Diet Soft Drink Consumption is Associated with an Increased Risk of Vascular Events in the Northern Manhattan Study

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BACKGROUND: Diet and regular soft drinks have been associated with diabetes and the metabolic syndrome, and regular soft drinks with coronary heart disease.
OBJECTIVE: To determine the association between soft drinks and combined vascular events, including stroke.
DESIGN: A population-based cohort study of stroke incidence and risk factors.
PARTICANTS: Participants (N=2564, 36% men, mean age 69±10, 20% white, 23% black, 53% Hispanic) were from the Northern Manhattan Study.
MAIN MEASURES: We assessed diet and regular soft drink consumption using a food frequency questionnaire at baseline, and categorized: none (<1/month, N=1948 diet, N=1333 regular), light (1/month-6/week, N=453 diet, N=995 regular), daily (≥1/day, N=163 diet, N=338 regular). Over a mean follow-up of 10 years, we examined the association between soft drink consumption and 591 incident vascular events (stroke, myocardial infarction, vascular death) using Cox models.
KEY RESULTS: Controlling for age, sex, race/ethnicity, education, smoking, physical activity, alcohol consumption, BMI, daily calories, consumption of protein, carbohydrates, total fat, saturated fat, and sodium, those who drank diet soft drinks daily (vs. none) had an increased risk of vascular events, and this persisted after controlling further for the metabolic syndrome, peripheral vascular disease, diabetes, cardiac disease, hypertension, and hypercholesterolemia (HR=1.43, 95% CI=1.06–1.94). There was no increased risk of vascular events associated with regular soft drinks or light diet soft drink consumption.
CONCLUSIONS: Daily diet soft drink consumption was associated with several vascular risk factors and with an increased risk for vascular events. Further research is needed before any conclusions can be made regarding the potential health consequences of diet soft drink consumption.

KEY WORDS: diet; epidemiology; myocardial infarction; stroke; cardiovascular disease.

Electronic supplementary material *The online version of this article (doi:10.1007/s11606-011-1968-2) contains supplementary material, which is available to authorized users.*

Received June 16, 2011
Revised October 14, 2011
Accepted December 2, 2011

Published online: 27 January 2012

J Gen Intern Med
DOI: 10.1007/s11606-011-1968-2

INTRODUCTION

An association between sugar-sweetened soft drinks and obesity, insulin sensitivity, and hypertension may be attributed to their high caloric and sugar load, and lack of nutrients.[1–3] The popularity of sugar-sweetened soft drinks and rising rate of obesity underscore the need for healthier beverages. Artificially-sweetened "diet" soft drinks have been marketed as healthier alternatives due to their lack of calories. However, recent studies suggested that diet soft drink consumption may also be associated with health consequences, particularly type 2 diabetes and the metabolic syndrome,[4–6] risk factors for cardiovascular disease (CVD), ischemic stroke, and all-cause mortality.[7–11]

A report from the Nurses' Health Study (NHS), which includes only women, showed an increased risk of coronary heart disease (CHD) with greater consumption of sugar-sweetened beverages, and particularly soft drinks.[12] In that study, an increased risk of CHD was associated with diet soft drink consumption after adjustment for age only, but the association was no longer significant after adjusting for other cardiac risk factors. To our knowledge these analyses have not been replicated, and no studies have examined the association between diet soft drink consumption and risk of all vascular events, including stroke. Therefore, the primary objective of this study is to examine the relationship between diet and regular soft drink consumption and risk for stroke, myocardial infarction (MI), and vascular death in a multi-ethnic population-based cohort.

METHODS

Study Population

The Northern Manhattan Study (NOMAS) is a cohort study designed to determine stroke incidence, risk factors, and

prognosis in a multi-ethnic urban population. Study details were published previously.[13]

Eligible participants: a) were stroke-free; b) >40 years old; and c) resided in Northern Manhattan for ≥ 3 months, with a household telephone. Subjects were identified by random-digit dialing (91% telephone response rate), and recruited to have an in-person interview and assessment. The enrollment response rate was 75%, and 3,298 subjects were enrolled. For this analysis, participants with a previous MI (n=175) and those without information on soft drink consumption (n=563) were excluded. The study was approved by the Columbia University and University of Miami IRBs and all subjects provided informed consent.

Baseline Evaluation (1993-2001)

Data were collected through interviews with trained research assistants in English or Spanish. Physical examinations were conducted by study physicians. Race-ethnicity was based upon self-identification using questions modeled after the US census and conforming to standard definitions outlined by Directive 15.[14] Standardized questions were adapted from the Behavioral Risk Factor Surveillance System by the Centers for Disease Control regarding hypertension, diabetes, smoking, and cardiac conditions.[15] Measurement of blood pressure (BP) and fasting blood specimens for glucose and lipids, and the definitions of moderate-heavy physical activity and moderate alcohol use have been described previously.[16–18] Metabolic syndrome was classified by the criteria of the Third Report of the National Cholesterol Education Program: Adult Treatment Panel III.[19]

Diet

At baseline, participants were administered a modified Block National Cancer Institute food frequency questionnaire by trained research assistants, in English or Spanish.[20] The questionnaire contained questions regarding the average consumption of diet soft drinks as well as regular soft drinks. The possible responses were: never or<1/month, 1-3/month, 1/week, 2-4/week, 5-6/week, 1/day, 2-3/day, 4-5/day, and ≥6/day.

The primary exposures of interest, average diet and regular soft drink consumption, were examined categorically: none (<1/month, referent), light (1/month-6/week), and daily (1+/day). Diet and regular soft drink consumption was also examined continuously as soft drinks per week, after assigning the middle value for each category (< 1/month=0/week, 1-3/month=0.47/week, 1/week, 2-4/week=3/week, 5-6/week=5.5/week, 1/day=7/week, 2-3/day=17.5/week, 4-5/day=31.5/week, ≥6/day=45.5/week).

Annual Prospective Follow-up

Participants were screened annually by telephone to determine changes in vital status, detect neurologic events, document interval hospitalizations, and review risk factor status, medication changes, and changes in functional status. Persons who screened positive had an in-person assessment, including chart review and physician examination. Hospital surveillance of admission and discharge data, including ICD-9 codes, also provided morbidity and mortality data.

Definition of Outcomes

The primary outcome was confirmed incident vascular event, defined as stroke, MI, or vascular death. Secondary outcomes were confirmed incident stroke, MI, and vascular death considered individually. Follow-up procedures and outcome classifications were detailed previously.[11,18]

Statistical Analysis

The unadjusted association between soft drink consumption and sociodemographics and vascular risk factors was examined using ANOVA and chi-square tests.

We constructed Cox proportional hazards models to examine the association between soft drink consumption and vascular events, and hazard ratios (HR) and 95% confidence intervals (CI) were calculated. Person-time of follow-up was accrued from baseline to the end of follow-up (March, 2011), outcome event, death or loss to follow-up, whichever came first. We used the following sequence of models: (1) adjusted for demographics (age, sex, race/ethnicity, education); (2) demographics, behavioral risk factors (smoking, physical activity, moderate alcohol consumption), daily diet (total kilocalories, grams of protein, total fat, saturated fat, carbohydrates, mg sodium), and BMI; (3) demographics, behavioral risk factors, diet, BMI, previous cardiac disease, peripheral vascular disease, metabolic syndrome, , history of diabetes, history of hypercholesterolemia, and history of hypertension; (4) demographics, behavioral risk factors, diet, waist circumference, previous cardiac disease, peripheral vascular disease, blood sugar, HDL cholesterol, LDL cholesterol, triglycerides, systolic BP, diastolic BP, and anti-hypertensive medication use. In all models, each type of soft drink was mutually adjusted. We examined possible interactions between each type of soft drink and age, sex, race/ethnicity, history of diabetes, BMI, and metabolic syndrome in model 3. Because self-reported kcal <500 or >4000 might indicate inaccurate reporting of dietary information, we conducted sensitivity analyses excluding these participants. We also conducted sensitivity analyses excluding all participants who were obese (BMI≥30), with a history of diabetes or metabolic

syndrome at baseline, to reduce the possibility of indication bias, or reverse causation, in which participants with preexisting vascular disease who are at an increased risk of vascular events may have switched from regular to diet soft drinks.

RESULTS

This study included 2,564 NOMAS participants with data on soft drink consumption. There was no association between availability of information on soft drink consumption and risk of vascular events, suggesting that selection bias was less likely to influence results. The mean age at baseline was 68.6±10.3 years, 36% of participants were men, 20% white, 23% black, 54% Hispanic, and 2% other race. Over a mean follow-up of 9.8 years, 591 vascular events accrued, including 225 strokes, 155 MIs, and 351 vascular deaths. Table 1 shows the frequency of diet and regular soft drink consumption.

In unadjusted analyses, frequent diet or regular soft drink consumption were associated with a number of baseline risk factors (Table 2), but there were some risk factors uniquely associated with only one type of soft drink. Frequent diet soft drink consumption was uniquely associated with white race, former smoking, hypertension, elevated blood sugar, lower HDL, elevated triglycerides, increased waist circumference, BMI, peripheral vascular disease, previous cardiac disease, and the metabolic syndrome. Frequent regular soft drink consumption was uniquely associated with male sex, black race, current smoking, carbohydrate consumption, greater diastolic BP, and lower prevalences of diabetes and hypercholesterolemia.

We found no association between regular soft drink consumption and risk of combined vascular events, adjusting for demographic and vascular risk factors (Table 3). Daily diet soft drink consumption was associated with an elevated risk of combined vascular events, adjusting for demographics. The association was attenuated after adjusting for vascular risk factors in models 3 and 4, but remained statistically significant. In model 3, those who drank diet soft drinks daily had a 43% increased risk of vascular events as compared to those who did not drink diet soft drinks. Light diet soft drink users did not have a significantly increased risk of vascular events. We observed no significant interaction between diet and regular soft drink consumption in relation to vascular disease risk.

While the number of daily diet soft drink consumers is too small to efficiently examine a dose-response relationship with vascular events within this group, it is interesting to note the relative distribution of cohort members and vascular event cases across daily diet soft drink consumption categories. Of the 163 daily diet soft drink consumers in the cohort (51 vascular events), 106 reported drinking 1/day (34 events), 42 reported 2-3/day (10 events), 14 reported 4-5/day (6 events), and 1 reported 6+/day (1 event).

Our findings remained significant in sensitivity analyses in which 75 participants with reported total daily kilocalorie consumption <500 or >4000 were excluded (not shown). The results also remained consistent when a score indicating adherence to a Mediterranean-style diet was included in the model (not shown). Adherence to a Mediterranean-style diet has been associated with decreased risk of vascular events in our cohort as well as others. We observed that the effect of diet soft drink consumption was greater among black participants vs. whites (interaction between continuous diet soft drinks/week and black vs. white race HR=1.06, 95% CI=1.01–1.11, p=0.03). In addition, we observed a negative interaction between regular soft drink consumption and BMI in relation to combined vascular events (interaction between continuous regular soft drinks/week and BMI HR=0.996, 95% CI=0.993–0.999, p=0.01).

When the vascular events were considered individually (Supplement Table 3b, available online), we observed no association for regular soft drink consumption after adjustment for vascular risk factors. We also observed no elevated risk of stroke or vascular death in relation to diet soft drink consumption. However, the data suggested a possible elevated risk of MI among daily diet soft drink consumers. In model 3, daily diet soft drink consumption was associated with a 66% increased risk of MI as compared to no diet soft drink consumption (95% CI=0.99–2.78, p=0.05). Light diet soft drink consumption was not associated with any of the separate vascular outcomes.

Table 4 shows the relationship between diet and regular soft drink consumption and combined vascular events after excluding all participants who were obese, with a history of diabetes or metabolic syndrome (N=1122 included, 237

Table 1. Frequency of Diet and Regular Soft Drink Consumption in NOMAS

Diet soft drinks	Regular soft drinks						
N (%)	<1/month	1–3/month	1/week	2–6/week	1/day	2+/day	Total
<1/month	901 (35)	258 (10)	144 (6)	359 (14)	184 (7)	82 (4)	1948 (76)
1–3/month	64 (3)	54 (2)	8 (<1)	12 (<1)	5 (<1)	2 (<1)	145 (6)
1/week	38 (1)	7 (<1)	35 (1)	13 (1)	5 (<1)	3 (<1)	101 (4)
2–6/week	112 (4)	7 (<1)	12 (<1)	65 (3)	5 (<1)	3 (<1)	207 (8)
1/day	76 (3)	5 (<1)	5 (<1)	1 (<1)	17 (1)	2 (<1)	106 (4)
2+/day	40 (2)	3 (<1)	2 (<1)	2 (<1)	3 (<1)	7 (<1)	57 (2)
Total	1231 (48)	337 (13)	206 (8)	452 (18)	219 (9)	119 (5)	2564 (100)

Table 2. Unadjusted Association of Demographics and Vascular Risk Factors Among Diet and Regular Soft Drink Consumption Subgroups

Demographics and vascular risk factors at baseline	Study cohort (N=2564)	Diet Soft Drink Consumption‡		Regular Soft Drink Consumption‡	
		<1/month (N=1948)	Daily (N=163)	<1/month (N=1231)	Daily (N=338)
Age, mean(SD)*†	69 (10)	69 (10)	68 (9)	70 (10)	69 (10)
Male sex, %†	36	36	42	33	43
Race/ethnicity, %*†					
White	20	18	26	26	15
Black	23	23	23	19	29
Hispanic	54	57	49	54	54
Other	2	2	1	2	2
Smoking, %*†					
Current	17	18	15	15	18
Former	36	34	44	38	36
Never	47	48	42	47	45
Moderate–heavy physical activity, %	9	8	9	9	7
Moderate alcohol use, %§	33	34	28	32	34
Total kcal/day, mean(SD)*†	1575 (738)	1552 (729)	1702 (701)	1431 (630)	2030 (925)
Protein (g)/day, mean(SD)*†	62 (31)	60 (31)	72 (33)	59 (28)	73 (39)
Saturated fat (g)/day, mean(SD)*†	21 (13)	20 (13)	23 (13)	18 (11)	27 (17)
Total fat (g)/day, mean(SD)*†	61 (34)	60 (33)	68 (35)	55 (29)	78 (44)
Carbohydrates (g)/day, mean(SD)†	189 (90)	187 (90)	195 (84)	171 (80)	254 (111)
Sodium (mg)/day, mean(SD)*†	3070 (1670)	3012 (1644)	3400 (1686)	2878 (1531)	3717 (2035)
History of hypertension, %*	52	50	56	53	51
Systolic blood pressure, mean(SD)	144 (21)	144 (21)	146 (22)	143 (21)	143 (19)
Diastolic blood pressure, mean(SD)†	83 (11)	83 (11)	84 (11)	83 (11)	83 (11)
History of diabetes, %*†	17	13	31	23	11
Blood sugar, mean(SD)*†	105 (49)	101 (43)	118 (50)	110 (56)	103 (48)
History of hypercholesterolemia, %†	37	37	45	40	35
LDL, mean(SD)	128 (36)	129 (36)	128 (41)	129 (35)	128 (40)
HDL, mean(SD)*	47 (15)	48 (15)	45 (15)	48 (15)	45 (14)
Triglycerides, mean(SD)*	134 (80)	131 (73)	146 (99)	135 (78)	131 (70)
Waist circumference (in), mean(SD)*	37 (5)	36 (5)	39 (6)	37 (5)	37 (5)
BMI, mean(SD)*	28 (6)	28 (5)	31 (7)	28 (6)	28 (6)
Peripheral vascular disease, %*	15	14	21	16	12
Previous cardiac disease, %*	19	18	23	20	20
Metabolic syndrome, %*	41	38	50	43	40

** $p < 0.05$ across categories of diet soft drink consumption (chi-square test, analysis of variance)*
† $p < 0.05$ across categories of regular soft drink consumption (chi-square test, analysis of variance)
‡ Light soft drink consumption subgroups not shown
§ Current drinking of >1 drink/month and ≤2 drinks/day

vascular events). In this restricted group, we observed effect estimates for both daily diet and regular soft drink consumption that were stronger than those observed in the full cohort. In fact, we observed a 57% increased risk of

Table 3. Diet and Regular Soft Drink Consumption and Risk of Vascular Events (N=2564)

Soft drink consumption	Combined vascular events HR (95% CI)				
	N events	Model 1*	Model 2†	Model 3‡	Model 4§
Regular soft drinks					
None (<1/mo, N=1333)	312	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Light (1/mo–6/wk, N=995)	189	0.83 (0.69–1.00)	0.82 (0.68–0.99)	0.87 (0.72–1.06)	0.87 (0.71–1.07)
Daily (1+/day, N=338)	90	1.15 (0.91–1.46)	1.12 (0.87–1.45)	1.14 (0.88–1.49)	1.09 (0.82–1.46)
Continuous (regular soft drinks/wk)		1.00 (0.99–1.02)	1.00 (0.99–1.02)	1.00 (0.99–1.02)	1.00 (0.98–1.02)
Diet soft drinks					
None (<1/mo, N=1948)	431	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Light (1/mo–6/wk, N=453)	109	1.19 (0.96–1.47)	1.12 (0.90–1.39)	0.94 (0.75–1.18)	1.08 (0.85–1.37)
Daily (1+/day, N=163)	51	1.66 (1.23–2.23)	1.46 (1.08–1.98)	1.43 (1.06–1.94)	1.44 (1.02–2.02)
Continuous (diet soft drinks/wk)		1.03 (1.02–1.05)	1.03 (1.01–1.05)	1.03 (1.01–1.04)	1.02 (1.00–1.05)

**Model 1: Adjusted for demographics (age, sex, race/ethnicity, education) and mutually adjusted for each type of soft drinks*
†Model 2: Adjusted for demographics, behavioral risk factors (smoking, moderate alcohol use, moderate to heavy physical activity), daily diet (total calories, grams of protein, grams of total fat, grams of saturated fat, grams of carbohydrates, mg of sodium), BMI, and mutually adjusted for each type of soft drinks
‡Model 3: Adjusted for demographics, behavioral risk factors, daily diet, BMI, vascular risk factors (previous cardiac disease, peripheral vascular disease, history of diabetes, history of hypercholesterolemia, history of hypertension, metabolic syndrome), and mutually adjusted for each type of soft drinks
§Model 4: Adjusted for demographics, behavioral risk factors, daily diet, waist circumference, vascular risk factors (previous cardiac disease, peripheral vascular disease, blood sugar, HDL, LDL, triglyecrides, systolic blood pressure, diastolic blood pressure, anti-hypertensive medication use), and mutually adjusted for each type of soft drinks

Table 4. Diet and Regular Soft Drink Consumption and Combined Vascular Events Among Those Who Were Healthier at Baseline

Soft drink consumption	HR (95% CI) for vascular events*
Regular soft drinks	
None (<1/mo, N=505, 114 events)	1.00 (ref)
Light (1/mo–6/wk, N=461, 82 events)	0.93 (0.68–1.25)
Daily (1+/day, N=156, 41events)	1.57 (1.05–2.35)†
Continuous (regular soft drinks /wk)	1.02 (0.99–1.04)
Diet soft drinks	
None (<1/mo, N=932, 192 events)	1.00 (ref)
Light (1/mo–6/wk, N=143, 30 events)	0.94 (0.62–1.41)
Daily (1+/day, N=47, 15 events)	1.59 (0.92–2.74)‡
Continuous (diet soft drinks /wk)	1.03 (1.00–1.07)†

** Restricted to those who were not obese (BMI< 30) and no history of diabetes or metabolic syndrome (N= 1122, 237 events); Adjusted for demographics, behavioral risk factors, BMI, daily diet, history of hypercholesterolemia, hypertension, cardiac disease, peripheral vascular disease, and mutually adjusted for each type of soft drinks*
† $p < 0.05$
‡ $0.05 < p < 0.10$

vascular events among those who consumed regular soft drinks daily (p=0.03), and a 59% increased risk among those who consumed diet soft drinks daily (p=0.09).

When we examined diet and regular soft drinks together in seven mutually exclusive categories with no diet or regular soft drink consumers as the referent (Supplement Table 5, available online), we also observed a suggestive yet not statistically significant increased risk of vascular events among those who consumed diet soft drinks daily, with (model 3 HR=1.48, 95% CI=0.64-3.39) or without (model 3 HR=1.37, 95% CI=0.83-2.25) regular soft drinks vs. no soft drinks. However, this analysis was underpowered.

DISCUSSION

Reported diet soft drink consumption in this multi-ethnic adult population was relatively uncommon, and was associated with many important vascular risk factors including diabetes, increased BMI, peripheral vascular disease, previous cardiac disease, metabolic syndrome, low HDL, elevated triglycerides, hypertension, elevated sodium consumption, and increased kilocalories/day. These associations suggest that individuals may consume diet soft drinks in an effort to reduce calories and sugar and lose weight to compensate for an underlying elevated risk of vascular disease. However, even after controlling for these potential confounders, daily diet soft drink consumption at baseline was associated with an increased risk for vascular events during follow-up. In contrast, consumption of regular soft drinks was not associated with an increased risk for vascular events in multivariable-adjusted analyses. Therefore, these results underscore the need for further studies on whether diet soft drinks are healthy substitutes for regular soft drinks.

To the best of our knowledge, our study is the first to examine the association between diet soft drink consumption and incident combined vascular events, including stroke. The association between diet and sugar-sweetened beverages with risk of CHD was previously assessed in the younger all-female NHS.[12] In contrast to our findings, they observed a robust increased risk of CHD among frequent drinkers of sugar-sweetened beverages, and in particular sugar-sweetened soda, but after adjustment for cardiac risk factors the association between diet soda and risk of CHD was attenuated and lost statistical significance. Beyond the inherent differences between our NOMAS cohort and the NHS in terms of age, sex, race-ethnic composition, and sample size, reasons for the discrepant results for the association between diet soft drinks and cardiovascular disease are not immediately obvious, underscoring the need for further study in other cohorts. We showed that the strength of the association was greater for black participants, which are not well-represented in the NHS. Our data also suggest that the effect of regular soft drinks may be greater for those with lower BMI, and the high mean BMI in our cohort may explain the lack of association observed for regular soft drinks in our full cohort analyses. Our sensitivity analysis of those participants free of obesity, diabetes, and metabolic syndrome suggested an increased risk of vascular events among daily regular soft drink consumers, contributing to a substantial literature on the negative health consequences of sugar-sweetened beverages. Likewise, our analysis of mutually exclusive categories of regular and diet soft drinks also supported a possible increased risk of vascular events among daily regular soft drink consumers, although the association was weaker than that observed for diet soft drinks. The power of these sensitivity analyses was limited and therefore results should be interpreted with caution.

Our data are consistent with findings of previous studies that have shown an association between diet soft drink consumption and metabolic syndrome and its components.[5] When the components of the metabolic syndrome were examined individually in the Multi-ethnic Study of Atherosclerosis, diet soft drinks were significantly associated with waist circumference and fasting glucose. In the Framingham Heart Study, only daily consumption of diet soft drinks, not regular soft drinks, was associated with incident metabolic syndrome after multivariate adjustment.

The health consequences associated with regular soft drink consumption may be attributed to its high caloric content, glycemic load and consequential inflammatory responses, and added sweeteners such as high fructose corn syrup, which may increase the risk of vascular disease due to its association with blood uric acid levels and triacylglycerol concentrations.[12] However, the mechanisms by which

diet soft drinks may affect vascular events are less clear. A prospective cohort study found that consumption of artificially sweetened drinks was associated with gaining weight.[21] In rats, consumption of artificial sweeteners weakened the ability to anticipate the caloric content of foods, and led to increased intake and body weight.[22] Previous prospective analyses of the association between diet soft drink consumption and metabolic syndrome suggest that the association between diet soft drinks and vascular events may be largely mediated by adiposity and fasting glucose.[6] We controlled for BMI, metabolic syndrome, blood sugar, blood pressure, and lipids at baseline, as well as intake of total calories, total fat, saturated fat, protein, carbohydrates, and sodium, but these variables may still be on the pathway linking diet soft drink consumption with vascular disease risk. Lastly, it has been suggested that the caramel coloring of both diet and regular soft drinks may contribute to increased levels of proinflammatory advanced glycation end products.[23]

The attenuation of effects observed after adjusting for behavioral and vascular risk factors indicates the bias due to confounding in the relationship between diet soft drink consumption and risk of vascular events, and some residual confounding in models 3 and 4 may be present. However, it is important to note that our multivariable models 3 and 4 included vascular risk factors that could be considered both as potential confounders and as intermediates on the causal pathway between soft drink consumption and vascular disease. It is possible that the attenuation of the associations seen when comparing the results of model 1 with models 3 and 4 was at least partly due to the control of potential mediators on the causal pathway, and therefore should be interpreted with caution.

Sensitivity analyses excluding obese individuals and those with diabetes or the metabolic syndrome showed that the strength of the association between diet soft drink consumption and vascular events persisted even among those without a preexisting vascular condition that might have motivated people to switch from regular to diet soft drinks. However, this analysis was underpowered and we are unable to rule out reverse confounding, or indication bias, such that people at increased risk of vascular events due to preexisting vascular conditions may be advised to switch from regular to diet soft drinks. Our finding that cohort participants at high risk for cardiovascular events, those with various vascular risk factors including diabetes, hypertension, and previous cardiac disease, consumed more diet soft drinks at baseline, suggests the possibility of bias due to reverse confounding.

The strong association between diet and regular soft drink consumption with other dietary behaviors and behavioral and vascular risk factors, coupled with the suggestive findings of a possible association between diet soft drink consumption and risk of vascular events, indicate that clinical trials on the relationship of diet and regular soft drinks with clinical and subclinical vascular outcomes may be warranted. Although randomized clinical trials on this topic are costly and difficult, such trials may be needed to advance knowledge on this association, and should therefore be considered, as should experimental studies using animals.

Strengths of our study include its prospective design, multi-ethnic population, excellent follow-up and validated outcomes, and comprehensive collection of other important vascular risk factors. However, despite the use of a valid and reliable food frequency questionnaire[20,24,25] to calculate soft drink consumption, a potential for both random misclassification and recall bias persists. The use of a prospective follow-up study design suggests that most of the misclassification would likely be random, but many factors can systematically affect the way people report their dietary patterns and those may be related to vascular disease risk. We lacked information on the type of diet and regular soft drinks consumed. It is possible that variations over time and across brands, in coloring and artificial sweetener used may be relevant. There is a possibility for residual confounding by both measured and unmeasured risk factors for vascular outcomes possibly associated with soft drink consumption. Most notably, we lacked information on recent weight changes, and we were unable to capture all potential differences in the dietary behaviors of frequent diet soft drink consumers that may account for the observed relationship with vascular event risk. Further, we only collected information on dietary behavior, including soft drinks, at baseline. Diet soft drink consumption was not reassessed during the regular follow-up of this cohort, and it is possible that participants may have changed their consumption during follow-up. Lastly, diet soft drink consumption was uncommon in our older, primarily Hispanic, population, limiting statistical power. The small number of daily diet soft drink consumers in the cohort (N=163, 51 events) impeded a thorough examination of a dose-response relationship between diet soft drink consumption and risk of vascular events among daily consumers.

This study suggests a potential association between daily diet soft drink consumption and vascular outcomes. However, additional large prospective studies as well as randomized trials are needed to confirm our findings before any conclusions can be made regarding the adequacy of diet soft drinks as substitutes for sugar-sweetened drinks. Future studies in younger populations in which diet soft drink consumption is more prevalent are particularly important, as are studies examining the associations between all beverages, including other non-soft drink sugar-sweetened and diet beverages, and vascular events. In addition, further study is needed on

the potential mechanisms by which diet soft drinks may affect the risk of vascular events.

Acknowledgements: Funding: *This work is supported by a grant from the National Institute of Neurological Disorders and Stroke (R37 NS 29993).*

The data described in this manuscript were presented at the International Stroke Conference in Los Angeles, CA on February 11, 2011.

Conflict of Interest: *The authors declare that they do not have a conflict of interest.*

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J Gen Intern Med. 2012 Jan 27. [Epub ahead of print]

Diet Soft Drink Consumption is Associated with an Increased Risk of Vascular Events in the Northern Manhattan Study.

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Source

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Abstract

BACKGROUND:

Diet and regular soft drinks have been associated with diabetes and the metabolic syndrome, and regular soft drinks with coronary heart disease.

OBJECTIVE:

To determine the association between soft drinks and combined vascular events, including stroke.

DESIGN:

A population-based cohort study of stroke incidence and risk factors. PARTICANTS: Participants (N = 2564, 36% men, mean age 69 ± 10, 20% white, 23% black, 53% Hispanic) were from the Northern Manhattan Study.

MAIN MEASURES:

We assessed diet and regular soft drink consumption using a food frequency questionnaire at baseline, and categorized: none (<1/month, N = 1948 diet, N = 1333 regular), light (1/month-6/week, N = 453 diet, N = 995 regular), daily (≥1/day, N = 163 diet, N = 338 regular). Over a mean follow-up of 10 years, we examined the association between soft drink consumption and 591 incident vascular events (stroke, myocardial infarction, vascular death) using Cox models.

KEY RESULTS:

Controlling for age, sex, race/ethnicity, education, smoking, physical activity, alcohol consumption, BMI, daily calories, consumption of protein, carbohydrates, total fat, saturated fat, and sodium, those who drank diet soft drinks daily (vs. none) had an increased risk of vascular events, and this persisted after controlling further for the metabolic syndrome, peripheral vascular disease, diabetes, cardiac disease, hypertension, and hypercholesterolemia (HR = 1.43, 95% CI = 1.06-1.94). There was no increased risk of vascular events associated with regular soft drinks or light diet soft drink consumption.

CONCLUSIONS:

Daily diet soft drink consumption was associated with several vascular risk factors and with an increased risk for vascular events. Further research is needed before any conclusions can be made regarding the potential health consequences of diet soft drink consumption.

PMID:
22282311
[PubMed - as supplied by publisher]