occurred in the treatment group. At 3 mo, the intervention group increased their consumption of vegetables and fruit compared with the control group, but this increase was not maintained at 12 mo relative to the control group. The cohort overall increased their consumption of fruit (48 ± 226 g/d), vegetables (14 ± 92 g/d), and dairy (33 ± 274 g/d) over the 12-mo period, which may explain the CCA IMT regression observed in both groups. A regression analysis conducted a baseline showed that 1 y of aging should increase CCA IMT by 0.006 mm. Therefore, the findings of this study suggest that greater consumption of fruit, vegetables, and dairy alters the natural progression of CCA IMT.

The clinical impact of the CCA IMT regression we observed with increased dietary quality remains unclear. A meta-regression showed that the change in CCA IMT (progression or regression), achieved with drugs or lifestyle interventions in trials of primary or secondary prevention, was not correlated with cardiovascular events (26). In a meta-analysis of 32 randomized controlled trials of drug therapy, it was shown that for each 0.01-mm reduction in carotid IMT progression per year, the OR for nonfatal myocardial infarction was 0.82 (95% CI: 0.69, 0.96; P = 0.018) (27). Currently, there are not enough data from cohorts with diabetes to determine the impact of the CCA IMT regression we observed in this study on cardiovascular outcomes. However, the CCA IMT regression we observed with a relatively simple dietary intervention is approximately equivalent to 50% of the reduction in CCA IMT progression achieved with statin treatment (weighted mean difference: −0.029 mm; 95% CI: −0.045, −0.013 mm) (28).

As previously reviewed (15), fruit and vegetables contain many components that may account for their beneficial effect on carotid IMT, including potassium, fiber, vitamins, minerals, carotenoids, and phytochemicals, including polyphenols. In this study, at 3 mo, fiber intake was increased by 5 g/d (95% CI: 1.8 g/d; P = 0.006) in the intervention group compared with the control group. Buil-Cosiales et al. (29) showed that a 10-g increase in fiber from <25 g/d to >35 g/d was associated with CCA IMT 0.051 mm lower, and only fiber consumption from fruit was inversely associated with CCA IMT. In addition, potassium intake was increased by 492 mg/d (95% CI: 94, 889 mg/d; P = 0.02) in the intervention group compared with the control group at 12 mo. Studies to date have not shown an association between potassium and CCA IMT, although there is evidence to show that potassium has a beneficial effect on vascular function (30).

A similar change in CCA IMT to what we observed in the current study was reported in a randomized controlled trial investigating the effect of supplementation with 27 g flavonoid-enriched chocolate/d [850 mg flavan-3-ols (90 mg epicatechin) + 100 mg isoflavones] in statin-treated postmenopausal women with type 2 diabetes (n = 93) (flavonoid treatment: 0.006 ± 0.008 mm/y; control group: −0.006 ± 0.007 mm/y) (31). The characteristics of the cohort in the study by Curtis et al. (31) were similar to the present study, with 57% of the cohort taking an antihypertensive medication and HbA1c ~7.2% (55 mmol/mol). More than half of the subjects in the present study were prescribed a lipid-lowering or antihypertensive medication (27). In addition, recommendations for blood pressure (<140/85 mm Hg), LDL cholesterol (<2.5 mmol/L), triglycerides (<2.2 mmol/L), and HDL cholesterol (>1 mmol/L) were met (32). At baseline, mean CCA IMT was lower than what has been observed in other populations with diabetes of a similar age. In a meta-analysis involving 4420 individuals with type 1 or type 2 diabetes, the mean CCA IMT was 0.79 ± 0.19 mm (mean age: 61 y; IQR: 36–76 y) compared with 0.73 ± 0.13 mm in our cohort (mean age: 56 ± 14 y) (33).

In our cohort, baseline HbA1c was an independent predictor of the change in mean CCA IMT. It was shown in the Epidemiology of Diabetes Interventions and Complications Trial/Diabetes Control and Complications Trial, involving people with type 1 diabetes, that change in HbA1c (measured annually) predicted CCA IMT progression after 12 y of follow-up (34). In addition, a study conducted in a population with type 2 diabetes showed that baseline HbA1c was a predictor of CCA IMT progression (35). Therefore, the lack of an increase in HbA1c during the study may also explain why CCA IMT progression was not observed.

Inflammation causes a cascade of events that includes the synthesis of MMP-7, which acts on collagen and elastin to cause degradation of the extracellular matrix, resulting in structural changes (36). MMP-7 is selectively produced in atherosclerotic lesions (37) and has been shown to be positively associated with carotid IMT (38). In the present study, MMP-7 concentration at baseline was correlated with the 12-mo change in mean maximum CCA IMT but not mean CCA IMT. Both CRP and MMP-7 concentration were unchanged after 12 mo of improved dietary quality. MMP-7 activity is also affected by blood lipids (39), which remained unchanged in the present study. We are not aware of any dietary or lifestyle interventions that have measured MMP-7.

A limitation of this study is that biomarkers of fruit, vegetable, and dairy intake were not measured to provide an objective measure of compliance with the intervention. Another limitation is the use of a random spot urine sample taken on one occasion to measure sodium and potassium excretion. Electrocardiogram gating was not used to measure CCA IMT at a specific point in the cardiac cycle, but rather, an average CCA IMT was determined by taking measurements across the cardiac cycle. The presence of carotid plaques was not measured. It has been shown that assessment of carotid plaques has greater diagnostic accuracy for predicting future vascular events compared with IMT (40).

In conclusion, in this cohort with well-controlled type 1 and type 2 diabetes, dietary quality improved in the short term in the intervention group, but this was not fully maintained over the 12-mo intervention period. Despite this, mean CCA IMT regressed over time (P = 0.001), and there was a significant time-by-treatment effect (P = 0.044). Peripheral diastolic blood pressure was reduced in the treatment group compared with the control group. Improving dietary quality may cause CCA IMT regression in people with diabetes.
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