Sugar-Sweetened Beverage Consumption Is Associated With Change of Visceral Adipose Tissue Over 6 Years of Follow-Up

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Background—Sugar-sweetened beverage (SSB) intake has been linked to abnormal abdominal adipose tissue. We examined the prospective association of habitual SSB intake and change in visceral adipose tissue (VAT) and subcutaneous adipose tissue.

Methods and Results—The quantity (volume, cm^3) and quality (attenuation, Hounsfield Unit) of abdominal adipose tissue were measured using computed tomography in 1003 participants (mean age 45.3 years, 45.0% women) at examination 1 and 2 in the Framingham's Third Generation cohort. The 2 exams were ≈6 years apart. At baseline, SSB and diet soda intake were assessed using a valid food frequency questionnaire. Participants were categorized into 4 groups: none to <1 serving/mo (nonconsumers), 1 serving/mo to <1 serving/week, 1 serving/week to 1 serving/d, and ≥1 serving/d (daily consumers) of either SSB or diet soda. After adjustment for multiple confounders including change in body weight, higher SSB intake was associated with greater change in VAT volume (*P* trend<0.001). VAT volume increased by 658 cm^3 (95% confidence interval [CI], 602 to 713), 649 cm^3 (95% CI, 582 to 716), 707 cm^3 (95% CI, 657 to 757), and 852 cm^3 (95% CI, 760 to 943) from nonconsumers to daily consumers. Higher SSB intake was also associated with greater decline of VAT attenuation (*P* trend=0.007); however, the association became nonsignificant after additional adjustment for VAT volume change. In contrast, diet soda consumption was not associated with change in abdominal adipose tissue.

Conclusions—Regular SSB intake was associated with adverse change in both VAT quality and quantity, whereas we observed no such association for diet soda. **(*Circulation*. 2016;133:370-377. DOI: 10.1161/CIRCULATIONAHA.115.018704.)**

Key Words: obesity ■ subcutaneous adipose tissue ■ visceral adipose tissue

Abdominal adipose tissue, particularly visceral adipose tissue (VAT), has been linked to the development of type 2 diabetes mellitus and cardiovascular disease.[1] Imaging techniques such as computed tomography (CT) can be exploited to assess the quantity of abdominal adipose tissue, including VAT and subcutaneous adipose tissue (SAT).[2] In addition, the quality of VAT and SAT can be indirectly assessed by adipose tissue attenuation obtained from CT images.[3] From the CT images, the radiodensity range from −195 to −45 Hounsfield units (HU) is typically attributed to adipose tissue.[4] Within this HU range, a lower HU in adipose tissue can be used as a proxy for lower fat quality.[5,6] Studies have shown that both quantity and quality of abdominal adipose tissue were associated with cardiometabolic risk.[2,3]

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Sugar-sweetened beverages (SSB) are the largest contributor of added sugar intake in the US.[7] Added sugar consumed from SSB alone, particularly in low socioeconomic populations, nearly exceeds the limits of added sugar intake recommended to maintain cardiometabolic health.[8,9] Recent data from the Global Burden of Diseases, Injuries, and Risk Factors 2010 Study showed a significant number of deaths from diabetes and cardiovascular disease may be attributed to excess SSB intake.[10] Sugars added in SSB are either sucrose or high fructose corn syrup, which both may contribute to metabolic disorders.[11,12] In contrast, diet soda is a popular beverage,[13] which contains no calories from added sugar. In a previous cross-sectional analysis of data from the Framingham Heart Study, SSB intake rather than diet soda intake was associated with VAT volume.[14] This observation was consistent with 1 other cross-sectional study.[15] However, these studies were limited by the cross-sectional design because the temporality of the association was not able to be established.

To date, data examining the association between either habitual intake of SSB or diet soda on the change in quantity

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and quality in abdominal adipose tissue over time have been limited. The objective of the present study was to examine the prospective association between habitual intake of SSB or diet soda and changes in VAT and SAT assessed by CT over a 6-year time frame in the Framingham Heart Study. We hypothesized that, independent of change in body weight, higher habitual SSB intake would be associated with a greater increase in VAT and SAT quantity and a greater decline in the quality of adipose tissue in these regions, whereas we hypothesized that no such association would be observed with diet soda.

Methods

Study Sample

Study participants were drawn from the Third Generation cohort of the Framingham Heart Study, which has been described elsewhere.[16] Enrollment of the Third Generation cohort was initiated in 2002, and 4095 participants (53.3% women, age range 19–72 years, 99.7% white) attended the first examination. In this cohort, participants were evaluated by a physician interview, a physical examination, and standard laboratory assessments of vascular risk factors. Of the 4095 participants who attended the first examination (2002–2005), 1994 participants underwent a multi-detector CT scan. Among these participants, 1160 participants also had CT scan at the second examination (2008–2011). To be eligible for the CT scan, participants' body weight had to be <160 kg because of the CT machine's restriction for weight. Compared with participants who attended both baseline and follow-up examinations but had no CT measurements at both exams (n=2251), those with CT measurements (n=1160) were older (45.3 versus 37.9 years), less likely to be women (44.7% versus 57.3%) or smokers (9.5% versus 16.7%), and had slightly higher body mass index (BMI) levels (27.3 versus 26.6 kg/m^2). It should be noted that, to be eligible for CT scans, men had to be age ≥35 years and women had to be ≥40 years. In addition, there was no substantial difference between the 2 groups for alcohol intake, waist circumference, lipid profiles and lipid lowering medication usage, antihypertensive medications usage, and fasting plasma glucose (all P>0.10). A total of 157 participants were additionally excluded for the following reasons: bariatric surgery (n=3), history of hard cardiovascular disease (myocardial infarction and stroke, n=9), history of cancer (excluding nonmelanotic skin cancer, n=16), missing data for SSB or diet soda (n=114), and missing important covariates such as physical activity, smoking status, and other dietary assessments (n=15) at baseline. The present study was completed on the final sample size of 1003 participants. All participants provided written informed consent and the Framingham Heart Study protocols and procedures were approved by the Institutional Review Board for Human Research at Boston University Medical Center.

Abdominal Adipose Tissue

The protocol for measuring abdominal adiposity has been previously described.[2,3] Briefly, participants underwent an abdominal scanning with an 8-slice multi-detector CT scan (LightSpeed Ultra; General Electric Health Care). The CT scanning obtained 25 contiguous slices covering 125 mm superiorly from the upper edge of the S1 vertebrae. Pixels of CT image between −195 to −45 Hounsfield units (HU) were defined as adipose tissue. VAT and SAT were separated by manually tracing the abdominal muscular wall. The quantity was determined by the volume of VAT and SAT, and a ratio of VAT to SAT volume (VAT:SAT ratio) was calculated to reflect the propensity of storing fat in VAT relative to SAT. The average attenuation (HU) was also measured as a proxy for VAT and SAT quality. The intraclass correlations were >0.99 for both VAT and SAT readings.[3]

Beverage Consumption

The Harvard semiquantitative food frequency questionnaire (FFQ)[17] was used to assess SSB and diet soda intake at baseline in the Third Generation cohort. This FFQ consisted of 126 food items with standard serving sizes. There were 9 frequency categories for each food item, ranging from none or <1 serving/mo to ≥6 servings/d. Dietary assessment was considered valid only if reported energy intake was ≥2.5 MJ/d (600 kcal/d) for both men and women, <16.7 MJ/d (4000 kcal/d) for women, <17.5 MJ/d (4200 kcal/d) for men, and if <13 food items were left blank.

To estimate SSB intake, we summed consumption of the following 4 types of beverages, including (1) caffeinated colas with sugar, (2) caffeine-free colas with sugar, (3) other carbonated beverages with sugar, and (4) fruit punches, lemonade, or other noncarbonated fruit drinks. Diet soda intake was assessed using the following 3 items: (1) low-calorie cola (2) low-calorie, caffeine-free cola, and (3) other low-calorie carbonated beverage. The relative validity of the Harvard FFQ has been tested by comparing with 7-day dietary records in other cohorts.[18–20] The correlation coefficient between the FFQ and dietary records was 0.51 for SSB and 0.66 for diet soda.[21]

Anthropometry and Covariate Assessment

Body weight was measured with light clothes, and was rounded to the nearest 0.5 pound. Standing height was measured using a vertical ruler, and measurement was recorded to the nearest ¼ inch. BMI was calculated as weight (kg) divided by height squared (m^2). Current smokers were defined when participants reported that they smoked regularly in the past year. Physical activity level was estimated using questionnaire-derived intensity of the activity and time spent on performing the activity in a typical day. All dietary factors were estimated using the abovementioned FFQ including total energy intake (kilocalories/d), saturated fatty acids (as % energy intake), alcohol intake (grams/d), multivitamin use (yes/no), and intake of individual foods including whole grain (grams/d), fruit(grams/d), vegetable (grams/d), coffee (servings/d), nuts (grams/d), and fish (grams/d). Type 2 diabetes mellitus was defined as fasting plasma glucose ≥7 mmol/L or the use of hypoglycemic medications.

Statistical Analysis

According to the frequency of SSB intake at baseline, we categorized participants as nonconsumers (none to <1 serving/mo) and consumers (3 categories): 1 serving/mo to <1 serving/week (occasional consumers), 1 serving/week to 1 serving/d (frequent consumers), and ≥1 serving/d (daily consumers). The same categorization strategy was applied for diet soda too. Mean and standard deviation or proportion and frequency were calculated for baseline characteristics of participants in each beverage consumption category. A median approach was used to examine the linear trend across consumption categories. The median intake value of SSB or diet soda in one category was assigned to all individuals in that category. The statistical significance of the linear trend was tested by linear or logistic regression model using the median intake value as a continuous independent variable.

Multiple linear regression models were used to examine the prospective association of beverage consumption and change in body weight and abdominal adipose tissue (volume and attenuation). Least-squares means of change in body weight and abdominal adipose tissue were estimated for each beverage consumption category with adjustment for baseline outcome values, sex, age, smoking status, physical activity level, alcohol intake, daily energy intake, saturated fatty acids (% energy), multivitamin use, and intakes of individuals foods including whole grain, fruit, vegetable, coffee, nuts, and fish. SSB and diet soda were mutually adjusted (ie, diet soda was adjusted for in analysis for SSB and vice versa). In a separate model, change in body weight was additionally adjusted to assess whether the association was independent of body weight change. To examine whether the change in attenuation (HU) was independent of change in volume, volume changes in VAT or SAT were additionally adjusted for in the analyses for the attenuation change in VAT or SAT. A linear trend across beverage categories was performed using the median method described above with adjustment for same covariates.

In the secondary analysis, we tested whether sex, BMI, or diabetes mellitus status modified the observed association between beverage intake and abdominal adipose tissue change. A cross-product term of beverage intake categories and dichotomous variables of sex, BMI (<25 and ≥25 kg/m^2), or type 2 diabetes mellitus status was included in the multiple regression models for trend analysis. The significance level for the interaction term was set as $P<0.02$ (0.05/3) to account for multiple comparisons.

All statistical analyses were conducted using SAS statistical software (version 9.3; SAS Institute, Cary, NC). A 2-tailed $P<0.05$ was considered statistically significant, unless otherwise specified.

Results

Baseline Characteristics

The majority of our study sample (85%, n=852) consumed a mixture of SSB and diet soda, and 1% (n=13) were daily consumers of both SSB and diet soda and 14% (n=138) were nonconsumers of both types of beverages. Among our study participants (Table 1), SSB nonconsumers, occasional, frequent, and daily consumers accounted for 32% (n=317), 20% (n=196), 35% (n=356), and 13% (n=134), respectively. SSB consumers were more likely to be men, younger, current smokers, engaged in slightly more physical activity, and less likely to have diabetes. Also, SSB consumers were not more likely to take multivitamins, consumed fewer nuts, and had higher daily energy intake. SSB intake was inversely associated with diet soda intake. As shown in Table 2, ≈50% (n=501) of study participants were diet soda nonconsumers, and 13% (n=128), 22% (n=221), and 15% (n=153) were occasional, frequent, and daily diet soda consumers, respectively. There was no significant difference in age, sex, current smoking status between diet soda consumption categories. Diet soda consumers were less likely to be engaged in physical activity, had higher BMI, and had higher prevalence of diabetes. Diet soda intake was directly associated with intake of saturated fat, nuts, and vegetables, but inversely associated with fruit intake.

SSB and Change in Abdominal Adipose Tissue

Over a 6-year interval, body weight increased by 2.4 kg (95% confidence interval [CI], 1.7–3.2), 2.8 kg (95% CI, 1.8–3.7), 2.4 kg (95% CI,: 1.7–3.0), and 1.7 kg (95% CI, 0.5–2.9) from SSB nonconsumers to daily consumers (Table 3). No significant association was observed between SSB intake and change in body weight (P trend=0.26).

There was a linear association between SSB intake and change in VAT volume (659 cm^3 among nonconsumers and 675, 709, and 809 cm^3 in occasional, frequent, and daily consumers, respectively), and this association became statistically significant after adjustment for change in body weight (P trend<0.001). Over follow-up, SAT increased by 586 cm^3

Table 1. Baseline Characteristics of Participants According to Sugar-Sweetened Beverage Consumption Categories*

	Nonconsumers (0 to <1/mo)	Occasional Consumers (1/mo to <1/week)	Frequent Consumers (1/week to <1/d)	Daily Consumers (≥1/d)	
N=1003	317	196	356	134	
Median intake, servings/week	0	0.5	3	11	*P* Trend
Age, y	47.2±6.0	45.6±5.9	44.3±6.2	43.2±5.6	<0.001
Women, %	65.0% (206)	55.6% (109)	31.2% (111)	18.7% (25)	<0.001
Current smoker, %	8.8% (28)	6.6% (13)	7.9% (28)	14.2% (19)	0.03
Alcohol, g/d	10.3±14.7	11.2±14.5	12.1±14.3	12.7±17.2	0.13
Physical activity score	36.1±6.8	37.0±6.9	37.5±8.0	40.4±10.5	<0.001
Multivitamin, %	55.8% (177)	58.7% (115)	40.2% (143)	33.6% (45)	<0.001
BMI, kg/m^2	27.5±5.7	26.2±5.1	27.4±4.7	27.0±3.9	0.87
VAT, cm^3	1454±902	1322±868	1731±896	1771±831	<0.001
VAT, HU	−93.2±4.5	−92.6±4.5	−94.9±4.7	−95.3±4.7	<0.001
SAT, cm^3	3081±1553	2572±1329	2676±1374	2391±1037	<0.001
SAT, HU	−101.1±5.8	−100.7±5.3	−100.7±4.8	−100.8±4.3	0.75
VAT(cm^3):SAT(cm^3) ratio†	0.44±0.30	0.47±0.33	0.62±0.43	0.72±0.39	<0.001
Type 2 diabetes mellitus, %	5.4% (17)	2.6% (5)	1.4% (5)	0.7% (1)	0.02
Daily energy intake, kcal	1816±610	1875±598	2087±590	2598±660	<0.001
Saturated fat, %energy	11.4±3.2	11.3±2.9	11.4±2.3	11.2±2.3	0.56
Whole grain, g/d	30.5±23.3	31.0±20.8	29.0±19.7	28.1±17.2	0.17
Fruits, g/d	270.4±220.0	267.3±200.9	275.2±192.2	249.6±185.3	0.35
Vegetables, g/d	241.4±152.2	243.6±161.9	217.0±130.4	218.4±125.2	0.06
Nuts, g/d	6.7±14.0	6.0±12.1	4.5±8.2	4.2±8.1	0.02
Fish, g/d	48.6±50.6	46.6±42.9	40.6±35.0	41.0±34.6	0.06
Coffee, servings/d	1.4±1.3	1.4±1.2	1.5±1.4	1.4±1.3	0.85
Diet soda, serving/week	4.5±8.6	3.1±7.0	2.6±5.4	2.4±6.4	0.01

BMI indicates body mass index; SAT, subcutaneous adipose tissue; and VAT, visceral adipose tissue.

*Mean and standard deviation or proportion and frequency.

†Geometric mean and standard deviation.

(95% CI, 500–672) in nonconsumers and 568 cm^3 (95% CI, 427–709) in daily consumers. SSB intake was not associated with change in SAT volume (*P* trend=0.70 and *P* trend=0.77 in models with additional adjustment for change in body weight).

The attenuation change of VAT was 0.4 HU (95% CI, −0.1 to 1.0) in nonconsumers and -0.6 HU (95% CI, −1.5 to 0.3) in daily consumers. After additional adjustment for change in body weight, a higher SSB intake was associated with a greater attenuation decline in VAT (*P* trend=0.007), which became nonsignificant on adjustment for change in VAT volume (*P* trend=0.24). We observed that SSB intake was not associated with attenuation change in SAT (*P* trend=0.92 and *P* trend=0.63 in model with additional adjustment for change in body weight).

SSB intake was positively associated with change in VAT:SAT ratio (*P* trend=0.007). The change in VAT:SAT ratio was 0.09 (95% CI, 0.06–0.11) in nonconsumers and 0.15 (95% CI, 0.11–0.18) in daily consumers. This association remained significant with additional adjustment for body weight change (*P* trend=0.004).

Diet Soda and Change in Abdominal Adipose Tissue

As shown in Table 4, body weight increased by 2.8 kg (95% CI, 2.2–3.3), 1.6 kg (95% CI, 0.5–2.7), 1.7 kg (95% CI, 0.8–2.5), and 2.7 kg (95% CI, 1.7–3.8) from diet soda nonconsumers to daily consumers during the 6-year interval. Diet soda intake was not associated with change in body weight (*P* trend=0.96). At follow-up, VAT volume increased by 709 cm^3 (95% CI, 652–766) in nonconsumers and 748 cm^3 (95% CI, 644–853) in daily consumers, whereas SAT volume increased by 588 cm^3 (95% CI, 525–652) in nonconsumers and 599 cm^3 (95% CI, 482–717) in daily consumers. There was no association between diet soda intake and change in either SAT volume (*P* trend=0.80) or VAT volume (*P* trend=0.38). Similarly, attenuation change in either VAT or SAT was similar across diet soda consumption categories. No association was observed between diet soda intake and attenuation change in VAT (*P* trend=0.72) and SAT (*P* trend=0.81). Diet soda intake was also not associated with change in VAT:SAT ratio (*P* trend=0.23). Additional adjustment for change in body weight did not change the observed associations.

Secondary Analysis

No significant interaction was observed between SSB intake and sex, BMI, or type 2 diabetes mellitus on the outcomes (Table 3). Nevertheless, sex-specified subgroup analyses were conducted for SSB intake (Tables I and II in the online-only Data Supplement). The association of higher SSB intake and adverse change in volume and attenuation of VAT was observed in both men and women (Figure, A and B). A significant interaction was observed between sex and diet soda

Table 2. Baseline Characteristics of Participants According to Diet Soda Consumption Categories*

	Nonconsumers (0 to <1/mo)	Occasional Consumers (1/mo to <1/week)	Frequent Consumers (1/week to <1/d)	Daily Consumers (≥1/d)	
N=1003	501	128	221	153	
Median intake, servings/week	0	0.5	3	12	*P* Trend
Age, y	45.5±6.3	45.6±6.1	44.8±5.7	45.2±6.4	0.51
Women, %	40.5% (203)	50.0% (64)	51.6% (114)	45.8% (70)	0.35
Current smoker, %	8.4% (42)	9.4% (12)	7.2% (16)	11.8% (18)	0.23
Alcohol, g/d	12.3±15.7	10.1±12.9	10.5±13.5	11.0±15.4	0.48
Physical activity score	38.0±8.7	37.2±8.2	36.7±6.3	36.2±6.7	0.02
Multivitamin, %	46.7% (234)	52.3% (67)	48.4% (107)	47.1% (72)	0.90
BMI, kg/m^2	26.6±4.8	26.5±4.7	27.7±5.2	28.9±5.5	<0.001
VAT, cm^3	1543±866	1437±953	1553±894	1787±947	0.001
VAT, HU	−93.8±4.7	−93.7±4.9	−94.0±4.6	−94.7±4.8	0.03
SAT, cm^3	2557±1316	2578±1380	2935±1368	3231±1613	<0.001
SAT, HU	−100.5±5.2	−100.6±5.2	−101.4±5.2	−101.1±5.1	0.18
VAT(cm^3):SAT(cm^3) ratio†	0.57±0.40	0.51±0.39	0.49±0.37	0.53±0.36	0.13
Type 2 diabetes mellitus, %	2.0% (10)	0.8% (1)	3.6% (8)	5.9% (9)	0.007
Daily energy intake, kcal	2011±645	1974±619	2053±692	2094±676	0.12
Saturated fat, %energy	11.1±2.7	11.6±3.1	11.4±2.6	11.9±2.6	0.005
Whole grain, g/d	29.9±21.0	31.5±22.2	28.8±19.2	29.2±21.1	0.58
Fruits, g/d	274.4±213.4	264.9±177.4	286.1±212.9	228.3±158.8	0.02
Vegetables, g/d	228.5±147.6	231.2±116.6	214.8±135.9	256.7±159.5	0.04
Nuts, g/d	5.1±10.2	5.5±10.4	4.7±10.9	7.3±14.6	0.04
Fish, g/d	44.3±44.0	42.1±36.3	45.4±43.1	44.8±38.9	0.80
Coffee, servings/d	1.3±1.3	1.4±1.3	1.5±1.3	1.6±1.5	0.06
SSB, serving/week	3.7±5.9	2.4±3.7	2.9±5.7	2.0±4.4	0.002

BMI indicates body mass index; SAT, subcutaneous adipose tissue; SSB, sugar-sweetened beverages; and VAT, visceral adipose tissue.
*Mean and standard deviation and proportion and frequency.
†Geometric mean and standard deviation.

intake for change in body weight and VAT volume (both *P* interaction=0.01, Table 4). However, diet soda intake was not associated with change in body weight or VAT volume in either men (Table III in the online-only Data Supplement) or women (Table IV in the online-only Data Supplement). The sex-specific analyses for diet soda intake and change in VAT volume and attenuation are shown in Figure, C and D.

Discussion

Principal Findings

In this prospective observational study of middle-aged adults, we observed that individuals who consumed ≥1 serving of SSB per day (SSB daily consumers) had a 29% greater increase in VAT volume over 6 years compared with nonconsumers. Coupled with this greater increase in VAT volume overtime, the decline in the attenuation of VAT was greater among daily SSB consumers as compared with SSB nonconsumers. In contrast, we observed no significant association between SSB intake and change in either volume or attenuation of SAT. In addition, we observed no significant association between diet soda intake and change in volume and attenuation of abdominal adipose tissue. Taken together, these findings suggest that habitual SSB intake was associated with a long-term adverse change in visceral adiposity (ie, increased VAT volume and decrease in VAT attenuation), independent of weight gain.

In the Context of Current Literature

In our previous study, using data collected from 2596 participants in the Framingham Offspring and Third Generation cohorts, we examined the cross-sectional association of SSB intake and abdominal adipose tissue.[14] In that study, SSB consumption was associated with greater VAT and greater VAT:SAT ratio after adjustment for potential confounders. Similarly, a cross-sectional study conducted in 791 non-Hispanic white adults showed that regular SSB intake was positively associated with the ratio of VAT to overall abdominal adipose tissue.[15] As far as we are aware, our study is the first observational study to prospectively link SSB consumption patterns to changes in VAT volume over time. Our findings are supported by a small (n=47) randomized intervention trial,[22] which demonstrated that a high daily consumption of 1 L of SSB for 6 months led to a 23% increase in VAT volume. As such, our data, together with others, support the hypothesis that regular SSB consumption may be associated with adverse changes in VAT.

In addition to VAT volume, it has been shown that adipose tissue attenuation is a marker of metabolic risk.[3] A lower HU reflects high lipid content in adipose tissue,[5,6] and perhaps a damaged cell growth (ie, adipocyte hypertrophy).[23,24] In the present study, we found that increased SSB intake was associated with a worsening (ie, lower) adipose tissue attenuation over time. Although evidence from human studies is limited, feeding

Table 3. Prospective Association of Sugar-Sweetened Beverage Intake and Change in Abdominal Fat in 1003 Adults

	Nonconsumers (0 to <1/mo)	Occasional Consumers (1/mo to <1/week)	Frequent Consumers (1/week to <1/d)	Daily Consumers (≥1/d)		*P* Interaction		
N=1003	317	196	356	134				
Median intake, servings/week	0	0.5	3	11	*P* Trend	Sex	BMI	T2D
ΔBody weight, kg								
Model 1	2.4 (1.7, 3.2)	2.8 (1.8, 3.7)	2.4 (1.7, 3.0)	1.7 (0.5, 2.9)	0.26	0.46	0.88	0.34
ΔVAT volume, cm^3								
Model 1	659 (582, 735)	675 (582, 767)	709 (640, 777)	809 (683, 935)	0.06	0.37	0.71	0.31
Model 1+Δ body weight	658 (602, 713)	649 (582, 716)	707 (657, 757)	852 (760, 943)	<0.001			
ΔVAT attenuation, HU								
Model 1	0.4 (−0.1, 1.0)	0.4 (−0.2, 1.1)	0.2 (−0.3, 0.7)	−0.6 (−1.5, 0.3)	0.07	0.48	0.02	0.95
Model 1+Δbody weight	0.4 (−0.1, 0.9)	0.5 (−0.0, 1.1)	0.2 (−0.2, 0.6)	−0.8 (−1.6, −0.0)	0.007			
Model 1+Δbody weight +ΔVAT volume	0.2 (−0.1, 0.6)	0.3 (−0.2, 0.7)	0.2 (−0.1, 0.5)	−0.2 (−0.7, 0.4)	0.24			
ΔSAT volume, cm^3								
Model 1	586 (500, 672)	631 (528, 735)	564 (487, 641)	568 (427, 709)	0.70	0.72	0.92	0.44
Model 1+Δbody weight	584 (524, 644)	612 (539, 684)	560 (507, 614)	611 (512, 710)	0.77			
ΔSAT attenuation, HU								
Model 1	−5.6 (−6.0, −5.2)	−5.4 (−5.8, −4.9)	−5.4 (−5.7, −5.1)	−5.5 (−6.2, −4.9)	0.92	0.17	0.47	0.40
Model 1+Δbody weight	−5.6 (−5.9, −5.3)	−5.3 (−5.7, −4.9)	−5.4 (−5.7, −5.1)	−5.6 (−6.2, −5.1)	0.63			
Model 1+Δbody weight +ΔSAT volume	−5.6 (−5.9, −5.3)	−5.2 (−5.6, −4.9)	−5.4 (−5.7, −5.2)	−5.6 (−6.1, −5.1)	0.61			
Δ VAT(cm^3):SAT(cm^3) ratio								
Model 1	0.09 (0.06, 0.11)	0.08 (0.05, 0.11)	0.12 (0.10, 0.14)	0.15 (0.11, 0.18)	0.007	0.39	0.90	0.80
Model 1+Δbody weight	0.09 (0.07, 0.11)	0.08 (0.05, 0.10)	0.12 (0.10, 0.14)	0.15 (0.11, 0.19)	0.004			

Model 1 adjusted for baseline outcome values, sex, age, smoking status (yes/no), physical activity score, energy intake (kcal/d), alcohol intake (g/d), saturated fat intake (%energy), diet soda intake (servings/week), multivitamin use (yes/no), whole grain, fruit, vegetable, coffee (servings/d), nuts, and fish. BMI indicates body mass index; SAT, subcutaneous adipose tissue; SSB, sugar-sweetened beverages; T2D, type 2 diabetes mellitus; and VAT, visceral adipose tissue.

Table 4. Prospective Association of Diet Soda Intake and Change in Abdominal Fat in 1003 Adults

	Nonconsumers (0 to <1/mo)	Occasional Consumers (1/mo to <1/week)	Frequent Consumers (1/week to <1/d)	Daily Consumers (≥1/d)		*P* Interaction		
N=1003	501	128	221	153				
Median intake, servings/week	0	0.5	3	12	*P* Trend	Sex	BMI	T2D
ΔBody weight, kg								
Model 1	2.8 (2.2, 3.3)	1.6 (0.5, 2.7)	1.7 (0.8, 2.5)	2.7 (1.7, 3.8)	0.85	0.01	0.99	0.57
ΔVAT volume, cm^3								
Model 1	709 (652, 766)	628 (517, 740)	685 (599, 771)	748 (644, 853)	0.38	0.01	0.24	0.30
Model 1+Δbody weight	680 (639, 722)	680 (599, 761)	737 (674, 799)	725 (650, 801)	0.27			
Δ VAT attenuation, HU								
Model 1	0.1 (−0.3, 0.5)	1.1 (0.3, 1.9)	−0.0 (−0.6, 0.6)	0.1 (−0.6, 0.9)	0.72	0.88	0.14	0.67
Model 1+Δbody weight	0.2 (−0.1, 0.6)	0.8 (0.1, 1.5)	−0.3 (−0.8, 0.2)	0.3 (−0.4, 0.9)	0.75			
Model 1+Δbody weight +ΔVAT volume	0.1 (−0.2, 0.4)	0.5 (0.0, 1.0)	−0.1 (−0.4, 0.3)	0.6 (0.1, 1.0)	0.19			
ΔSAT volume, cm^3								
Model 1	588 (525, 652)	556 (431, 680)	584 (488, 679)	599 (482, 717)	0.80	0.92	0.73	0.46
Model 1 + Δbody weight	555 (511, 600)	616 (528, 703)	637 (570, 704)	579 (497, 662)	0.72			
ΔSAT attenuation, HU								
Model 1	−5.5 (−5.8, −5.2)	−5.4 (−6.0, −4.9)	−5.4 (−5.8, −5.0)	−5.6 (−6.1, −5.0)	0.81	0.68	0.76	0.60
Model 1+Δbody weight	−5.4 (−5.6, −5.1)	−5.6 (−6.1, −5.2)	−5.6 (−5.9, −5.2)	−5.5 (−5.9, −5.1)	0.64			
Model 1+Δ body weight + ΔSAT volume	−5.4 (−5.7, −5.2)	−5.6 (−6.0, −5.2)	−5.4 (−5.7, −5.1)	−5.5 (−5.9, −5.1)	0.95			
ΔVAT(cm^3):SAT(cm^3) ratio								
Model 1	0.11 (0.09, 0.12)	0.07 (0.04, 0.11)	0.10 (0.08, 0.13)	0.12 (0.09, 0.15)	0.23	0.18	0.54	0.58
Model 1 + Δbody weight	0.10 (0.09, 0.12)	0.08 (0.05, 0.11)	0.11 (0.08, 0.13)	0.12 (0.09, 0.15)	0.19			

Model 1 adjusted for baseline outcome values, sex, age, smoking status (yes/no), physical activity score, energy intake (kcal/d), alcohol intake (g/d), saturated fat intake (%energy), sugar-sweetened beverage intake (servings/week), multivitamin use (yes/no), whole grain, fruit, vegetable, coffee (servings/d), nuts, and fish. BMI indicates body mass index; SAT, subcutaneous adipose tissue; SSB, sugar-sweetened beverages; T2D, type 2 diabetes mellitus; and VAT, visceral adipose tissue.

a high fructose diet (fructose accounting for 30% of energy) for 8 weeks significantly increased volume of intra-abdominal adipose tissue, as well as the size of adipocytes in this tissue compared with a standard chow diet in male Sprague-Dawley rats.[25] In contrast, this animal study observed no effect of high-fructose diet on SAT, which is consistent with our observation that SSB intake was not associated with SAT attenuation in humans. However, lipid metabolism and the structure of adipose tissue in rats are different from humans, and the actual intake of fructose in the human diet is lower than 30% of energy intake.[26] Further studies in humans that seek to examine the relationship of SSB or added sugar intake and VAT quality are needed.

Multiple factors may confound our lack of association between baseline SSB intake and weight change. Participants may have stopped drinking SSB after the baseline examination. It is also possible that some individuals, particularly those with overweight and obesity, may underestimate their SSB intake.[27]

Potential Mechanisms

Several mechanisms may explain the observed association between SSB intake and adverse changes in VAT. Under normal conditions, circulating triglycerides deposition is more efficient in SAT compared with VAT because lipoprotein lipase, the rate-limiting enzyme, is more sensitive to insulin in SAT than that in VAT.[28,29] In contrast, under conditions of insulin resistance, lipoprotein lipase activity in SAT may be suppressed[28,29] and greater amounts of triglycerides flux in VAT. It has been hypothesized that excess fructose, the major component in SSB, may trigger insulin resistance and increase fat accumulation in VAT.[30] Fructose is primarily metabolized in the liver, where it is converted to triglycerides.[31] This pathway is not regulated by phosphofructokinase, the main rate-limiting enzyme in glycolysis.[32] When triglycerides are over produced, some may convert to intermediate products such as diacylglycerols, which may impair insulin signaling pathways.[33] It is also possible that fructose may directly promote fat deposition in VAT by activating intracellular glucocorticoids.[34] Because glucocorticoids receptors are more prominent in VAT than SAT,[28] triglycerides may be more likely to be stored in VAT when excess SSB is consumed. Nevertheless, the exact underlying mechanisms remain to be determined.

Implications

Excess SSB consumption has been linked to increased risk of type 2 diabetes mellitus and cardiovascular disease.[35] The present study provides a useful hypothesis for further analysis regarding the pathways leading SSB to cardiometabolic diseases. SSB consumption is currently high in both children and adults, particularly in populations with low socioeconomic status.[8] Our findings also emphasize the importance of the current dietary guideline recommendations[36] (ie, limiting SSB consumption as much as possible may be an efficient strategy to reduce the burden of cardiometabolic disease).

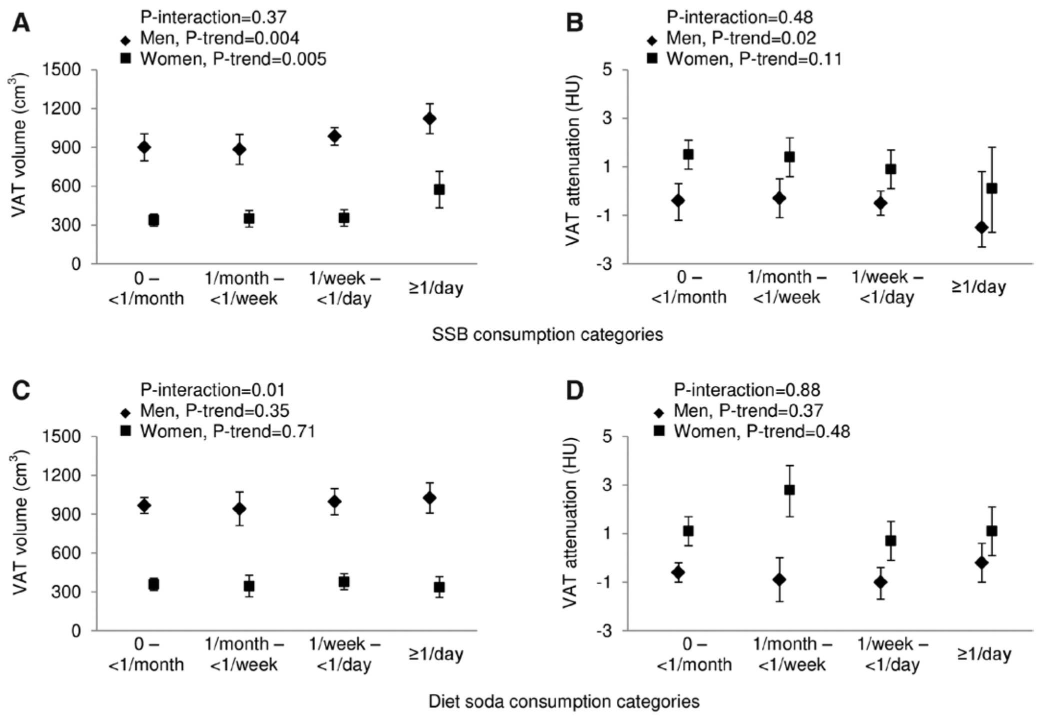

Figure. Sex-specific analysis (552 men and 451 women) of association of sugar-sweetened intake (SSB) and change in visceral adipose tissue (VAT) volume (**A**) and Hounsfield Unit (**B**); diet soda intake and change in visceral adipose tissue (VAT) volume (**C**) and Hounsfield Unit (**D**). In analysis for linear trend, multiple linear regression model was used with adjustment for baseline VAT volume, age, smoking status (yes/no), physical activity score, energy intake, alcohol intake, saturated fat intake, diet soda intake or SSB intake, multivitamin use, whole grain, fruit, vegetable, coffee, nuts, and fish.

Strengths and Limitations

Strengths of the present study include its prospective study design with utilization of highly specific and reproducible measurements of abdominal adipose tissue, and comprehensive dietary, lifestyle, and clinical data collected in the Framingham Heart Study. With respect to limitations, given that the majority of the study sample were white, this limits the generalizability to other ethnically diverse populations. In the present study sample, only 1 estimate of SSB or diet soda intake was assessed at baseline. We cannot rule out that participants may have changed their beverage consumption intake over time. In addition, beverages such as sports drinks, energy drinks, and sweetened teas were not specifically assessed by the FFQ. Individuals with overweight or obesity may underestimate their SSB intake,[27] which may partly explain why we observed no association between SSB intake and change in body weight. However, this type of misclassification is likely to attenuate our findings to the null rather than strengthen the association between SSB intake and change in VAT. Therefore, it is unlikely to account for our primary findings. We adjusted for a variety of dietary and lifestyle factors, but residual confounding may still exist. Finally, the assessment of diet soda intake did not include all consumption of low calorie and artificially sweetened, noncarbonated beverages.

Conclusions

Regular SSB intake at baseline was associated with an adverse change in VAT in a group of middle-aged adults over 6 years of follow-up. In contrast, we observed no such association for diet soda intake. The present study supports current dietary recommendations that limiting SSB consumption may be helpful to prevent cardiometabolic diseases.

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Disclosure

None.

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CLINICAL PERSPECTIVE

Excess sugar-sweetened beverage consumption has been linked to increased risk of cardiovascular disease and type 2 diabetes mellitus. In this study, we conducted a prospective observational study that examined the association between habitual intake of sugar-sweetened beverages and change in visceral adipose tissue. We examined data collected from 1,003 middle-age adults, mean age 45.3 years and 45% women, who attended the Framingham Heart Study's Third Generation Cohort. These participants were examined at baseline and approximately 6 years later. This study demonstrated a dose–response relationship between sugar-sweetened beverage consumption and change in visceral adipose tissue. Higher sugar-sweetened beverage consumption was associated with higher fat accumulation and adverse change of quality in visceral adipose tissue. Our findings provide evidence for further studies regarding underlying mechanisms leading sugar-sweetened beverage intake to cardiometabolic diseases. Our observations highlight the importance of the current dietary recommendations to limit sugar-sweetened beverage consumption.