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Association of soda consumption with subclinical cardiac remodeling in the Framingham Heart Study

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Abstract

Objective—Diet soda consumption increases cardiometabolic risk. The aim of this investigation was to assess the relations between self-reported soda consumption and subclinical cardiac remodeling.

Methods—We assessed the relations between self-reported soda consumption and left ventricular mass (LVM) and left atrial dimension (LAD) (both standardized within sex) in a sample of middle-aged attendees from the Framingham Heart Offspring cohort examination 5 and 6.

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Authors' contributions

CA and RSV came up with study design. LS performed the statistical analyses. All authors contributed with important intellectual input and critical revision of the paper.

Disclosures: None

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Results—The overall mean age was 55 years and 59% of the participants were women. Compared to non-consumers (n=1010), soda consumers (n=3192) had greater body weight (mean 86 vs. 82 kg among men, and 70 vs. 67 kg among women). Compared with non-consumers, age- and height-adjusted LAD was increased (standard deviation units) among soda consumers by 0.15 standard error 0.042, $p<0.001$) for those drinking $>0-7$ diet soda (n=1023), -0.010 (0.043, $p=0.82$) for people drinking $>0-7$ regular soda (n=907), 0.22 (0.057, $p<0.0001$) for individuals consuming >7 diet soda (n=372), and 0.20 (0.092, $p=0.034$) for participants drinking >7 regular soda (n=116) per week. LVM was increased among participants consuming diet soda ($p<0.05$), but not in regular soda consumers ($p>0.05$). Upon adjustment for weight, however, all aforementioned associations were attenuated.

Conclusion—The observed associations between soda consumption and LAD or LVM were likely related to the greater body weight of soda drinkers relative to non-drinkers.

Keywords

Soda consumption; body weight; cardiac remodeling; cardiovascular disease

1. Introduction

Consumption of both sugar and aspartame-containing beverages has increased rapidly during the last couple of decades.[1] During the same time period, the prevalence and incidence of the metabolic syndrome, atrial fibrillation, and heart failure have increased as well.[2] The temporal increases in the prevalence and incidence of these conditions have been particularly pronounced among younger individuals and women,[3–5] who often are the greatest consumers of soda. Soda consumption previously has been shown to increase the risk of developing the metabolic syndrome,[4, 6] but the relations between soda consumption and cardiovascular disease (CVD) have been less well investigated. Two recent epidemiological studies reported increased risks of stroke associated with diet soda, but not with regular soda consumption, whereas another study showed increased risk of coronary heart disease and adverse changes in metabolic risk factors among people consuming sugar-, but not artificially-sweetened soda beverages.[7–9] In order to explore one potential mechanism by which soda consumption might lead to CVD, we assessed the association between soda consumption and subclinical cardiac remodeling (using left ventricular mass [LVM] and left atrial [LA] size as endophenotypes for CVD and atrial fibrillation, respectively) in a middle-aged to older adult community-based sample of individuals free from overt CVD.

2. Material and methods

The Framingham Heart Study is a prospective community-based observational study aiming to investigate risk factors for CVD. The participants of the original cohort were enrolled in 1948. In 1971 the children of the original cohort and the spouses of the children were enrolled into the Offspring cohort.[10] For the present investigation, we used a pooled sample of participants from the 5th (1991–1995) and 6th (1995–1998) quadrennial examination cycles of the Offspring cohort when routine echocardiography was performed and information on soda consumption was collected (n=7331 person-observations). We

excluded participants with prevalent CVD (including significant valve disease, prior acute myocardial infarction, clinical heart failure, atrial fibrillation, and/or cerebrovascular disease, n=790), inadequate echocardiograms (n=1715), incomplete data on soda consumption (n=579), or other important covariates (n=45), leaving 4202 person-observations for analyses. Of these 896 people contributed data from one examination cycle, and 1653 from two examination cycles.

Consumption of soda was based on self-reported questionnaires. Questions included how many soda drinks the participants consumed in a week and distinguished use of diet from regular soda. For the present purpose, weekly soda consumption was divided into six groups: “non-consumers” (n=1010), “consumption of >0–7” (n=1023 diet and n=907 regular consumers), or “>7” diet/regular soda drinks (n=372 diet and n=116 regular consumers) and a “mixed group” (n=774) including participants who consumed both diet and regular soda (see Table 1). All participants had fasting blood samples drawn at the Framingham Heart Study clinic as well as standardized measures of anthropometric variables.

2.1 Echocardiograms

Experienced sonographers performed transthoracic echocardiographic examination of all participants using a standardized protocol. Measurements of left ventricular size and left atrial end-systolic dimensions (LAD) were performed from M-mode echocardiograms obtained from the parasternal long axis view. For calculation of left ventricular mass, we used the following formula:

$LV\ mass\ (LVM) = 0.8\ (1.04\ ([LVIDD + PWTD + IVSTD]^3 - [LVIDD]^3)) + 0.6\ g$, where LVIDD is LV end-diastolic dimension, PWTD left ventricular posterior wall thickness, and IVSTD interventricular septum thickness.

2.2 Ethics

The study was approved by the Institutional Review Board of the Boston University Medical Center. All participants provided written informed consent before participation.

3. Calculations

Multivariable linear regression models were used to estimate the associations between soda consumption category and different echocardiographic variables. LVM and LAD were included as dependent variables in analyses after being standardized within sex. All models were adjusted for age and height initially. In subsequent steps, we additionally adjusted for: 1) weight, and 2) systolic blood pressure, anti-hypertensive treatment, smoking, dyslipidemia, and diabetes. We repeated all analyses using generalized estimation equation models, which accounts for the dependence between observations and unless specified, similar results were observed. All analyses were performed in SAS version 9.3 (Cary, NC, USA). A two-sided p-value <0.05 was considered statistically significant for all analyses.

4. Results

The overall mean age was 55 years and 59% of the participants were women. Twenty-four percent of the participants did not consume any soda, whereas 33% consumed diet soda

only, 25% regular soda only, and 18% consumed both diet and regular soda. Soda consumers were younger, had a higher body mass index, and lower serum high-density lipoprotein concentrations than non-consumers (Table 1). Moreover, the total daily energy intake was higher for the regular and high diet soda consumption groups compared to the soda non-consumer group. The prevalence of diabetes was also higher in the high diet soda consumption group.

4.1 Association between soda consumption and cardiac remodeling

All of the soda consumption groups, except for the >0–7 regular soda intake per week group, were associated with higher mean LAD, compared with the non-consumer group in analyses adjusting for age and height, with the highest LAD seen in the higher soda consumption groups (Table 2). Similarly, higher adjusted-mean LVM was observed for the diet soda consumption groups relative to non-consumers, but this was not observed for the regular soda consumption groups. Upon additional adjustment for weight, the association of soda consumption with LAD and LVM were largely rendered statistically non-significant. We did not observe effect modification by weight for the associations of soda consumption groups with LAD and LVM (p for interactions between soda consumption groups and weights >0.10 in fully adjusted models). In models adjusting for waist-hip-ratio instead of weight some significant association between soda consumption groups and LAD and LVM remained, but these models had much lower R^2 values than those including weight, indicating that waist-hip-ratio is not as closely related to cardiac remodeling as body weight, Table 2.

5. Discussion

In our cross-sectional study of middle-aged and older community-dwelling individuals free of overt CVD we investigated the relations between soda consumption and echocardiographic indices of left ventricular remodeling. We observed that consumption of both diet and regular soda was associated with higher mean LAD. Furthermore, we observed that consumption of diet soda was associated with greater LVM after adjustment for age and height. Upon adjustment for weight, however, all aforementioned associations were attenuated, suggesting that any observed association between soda consumption and LAD or LVM was likely related to the higher weight of soda drinkers relative to non-consumers.

Several observational studies have shown that soda consumption was associated with an increased risk of obesity, even after adjustment for total calorie intake.[11, 12] This has been demonstrated in cross-sectional as well as longitudinal studies, which raises the possibility of a potentially causal relation.[11] Recently, diet soda was confirmed to be associated with impaired glucose tolerance in mice, presumably by altering intestinal microbiota and the effects were reversed by antibiotics.[13] Moreover, the Framingham Heart Study, as well as other data has previously demonstrated that higher soda consumption may be associated with increased waist circumference and the metabolic syndrome.[6, 12] Cardiac remodeling is also a well-known consequence of both obesity and the metabolic syndrome (including impaired glucose tolerance and diabetes).[14] Taken together the present investigation and prior evidence suggest that the greater body weight among soda drinkers may be associated

with adverse left ventricular remodeling, which in turn may be the substrate for other forms of CVD, including atrial fibrillation, stroke, and heart failure.

5.1 Strengths and limitations

The present study was based on a rather larger sample with well-validated data collected during 1991–1998. It may, however, not be completely generalizable in terms of contemporary amounts of soda consumption in the United States. Further, all analyses were cross-sectional and based on observations on middle-aged to older adult white individuals; our results may not be generalizable to other age groups or ethnicities. Additionally, both soda consumption and total calorie intake were self-reported, and may be inherently subject to inaccuracies. Finally, the study may have also been underpowered in a statistical sense. We had 80% power to detect effect sizes (standardized differences in mean LAD and LVM) as small as 0.16 standard deviation units when comparing non-consumers to those consuming 0–7 diet, 0–7 regular soda drinks per week, or those with a mixed soda use pattern. However, when comparing non-consumers to those drinking >7 regular sodas we would need to see far larger differences (0.45 standard deviation units) to ensure 80% statistical power.

5.2 Conclusions

Soda consumption, especially diet soda, was associated with higher LAD and LVM, compared to no soda consumption, but these findings were likely related to greater body weight of soda drinkers relative to that of non-consumers.

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Abbreviations

BMI	body mass index
CVD	cardiovascular disease
LAD	left atrial end-systolic dimension
LVM	left ventricular mass

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Table 1

Study Sample characteristics according to weekly soda consumption

	Non-consumer	>0-7 diet soda/week	>0-7 regular soda/week	>7 diet soda/week	>7 regular soda/week	Mixed use of soda/ week
Numbers	1010 (24%)	1023 (24%)	907 (22%)	372 (9%)	116 (3%)	774 (18%)
Age (years)	58±10	55±9	54±9	53±9	52±9	54±10
Men (%)	304 (30%)	301 (29%)	476 (52%)	140 (38%)	72 (62%)	449 (58%)
<i>Numbers of sodas per week</i>						
Diet, mean (min, max)	0 (0-0)	3.2 (0.5-7.0)	-	17.7 (7.5-63.0)	-	5.0 (0.5-49.0)
Regular, mean (min, max)	0 (0-0)	-	2.4 (0.5-7.0)	-	18.1 (7.5-84.0)	2.4 (0.5-59.5)
Weight, men (kg)	82±12	86±12	84±12	92±16	84±12	88±13
Weight, women (kg)	67±13	70±13	66±13	73±14	74±18	71±14
Body mass index (kg/m2)	25.9±4.3	27.2±4.4	26.3±4.2	28.4±5.0	27.5±4.9	27.7±4.4
Waist-hip-ratio, men	0.96±0.05	0.97±0.05	0.96±0.06	0.98±0.06	0.97±0.06	0.97±0.05
Waist-hip-ratio, women	0.86±0.09	0.86±0.08	0.86±0.08	0.86±0.09	0.87±0.08	0.86±0.09
Left ventricular mass, men (g)	185±36	193±40	187±39	194±41	189±43	190±39
Left ventricular mass, women (g)	141±31	143±29	136±29	142±30	149±30	143±30
Left atrial dimension, men (cm)	4.1±0.5	4.1±0.5	4.1±0.5	4.2±0.5	4.1±0.4	4.1±0.5
Left atrial dimension, women (cm)	3.6±0.5	3.6±0.5	3.5±0.5	3.6±0.5	3.7±0.5	3.6±0.4
Left ventricular end diastolic dimension, men (cm)	5.0±0.4	5.0±0.4	4.9±0.4	5.0±0.4	5.0±0.4	5.0±0.5
Left ventricular end diastolic dimension, women (cm)	4.6±0.4	4.6±0.4	4.5±0.3	4.6±0.3	4.7±0.4	4.6±0.4
Left ventricular wall thickness (septum+posterior wall; men; cm)	2.0±0.2	2.0±0.3	2.0±0.2	2.0±0.2	2.0±0.3	2.0±0.3
Left ventricular wall thickness (septum+posterior wall; women; cm)	1.8±0.2	1.8±0.2	1.8±0.2	1.8±0.2	1.8±0.2	1.8±0.2
Systolic blood pressure (mmHg)	125±20	125±18	124±19	123±18	128±19	126±17

	Non-consumer	>0–7 diet soda/week	>0–7 regular soda/week	>7 diet soda/week	>7 regular soda/week	Mixed use of soda/ week
Diastolic blood pressure (mmHg)	73±10	74±9	75±10	75±10	75±10	75±9
Treatment for hypertension (%)	183 (18%)	187 (18%)	150 (17%)	72 (19%)	23 (20%)	120 (16%)
Total cholesterol (mg/dL)	208±35	206±37	203±37	201±36	198±34	202±36
HDL cholesterol (mg/dL)	55±16	54±16	50±15	51±15	44±12	50±15
Treatment for dyslipidemia (%)	15 (1%)	30 (3%)	11 (1%)	11 (3%)	2 (2%)	16 (2%)
Diabetes mellitus (%)	47 (5%)	76 (7%)	33 (4%)	60 (16%)	9 (8%)	46 (6%)
Total energy intake per day (kcal)	1783±577	1776±587	2055±626	1874±1204	2142±706	2060±669

Footnote: Values are n(%) or mean ± SD

Table 2

Associations between weekly soda consumption and echocardiographic measures.

	Non-consumer	>0-7 diet soda/week	>0-7 regular soda/week	>7 diet soda/week	>7 regular soda/week	Mixed use of soda/week
<i>Left Atrial Dimension</i>						
<i>Model 1</i> ($R^2=0.0521$)	-	0.15 (0.042) ***	-0.010 (0.043)	0.22 (0.057) ***	0.20 (0.092) *	0.11 (0.045) *
<i>Model 2</i> ($R^2=0.1965$)	-	0.041 (0.038)	-0.038 (0.040)	0.0094 (0.053)	0.077 (0.085)	-0.030 (0.042)
<i>Model 3</i> ($R^2=0.2099$)	-	0.027 (0.038)	-0.035 (0.040)	-0.0042 (0.053)	0.066 (0.085)	-0.033 (0.042)
<i>Model 4</i> ($R^2=0.1039$)	-	0.11 (0.041) **	-0.041 (0.042)	0.16 (0.056) **	0.099 (0.090)	0.056 (0.045)
<i>Left Ventricular Mass</i>						
<i>Model 1</i> ($R^2=0.0331$)	-	0.13 (0.043) **	-0.060 (0.045)	0.14 (0.059) *	0.14 (0.095)	0.067 (0.047)
<i>Model 2</i> ($R^2=0.1453$)	-	0.039 (0.040)	-0.086 (0.042) *	-0.054 (0.056)	0.033 (0.089)	-0.060 (0.044)
<i>Model 3</i> ($R^2=0.1707$)	-	0.029 (0.040)	-0.094 (0.041) *	-0.065 (0.055)	-0.0044 (0.088)	-0.069 (0.044)
<i>Model 4</i> ($R^2=0.0863$)	-	0.10 (0.042) *	-0.10 (0.044) *	0.086 (0.056)	0.028 (0.093)	0.014 (0.046)

Footnote: Estimated association of soda consumption on L/A dimension and LVM on sex-standardized measures, compared with no soda consumption. Estimates refer to numbers of standard deviations. Model 1: Adjusted for age and height. Model 2: Adjusted for age, height, and weight. Model 3: Adjusted for age, height, weight, systolic blood pressure, smoking, hypertension, diabetes, and total cholesterol:HDL ratio. Model 4: Adjusted for waist-hip ratio plus all variables in model 3, except for weight.

* $p<0.05$,

** $p<0.01$,

*** $p<0.001$.

R^2 values refer to the adjusted R^2 values from the different models.