ORIGINAL RESEARCH

Annals of Internal Medicine

Associations Between Dietary Patterns and Subclinical Cardiac Injury

An Observational Analysis From the DASH Trial

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Background: The DASH diet has been found to lower blood pressure (BP) and low-density lipoprotein cholesterol levels.

Objective: To compare diets rich in fruits and vegetables with a typical American diet in their effects on cardiovascular injury in middle-aged adults without known preexisting cardiovascular disease (CVD).

Design: Observational study based on a 3-group, parallel-design, randomized trial conducted in the United States from 1994 to 1996. (ClinicalTrials.gov: NCT00000544)

Setting: 3 of the 4 original clinical trial centers.

Participants: 326 of the original 459 trial participants with available stored specimens.

Intervention: Participants were randomly assigned to 8 weeks of monitored feeding with a control diet typical of what many Americans eat; a diet rich in fruits and vegetables but otherwise similar to the control diet; or the DASH diet, which is rich in fruits, vegetables, low-fat dairy, and fiber and has low levels of saturated fat and cholesterol. Weight was kept constant throughout feeding.

Measurements: Biomarkers collected at baseline and 8 weeks: high-sensitivity cardiac troponin I (hs-cTnI), *N*-terminal pro–B-type natriuretic peptide (NT-proBNP), and high-sensitivity C-reactive protein (hs-CRP).

Results: The mean age of participants was 45.2 years, 48% were women, 49% were black, and mean baseline BP was 131/85 mm Hg. Compared with the control diet, the fruit-and-vegetable diet reduced hs-cTnI levels by 0.5 ng/L (95% CI, −0.9 to −0.2 ng/L) and NT-proBNP levels by 0.3 pg/mL (CI, −0.5 to −0.1 pg/mL). Compared with the control diet, the DASH diet reduced hs-cTnI levels by 0.5 ng/L (CI, −0.9 to −0.1 ng/L) and NT-proBNP levels by 0.3 pg/mL (CI, −0.5 to −0.04 pg/mL). Levels of hs-CRP did not differ among diets. None of the markers differed between the fruit-and-vegetable and DASH diets.

Limitation: Short duration, missing specimens, and an inability to isolate the effects of specific foods or micronutrients.

Conclusion: Diets rich in fruits and vegetables given over 8 weeks were associated with lower levels of markers for subclinical cardiac damage and strain in adults without preexisting CVD.

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Cardiovascular disease (CVD) is the leading cause of death in the United States (1). Observational studies show that a healthy diet is linked to a reduced risk for CVD events, leading many to advocate for stronger public policy to promote healthy food choices (2). Critics, however, point to a dearth of evidence to support the hypothesis that adopting a healthy diet directly reduces CVD injury (3–5), and few feeding studies of healthy diets have addressed primary prevention of CVD (6).

The DASH trial was an 8-week parallel-group feeding study in adults with systolic blood pressures (SBPs) less than 160 mm Hg and diastolic blood pressures (DBPs) of 80 to 95 mm Hg (7). Participants were fed a typical American diet; a fruit-and-vegetable diet; or the DASH diet, which is rich in fruits, vegetables, low-fat dairy, and fiber and contains lower levels of saturated fat and cholesterol. The DASH diet, which lowered blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C) levels compared with a typical American diet, was considered by many to be a bedrock of dietary guidelines for CVD risk prevention (8). However, whether the observed improvements in CVD risk factors had an impact on cardiac injury has not been reported.

In this study, we examined 3 biomarkers in stored specimens from a subpopulation of DASH trial participants to determine the effects of diet on subclinical cardiac damage (high-sensitivity troponin I [hs-cTnI]), cardiac strain (*N*-terminal pro–B-type natriuretic peptide [NT-proBNP]), and inflammation (high-sensitivity C-reactive protein [hs-CRP]).

See also:

Editorial comment 826

Web-Only
Supplement

Methods

The DASH trial was conducted between September 1994 and March 1996 at 4 clinical centers in the United States (Baltimore, Maryland; Boston, Massachusetts; Durham, North Carolina; and Baton Rouge, Louisiana). The study was sponsored by the National Heart, Lung, and Blood Institute (NHLBI). A detailed description and the primary results of the study have been published (7). In brief, DASH compared the effects of 3 diets on SBP. The 459 trial participants were randomly assigned at each site to a control diet typical of what many Americans eat, a fruit-and-vegetable diet, or the DASH diet. At the time of the study, all participants provided written informed consent for specimen storage.

The present study used specimens curated by the NHLBI Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) to measure the biomarkers described earlier. Institutional review boards at each institution approved the original study protocol. Only 3 of the original 4 sites contributed specimens for this analysis.

Participants

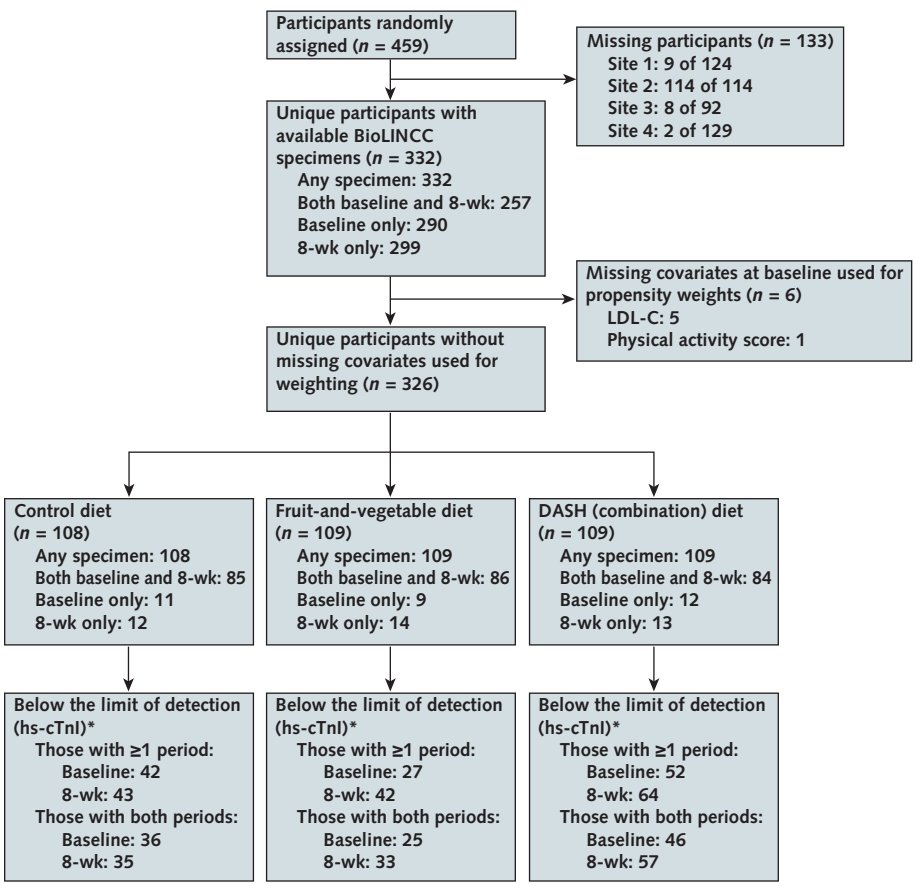
DASH participants were aged 22 years and older with an average SBP of 120 to 159 mm Hg and average DBP of 80 to 95 mm Hg. Adults with diabetes mellitus, a cardiovascular event within the previous 6 months, a body mass index (BMI) greater than 35 kg/m^2, renal insufficiency, or a self-reported alcoholic beverage intake of more than 14 drinks per week were excluded, as were those receiving antihypertensive medications. Of the original 459 participants in the trial, 326 had stored specimens that were used for this analysis. Details regarding these participants, assignments, and specimen availability are in Figure 1.

Dietary Interventions

Following a parallel design, each site randomly assigned participants to 1 of 3 diets: a control diet, a fruit-and-vegetable diet, or the DASH diet (called "the combination diet" in the original publication [Supplement Table 1, available at Annals.org]). The control diet was designed to represent a typical American diet, with potassium, magnesium, and calcium levels reflecting the 25th percentile of U.S. consumption and macronutrient profiles and fiber amounts reflecting average U.S. consumption (7). By contrast, the fruit-and-vegetable diet provided potassium and magnesium levels at the 75th percentile of U.S. consumption and provided higher amounts of fiber. This diet provided more fruits and vegetables with fewer snacks and sweets than the control diet but was otherwise similar.

Like the fruit-and-vegetable diet, the DASH diet provided potassium and magnesium at levels reflecting the 75th percentile of U.S. consumption and was higher in fiber and protein (7). In addition, the DASH diet provided calcium at a level reflecting the 75th percentile of U.S. consumption; emphasized fat-free or low-fat dairy

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram of participants and specimens.



BioLINCC = Biologic Specimen and Data Repository Information Coordinating Center; hs-cTnI = high-sensitivity cardiac troponin I; LDL-C = low-density lipoprotein cholesterol.
* Because there were few undetectable measures for *N*-terminal pro–B-type natriuretic peptide or high-sensitivity C-reactive protein, this figure presents only the number under the limit of detection for hs-cTnI.

products; was reduced in saturated fat, total fat, cholesterol, sweets, and sugar-containing beverages; and included whole grains, poultry, fish, and nuts. All 3 diets were designed to provide a similar amount of sodium (approximately 3 g/d).

Isocaloric diets were administered as part of a 7-day menu cycle, which included 21 meals at 4 Calorie levels (1600, 2100, 2600, and 3100 Cal). Each weekday, participants ate 1 principal meal (lunch or dinner) onsite. The remaining meals (including weekend meals) were sent home in coolers to be consumed offsite. Feeding and participants' weights were closely monitored. Participants recorded intake of beverages, salt, and nonstudy foods. Adherence was high, with participants attending more than 95% of person-days at scheduled onsite meals and adhering to the study protocol offsite (all study foods and no nonstudy foods) over 93% of person-days.

Outcomes of Interest

Biomarker outcomes of interest for this analysis (hs-cTnI, NT-proBNP, and hs-CRP) were measured in 2019 from stored specimens. The biomarkers were selected on the basis of their relationship to subclinical myocyte damage (hs-cTnI), cardiac strain (NT-proBNP), and inflammation (hs-CRP), which have been shown to predict CVD events in adults without known CVD (9–15). Serum specimens were collected from participants after a 12-hour fast at baseline before feeding (n = 290) and at the conclusion of the 8-week feeding period (n = 299) for each of the 3 diets. All serum had been stored at −70 °C and underwent at least 1 freeze–thaw cycle before being measured in the present study. All 3 markers were measured in all available specimens.

Assays and kits were donated by Siemens Healthineers for the following markers: ADVIA Centaur High-Sensitivity Troponin I (reported within-run coefficient of variation [CV] of 4.8% for a mean of 13.11 ng/L [or pg/mL]), Dimension Vista N-terminal Pro-Brain Natriuretic Peptide (reported within-run CV of 1.4% for a mean of 120 pg/mL), and Dimension Vista hs-CRP assay (reported within-run CV of 5.2% for a mean of 2.39 mg/L). Laboratory inserts from the manufacturer with assay accuracy and precision performance data are provided in the **Supplement** (available at Annals.org). A total of 332 participants had specimens at either baseline or the 8-week visit. Biomarker assays were restricted by the following limits of detection: less than 1.60 ng/L for hs-cTnI, less than 5 pg/mL for NT-proBNP, and less than 0.160 mg/L for hs-CRP. Given the larger number of hs-cTnI values below the limit of detection, we also examined an alternate measurement cut point based on the hs-cTnI assay's limit of blank (<0.5 ng/L) (**Supplement Table 2**, available at Annals.org). The limit of detection is defined by the manufacturer as the lowest concentration of hs-cTnI that can be detected with 95% probability, whereas the limit of blank is defined as the highest measurement that might be observed for a blank sample. Note the following conversions for SI units: 1 ng/L of hs-cTnI = 0.001 mg/L, 1 pg/mL of NT-proBNP = 1 ng/L or 0.1182 pmol/L, and 1 mg/L of hs-CRP = 9.5238 nmol/L.

Covariates

Other participant characteristics were determined via questionnaire, laboratory specimens, and physical examination. Race was examined in categories of black and nonblack. Body mass index was derived from measured height and weight; obesity was defined as a BMI of 30 kg/m^2 or greater. Seated SBP and DBP were measured with random-zero sphygmomanometers. Blood pressure at baseline was based on the average of 3 pairs of measurements during screening and 4 pairs during the run-in phase, whereas BP at follow-up was based on the average of 4 or 5 pairs of measurements during weeks 7 and 8 of the intervention phase. Hypertension was defined in DASH as an SBP of 140 mm Hg or higher or a DBP of 90 mm Hg or higher. Total cholesterol, high-density lipoprotein cholesterol, and triglyceride levels were measured with enzymatic colorimetry and used to estimate LDL-C levels (16). Number of alcoholic drinks per day was self-reported. Participants also were asked to quantify the time they spent on "moderate," "hard," or "very hard" tasks during the preceding 7 days to estimate their physical activity score (calories per kilogram per day).

Statistical Analysis

All analyses were up-weighted (via the "pw" option) with inverse propensity score weights (17) to account for missing specimens and thus reflect the characteristics of the original randomized sample of the 3 sites included in this study (n = 345). Propensity scores were determined via a logit function in which specimen variability was the dependent variable of the following participant characteristics (independent variables): age; female sex; black race; and baseline SBP, DBP, LDL-C, BMI, hypertension status, obesity, alcohol use, and physical activity score.

We described baseline population characteristics, by diet assignment, by using weighted means (SD) and proportions. Individual changes in biomarkers were examined via spaghetti plots. The distribution of natural log-transformed cardiac biomarkers at baseline and 8 weeks was examined by using kernel density plots. Given data skew, we determined the geometric mean of serum concentrations (SD) of biomarkers at baseline and 8 weeks and used both the absolute difference (the difference in geometric means) and the percentage change (derived by exponentiating the log-transformed difference) to compare change from baseline.

We compared log-transformed cardiac markers across dietary assignments by using the following contrasts: fruit-and-vegetable versus control diet, DASH versus control diet, and fruit-and-vegetable versus DASH diet. We report both the difference in exponentiated values (geometric means) to estimate change on the original marker scale and exponentiated differences to present percentage difference between diets.

All comparisons (both baseline and between diets) were performed via mixed-effects tobit regression mod-

els (*metobit* command) that were left-truncated for the limits of detection or blank described earlier. We used a tobit model to address informative left-censoring that occurs below the limit of detection (or blank) for each assay. The tobit model allowed us to fit a linear regression model in the detectable range while designating undetectable biomarkers as below the detectable range (18). The fixed-effects portion of the tobit model included diet assignment, visit (baseline or follow-up), and the interaction of these terms. The random-effects portion of the tobit model included participant identification numbers (introducing a random intercept). Although we attempted to produce mixed-effects models with a random slope for study visit, these models would not converge. For a sensitivity analysis, we used marginal, longitudinal tobit models with the variance clustered by participant, assuming that missing specimens occurred completely at random. These models yielded similar results.

Standardized mean difference E-values (using unclustered SDs) were calculated for each of the between-diet contrasts to estimate the minimum strength of association an unmeasured confounder would need to explain away the dietary associations with each cardiac biomarker (19). These sensitivity analyses are needed in this observational follow-up study.

Note that for kernel density plots, we imputed the undetectable range of the biomarkers as two thirds the distance to 0, using 0.333 for hs-cTnI (limit of blank), 1.067 for hs-cTnI (limit of detection), 3.333 for NT-proBNP, and 0.1067 for hs-CRP.

All analyses were conducted by using Stata, version 15.0 (StataCorp) (for code details, see the **Supplement**). Missing data were distributed evenly across dietary assignments.

Role of the Funding Source

The funding source had no role in the study design, conduct, or analysis, or the decision to submit the manuscript for publication.

RESULTS

Baseline Characteristics

Weighted and unweighted baseline characteristics of the DASH trial participants are shown in **Table 1** (for unweighted characteristics by diet, see **Supplement Table 3**, available at Annals.org). The differences across dietary assignments were minimal. From the 3 sites that contributed specimens, 19 participants were missing. These participants were more likely to be black and have higher LDL-C levels. Nevertheless, weighted characteristics were balanced across dietary assignments.

Change in Cardiac Biomarkers From Baseline

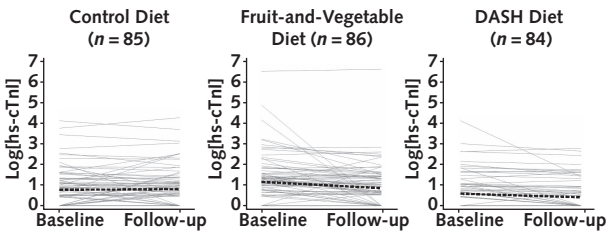
Individual changes in biomarkers from baseline, according to diet assignment, are shown in **Supplement Figure 1** (available at Annals.org) and **Figures 2** to **4**. Mean baseline concentrations of biomarkers were similar across diet assignments with the exception of hs-cTnI, which was higher in those assigned to the fruit-and-vegetable diet (**Table 2**; **Supplement Figures 2** to **4**, available at Annals.org). Statistically significant changes in hs-cTnI levels (limit of detection) from baseline were seen among participants on the fruit-and-vegetable diet (−0.9 ng/L [95% CI, −1.5 to −0.3 ng/L]) and the DASH diet (−0.4 ng/L [CI, −0.6 to −0.2 ng/L]). Statistically significant changes were also observed in NT-proBNP levels from baseline among those assigned to the fruit-and-vegetable diet (−4.6 pg/mL [CI, −7.9 to −1.2 pg/mL]) and the DASH diet (−4.0 pg/mL [CI, −7.3

Table 1. Weighted Baseline Characteristics, According to Diet Assignment

Characteristic	Diet			Unweighted Overall Characteristics of Those Included (*n* = 326)*	Unweighted Characteristics of Those Not Included (*n* = 19)†
	Control (*n* = 108)	Fruit-and-Vegetable (*n* = 109)	DASH (Combination) (*n* = 109)		
Mean age (SD), *y*	44.7 (1.1)	45.9 (1.1)	44.5 (1.0)	45.2 (0.6)	47.2 (2.2)
Female, %	45.1	43.4	52.0	48.2	31.6
Black, %	49.1	46.3	52.6	49.4	63.2
BMI					
≥30 kg/m^2, %	36.2	34.8	34.4	36.2	31.6
Mean (SD), *kg/m^2*	28.0 (0.4)	27.8 (0.4)	28.2 (0.4)	28.1 (0.2)	27.4 (0.7)
Hypertension, %	26.0	26.3	25.1	25.8	36.8
Mean SBP (SD), *mm Hg*	130.5 (1.1)	131.3 (1.1)	130.8 (1.0)	131.0 (0.6)	129.6 (2.5)
Mean DBP (SD), *mm Hg*	84.8 (0.4)	84.3 (0.5)	84.1 (0.4)	84.5 (0.3)	83.9 (0.8)
Mean LDL-C level (SD)					
mg/dL	120.9 (2.9)	127.9 (2.9)	118.7 (3.3)	121.7 (1.8)	141.7 (6.7)
mmol/L	3.1 (0.1)	3.3 (0.1)	3.1 (0.1)	3.1 (0.0)	3.7 (0.2)
Mean alcohol consumption (SD), *drinks per day*	1.4 (0.2)	1.2 (0.2)	1.2 (0.2)	1.2 (0.1)	1.0 (0.3)
Mean physical activity (SD), *cal/kg/d*	37.6 (0.6)	37.7 (0.6)	37.7 (0.6)	37.8 (0.4)	36.9 (1.5)

BMI = body mass index; DBP = diastolic blood pressure; LDL-C = low-density lipoprotein cholesterol; SBP = systolic blood pressure.
* Of the 332 participants with cardiac biomarkers measured from at least 1 visit, 5 did not have a baseline LDL-C measurement and 1 did not have a baseline activity score. As a result, our analytic sample included 326 participants.
† This number is based on the 3 research sites that provided specimens. In the original DASH study, there were 4 research sites. One site, with 114 participants, did not provide any specimens. Of the 19 participants not included in our study from the 3 research sites with specimens, only 13 had a measured LDL-C level at baseline and only 18 had a physical activity score measured at baseline. The vast majority (13 of 19) were excluded because they did not have specimens available to measure cardiac biomarkers.

Figure 2. Spaghetti plots of hs-cTnI (limit of detection, 1.6 ng/L).



Spaghetti plots of the within-person change in natural log-transformed hs-cTnI (nanograms per liter), created by using the limit of detection (1.6 ng/L) at baseline and the follow-up visit after 8 weeks. These plots are limited to the 255 participants with both baseline and follow-up measurements. Values below the limit of blank were imputed as two thirds the distance to zero (1.067 ng/L). The thick dashed line represents the average slope and intercept. hs-cTnI = high sensitivity cardiac troponin I.

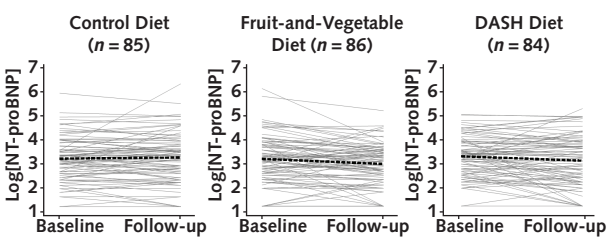
to −0.8 pg/mL]). No change was seen in baseline hs-CRP levels during any of the 3 diets.

Comparison Among Randomized Dietary Assignments

Compared with the control diet, the fruit-and-vegetable diet reduced hs-cTnI levels (limit of detection) by 0.5 ng/L (CI, −0.9 to −0.2 ng/L) and NT-proBNP levels by 0.3 pg/mL (CI, −0.5 to −0.1 pg/mL) (**Table 3**; **Supplement Figures 5** to **7**, available at Annals.org). Compared with the control diet, the DASH diet reduced hs-cTnI levels by 0.5 ng/L (CI, −0.9 to −0.1 ng/L) and NT-proBNP levels by 0.3 pg/mL (CI, −0.5 to −0.04 pg/mL). Levels of hs-CRP did not differ among diets (**Supplement Figure 8**, available at Annals.org), and none of the markers differed between the DASH and fruit-and-vegetable diets.

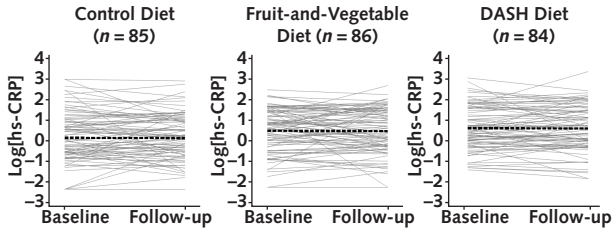
E-values were greater for the contrast between the fruit-and-vegetable and control diets with respect to hs-cTnI and NT-proBNP levels and for the contrast between the DASH and control diets with respect to hs-cTnI and NT-proBNP levels (**Supplement Table 4**, available at Annals.org). This finding implies that only a strong confounder could explain away some of the estimated differences in outcome between diets, and shift the estimates toward the null far enough that the confidence bounds include zero.

Figure 3. Spaghetti plots of NT-proBNP.



Spaghetti plots of the within-person change in natural log-transformed NT-proBNP (picograms per milliliter) at baseline and the follow-up visit after 8 weeks. These plots are limited to the 255 participants with both baseline and follow-up measurements. The thick dashed line represents the average slope and intercept. NT-proBNP = *N*-terminal pro–B-type natriuretic peptide.

Figure 4. Spaghetti plots of hs-CRP.



Spaghetti plots of the within-person change in natural log-transformed hs-CRP (milligrams per liter) at baseline and the follow-up visit after 8 weeks. These plots are limited to the 255 participants with both baseline and follow-up measurements. The thick dashed line represents the average slope and intercept. hs-CRP = high-sensitivity C-reactive protein.

DISCUSSION

Both a diet rich in fruits and vegetables and the DASH diet were associated with lower subclinical cardiac damage and strain within an 8-week period. These associations did not differ between the DASH and fruit-and-vegetable diets, and none of the diets affected hs-CRP, a marker of inflammation. We believe these findings strengthen recommendations for the DASH diet and, more generally, for increased consumption of fruits and vegetables as a means of optimizing cardiovascular health.

Observational evidence has consistently demonstrated that greater consumption of the DASH diet is associated with a lower risk for CVD events over time (20–22). Furthermore, we recently showed that 3 healthy DASH-like diets lowered hs-cTnI levels over 6 weeks, regardless of differences in their macronutrient content. However, the pre–post comparisons in our previous study were not controlled. In the present study, we demonstrated that compared with a typical American diet, 2 healthful diets rich in fruits and vegetables reduced subclinical cardiac damage and strain.

Our study demonstrated that both the DASH and fruit-and-vegetable diets reduced levels of NT-proBNP, a marker of cardiac strain (23). Observational studies have shown that the DASH diet is associated with favorable left ventricular function (24) and a lower risk for heart failure (25–27), as well as greater exercise capacity (28) and a lower risk for death among those with heart failure (29). Our study suggests that dietary features common to both the DASH and fruit-and-vegetable diets, including but not limited to higher potassium, magnesium, and fiber content, may be causative factors. Further research is needed to confirm whether similar diets can improve cardiac function in adults with established heart failure.

Several observational studies have described inverse relationships between DASH-patterned diets and CRP levels (30–32). Furthermore, several lifestyle interventions demonstrated CRP reduction in the setting of

Table 2. Baseline and 8-Week Concentrations of Cardiac Biomarkers and Their Differences, by Diet Assignment*

Biomarker and Diet†	Baseline‡	8-Week‡	Absolute Change From Baseline (95% CI)§	Difference From Baseline (95% CI), %‖
Mean hs-cTnI (SD), *ng/L*				
Limit of blank: 5				
Control	1.4 (0.2)	1.5 (0.2)	0.1 (−0.2 to 0.3)	6.3 (−10.8 to 26.5)
Fruit-and-vegetable	2.4 (0.4)	1.5 (0.2)	−0.9 (−1.4 to −0.4)	−37.2 (−49.5 to −21.8)
DASH (combination)	1.2 (0.2)	0.9 (0.1)	−0.3 (−0.6 to −0.1)	−27.1 (−39.5 to −12.3)
Limit of detection: 1.6				
Control	1.6 (0.2)	1.7 (0.2)	0.0 (−0.2 to 0.3)	2.8 (−13.5 to 22.2)
Fruit-and-vegetable	2.7 (0.4)	1.8 (0.2)	−0.9 (−1.5 to −0.3)	−33.6 (−47.3 to −16.4)
DASH (combination)	1.3 (0.2)	0.9 (0.1)	−0.4 (−0.6 to −0.2)	−30.4 (−42.0 to −16.4)
Mean NT-proBNP (SD), *pg/mL*				
Control	23.1 (2.0)	24.2 (2.3)	1.0 (−1.7 to 3.8)	4.5 (−6.7 to 17.0)
Fruit-and-vegetable	25.0 (2.3)	20.4 (1.6)	−4.6 (−7.9 to −1.2)	−18.3 (−29.0 to −6.0)
DASH (combination)	24.6 (2.0)	20.5 (2.0)	−4.0 (−7.3 to −0.8)	−16.5 (−27.9 to −3.2)
Mean hs-CRP (SD), *mg/L*				
Control	1.2 (0.2)	1.2 (0.1)	−0.0 (−0.2 to 0.2)	−0.6 (−17.1 to 19.1)
Fruit-and-vegetable	1.6 (0.2)	1.5 (0.2)	−0.0 (−0.3 to 0.2)	−2.8 (−19.2 to 16.9)
DASH (combination)	1.7 (0.2)	1.7 (0.2)	−0.0 (−0.3 to 0.2)	−0.8 (−14.7 to 15.2)

hs-CRP = high-sensitivity C-reactive protein; hs-cTnI = high-sensitivity cardiac troponin I; NT-proBNP = *N*-terminal pro–B-type natriuretic peptide.
* Note that 108 participants were assigned to the control diet, 109 to the fruit-and-vegetable diet, and 109 to the DASH diet. Estimates were derived via weighted mixed-effects tobit models. Please refer to the main text for details.
† Conversions: 1 ng/L of hs-cTnI = 0.001 mg/L, 1 pg/mL of NT-proBNP = 1 ng/L or 0.1182 pmol/L, and 1 mg/L of hs-CRP = 9.5238 nmol/L.
‡ Exponentiated log-transformed markers or the geometric mean.
§ Difference in exponentiated log-transformed markers (i.e., difference in geometric means).
‖ Exponentiated differences of the change on the log-scale.

weight loss (33, 34). In another trial, we demonstrated that 3 isocaloric DASH-like diets reduced hs-CRP levels from baseline, but these comparisons lacked a temporal control (35). One controlled trial of an isocaloric, high-fiber DASH diet demonstrated CRP reduction only in a lean subpopulation (BMI <25 kg/m^2) (36). The present study, with an average BMI of 28 kg/m^2 among participants, did not observe any effect from diet on hs-CRP levels. We speculate that weight is a principal determinant of elevated hs-CRP levels among overweight and obese adults such that improvements in diet that do not reduce weight may not influence hs-CRP concentrations.

In the original study, the DASH diet had greater effects on SBP, DBP, and LDL-C levels than the fruit-and-vegetable diet (7, 16). However, these differences in CVD risk factors did not translate into significant differences in hs-cTnI and NT-proBNP levels between the fruit-and-vegetable and DASH diets at 8 weeks. Although reductions in these markers reflect short-term improvements in subclinical CVD injury, their relationships with CVD events have been observed indepen-

Table 3. Weighted Differences in Cardiac Biomarkers Between Diets

Biomarker and Diet*	Absolute Difference (95% CI)	Difference (95% CI), %
hs-cTnI, *ng/L*		
Limit of blank: 0.5		
Fruit-and-vegetable vs. control	−0.6 (−0.9 to −0.3)	−40.8 (−55.3 to −21.7)
DASH vs. control	−0.5 (−0.9 to −0.1)	−31.4 (−46.9 to −11.5)
Fruit-and-vegetable vs. DASH	−0.1 (−0.3 to 0.1)	−13.7 (−35.1 to 14.7)
Limit of detection: 1.6		
Fruit-and-vegetable vs. control	−0.5 (−0.9 to −0.2)	−35.4 (−51.5 to −13.9)
DASH vs. control	−0.5 (−0.9 to −0.1)	−32.3 (−47.4 to −12.9)
Fruit-and-vegetable vs. DASH	−0.0 (−0.2 to 0.2)	−4.6 (−27.8 to 26.1)
NT-proBNP, *pg/mL*		
Fruit-and-vegetable vs. control	−0.3 (−0.5 to −0.1)	−21.8 (−34.7 to −6.4)
DASH vs. control	−0.3 (−0.5 to −0.0)	−20.1 (−33.7 to −3.7)
Fruit-and-vegetable vs. DASH	−0.0 (−0.2 to 0.1)	−2.2 (−20.2 to 19.9)
hs-CRP, *mg/L*		
Fruit-and-vegetable vs. control	−0.0 (−0.3 to 0.2)	−2.2 (−24.5 to 26.6)
DASH vs. control	−0.0 (−0.2 to 0.2)	−0.2 (−21.2 to 26.3)
Fruit-and-vegetable vs. DASH	−0.0 (−0.3 to 0.2)	−2.0 (−22.8 to 24.3)

hs-CRP = high-sensitivity C-reactive protein; hs-cTnI = high-sensitivity cardiac troponin I; NT-proBNP = *N*-terminal pro–B-type natriuretic peptide.
* Conversions: 1 ng/L of hs-cTnI = 0.001 mg/L, 1 pg/mL of NT-proBNP = 1 ng/L or 0.1182 pmol/L, and 1 mg/L of hs-CRP = 9.5238 nmol/L.

dent of pathways predicted by traditional risk factors (9–12). Thus, they do not necessarily capture, for example, long-term ischemic risk from atherosclerotic plaque burden and potential rupture (37). This distinction is important, because the BP- and cholesterol-reducing features of the DASH diet probably still play an important role in long-term CVD risk prevention. Further research is needed to study the longitudinal effects of the DASH diet on CVD events.

Our study has limitations. Because specimens that had been collected in the DASH trial were not available for several of the original participants, our findings are observational and susceptible to confounding. Nevertheless, E-values for hs-cTnI and NT-proBNP levels suggest that unmeasured confounding cannot explain the larger observed associations. The study duration of 8 weeks was short; effects of diet on clinical events could not be evaluated. Specimens were stored for at least 2 decades before measurement. Although hs-CRP is thought to be robust to freeze–thaw cycling (38, 39), its measurements may have been affected by drift, contributing to its null relationship with the diets. Specific food groups or micronutrients that affect cardiac biomarker changes could not be isolated, although the similar changes seen with the DASH and fruit-and-vegetable diets suggest that micronutrients or food groups common to those 2 diets are probably involved. Of note, minor differences in sodium intake were seen between diets, which we could not adjust for in our analyses. In many cases, troponin concentrations were undetectable, introducing model uncertainty. Although protocol adherence was high, consumption of nonstudy foods may have biased the findings and increased imprecision. Variables used for weighting (such as self-reported alcohol use or physical activity) have measurement error and also may increase imprecision.

Our study also has several strengths. The dietary interventions were tightly controlled and administered in a randomized fashion. We examined highly sensitive cardiac markers in adults without established CVD. As a result, our study shows the short-term effects of diet on cardiac damage and strain, observations more proximal to actual CVD events. The use of isocaloric diets minimized the possibility of weight change and its effects on biomarkers, particularly hs-CRP. Higher E-values for the fruit-and-vegetable and DASH diets versus the control diet with respect to levels of the biomarkers hs-cTnI and NT-proBNP suggest that unmeasured confounding cannot explain the larger observed associations.

Our study has potential clinical implications. Cardiovascular disease is the leading cause of death in the United States (1). Large observational studies have consistently demonstrated that unhealthy food consumption is associated with a greater risk for CVD events (20–22). As a result, many advocate for stronger government policies aimed at promoting healthier lifestyle behaviors (40). Meanwhile, critics point out the lack of causal evidence that a healthy diet prevents CVD (41) and the lack of consensus on what defines a "heart-healthy" diet (42). Our study shows that what we eat has an impact on cardiac damage and strain over 8 weeks. Moreover, it simplifies what is known about the minimum requirements for healthy eating for short-term cardiac benefits to the following advice: Consume more fruit, vegetables, nuts, seeds, and legumes and eat fewer snacks and sweets. This distilled list of food groups may be more easily targeted by public policy.

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Data Sharing Statement: The following data will be made available with publication: deidentified participant data and data dictionary. The data from the original trial are available via the NHLBI BioLINCC (https://biolincc.nhlbi.nih.gov/home), which maintains a formal proposal submission and review process. The following supporting documents will be made available with publication: manual of procedures (available at ClinicalTrials.gov). These data will be made available to all investigators after approval of a proposal with a signed data sharing agreement.

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