Published in final edited form as:

Atherosclerosis. 2016 August ; 251: 361–366. doi:10.1016/j.atherosclerosis.2016.05.024.

Polyunsaturated fats, carbohydrates and carotid disease: The Atherosclerosis Risk in Communities (ARIC) Carotid MRI study

Jennifer L. Dearborn, MD MPH¹, Ye Qiao, PhD², Eliseo Guallar, PhD³, Lyn M. Steffen, PhD MPH RD⁴, Rebecca F. Gottesman, MD PHD^{3,5}, Yiyi Zhang, PhD MHS³, and Bruce A. Wasserman, MD²

¹Department of Neurology, Yale University School of Medicine, New Haven, CT

²The Russell H. Morgan Department of Radiology and Radiological Sciences, Johns Hopkins University School of Medicine, Baltimore, MD

³Department of Epidemiology and Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, USA

⁴Division of Epidemiology and Community Health, University of Minnesota School of Public Health, Minneapolis, MN

⁵Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD Subject codes: Cardiovascular disease; Diet and nutrition; Epidemiology; Vascular disease

Abstract

Background and aims—Carbohydrates and fat intake have both been linked to development of atherosclerosis. We examined associations between glycemic index GI and fat intake with carotid atherosclerosis.

Methods—The Atherosclerosis Risk in Communities (ARIC) cohort enrolled participants during the period 1987–1989 and the Carotid MRI sub-study occurred between 2004 and 2006 (1,672 participants attending both visits). Measures of carbohydrate quality (usual GI), fat intake (total, polyunsaturated and saturated) and overall dietary quality index (DASH Diet Score) were derived from a 66-item food frequency questionnaire administered at baseline. Trained readers measured lipid core presence and maximum wall thickness. Using multivariate logistic regression, we determined the odds of lipid core presence by quintile (Q) of energy-adjusted dietary components. Restricted cubic spline models were used to examine non-linear associations between dietary components and maximum wall thickness.

Results—Mean daily polyunsaturated fat intake was 5 g (SD 1.4). GI and polyunsaturated fat intake had a nonlinear relationship with maximum wall thickness. Low (1–4 g) and high (6–12 g)

Corresponding Author: Jennifer L. Dearborn, Yale University School of Medicine, Department of Neurology, PO Box 208018 New Haven, CT 06520-8018, Tel: 203-737-1057, Fax: 203-737-4382, Jennifer.dearborn@yale.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of interest

The authors declared that they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

polyunsaturated fat intake were associated with a statistically significant decreased odds of lipid core presence compared to intake in a majority of participants (OR Q5 vs. Q2–4: 0.64, 95% CI 0.42 to 0.98; OR Q1 vs. Q2–4: 0.64, 95% CI 0.42, 0.96), however, the association with lipid core was attenuated by adjustment for maximum wall thickness, hypertension, hyperlipidemia, and diabetes.

Conclusions—GI and polyunsaturated fat intake were not associated with high-risk plaque features, such as lipid core presence, independent of traditional vascular risk factors.

Keywords

diet; carotid atherosclerosis; polyunsaturated fats; glycemic index

Introduction

The carotid artery is particularly susceptible to plaque formation, with a general population prevalence of plaque presence of 62% in women and 75% in men in the U.S.¹ Healthy dietary patterns are protective against carotid disease^{2,3} and unhealthy diets are associated with higher disease burden.^{4,5} Particular dietary components, such as carbohydrates and fats, have patho-etiological links to atherosclerosis. For example, high carbohydrate diets may be particularly atherogenic because postprandial hyperglycemia results in elevated triglycerides and increased oxidative stress, which can negatively impact the vascular endothelium.⁶ Additionally, although saturated fats are postulated to be atherogenic, the association may be overstated.⁷ Emerging data suggest that intake of polyunsaturated fats results in improved markers of vascular endothelial health.⁸ Conflicting epidemiologic data about the positive or negative effects of these dietary components may be a result of not considering overall diet composition and the balance between potentially protective and detrimental foods.

Carotid artery plaque characteristics that lead to rupture and subsequent stroke are well established.⁹ For example, presence of a lipid rich or necrotic core is a key element of the “vulnerable” plaque.¹⁰ Known associations with lipid core presence include total and low density lipoprotein (LDL) cholesterol.¹¹ No studies to date have examined the impact of nutritional factors on high-risk plaque features. More refined characterization of the arterial wall, as defined by magnetic resonance imaging (MRI), may allow for unique observations regarding dietary impact on disease. We hypothesized that a high midlife usual glycemic index (GI) would be associated with lipid core presence, and that high polyunsaturated fat intake may be less associated with carotid disease.

Materials and methods

Study population

The Atherosclerosis Risk in Communities Study (ARIC) is a prospective, predominantly biracial (black and white) prospective study of persons from four U.S. communities, designed to examine the natural life course of atherosclerotic disease.¹² At the baseline visit (1987–1989), participants were aged 45 to 64 years. The ARIC Carotid MRI study was performed in a subset of participants in 2004–2006, approximately 18 years after study initiation. Participants were selected using a stratified sampling plan to oversample

participants with carotid plaques based on previously measured intima media thickness measured on B-mode ultrasound from 1993 to 1998.¹³ The goal was to recruit more participants with high values of maximum carotid artery intimal medial thickness with the remainder randomly selected from the remainder of the distribution. Field center-specific cut points were adjusted over the recruitment period to meet desired enrollment targets. Further details of recruitment are previously reported.¹¹ The institutional review board at all participating centers approved the study and all participants provided informed consent.

Analytic population

Only participants with good image quality and good protocol adherence were included (n=1740, Supplemental Figure). Exclusions from the analysis were missing nutrition data or had implausible caloric intake, as defined by the top or bottom 1% stratified by sex (n=61). The total population for the analysis of maximum wall thickness included 1,679 participants. Analyses of lipid core presence were restricted to participants with a wall thickness greater than or equal to 1.5 mm (n=1120) due to the resolution constraints of the MRI scan.¹⁴

Definitions of dietary components

Dietary intake was assessed by an interviewer-administered 66-item semi-quantitative food frequency questionnaire at baseline (1987–1989). GI for each food is defined as the increase in the area under the glucose response curve after ingestion of 50 g of the available carbohydrate compared with the reference food (white bread), expressed as a percentage compared to white bread. Glycemic load (GL) represents the postprandial blood glucose based on the entire day's intake of food. For this study, usual dietary GL was calculated by: (carbohydrate content per serving of food) × (average number of servings of food per day) × (GI for that food). Usual dietary GI was computed by dividing the GL by the total carbohydrate intake for the individual.¹⁵ Dietary fat intakes, including total, polyunsaturated and saturated fats, are nutrients calculated from reported food intakes. Energy-adjusted values were used in all analyses.

Overall diet quality was derived from an index using nutrient values based on the Dietary Approaches to Stop Hypertension (DASH) diet, herein referred to as the DASH Diet Score.¹⁶ The five beneficial nutrients used in the score are: protein, fiber, magnesium, calcium and potassium. Presumed detrimental nutrients are: total fat, saturated fat, sodium and dietary cholesterol. This score reasonably approximates healthy eating targets in men and women based on a 2,100 calorie diet. Participants received one point for each nutrient meeting the recommended goal and half a point for meeting an intermediate goal (defined as intermediate target between DASH and control diet).¹⁶ This score was chosen over other measures of overall diet quality because of its emphasis on specific guidelines for nutrient intake to allow for patient-level interpretations.

Magnetic resonance imaging and analysis

MRI studies were performed on 1.5T scanners (GE Medical Systems, Milwaukee, Wis at three field sites; Siemens Medical Solutions, Ehrlangen, Germany at 1 field site) using a bilateral 4-element phased array carotid coil (Machnet, The Netherlands). Details of the carotid MRI protocol have been previously described.^{13,17} Briefly, a 3D time-of-flight MR

angiogram was acquired through both carotid bifurcations. BBRMI imaging was achieved using a 2D cardiac-gated double-inversion recovery fast spin-echo sequence with fat signal suppression before and after an intravenous injection of gadodiamide (Omniscan, GE Amersham, Buckinghamshire, England; 0.1 mmol/kg body weight). Sixteen BBRMI slices were oriented perpendicular to the vessel and centered through the thickest part of the carotid plaque on the side with the thicker wall (acquired resolution, $0.51 \times 0.58 \times 2.00$ mm³).¹³

Seven readers who were blinded to patient characteristics were certified to interpret the MRI images using semi-automated software (VesselMASS, Leiden University Medical Center). Post-contrast images were used to draw contours to delineate the lipid core and outer wall, as contrast helps delineate these features. The semi-automated software divided vessel walls into 12 radial segments, of which the maximum segmental wall thickness was used for analysis.¹³

Covariates

Measurement protocols were identical at study baseline and in the Carotid MRI sub-study. Confounders at baseline included: age, race-center (Forsyth County-white; Forsyth County-black; Washington County-white; Mississippi-black; Minnesota-white), sex, height, history of smoking, history of hypertension, and history of diabetes. Because of the close association with cholesterol and atherosclerosis, we used a time-weighted average across five preceding study visits for total cholesterol rather than a cross-sectional measurement.¹⁸ This value was calculated by plotting the cholesterol and study time and dividing the area under this curve by total time of follow-up. At visit 1–4 and the Carotid MRI visit, fasting measurements of plasma lipids were performed using conventional techniques. At baseline, hypertension was defined as a systolic or diastolic blood pressure greater than or equal to 140 or 90 mmHg, respectively, or use of antihypertensive medication. Diabetes was defined as a fasting glucose greater than or equal to 126 mg/dl or a self-report of physician-diagnosed diabetes or on treatment.

Statistical analysis

To account for the stratified sampling design of the Carotid MRI sub-study, the data were weighted by the inverse of the sampling fractions in the eight sampling strata (four field centers X two intima media thickness groups). Participant characteristics were evaluated across diet quality subgroups, using a score of >4.5 to approximate good diet quality, as this signified participants that met at least half of the recommended daily intake as specified by the DASH diet.¹⁶

Dietary components were divided into quintiles to examine nonlinear associations with carotid plaque characteristics (Q1, Q2–4, Q5) and the percentage of participants with and without a lipid core was investigated. The odds of lipid core presence for GI and GL, and fat intake were compared using multivariate logistic regression using Q2–4 as the reference for high (Q5) and low (Q1) intake. ‘Model 1’, was adjusted for: age, sex, race-center, height, height squared and history of smoking. Model 2 was adjusted for variables in Model 1 plus

maximum wall thickness because of the previously described strong association with lipid core¹¹ and model 3 added adjustments for cholesterol, diabetes and history of hypertension.

Restricted cubic splines, a type of regression where polynomials are defined across a small number of “knots” which define adjacent intervals, were used to depict the nonlinear associations between dietary components and maximum wall thickness. The reference category was set at the 50th percentile for each dietary component, and the knots are at the 5, 35, 65 and 95 percentile. Adjustments for nonlinear models were the same as in Model 1.

Results

In late midlife, at study baseline (mean age 53.7 ± 5.5 years), mean caloric intake was 1599 ± 557 kcal. At the time of the MRI exam, participants were on average, 70.8 years old (SD 5.6), over half (51.3%) were women, and 21.4% were black. Participants who had a better DASH Diet Score (Score ≥ 4.5) were slightly older and more likely to be women and white (Table 1). Participants with a higher score were also less likely to be smokers and less likely to be hypertensive at year 18. They consumed fewer calories, and had lower fat intake (total, polyunsaturated and saturated) and also had a higher GI and GL. Q1 of polyunsaturated fat intake was 1–4 g/day and Q5 of intake represented 6–12 g/day.

The correlations of dietary components are summarized as follows (Table 2): total fat and saturated fat intake were correlated ($R = 0.787$), and there was a weak correlation with polyunsaturated fat intake. Total fat was inversely correlated with GI and GL, while polyunsaturated fat demonstrated weak correlations with carbohydrate intake (GI $R = -0.147$; GL $R = -0.286$, Table 2). A higher DASH Diet Score had weak correlations with GI, GL and polyunsaturated fat. A higher DASH Diet Score had modest inverse correlations with total fat (Table 2).

Associations with lipid core presence

542 of 1120 participants with wall thickness ≥ 1.5 mm (48.4%) had an identifiable lipid core. Dietary component intake across quintiles was not significantly different in participants with and without a lipid core (Table 3). The odds of lipid core presence for GI and GL was not significantly increased in Q1 or Q5 (Table 4). Total and saturated fat were not associated with lipid core presence, nor was overall diet quality. Polyunsaturated fat was associated with decreased odds of lipid core presence in Q1 (Model 1 adjusted odd ratio, OR Q1 vs. Q2–4 0.64, 95% CI 0.42, 0.96, Table 4) and Q5 (Model 1 adjusted OR Q5 vs. Q2–4 0.64, 95% CI 0.42, 0.98, Table 4) as compared to Q2–4. This result was attenuated by adjustment for wall thickness and no longer reached significance for the Q5 of polyunsaturated fat intake (Model 2, Table 4). This supports that the association of polyunsaturated fat with maximum wall thickness is mediated by lipid core. Further adjustments for cholesterol, hypertension and diabetes did not significantly alter the results (Model 3, Table 4).

The associations of GI and polyunsaturated fats with wall thickness appeared to be nonlinear (p -values for the spline terms = 0.412; 0.060; 0.031 for GI and for polyunsaturated fats, 0.083; 0.044; 0.032, Figure 1). In the nonlinear models, GI showed a nominal association

toward increasing wall thickness at the lowest and highest values, with a no association towards decreasing wall thickness in mid-range GI (approximate GI 75–85, Figure 1). Polyunsaturated fats also had a nominal association of decreasing wall thickness in those with the highest intake (greater than 7 g/day, Figure 1). There was no apparent association with total fat intake or DASH Diet Score and wall thickness in nonlinear models (Figure 1).

Discussion

This study demonstrates two important points. First, we observed that dietary components are not strongly associated with carotid atherosclerosis. GI is not strongly associated, and low and high polyunsaturated fat intake are inversely associated with maximum wall thickness. Second, there is a suggestion that low and high polyunsaturated fats compared to “average” intake, was protective against lipid core development, but this was not independent of vascular risk factors. These associations were not surprisingly attenuated with adjustment for maximum wall thickness, as lipid deposition occurs first resulting in an increase in wall thickness. This suggests that dietary factors are not associated with plaque presence independent of wall thickness or known risk factor associations such as diabetes, hypertension and hyperlipidemia.

The trend of low polyunsaturated fat intake and lower odds of lipid core presence was surprising. It is possible that the trend of low polyunsaturated fat intake and a lower burden of carotid disease may be from improved overall diet quality (DASH Diet Score). The trend in high polyunsaturated fat is easier to interpret, as high polyunsaturated fat intake may be protective against atherogenesis because of direct effects of vascular health. For example, one study demonstrated reduced LDL levels and other pro-atherogenic markers with increasing intake.¹⁹ Additionally a large clinical trial that demonstrated improved carotid plaque characteristics with dietary modification that included higher polyunsaturated fat intake.²⁰

Measures of dietary quality were not always concordant. For example, although GI and GL are markers of carbohydrate quality, they did not correlate with another accepted marker of overall dietary quality, the DASH Diet Score. This illustrates that defining the impact of a single dietary component is difficult, in that it is impossible to control for other aspects of diet that may also affect vascular health in a dose dependent fashion. It is likely that those consuming more carbohydrates also were consuming lower total fat. Additionally, finding that low GI intake, which we hypothesized to be protective, was associated with increased wall thickness was surprising. This may be explained by the low correlation between GI and overall diet quality.

A dietary pattern that is increasingly gaining recognition for its vascular benefits, including reduced incidence of stroke, is the Mediterranean Diet.²¹ This diet is rich in olive oil, nuts, fish, fruits and vegetables and low in refined grains and dairy. The “average” diet measured in the ARIC population is likely not close to this dietary pattern, and olive oil intake was not measured specifically. Both the DASH diet and the Mediterranean diet encourage low GI food (i.e. fruits and vegetables), but the Mediterranean Diet encourages high consumption of poly and monounsaturated fats (olive oil and nuts). In our study population, high

polyunsaturated fats (6–12 g per day) may be protective against atherosclerosis, even though overall diet quality was not. This intake is within the range of polyunsaturated fat consumption reported in a clinical trial of olive oil and nut supplementation to reduce cardiovascular endpoints.²¹

Described epidemiologic associations of diet and carotid disease are supported by known physiologic mechanisms of atherosclerosis development. For example, feeding studies have suggested that polyunsaturated fat consumption reduces systemic markers of inflammation such as C-reactive protein and replacement of dietary saturated fats with polyunsaturated fats directly reduces low-density lipoprotein concentration.²² Lower GI diets result in lower postprandial blood sugar. Postprandial hyperglycemia is a recognized risk factor for cardiovascular disease in both diabetics and non-diabetics.²³ One possibility is that fat consumption may be more important than the effect of GI for atherosclerosis development, which is supported by a recent clinical trial that demonstrated no impact of low GI diets in cardiovascular disease prevention.²⁴ We suggest that these mechanisms may be relevant to disease progression and agree that polyunsaturated fat intake requires further study to confirm the effect on cardiovascular disease prevention.

There are several limitations to our study. Although it is a strength is that we are able to prospectively capture midlife eating patterns and the impact on carotid disease later in life, a limitation is that dietary patterns at study onset may not reflect the lifelong eating habits of participants. It is possible that participants switch toward an unhealthy diet as they age, resulting in underestimation of effect size by misclassification. Additionally, food frequency questionnaires are prone to over or underreporting consumption, and therefore the baseline measurements in our study may not reflect a participant's actual diet. It is possible that reverse causation is present, meaning that those with underlying risk factors for cardiovascular disease are more likely to modify their diet toward a healthier pattern to prevent disease progression. Finally, the number of participants with a lipid core is small compared to the total sample size; therefore we may not have adequate power to detect a small effect size. It is also possible we may have seen stronger associations with diet and carotid disease in a higher risk population, such as diabetic patients or participants with cardiovascular disease. A strength of the current study is that confounders were rigorously measured as a part of the ARIC cohort. MRI protocols, patient recruitment and MRI interpretation was standardized across centers. Additionally, there were high rates of patient follow-up within the ARIC cohort, allowing longitudinal data to be collected over 18 years.

This work is important because carotid wall thickness is a surrogate for systemic vascular disease (both coronary artery disease and peripheral vascular disease),²⁵ and is a risk factor for subsequent plaque development, which is a direct cause of ipsilateral stroke.²⁶ Understanding the association of dietary components with high-risk plaques can lead to improved patient counseling and novel non-pharmacologic interventions to reduce disease burden. The association with diet and carotid disease is not greater than that of vascular risk factors diabetes, hypertension and cholesterol level. Diet may be a modest contributor to the development of lipid cores (likely via lipid accumulation in the carotid wall, as measured by wall thickness) that may lead to stroke. Because dietary modification is safe and part of

overall health and well being, dietary influences on vascular health require more investigation to inform patient-based interventions of dietary modification.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank the staff and participants of the ARIC study for their important contributions.

Financial support

The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C) with the ARIC carotid MRI examination funded by U01HL075572-01.

References

1. O'Leary DH, Polak JF, Kronmal RA, et al. Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. The CHS Collaborative Research Group. *Stroke*. 1992; 23(12):1752–1760. [PubMed: 1448826]
2. Petersen KS, Clifton PM, Keogh JB. The association between carotid intima media thickness and individual dietary components and patterns. *Nutr Metab Cardiovasc Dis*. 2014; 24(5):495–502. [PubMed: 24374005]
3. Nettleton JA, Schulze MB, Jiang R, Jenny NS, Burke GL, Jacobs DR. A priori-defined dietary patterns and markers of cardiovascular disease risk in the Multi-Ethnic Study of Atherosclerosis (MESA). *The American Journal of Clinical Nutrition*. 2008; 88(1):185–194. [PubMed: 18614740]
4. Millen BE, Quatromoni PA, Nam B-H, O'Horo CE, Polak JF, D'Agostino RB. Dietary Patterns and the Odds of Carotid Atherosclerosis in Women: The Framingham Nutrition Studies. *Preventive Medicine*. 2002; 35(6):540–547. [PubMed: 12460521]
5. Liese AD, Nichols M, Hodo D, et al. Food intake patterns associated with carotid artery atherosclerosis in the Insulin Resistance Atherosclerosis Study. *British Journal of Nutrition*. 2010; 103(10):1471–1479. [PubMed: 20092665]
6. Dickinson S, Brand-Miller J. Glycemic index, postprandial glycemia and cardiovascular disease. *Current opinion in lipidology*. 2005; 16(1):69–75. [PubMed: 15650566]
7. Tell GS, Evans GW, Folsom AR, Shimakawa T, Carpenter MA, Heiss G. Dietary fat intake and carotid artery wall thickness: the Atherosclerosis Risk in Communities (ARIC) Study. *American journal of epidemiology*. 1994; 139(10):979–989. [PubMed: 8178786]
8. Fitó M, Guxens M, Corella D, et al. Effect of a traditional mediterranean diet on lipoprotein oxidation: A randomized controlled trial. *Archives of Internal Medicine*. 2007; 167(11):1195–1203. [PubMed: 17563030]
9. Lindsay AC, Biasioli L, Lee JMS, et al. Plaque Features Associated With Increased Cerebral Infarction After Minor Stroke and TIA: A Prospective, Case-Control, 3-T Carotid Artery MR Imaging Study. *JACC: Cardiovascular Imaging*. 2012; 5(4):388–396. [PubMed: 22498328]
10. Saam T, Ferguson MS, Yarnykh VL, et al. Quantitative evaluation of carotid plaque composition by in vivo MRI. *Arteriosclerosis, thrombosis, and vascular biology*. 2005; 25(1):234–239.
11. Wagenknecht L, Wasserman B, Chambless L, et al. Correlates of carotid plaque presence and composition as measured by MRI: the Atherosclerosis Risk in Communities Study. *Circulation. Cardiovascular imaging*. 2009; 2(4):314–322. [PubMed: 19808612]
12. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. The ARIC investigators. *American journal of epidemiology*. 1989; 129(4):687–702. [PubMed: 2646917]

13. Wasserman BA, Astor BC, Sharrett AR, Swingen C, Catellier D. MRI measurements of carotid plaque in the atherosclerosis risk in communities (ARIC) study: Methods, reliability and descriptive statistics. *Journal of Magnetic Resonance Imaging*. 2010; 31(2):406–415. [PubMed: 20099354]
14. Wasserman BA, Sharrett AR, Lai S, et al. Risk factor associations with the presence of a lipid core in carotid plaque of asymptomatic individuals using high-resolution MRI: the multi-ethnic study of atherosclerosis (MESA). *Stroke*. 2008; 39(2):329–335. [PubMed: 18174475]
15. Stevens J, Ahn K, Juhaeri, Houston D, Steffan L, Couper D. Dietary Fiber Intake and Glycemic Index and Incidence of Diabetes in African-American and White Adults: The ARIC Study. *Diabetes Care*. 2002; 25(10):1715–1721. [PubMed: 12351467]
16. Mellen PB, Gao SK, Vitolins MZ, Goff DC Jr. Deteriorating dietary habits among adults with hypertension: DASH dietary concordance, NHANES 1988–1994 and 1999–2004. *Arch Intern Med*. 2008; 168(3):308–314. [PubMed: 18268173]
17. Astor BC, Sharrett AR, Coresh J, Chambless LE, Wasserman BA. Remodeling of Carotid Arteries Detected with MR Imaging: Atherosclerosis Risk in Communities Carotid MRI Study. *Radiology*. 2010; 256(3):879–886. [PubMed: 20651061]
18. Virani SS, Nambi V, Hoogeveen R, et al. Relationship between circulating levels of RANTES (regulated on activation, normal T-cell expressed, and secreted) and carotid plaque characteristics: the Atherosclerosis Risk in Communities (ARIC) Carotid MRI Study. *Eur Heart J*. 2011; 32(4):459–468. [PubMed: 20943669]
19. Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Saturated fat, carbohydrate, and cardiovascular disease. *Am J Clin Nutr*. 2010; 91(3):502–509. [PubMed: 20089734]
20. Sala-Vila A, Romero-Mamani ES, Gilabert R, et al. Changes in ultrasound-assessed carotid intima-media thickness and plaque with a Mediterranean diet: a substudy of the PREDIMED trial. *Arteriosclerosis, thrombosis, and vascular biology*. 2014; 34(2):439–445.
21. Estruch R, Ros E, Salas-Salvado J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *The New England journal of medicine*. 2013; 368(14):1279–1290. [PubMed: 23432189]
22. Hodson L, Skeaff CM, Chisholm WA. The effect of replacing dietary saturated fat with polyunsaturated or monounsaturated fat on plasma lipids in free-living young adults. *European journal of clinical nutrition*. 2001; 55(10):908–915. [PubMed: 11593354]
23. Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *Jama*. 2002; 287(18):2414–2423. [PubMed: 11988062]
24. Sacks FM, Carey VJ, Anderson CA, et al. Effects of high vs low glycemic index of dietary carbohydrate on cardiovascular disease risk factors and insulin sensitivity: the OmniCarb randomized clinical trial. *JAMA*. 2014; 312(23):2531–2541. [PubMed: 25514303]
25. Zureik M, Touboul PJ, Bonithon-Kopp C, et al. Cross-sectional and 4-year longitudinal associations between brachial pulse pressure and common carotid intima-media thickness in a general population. The EVA study. *Stroke*. 1999; 30(3):550–555. [PubMed: 10066851]
26. Touboul PJ, Labreuche J, Vicaud E, Amarenco P. Carotid intima-media thickness, plaques, and Framingham risk score as independent determinants of stroke risk. *Stroke*. 2005; 36(8):1741–1745. [PubMed: 16020769]

Highlights

- Diet measured at midlife, particularly carbohydrate and fat intake, may predict carotid atherosclerosis development 18 years later.
- Low and high polyunsaturated fat intake was associated with reduced odds of lipid core presence compared to those with intermediate intake.
- GI and polyunsaturated fat intake were not associated with high-risk plaque features such as lipid core presence independent of traditional vascular risk factors.

Figure 1. Change in maximum wall thickness by diet components

Figure 1 shows the change in maximum wall thickness per unit increase in energy-adjusted dietary components, as is modeled by a cubic spline. The reference category is the 50th percentile for each panel, and the knots are at the 5, 35, 65 and 95 percentile. Associations for glycemic index (1A), polyunsaturated fat (1B), saturated fat (1C), and total fat (1D) are shown. Models are adjusted for total calories, age, sex, race-center, height and height-squared and history of smoking.

Table 1

Participant characteristics by DASH Diet Score.

	DASH ≥ 4.5	DASH < 4.5	<i>p</i> -value
Women, %	60.9	47.6	<0.001
<u>Age (years)</u>			
Baseline	54.5 (5.5)	53.4 (5.5)	<0.001
Year 18	72.0 (5.5)	70.9 (5.5)	<0.001
Black, %	15.7	23.7	<0.001
<u>Education</u>			
Less than high school	8.6	18.8	<0.001
High school graduate ^a	41.6	42.5	
More than high school	49.8	38.7	
Height (m)	1.66 (0.09)	1.68 (0.10)	<0.001
Current or former smoking, %	50.3	56.0	0.037
Total cholesterol (mg/dl)			
Baseline	215.3 (40.0)	214.2 (39.1)	0.600
Year 18 ^b	206.2 (29.0)	201.2 (28.8)	0.002
History of hypertension, %			
Baseline	24.4	22.1	0.308
Year 18	63.5	69.2	0.025
History of diabetes, %			
Baseline	6.5	6.1	0.814
Year 18	21.4	25.7	0.069
Total calories (kcal/day)	1398.3 (459.6)	1676.7 (571.3)	<0.001
Glycemic index (daily intake)	77.5 (12.2)	72.6 (16.7)	<0.001
Glycemic load (daily intake)	140.7 (19.0)	131.4 (23.1)	<0.001
Total fat (g/day)	67.8 (9.8)	80.5 (11.2)	<0.001
Polyunsaturated fat (g/day)	4.5 (1.3)	5.2 (1.4)	<0.001
Saturated fat (g/day)	9.8 (2.3)	12.9 (2.6)	<0.001

The Dietary Approaches to Stop Hypertension (DASH) Diet Score was used to define better diet quality (>4.5) and non-optimal diet quality (<4.5). Participants with better diet quality met at least half of the recommended daily intake as specified by the DASH diet. Estimates are mean (SD) or percent.

^aIncludes vocational school;

^btime-weighted average over 5 visits.

Table 2

Partial correlations of energy-adjusted dietary scores to covariates.

	Glycemic index	Glycemic load	Total carbohydrates	Total fat	Polyunsaturated fat	Saturated fat
Glycemic index	1.0					
Glycemic load	0.575	1.0				
Total carbohydrates	0.533	0.949	1.0			
Total fat	-0.429	-0.768	-0.827	1.0		
Polyunsaturated fat	-0.147	-0.286	-0.328	0.440	1.0	
Saturated fat	-0.426	-0.647	-0.658	0.787	0.184	1.0
DASH Diet Score	0.127	0.158	0.300	-0.524	-0.238	-0.522

All values represent partial correlation, R. All *p* values were <0.001.

The Dietary Approaches to Stop Hypertension (DASH) Diet Score was used to define better diet quality with a higher score defined as better diet quality.

Table 3

Quintiles (Q) of dietary components and lipid core presence.

	Lipid core absent	Lipid core present	p-value
Glycemic index			
Q1	121 (20.9)	105 (19.4)	0.413
Q2–4	343 (59.3)	313 (57.8)	
Q5	114 (19.7)	124 (22.9)	
Glycemic load			
Q1	113 (19.6)	116 (21.6)	0.235
Q2–4	356 (61.6)	307 (56.6)	
Q5	109 (18.9)	118 (21.8)	
Total carbohydrates			
Q1	117 (20.2)	121 (22.3)	0.518
Q2–4	353 (61.1)	313 (57.8)	
Q5	108 (18.7)	108 (19.9)	
Total fat			
Q1	110 (19.0)	115 (21.2)	0.610
Q2–4	342 (59.2)	317 (58.5)	
Q5	126 (21.8)	110 (20.3)	
Polyunsaturated fat			
Q1	134 (23.2)	107 (19.7)	0.284
Q2–4	324 (56.1)	327 (60.3)	
Q5	120 (20.8)	108 (19.9)	
Saturated fat			
Q1	113 (19.6)	114 (21.0)	0.817
Q2–4	351 (60.7)	325 (60.0)	
Q5	114 (19.7)	103 (19.0)	
DASH Diet Score			
Q1	141 (24.4)	146 (26.9)	0.622
Q2–4	324 (56.1)	294 (54.2)	
Q5	113 (19.6)	102 (18.8)	

Values are N (%).

The Dietary Approaches to Stop Hypertension (DASH) Diet Score defines better diet quality with a higher score.

Table 4

Odds of lipid core presence by quintile (Q) of dietary components.

Glycemic index	Model 1	p-value	Model 2	p-value	Model 3	p-value
	Q1 0.94 (0.61, 1.46)	0.795	0.80 (0.50, 1.28)	0.349	0.85 (0.53, 1.37)	0.505
	Q5 0.95 (0.64, 1.40)	0.773	1.05 (0.68, 1.62)	0.833	1.09 (0.70, 1.71)	0.706
Glycemic load	Q1 1.45 (0.94, 2.25)	0.093	1.53 (0.96, 2.44)	0.076	1.51 (0.94, 2.41)	0.086
	Q5 1.19 (0.80, 1.77)	0.397	1.30 (0.83, 2.04)	0.253	1.28 (0.81, 2.03)	0.288
Total fat	Q1 1.08 (0.72, 1.62)	0.706	0.95 (0.61, 1.49)	0.635	0.89 (0.57, 1.41)	0.624
Polyunsaturated fat	Q1 0.64 (0.42, 0.96)	0.029	0.62 (0.40, 0.95)	0.028	0.58 (0.37, 0.89)	0.013
	Q5 0.64 (0.42, 0.98)	0.041	0.69 (0.43, 1.11)	0.122	0.69 (0.43, 1.12)	0.135
Saturated fat	Q1 1.14 (0.77, 1.69)	0.503	1.08 (0.69, 1.68)	0.740	1.07 (0.68, 1.68)	0.782
	Q5 1.05 (0.67, 1.62)	0.841	1.01 (0.63, 1.61)	0.958	1.04 (0.65, 1.68)	0.866
DASH Diet Score	Q1 0.97 (0.66, 1.44)	0.895	1.01 (0.66, 1.56)	0.840	0.99 (0.64, 1.54)	0.966
	Q5 0.76 (0.51, 1.14)	0.189	0.80 (0.51, 1.26)	0.337	0.74 (0.47, 1.17)	0.195

Restricted to wall thickness >1.5 mm (n=1120); reference group is Q2-4.

Values displayed are odds ratio (95% confidence interval), *p*-value.

Model 1: adjusted for total calories, age, sex, race-center, height and height-squared, history of smoking.

Model 2: adjusted for variables in Model 1 and maximum wall thickness.

Model 3: adjusted for variables in Model 2 and total cholesterol, cumulative (5 visits), history of diabetes, history of hypertension. The Dietary Approaches to Stop Hypertension (DASH) Diet Score defines better diet quality with a higher score.