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Carbohydrate Intake in Relation to Cardiovascular Risk Factors in the National Health and Nutrition Examination Survey (NHANES) – A Cross-sectional Study

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2019

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An abstract of
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Abstract

Carbohydrate Intake in Relation to Cardiovascular Risk Factors in the National Health and Nutrition Examination Survey (NHANES) – A Cross-sectional Study

By Aolei Chen

Background: Cardiovascular disease is the leading cause of mortality in many western countries. Previous studies have shown that dietary practices might impact cardiovascular health. We aimed to investigate the association between low carbohydrate diets and cardiovascular risk factors using nationally representative U.S. data.

Methods: We conducted a cross-sectional study among U.S. adults 18 years or older using data from the National Health and Nutrition Examination Survey (NHANES) cycles 2015 to 2018. Demographic data, current health status, physical activities, anthropometric measurements, dietary data (total energy, carbohydrate, fat, protein intake), cardiovascular biomarkers (systolic blood pressure, blood levels of total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, C-reactive protein) and type-2 diabetes indicators (fasting blood glucose and insulin) were included in the study. Low-carbohydrate-diet scores were developed using deciles of percentages of energy provided by protein, carbohydrate and fat. Participants in the lowest decile of carbohydrate intake received 10 points and those in the highest decile of carbohydrate intake were given 1 point. Other deciles received the corresponding score (9,8,7,6,5,4,3 and 2, respectively). For protein and fat intakes, the scoring procedure was reversed with lowest intakes receiving the lowest scores. The overall low-carbohydrate-diet score was computed by summing all points across the three macronutrients. The lowest scores represented participants having highest carbohydrate intakes and lowest fat and protein intakes, while the highest scores indicated the lowest carbohydrate intakes and highest fat and protein intakes. Simple and multiple linear regression analyses were conducted. Age, sex, race, family poverty income ratio, physical activity, educational level, weight status, smoking status and alcohol consumption were included as confounders in multivariate models.

Results: After controlling for all potential confounders, the low-carbohydrate-diet score was inversely associate with triglyceride level (β=0.87; 95%CI, 0.75-0.99) and positively associated with high-density lipoprotein cholesterol level (β=1.08; 95%CI, 1.03-1.14). The low-carbohydrate-diet score was not associated with systolic blood pressure, total cholesterol, low-density lipoprotein cholesterol, fasting insulin and the Homeostatic Model Assessment for Insulin Resistance.

Conclusion: This study supports the premise that low carbohydrate dietary practices may be associated with selected markers of lower cardiovascular risk among U.S. adults. Long-term prospective cohort studies are needed to confirm these findings.

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Introduction

Cardiovascular disease is the leading cause of death for most racial and ethnic groups in western countries (1). Worldwide, approximately 18 million people die from cardiovascular diseases annually, contributing to 31% of all deaths (2, 3). It is estimated that the U.S. national annual costs for care of adults with cardiovascular disease will increase to $1.5 trillion by 2030 (4).

Various risk factors including age (5), sex (6), smoking (7), obesity and physical activity (8) are related to cardiovascular health. Dietary practices, especially consuming a low-carbohydrate diet, may also play a vital role in affecting cardiovascular health (9).

Previous research has suggested that a low-carbohydrate diet may be effective for promoting weight loss (10, 11). According to a six-month randomized trial of 53 healthy, obese female volunteers, restricting the daily intake of carbohydrate to a very low level, less than 30% of total energy intake, increases lipid oxidation and energy expenditure, thus promoting a negative energy balance to facilitate weight loss (9). The analysis of a dietary pattern, such as a low-carbohydrate diet, considers the whole diet rather than individual nutrients or foods. Examining the totality of diet captures synergistic relationships between various dietary constituents (12, 13). For example, those on a low-carbohydrate diet would alternatively derive most of their energy intake from fat and protein (14). As high intakes of fat might detrimentally affect cardiovascular health, several studies have been conducted to estimate the potential association between low-carbohydrate diet and cardiovascular risk (4, 9, 14), but the results remain inconsistent. Findings from a recent meta-analysis of 38 randomized controlled trials conducted in many countries with the number of participants ranging from 28 to 811 showed that low-carbohydrate diets are effective at improving lipid profiles, compared to low-fat diets (15). However, an earlier meta-analysis of 5 trials including 447 individuals showed no significant association between low-carbohydrate diets and deleterious effects on cardiovascular risk (14). Few of the existing studies above were conducted on nationally representative populations.

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative dataset that features data on the nutrition and cardiovascular health status of the U.S. population. The goal of our study is to evaluate the cardiovascular health benefits or risks related to consumption of a low-carbohydrate diet.

Methods

Study Design

The NHANES is a large cross-sectional survey that is designed to assess the health and nutritional status of U.S. civilians. Data collection is ongoing with releases in 2-

year cycles. Detailed information of survey methods, data collection and interview procedures can be found on the NHANES website (16). We combined data from 2015-2016 and 2017-2018 survey cycles to increase statistical power.

Participants

In this study, participants aged 18 years or older from NHANES 2015 to 2018 were included. We excluded subjects who were pregnant or breast-feeding, missing dietary recall data, or missing outcome measures (e.g., blood levels of total cholesterol and high-density lipoprotein cholesterol). After exclusions, a total of 6,926 participants were included in the study (Figure 1).

Data collection

Demographic data

Demographic characteristics were collected in participants' homes by trained interviewers using a Computer-Assisted Personal Interviewing (CAPI) system. The CAPI system is programmed with built-in consistency checks to reduce data entry errors. It also uses online help screens to assist interviewers in defining key terms used in the questionnaire. Age, gender, race/ethnicity, education level and family income were recorded. Age in years at screening was reported for subjects under 79 years, while subjects aged 80 years or older were coded as '80'. Race/ethnicity was self-reported as Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black and other race, including multiracial. Education level was self-reported as less than high school, high school graduate/GED or equivalent and college graduate or above. Family income was calculated as the ratio of family income to poverty threshold, ranging from 0 to 5. Values of 5 or greater were recorded as 5.

Dietary data

Dietary variables were collected by two 24-hour dietary recall interviews. The first interview was collected in-person in the Mobile Examination Center and the second interview was collected by telephone 3 to 10 days later. All foods and beverages consumed during the 24-hour period prior to the interview (midnight to midnight) were collected to estimate intakes of energy, nutrients, and other food components. Energy (kcal), protein (gm), carbohydrate (gm), total fat (gm), cholesterol (mg) were estimated from the available recall data. Percent (%) energy from carbohydrate, protein, and fat were also estimated.

Other questionnaire data

Other potentially confounding variables including body mass index (BMI, weight in kg/ height in m^2), smoking status, physical activity level and alcohol consumption were collected. The body measurement data were collected in the Mobile Examination Center by trained health technicians. According to the CDC-definition for adult overweight and obesity (17), we further categorized the weight status as obese (BMI $\geq$30.0), overweight (BMI 25.0 to <30), normal weight (BMI 18.5 to <25) and underweight (BMI <18.5). Smoking status, alcohol use, physical activity level and history of diabetes were ascertained by trained interviewers using the CAPI system.

Subjects were asked about their current smoking status, and we further categorized the subjects into current smoker and current non-smoker (including non-smokers and former smokers). Alcohol consumption was categorized into risky alcohol use and non-risky alcohol use, according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA) recommendations (18). Risky alcohol use was defined for men younger than 65 years old as drinking more than 4 drinks per day or more than 14 drinks per week, and for women of all ages and men 65 years or older as drinking more than 3 drinks per day or more than7 drinks per week. Physical activity level was estimated using metabolic equivalent of task (MET) scores. According to WHO recommendations (19), a MET score at 600 MET-min/week was categorized as having moderate physical activity.

Examination and laboratory data

The outcomes of interest in this study are systolic blood pressure and other laboratory indicators that are associated with cardiovascular risk. Systolic blood pressure was measured by certified blood pressure examiners. Three consecutive systolic blood pressure readings were obtained, and the mean blood pressure was calculated and used for analysis. Total cholesterol (TC, mg/dL), triglycerides (TG, mg/dL), low-density lipoprotein cholesterol (LDL-C, mg/dL), high-density lipoprotein cholesterol (HDL-C, mg/dL), C-reactive protein (CRP, mg/L), fasting glucose (mmol/L) and fasting insulin (μU/mL) were measured using serum samples. Serum samples were processed, stored, and shipped to the University of Minnesota, Minneapolis, MN for analysis. Homeostatic model assessment (HOMA) was derived to gauge insulin resistance, and was calculated as fasting insulin (μU/ mL)×fasting glucose (mmol/L)/22.5 (20).

Calculation of the low-carbohydrate-diet Score

The exposure measure in this study was daily carbohydrate intake. To estimate the actual carbohydrate intake level, we computed a low-carbohydrate-diet (LCD) score (21-23) for each participant using deciles of percentages of energy provided by protein, carbohydrate and fat. Participants in the lowest decile of carbohydrate intake received 10 points and those in the highest decile of carbohydrate intake were given 1 point. Other deciles received the corresponding score (9,8,7,6,5,4,3 and 2, respectively). For protein and fat intakes, the scoring procedure was reversed with lowest intakes receiving the lowest scores. We then created the overall low-carbohydrate-diet score (continuous) by summing all the points for the three macronutrients, yielding total scores ranging from 3 to 30. The lowest scores indicated the highest carbohydrate intakes and lowest fat and protein intakes, while the highest scores indicated the lowest carbohydrate intakes and highest fat and protein intakes. Participants were also categorized by quintiles of low-carbohydrate-diet score (quintile 1: <11 (lowest carbohydrate intakes); quintile 2: 11-14; quintile 3: 15-18; quintile 4: 18-22; quintile 5: >22 (highest carbohydrate intakes)). We created a categorical LCD quintile based on the ranked variable to use in trend analyses. Participants in 1st quintile were coded as 1, and other quintiles received the corresponding values.

Statistical Analysis

All data were analyzed using R studio (version 3.6.2; R studio, Boston, Massachusetts). Sample weighting and specific survey procedures were used to account for the unequal selection probability and clustered design of the NHANES data. One-way analysis of variance (ANOVA) was used for continuous variables, and chi-square tests were used for categorical variables to compare participant characteristics and dietary intake across quintiles of the low-carbohydrate-diet score. Simple and multiple linear regression analyses were conducted to estimate the association between cardiovascular risk indicators and the low-carbohydrate-diet score as both continuous and as categorical predictor variables. Potential confounders including age (continuous), sex (male/female), race (Mexican American, Other Hispanic, non-Hispanic White, non-Hispanic Black, other race), family poverty income ratio (continuous), physical activity (MET≥600/MET<600), educational level (<high school/high-school graduate/>college graduate), weight status (underweight/normal/overweight/obese), current smoking status (current smoker/non-current smoker) and alcohol consumption (risky/non-risky alcohol use) were included in the multivariate models. All confounders were chosen a priori based on their importance as potential confounders as noted in previous publications. Statistical tests were two-sided, and significance was determined as $p<0.05$.

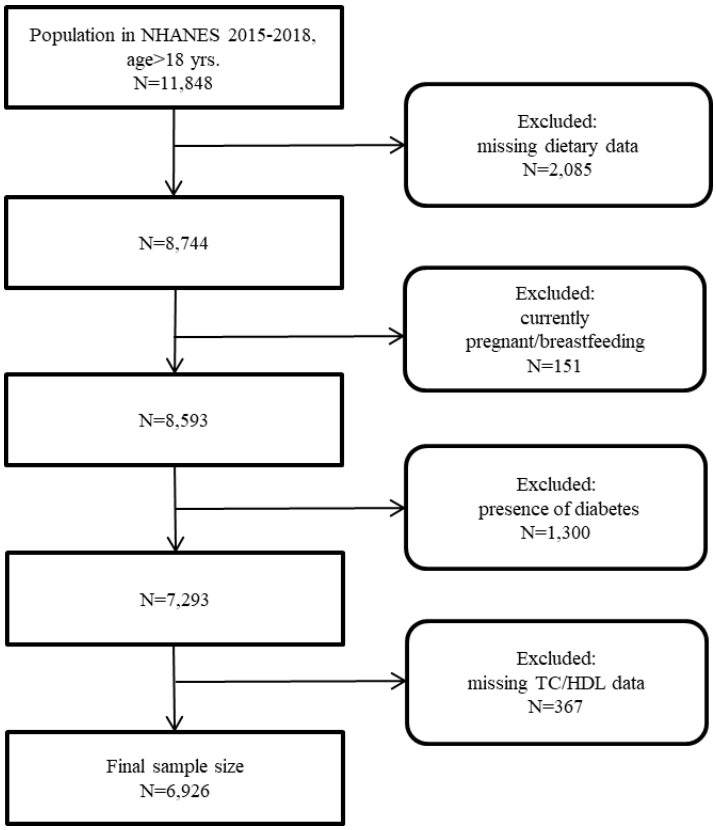

Figure 1. Flow Chart of Adult NHANES Participants 2015-2018 and Inclusion in Analyses

Results

A total of 6,926 participants were included in the analysis. Selected demographic characteristics of study participants across quintiles of the low-carbohydrate-diet (LCD) score are presented in Table 1. As expected, participants in the highest quintile of LCD score had the lowest carbohydrate intakes (36.7% of total energy intake) and highest protein and fat intake level (19.6% and 42.8% of total energy intake, respectively). No differences were found in mean age, sex distribution and physical activity level across quintiles of the LCD score. Compared to lower quintiles, participants in the highest quintile of LCD score were more likely to be non-Hispanic White and non-smokers and to have higher BMIs, educational attainment and physical activity levels ($p<0.05$).

The distributions of cardiovascular risk factors across quintiles of LCD score are presented in Table 2. Compared to participants in the lowest quintile of LCD score, mean HDL-C level in the 2nd, 3rd, 4th and 5th quintiles had significantly higher levels of HDL-C (51.8±15.5mg/dL vs. 54.5±16.6 mg/dL, 54.4±16.3 mg/dL, 55.6±17.6 mg/dL, 55.8±16.5mg/dL, respectively; $P_{trend}<0.05$). We did not observe significant differences for systolic blood pressure, or concentrations of serum TC, fasting TG, LDL-C, CRP, fasting glucose, fasting insulin and HOMA across quintiles of LCD score.

Regression coefficients for the association of cardiovascular risk factors with LCD scores are presented in Table 3. The LCD score was inversely associated with fasting TG levels. Compared to the lowest quintile, participants in the highest quintile of LCD score had lower fasting TG concentrations (crude: β=0.91; 95%CI, 0.86-0.97; $P_{trend}<0.01$). This association remained significant (β=0.86; 95%CI, 0.74-0.99; $P_{trend}=0.03$) after controlling for potential confounding factors (age, sex, educational level, current smoking status, physical activity level, alcohol consumption and family poverty income ratio). Further controlling for BMI did not meaningfully change the relationship between fasting TG and LCD score (β=0.87; 95%CI, 0.75-0.99; $P_{trend}=0.02$). Moreover, a positive relationship between HDL-C level and LCD score was found in the regression model. Both the crude and adjusted models showed that participants in the highest quintile of LCD score had 7 higher HDL-C concentrations than those in the lowest quintile (adjusted β=1.07; 95%CI,1.02-1.12; $P_{trend}<0.01$). Additional adjustment for BMI had little effect on the association between HDL-C and LCD score (β=1.08; 95%CI, 1.03-1.14; $P_{trend}<0.01$). We did not find a significant association between CRP level and LCD score in the crude or adjusted model 1 ($P_{trend}=0.68$ & 0.12, respectively). However, the association was strengthened after further adjustment for BMI. Compared to the lowest quintile, participants in the highest quintile of LCD score had lower CRP concentrations after adjustment for all confounding variables (β=0.80; 95%CI, 0.67-0.96; $P_{trend}=0.02$). Fasting glucose level was marginally associated with LCD score in the crude model only (β=1.01; 95%CI, 1.00-1.03; $P_{trend}=0.04$). Systolic blood pressure and other biomarkers including TC, LDL-C, fasting insulin and HOMA were not associated with the LCD score, either in crude or adjusted models.

Table 1. Demographic characteristics of the sample: NHANES 2015-2018[a]

	Quintiles of LCD score									
	1		2		3		4		5	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Cut points of quintiles										
	<11		11-14		15-18		18-22		>22	
Participants										
	1363		1364		1434		1366		1399	
Age (years)										
	47.4	18.0	48.7	18.4	47.1	18.5	47.4	18.3	47.4	18.1
Daily dietary intake										
Total energy (kcal)[b]	1969.1	790.6	2018.1	816.7	2069.5	821.0	2112.5	857.88	1988.7	818.1
Carbohydrate (%energy)[b]	60.2	5.9	52.1	5.2	47.6	4.1	43.1	4.1	36.7	5.7
Protein (%energy)[b]	12.3	2.5	14.6	3.5	15.9	3.8	17.0	4.4	19.6	4.4
Fat (%energy)[b]	27.7	5.2	31.8	5.8	35.0	5.3	38.4	5.7	42.8	5.4
Cholesterol (mg)[b]	188.2	133.6	251.2	147.2	295.8	167.6	344.8	193.7	412.1	239.8
Family poverty income ratio	2.8	2.8	2.3	1.5	2.4	1.6	2.5	1.6	2.7	1.7
Sex %										
Male	47		45		48		48		50	
Female	53		55		52		52		50	
Race/ethnicity % [b]										
Mexican American	14		15		17		13		14	
Other Hispanic	15		12		11		10		7	
Non-Hispanic White	32		35		35		40		41	
Non-Hispanic Black	22		21		22		23		23	
Other Race	17		16		15		16		15	
Educational level % [b]										
< High school	23		19		17		15		15	
High-school Graduate	52		55		57		56		56	
College graduate or above	26		26		26		29		29	
Current smoking status % [b]										
Non-current smoker	54		50		44		45		40	
Current Smoker	46		50		56		55		60	
Current weight status % [b, c]										
Underweight	3		1		1		1		1	
Normal	29		30		26		28		24	
Overweight	33		34		33		30		31	
Obese	36		35		40		41		44	
Physical Activities %										
MET scores <600	66		66		66		65		65	
MET scores ≥600	34		34		34		35		35	

Alcohol Consumption % [b]					
Risky alcohol use	34	29	30	26	27
Non-risky alcohol use	66	71	70	74	73

a: Values are means ± SD unless indicated.

b: p<0.05. P values result from ANOVA for continuous variables and chi-square test for categorical variables.

c: The weight status was classified as underweight (BMI <18.5), normal weight (BMI 18.5 to <25), overweight (BMI 25.0 to <30) and obese (BMI ≥30.0).

Table 2. Distribution of cardiovascular risk factors by LCD score categories: NHANES 2015-2018 [a]

	Quintiles of LCD score									
	1		**2**		**3**		**4**		**5**	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Cut points of quintiles	<11		11-14		15-18		18-22		>22	
Participants	1363		1364		1434		1366		1399	
Total Cholesterol (mg/dL)	190.0	40.7	188.8	39.5	190.2	40.7	191.0	41.2	190.8	41.0
Triglyceride (mg/dL)	110.4	78.5	108.2	120.8	109.3	77.1	106.1	123.9	100.9	65.2
LDL-Cholesterol (mg/dL)	113.5	35.7	110.3	34.5	113.7	34.0	111.3	33.9	113.9	37.2
HDL-Cholesterol (mg/dL) [b]	51.8	15.5	54.5	16.6	54.4	16.3	55.6	17.6	55.8	16.5
C-Reactive Protein (mg/L)	3.9	7.4	3.8	8.1	3.8	6.0	3.9	7.5	3.6	6.1
Fasting glucose (mmol/L)	5.7	0.8	5.7	0.9	5.8	1.0	5.8	1.0	5.8	0.9
Fasting insulin (μU/mL)	11.5	8.6	11.9	9.2	12.3	9.3	12.5	10.9	12.0	8.9
HOMA [c]	3.0	2.6	3.1	2.8	3.3	2.8	3.4	3.4	3.2	2.7

a: Values are means ± SD.

b: p<0.05 resulting from ANOVA.

c: HOMA (homeostatic model assessment) = fasting insulin (μU/ mL) x fasting glucose (mmol/L)/22.5.

Table 3. Association between cardiovascular risk factors and LCD score categories

	Quintiles of LCD score									
	1	**2**		**3**		**4**		**5**		**P_{trend}**
	β	β	95% CI	β	95% CI	β	95% CI	β	95% CI	
Cut points of quintiles	<11	11-14		15-18		18-22		>22		
Participants	1363	1364		1434		1366		1399		
Systolic blood pressure (mmHg)										
Crude	1	1.00	0.98-1.01	1.00	0.99-1.02	1.00	0.99-1.02	0.99	0.99-1.02	0.24
Model 1	1	0.99	0.97-1.02	0.99	0.97-1.02	1.00	0.97-1.03	1.00	0.97-1.02	0.85
Model 2	1	0.99	0.97-1.02	0.99	0.96-1.01	1.00	0.97-1.02	1.00	0.97-1.02	0.85
Total Cholesterol (mg/dL)										
Crude	1	0.99	0.98-1.01	1.00	0.99-1.02	1.01	0.99-1.02	1.01	0.99-1.02	0.27
Model 1	1	0.98	0.94-1.02	0.99	0.95-1.03	0.98	0.94-1.02	1.00	0.96-1.04	0.98

Model 2	1	0.99	0.95-1.03	0.99	0.95-1.03	0.98	0.94-1.02	1.00	0.96-1.04	0.94
Triglyceride (mg/dL)										
Crude	1	0.97	0.91-1.03	0.98	0.92-1.05	0.91	0.86-0.98	0.91	0.86-0.97	<0.01
Model 1	1	0.91	0.78-1.05	0.95	0.82-1.10	0.82	0.70-0.95	0.86	0.74-0.99	0.03
Model 2	1	0.93	0.80-1.08	0.95	0.82-1.10	0.81	0.70-0.95	0.87	0.75-0.99	0.02
LDL-Cholesterol (mg/dL)										
Crude	1	0.97	0.94-1.01	1.01	0.97-1.04	0.99	0.96-1.02	1.00	0.97-1.04	0.64
Model 1	1	0.99	0.91-1.09	1.01	0.93-1.11	0.97	0.89-1.06	1.02	0.94-1.12	0.69
Model 2	1	1.01	0.92-1.10	1.02	0.93-1.11	0.97	0.89-1.06	1.03	0.94-1.12	0.69
HDL-Cholesterol (mg/dL)										
Crude	1	1.05	1.03-1.07	1.05	0.13-1.07	1.07	1.05-1.10	1.07	1.05-1.10	<0.01
Model 1	1	1.02	0.97-1.07	1.05	1.00-1.10	1.09	1.03-1.14	1.07	1.02-1.12	<0.01
Model 2	1	1.02	0.97-1.07	1.06	1.01-1.11	1.09	1.03-1.14	1.08	1.03-1.14	<0.01
C-Reactive Protein (mg/L)										
Crude	1	0.97	0.88-1.07	1.02	0.94-1.12	1.00	0.91-1.10	1.01	0.92-1.10	0.68
Model 1	1	0.86	0.71-1.06	0.91	0.74-1.11	0.86	0.70-1.05	0.84	0.69-1.02	0.12
Model 2	1	0.89	0.74-1.06	0.86	0.72-1.03	0.86	0.72-1.04	0.80	0.67-0.96	0.02
Fasting glucose (mmol/L)										
Crude	1	1.00	0.99-1.02	1.02	1.00-1.03	1.01	0.99-1.02	1.01	0.99-1.03	0.04
Model 1	1	1.00	0.96-1.04	1.02	0.99-1.06	1.04	0.99-1.07	1.01	0.98-1.05	0.24
Model 2	1	1.01	0.97-1.04	1.02	0.99-1.06	1.04	0.99-1.07	1.01	0.98-1.05	0.23
Fasting insulin (μU/mL)										
Crude	1	1.03	0.96-1.11	1.06	0.98-1.14	1.03	0.96-1.11	1.05	0.97-1.13	0.23
Model 1	1	0.94	0.77-1.14	1.02	0.83-1.24	0.99	0.81-1.22	0.93	0.76-1.12	0.58
Model 2	1	1.02	0.86-1.20	1.00	0.85-1.17	0.99	0.83-1.16	0.96	0.82-1.12	0.50
HOMA										
Crude	1	1.03	0.95-1.12	1.08	0.99-1.17	1.04	0.96-1.13	1.06	0.98-1.15	0.14
Model 1	1	0.93	0.75-1.15	1.04	0.84-1.29	1.02	0.82-1.28	0.94	0.76-1.15	0.78
Model 2	1	1.01	0.85-1.21	1.02	0.85-1.21	1.02	0.85-1.22	0.97	0.82-1.15	0.74

a: Outcome variables for 2nd, 3rd, 4th and 5th quintile groups are compared to 1st quintile group (referent)

b: Adjusted for age, gender, race/ethnicity, educational level, current smoking status, physical activities, alcohol consumption and family income.

c: Adjusted all variables in Model 1 + BMI.

Discussion

This cross-sectional study observed that a low-carbohydrate-diet (LCD) score was inversely associated with serum TG and positively associated with HDL-C levels. This association persisted in multivariate models accounting for several confounders. We failed to find significant associations between this score and SBP, or other serum biomarkers including TC, LDL-C, fasting insulin and HOMA-IR. To the best of our knowledge, this is the first observational study to investigate the relationship between the LCD score and cardiovascular biomarkers in a nationally representative sample of

U.S. adults. As cardiovascular disease is the leading cause of mortality in the U.S., our study does have significant public health implications. Aside from being an efficient way to lose weight, findings from this study provide additional evidence for the benefit of a LCD on cardiovascular health.

Low-carbohydrate diets have a relatively lower level of carbohydrate intake with higher levels of fat and protein. This type of dietary pattern had been primarily suggested for management of diabetes and other related metabolic syndromes (24). However, previous studies on potential cardiovascular benefits and LCD remains inconsistent. In the present study, we found an inverse association between LCD score and TG level. The findings are in agreement with several randomized trials and meta-analysis in weight-loss patients (4, 14). For example, a randomized trial with 148 participants enrolled in New Orleans, Louisiana from 2008 to 2011 showed that aside from weight loss, restricting carbohydrate intake might be an option to reduce cardiovascular risk. Previous studies suggested that the reduction of TG observed with a LCD only appeared in obese patients who experienced weight loss (25). However, in our cross-sectional study, participants were not limited to the obese population. We adjusted for BMI as a confounder in the multivariate analysis, and the results remained significant (β=0.87; P_{trend}=0.023). Therefore, our results suggested that the benefit of LCD on TG level might be independent of body size or weight loss.

We also found a positive relationship between LCD score and HDL-C level in the present study. This result is consistent with other cross-sectional studies from various regions (26-29), where multiple races of participants were enrolled. Since our study used national representative data from U.S. adults and was not limited to specific racial/ethnic groups, these findings provide additional evidence for the effect of LCD on HDL-C in a broader population. HDL-C had been proven to play a key role in reverse cholesterol transport and mediating molecular mechanisms to promote cardiovascular health (30). Therefore, our finding on the relationship between HDL-C and LCD provides additional evidence for the cardiovascular benefit of LCD.

Our results showed that LCD was not associated with levels of SBP, TC and LDL-C. The findings are consistent with cross-sectional results in a sample of 2,941 Framingham Offspring Participants (31) of no significant relationship between total carbohydrate intake and TC or LDL-C levels. However, our findings are in disagreement with a recent meta-analysis of 12 studies (4 randomized trials, 5 prospective cohorts, 1 retrospective cohort, with sample sizes ranging from 20 to 178) (32), in which inverse associations between consumption of a very-low-calorie ketogenic diet with SBP and TC level were observed. Notably, this meta-analysis included only overweight and obese patients. If patients were following a ketogenic diet to lose weight, even losses of only 5-10% body weight improves lipid profiles (33).

In the current study, a trend for a reduction in CRP levels across LCD score groups were detected after controlling for all confounders, including BMI. This result is in line with a recent cross-sectional study from NHANES (34), which suggested a positive relationship between dietary carbohydrate intake and blood CRP concentrations in BMI-adjusted analyses. It has been reported that CRP level may be

positively associated with metabolic syndrome (35, 36) and may be an important indicator of future cardiovascular disease (34). Therefore, our study helps to strengthen the evidence that LCD is related to lower risk of cardiovascular disease. Finally, no significant associations were found between LCD and type 2 diabetes risk factors (fasting glucose, fasting insulin and HOMA) in the current study. This finding conflicts with existing evidence for the use of a LCD as an effective strategy for glycemic control in diabetic populations (37, 38). Our study excluded participants who had current diabetes or had a history of diabetes (either type 1 or type 2) because of the cross-sectional design.

The biggest strength of our study is that we examined the association between LCD and cardiovascular risk factors in the nationally representative U.S. NHANES, thus, can be generalized nationwide. Additionally, compared to self-reported data, the anthropometry data in our study were measured using standardized methods. We also took several confounders into account in the multivariate analysis.

Some limitations need to be considered in the current study as well. Firstly, this is a cross-sectional study. We were unable to determine the cause-and-effect between LCD and cardiovascular risk factors due to the study design. Secondly, the dietary intake information was collected via self-reported 24-hour dietary recalls on two days, which might lead to information bias. To minimize misclassification of participants due to under-reporting of total intake, we used the LCD score based on percentage of energy derived from carbohydrate in the analysis. Thirdly, other unmeasured confounding might still exist. It has been suggested that the potential efficacy of LCD might be influenced by the overall quality of the diet (38), which we did not assess. This could be an important confounder to be addressed in a future study. Finally, some of the observed associations were relatively small and may not be biologically meaningful.

In conclusion, findings from this large cross-sectional study add to the growing evidence that a low carbohydrate diet pattern may be associated with lower cardiovascular risk among U.S. adults. Future long-term prospective cohort studies and randomized controlled dietary studies are warranted to confirm the findings.

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