Mediterranean diet score and left ventricular structure and function: the Multi-Ethnic Study of Atherosclerosis[1,2]

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ABSTRACT

Background: Data are limited on the relation between dietary patterns and left ventricular (LV) structure and function.

Objective: We examined cross-sectional associations of a diet-score assessment of a Mediterranean dietary pattern with LV mass, volume, mass-to-volume ratio, stroke volume, and ejection fraction.

Design: We measured LV variables with the use of cardiac MRI in 4497 participants in the Multi-Ethnic Study of Atherosclerosis study who were aged 45–84 y and without clinical cardiovascular disease. We calculated a Mediterranean diet score from intakes of fruit, vegetables, nuts, legumes, whole grains, fish, red meat, the monounsaturated fat:saturated fat ratio, and alcohol that were self-reported with the use of a food-frequency questionnaire. We used linear regression with adjustment for body size, physical activity, and cardiovascular disease risk factors to model associations and assess the shape of these associations (linear or quadratic).

Results: The Mediterranean diet score had a slight U-shaped association with LV mass (adjusted means: 146, 145, 146, and 147 g across quartiles of diet score, respectively; *P*-quadratic trend = 0.04). The score was linearly associated with LV volume, stroke volume, and ejection fraction: for each +1-U difference in score, LV volume was 0.4 mL higher (95% CI: 0.0, 0.8 mL higher), the stroke volume was 0.5 mL higher (95% CI: 0.2, 0.8 mL higher), and the ejection fraction was 0.2 percentage points higher (95% CI: 0.1, 0.3 percentage points higher). The score was not associated with the mass-to-volume ratio.

Conclusions: A higher Mediterranean diet score is cross-sectionally associated with a higher LV mass, which is balanced by a higher LV volume as well as a higher ejection fraction and stroke volume. Participants in this healthy, multiethnic sample whose dietary patterns most closely conformed to a Mediterranean-type pattern had a modestly better LV structure and function than did participants with less–Mediterranean-like dietary patterns. This trial was registered at clinicaltrials.gov as NCT00005487. *Am J Clin Nutr* 2016;104:595–602.

Keywords: cardiovascular disease, epidemiology, Mediterranean diet pattern, left ventricular structure, left ventricular function, subclinical cardiovascular disease

INTRODUCTION

Subclinical changes in heart structure and function often precede symptomatic heart failure (1, 2); these changes are considered a stage in development of heart failure (3). In asymptomatic individuals, an elevated left ventricular (LV)[12] mass and volume and reduced ejection fraction are risk factors for incident symptomatic heart failure (2, 4–6). A higher LV mass-to-volume ratio is indicative of adverse remodeling and is associated with cardiovascular disease (CVD) (7, 8). Prudent dietary patterns, including the Mediterranean dietary pattern, are recommended to reduce risk of ischemic heart disease and to prevent or mitigate other heart-failure risk factors including hypertension and diabetes (3, 9). The 2015–2020 US federal dietary guidelines include a Mediterranean-style dietary pattern as one of several examples of healthy eating patterns (10). Low risk of ischemic heart disease in populations who follow Mediterranean dietary patterns has been documented in observational studies, including the landmark Seven Countries study (11–14). Although low-fat dietary advice has been commonly recommended to reduce risk of CVD, trials of Mediterranean-style dietary advice and supplemental foods that are high in monounsaturated fat have shown benefits for the prevention of CVD (15–17). In the 7447 participants in the Prevención con Dieta Mediterránea trial (also known as PREDIMED), high-risk

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[2] Supplemental Figure 1 and Supplemental Table 1 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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[12] Abbreviations used: CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; FFQ, food-frequency questionnaire; LV, left ventricular; MESA, Multi-Ethnic Study of Atherosclerosis.

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individuals in the Mediterranean diet arms had 30% lower risk of first CVD events than did participants who were randomly assigned to receive low-fat dietary advice (17). Mediterranean style dietary advice reduced blood pressure, fasting glucose and insulin, and the total cholesterol:HDL-cholesterol ratio in the Prevención con Dieta Mediterránea sample (18). In 505 participants enrolled in the Lyon Diet Heart Study after a myocardial infarction, those who were randomly assigned to the Mediterranean diet arm had a 72% lower rate of cardiac mortality or nonfatal myocardial infarction (15).

A previous study showed an inverse association between a Mediterranean diet score and LV mass (19). Other prudent dietary patterns have also been associated with LV structure and function. There were modest, favorable associations of the DASH (Dietary Approaches to Stop Hypertension) dietary pattern (20) and unfavorable associations of a dietary pattern that was characterized by high processed food and low fruit and vegetable intakes (21) with LV structure and function in adults who were free of clinical CVD in the MESA (Multi-Ethnic Study of Atherosclerosis). Although Mediterranean diet scores share many characteristics with other diet scores that capture a prudent dietary pattern, Mediterranean diet scores also have distinctive characteristics including a focus on monounsaturated fat intake and moderate alcohol consumption (22). Therefore, we explored the cross-sectional associations of a Mediterranean diet score that was designed to capture a Mediterranean-type dietary pattern with LV structure and function in 4497 participants in the MESA. This score was created by Trichopoulou et al. (23) in a Greek population and modified for a US population by Fung et al. (12).

METHODS

Study population

The MESA is a prospective cohort study of 6814 men and women who were recruited between 2000 and 2002 from Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; northern Manhattan and Bronx, New York; and St. Paul, Minnesota (24). Eligible participants were white, African American, Hispanic, or Chinese adults who were 45–84 y of age and without clinically recognized CVD at enrollment. For this cross-sectional analysis, we used participant data from the baseline examination that included assessments of medical histories and medication use, demographic and socioeconomic factors, dietary intakes, physical activity, family histories, anthropometric measures, and blood pressure. Blood and urine samples were collected, and measures of subclinical atherosclerosis were obtained (24, 25). Seventy-three percent of MESA participants (n = 5004) had a technically adequate cardiac MRI, and 90% of those participants (n = 4497) completed the food-frequency questionnaire (FFQ) and reported energy intakes between 600 and 6000 kcal/d (**Supplemental Figure 1**). Institutional review boards at each center approved the MESA protocols, and all participants provided written informed consent.

Dietary assessment

The self-administered FFQ was modified from a Block-style questionnaire that was originally designed for the Insulin Resistance and Atherosclerosis Study (26). Items were added to the FFQ to accommodate the demographics of the MESA sample (17, 21, 27). In 186 participants in the Insulin Resistance and Atherosclerosis Study, nutrient intakes that were calculated from the FFQ were compared with nutrient intakes that were calculated from eight 24-h recalls; the median correlation coefficient was 0.49 (26). In the MESA population, the criterion validity of the FFQ was established through a demonstration of known associations between macronutrients and plasma lipids (27). Participants reported the average frequency of consumption and the usual serving size (small, medium, or large) of 120 foods and beverages over the previous year. Nine predefined frequencies ranged from rare or never to ≥2 times/d for foods and ≥6 times/d for beverages. A medium portion size was considered to be 1 serving, a small portion size considered to be 0.5 servings, and a large portion size was considered to be 1.5 servings. In 2013, a programming error was discovered that caused data on 19 items to be missing for ∼30% of participants. Data were rekeyed for most participants; in 2 centers that did not keep original records, values for these 19 items were imputed with the use of a chained equation approach by the MESA coordinating center.

The Mediterranean diet score included the following food groups and nutrients: *1*) fruit, *2*) vegetables, *3*) nuts, *4*) legumes, *5*) whole grains, *6*) fish, *7*) ratio of monounsaturated to saturated fat, *8*) red and processed meats, and *9*) alcohol as previously described (12, 23). The food items included in each food group are described in **Supplemental Table 1**. Participants whose intakes were above the sex-specific MESA sample medians for fruit, vegetables, nuts, legumes, whole grains, fish, or the ratio of monounsaturated fat to saturated fat received 1 point for each dietary component. The consumption of red and processed meats below the median was awarded 1 point. In women, alcohol intake between 5 and 25 g/d was awarded 1 point, and in men, alcohol intake between 10 and 50 g/d was awarded 1 point (23). The total score could range from 0 to 9 with higher scores reflecting dietary intake that was more similar to a Mediterranean pattern.

LV structure and function

LV mass, end-diastolic volume, the mass-to-volume ratio, stroke volume, and ejection fraction were measured with the use of cardiac MRI at baseline. MESA participants underwent cardiac MRI with the use of scanners with 1.5-T magnets (25). Images were obtained with the use of a 4-element, phased-array surface coil that was positioned anteriorly and posteriorly, electrocardiographic gating, and brachial artery blood pressure monitoring. Trained readers at a single center read all images with the use of MASS software (version 4.2; Medis). Papillary muscles were included in LV volumes and excluded from LV mass. The ejection fraction was calculated as the stroke volume divided by the end-diastolic volume multiplied by 100%. The LV mass-to-volume ratio was calculated as LV mass divided by LV end-diastolic volume (8). Reproducibility was assessed with 155 duplicate readings (25). For LV mass, the intraclass correlation was 0.97 (95% CI: 0.96, 0.98) (25).

Covariate assessment

Heart rate was obtained at the time of the cardiac MRI. Physical activity (total intentional metabolic equivalent minutes per week) was measured with the use of a semiquantitative questionnaire (24). We classified participants who self-reported a diagnosis of diabetes, were taking medications for diabetes, or

TABLE 1
Selected foods and nutrients by quartiles of Mediterranean diet score in MESA participants[1]

	Mediterranean diet score				
	Quartile 1 (n = 896; score range: 0–2)	Quartile 2 (n = 1614; score range: 3–4)	Quartile 3 (n = 838; score range: 5–5)	Quartile 4 (n = 1149; score range: 6–9)	P
Fruit, servings/d	1.01 ± 1.01/0.81 (0.38–1.34)[2]	1.68 ± 1.35/1.40 (0.75–2.23)	2.31 ± 1.68/1.95 (1.23–2.90)	3.07 ± 1.82/2.74 (1.90–3.77)	<0.001
Vegetables, servings/d	1.36 ± 1.01/1.26 (0.82–1.81)	2.15 ± 1.30/1.93 (1.29–2.73)	3.03 ± 1.54/2.80 (1.98–3.72)	3.67 ± 1.71/3.31 (2.60–4.27)	<0.001
Nuts, servings/d	0.09 ± 0.17/0.04 (0.00–0.09)	0.20 ± 0.33/0.08 (0.03–0.25)	0.34 ± 0.44/0.19 (0.07–0.50)	0.51 ± 0.59/0.33 (0.16–0.65)	<0.001
Legumes, servings/d	0.17 ± 0.27/0.08 (0.03–0.16)	0.35 ± 0.55/0.16 (0.06–0.38)	0.47 ± 0.63/0.27 (0.11–0.57)	0.67 ± 0.80/0.42 (0.21–0.87)	<0.001
Whole grains, servings/d	0.40 ± 0.45/0.29 (0.08–0.53)	0.66 ± 0.62/0.52 (0.16–1.00)	0.89 ± 0.72/0.79 (0.35–1.24)	1.25 ± 079/1.10 (0.75–1.64)	<0.001
Fish, servings/d	0.14 ± 0.17/0.10 (0.04–0.17)	0.24 ± 0.25/0.16 (0.08–0.31)	0.38 ± 0.39/0.27 (0.15–0.48)	0.48 ± 0.43/0.37 (0.23–0.59)	<0.001
Red meat, servings/d	0.67 ± 0.48/0.58 (0.32–0.91)	0.63 ± 0.53/0.49 (0.26–0.86)	0.69 ± 0.61/0.53 (0.25–0.96)	0.62 ± 0.61/0.46 (0.22–0.81)	0.01
Ratio of monounsaturated fat to saturated fat, g/g	1.08 ± 0.19/1.07 (0.96–1.18)	1.19 ± 0.24/1.17 (1.02–1.33)	1.27 ± 0.26/1.26 (1.10–1.42)	1.38 ± 0.29/1.35 (1.21–1.51)	<0.001
Alcohol intake,[3] g/d	4.91 ± 16.27/0 (0–2.08)	4.94 ± 13.58/0 (0–3.78)	4.90 ± 10.33/0.47 (0–5.29)	7.27 ± 12.77/1.60 (0–10.04)	<0.001
Low, %	89.1	83.4	80.0	67.0	<0.001
Moderate, %	7.4	14.5	18.1	30.5	—
High, %	3.6	2.1	1.9	2.5	—

[1]Number of participants varied across quartiles because of the large number of ties in diet scores. Percentages do not sum to 100 because of rounding. P values were calculated with the use of an ANOVA for differences in means, and chi-square tests were used for differences in proportions. MESA, Multi-Ethnic Study of Atherosclerosis.

[2]Mean ± SD/median; IQR in parentheses (all such values).

[3]Low alcohol intake was defined as <5 g/d in women and <10 g/d in men, moderate alcohol intake was defined as 5–25 g/d in women and 10–50 g/d in men, and high alcohol intake was defined as >25 g/d in women and >50 g/d in men.

had fasting blood glucose concentrations ≥126 mg/dL as having a history of diabetes. The estimated glomerular filtration rate was calculated with the use of the Chronic Kidney Disease Epidemiology Collaboration equation (28).

Statistical analysis

We calculated medians and IQRs, means ± SDs, or percentages of MESA-participant dietary intakes and other characteristics by approximate quartiles of the Mediterranean diet score. Quartiles did not have equal numbers of participants because of ties in diet scores. We calculated means and 95% CIs of the LV mass, end-diastolic volume, mass-to-volume ratio, stroke volume, and ejection fraction by quartiles of the Mediterranean diet score. Adjusted means were calculated with the use of linear regression models with the covariates age (continuous; in y), sex, race-ethnicity, total energy intake (continuous; in kcal/d), cigarette smoking (current, past, and never), education (less than high school, high school graduate or some college, and college graduate), intentional physical activity (continuous; in metabolic equivalent minutes per week), height (continuous; in cm), and weight (continuous; in lb). We further adjusted for factors that could be either confounders or mediators of the association between the Mediterranean diet score and LV structure and function including heart rate (continuous; in beats/min), history of diabetes, systolic blood pressure (continuous; in mm Hg), use of antihypertensive medications, HDL cholesterol (continuous; in mg/dL), LDL cholesterol (continuous; in mg/dL), use of lipid-lowering medications, C-reactive protein (continuous; in mg/L), estimated glomerular filtration rate (≥90, 60–89, and <60 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$), and albumin-to-creatinine ratio (<30, 30–300, and >300 mg/g).

We conducted tests of linear trend by entering Mediterranean diet score as a continuous value and tests of quadratic trend by entering the diet score and diet score squared into the models. If there was no evidence for a quadratic trend, we calculated the difference in LV variables for each +1-U difference in the Mediterranean diet score with the use of linear regression models that were adjusted as previously described. Because risk of heart failure associated with LV mass was primarily observed in individuals in this sample at or above the 95th percentile of LV mass for height, weight, and sex (4), we examined the association between the diet score and being at or above this LV-mass threshold with the use of logistic regression models that were adjusted as previously described. LV mass was adjusted for height, weight, and sex as previously described (4, 29). In addition, we examined the association between the Mediterranean diet score and heart rate because ventricular filling is greater at lower heart rates, which, therefore, favors larger end-diastolic volumes and greater stroke volumes.

In sensitivity analyses, we limited the population to participants without diabetes and, separately, to participants who did not use antihypertensive medications because individuals diagnosed with diabetes or hypertension may change their diets. Because diet and physical activity may have synergistic effects on LV structure and function, we conducted analyses of the association of the Mediterranean diet score stratified by physical activity above and below the population median (intentional exercise of 840 metabolic-equivalent minutes/wk) and tested for an interaction between physical activity and the Mediterranean diet score.

We examined associations of the components of the Mediterranean diet score with LV-structure and -function variables. For each diet-score component, we calculated the difference in LV variables associated with receiving compared with not receiving the point associated with that component with the use of linear regression models. Models were mutually adjusted for each diet-score component and for the covariates previously described.

Two percent of participants (n = 111) were missing data for one or more covariates. Information on LDL cholesterol was most-frequently missing (n = 66) primarily because of elevated triglyceride concentrations that made the estimation of LDL-cholesterol concentrations, with the use of Friedewald's equation, unreliable. Missing data for covariates were imputed with the use of the chained-equations approach (30); 10 complete data sets were simulated, and estimates were combined, to get appropriate P values and CIs (31). The data analysis was conducted with the use of SAS version 9.3 software (SAS Institute Inc.). Two-side P values <0.05 were considered statistically significant. No adjustment was made for multiple comparisons.

RESULTS

MESA-participant means ± SDs and medians and IQRs of selected foods and nutrients across quartiles of the Mediterranean

TABLE 2
Characteristics of MESA participants by quartiles of Mediterranean diet score[1]

	Mediterranean diet score				
	Quartile 1 (n = 896; score range: 0–2)	Quartile 2 (n = 1614; score range: 3–4)	Quartile 3 (n = 838; score range: 5–5)	Quartile 4 (n = 1149; score range: 6–9)	P
Age, y	60.3 ± 9.9[2]	61.3 ± 10.3	61.9 ± 10.0	62.8 ± 10.1	<0.001
Sex, %					0.85
F	52.7	51.6	52.3	50.8	
M	47.3	48.4	47.7	49.2	
Race-ethnicity, %					<0.001
White	39.5	37.9	37.5	46.6	
Chinese	6.6	12.3	19.3	13.7	
African American	27.7	22.6	25.1	24.7	
Hispanic	26.2	27.1	18.1	15.1	
Education, %					<0.001
Less than high school	18.2	20.2	15.5	10.3	
High school graduate/some college	49.1	42.0	35.9	33.1	
College graduate	32.7	37.8	48.6	56.6	
Cigarette smoking, %					<0.001
Never	47.5	51.2	55.0	50.8	
Former	34.4	35.8	34.3	40.8	
Current	18.1	13.0	10.7	8.5	
Height, cm	166 ± 10	166 ± 10	166 ± 10	167 ± 10	0.003
Weight, lb	175 ± 38	169 ± 35	168 ± 36	168 ± 33	<0.001
BMI, kg/m^2	28.6 ± 5.3	27.7 ± 4.7	27.6 ± 5.0	27.1 ± 4.5	<0.001
Total calorie intake, kcal/d	1428 ± 612	1577 ± 725	1791 ± 848	1936 ± 855	<0.001
Intentional physical activity, MET-min/wk	630 (0–1680)[3]	735 (0–1890)	945 (210–1933)	1260 (473–2520)	<0.001
History of diabetes, %	14.0	12.6	13.4	10.3	0.056
Systolic blood pressure, mm Hg	125 ± 21	125 ± 21	125 ± 20	126 ± 21	0.61
Current antihypertensive use, %	29.8	31.4	34.1	29.8	0.15
Heart rate, beats/min	67.4 ± 11.2	66.7 ± 12.1	66.6 ± 11.7	65.3 ± 11.5	<0.001
Estimated glomerular filtration rate, mL · min^{-1} · 1.73 m^{-2}, %					0.13
≥90	26.0	23.3	23.4	20.5	
60–89	62.2	63.9	64.6	67.5	
<60	11.8	12.9	12.1	12.0	
Albumin-to-creatinine ratio, mg/g, %					0.87
<30	90.9	91.2	92.5	91.7	
30–300	7.5	7.6	6.6	7.0	
>300	1.6	1.2	1.0	1.3	
C-reactive protein, mg/L	2.28 (0.99–4.81)	1.81 (0.82–4.13)	1.62 (0.74–3.44)	1.54 (0.64–3.71)	<0.001
HDL cholesterol, mg/dL	50 ± 15	50 ± 15	52 ± 15	52 ± 16	0.002
LDL cholesterol, mg/dL	118 ± 32	118 ± 31	116 ± 30	116 ± 30	0.27
Current use of lipid-lowering therapy, %	15.2	16.8	15.1	15.6	0.73

[1]Percentages do not sum to 100 because of rounding. P values were calculated with the use of an ANOVA for differences in means, Kruskal-Wallis tests for differences in medians, and chi-square tests for differences in proportions. MESA, Multi-Ethnic Study of Atherosclerosis; MET-min, metabolic equivalent task minutes.

[2]Mean ± SD (all such values).

[3]Median; IQR in parentheses (all such values).

diet score are shown in **Table 1**. As expected, because of the method used to calculate the Mediterranean diet score, participants in the top quartile (i.e., subjects whose diets most conformed to a Mediterranean-type pattern) had, on average, higher intakes of fruit, vegetables, nuts, legumes, whole grains, and fish, to have lower intake of red meat and a higher ratio of monounsaturated fat to saturated fat, and were more likely to have moderate alcohol intake than were participants in the bottom quartile of the Mediterranean diet score (i.e., subjects whose diets least conformed to a Mediterranean-type pattern). Compared with participants with lower Mediterranean diet scores, MESA participants with higher Mediterranean diet scores were, on average, older, less likely to be Hispanic, more likely to be college graduates, and less likely to be cigarette smokers (**Table 2**). Weight, BMI, heart rate, and C-reactive protein were inversely associated with the Mediterranean diet score, and total energy intake, physical activity, and HDL cholesterol were positively associated with the Mediterranean diet score.

There was a slight but statistically significant U-shaped association between the Mediterranean diet score and LV mass (**Table 3**). In fully adjusted models that included demographics, physical activity, CVD risk factors, and other potential confounders, mean LV mass was 146, 145, 146, and 147 g across quartiles of the diet score (*P*-quadratic trend = 0.04). There was no association between Mediterranean diet scores and LV mass at or above the 95th percentile; ORs were 1 (reference), 0.74 (95% CI: 0.50, 1.11), 1.07 (95% CI: 0.68, 1.68), and 0.79 (95% CI: 0.51, 1.25) across quartiles of the diet score in fully adjusted models (*P*-linear trend = 0.86, *P*-quadratic trend = 0.95). The Mediterranean diet score was positively associated with LV end-diastolic volume, stroke volume, and ejection fraction, although the association with the end-diastolic volume was NS in the fully adjusted model (*P* = 0.055). The Mediterranean diet score was not associated with LV mass-to-volume ratio in crude or adjusted models. In fully adjusted models, heart rate was slightly lower comparing individuals in the highest quartile of the Mediterranean diet score compared with the other quartiles (adjusted means: 67.1, 66.6, 66.6, and 65.6 beats/min across quartiles, respectively; *P*-linear trend = 0.002, *P*-quadratic trend = 0.06). The associations of Mediterranean diet score with the LV metrics were similar when the population was limited to people without diabetes and when the population was limited to people who were not taking antihypertensive medications. There were no significant interactions between the Mediterranean diet score and physical activity.

Moderate alcohol intake, compared with higher or lower alcohol intake, was independently associated with higher LV mass, end-diastolic volume, and stroke volume (**Table 4**). Fruit intake and the monounsaturated fat:saturated fat ratio above the median were associated with a greater ejection fraction, intake of vegetables above the median was associated with lower LV mass, intake of legumes above the median was associated with higher LV mass, and intake of red meat below the median was associated with higher LV end-diastolic volume and stroke volume and a lower LV mass-to-volume ratio in adjusted models.

TABLE 3
Association of Mediterranean diet score with left ventricular structure and function measured with the use of cardiac MRI in MESA participants[1]

	Mediterranean diet score						
	Quartile 1 (*n* = 896; score range: 0–2)	Quartile 2 (*n* = 1614; score range: 3–4)	Quartile 3 (*n* = 838; score range: 5–5)	Quartile 4 (*n* = 1149; score range: 6–9)	*P*-linear trend	*P*-quadratic trend	Difference per 1-point higher diet score[2]
Left ventricular mass, g	149 (146, 151)	144 (142, 146)	144 (142, 147)	146 (144, 149)	0.61	0.003	—
Model 1	146 (144, 147)	144 (143, 146)	146 (144, 148)	147 (146, 149)	0.02	0.007	—
Model 2	146 (145, 148)	145 (143, 146)	146 (144, 148)	147 (145, 148)	0.19	0.04	—
Left ventricular end diastolic volume, mL	128 (126, 130)	126 (124, 128)	126 (123, 128)	127 (125, 129)	0.68	0.02	—
Model 1	126 (124, 127)	126 (125, 127)	127 (125, 129)	128 (127, 130)	0.004	0.10	0.6 (0.2, 1.0)
Model 2	126 (125, 128)	126 (125, 127)	127 (126, 129)	128 (126, 129)	0.055	0.32	0.4 (0.0, 0.8)
Left ventricular mass-to-volume ratio, g/mL	1.18 (1.16, 1.19)	1.16 (1.15, 1.18)	1.17 (1.15, 1.18)	1.17 (1.16, 1.18)	0.55	0.46	0.00 (−0.01, 0.00)
Model 1	1.18 (1.16, 1.19)	1.17 (1.16, 1.18)	1.17 (1.15, 1.18)	1.16 (1.15, 1.18)	0.20	0.68	0.00 (−0.01, 0.00)
Model 2	1.18 (1.16, 1.19)	1.17 (1.16, 1.18)	1.16 (1.15, 1.18)	1.16 (1.15, 1.17)	0.17	0.71	0.00 (−0.01, 0.00)
Left ventricular stroke volume, mL	86.3 (85.0, 87.6)	86.3 (85.3, 87.3)	86.4 (85.0, 87.7)	87.5 (86.3, 88.6)	0.08	0.03	—
Model 1	84.9 (83.8, 86.0)	86.3 (85.4, 87.1)	87.1 (85.9, 88.2)	88.0 (87.0, 89.0)	<0.001	0.06	0.7 (0.4, 1.0)
Model 2	85.3 (84.2, 86.4)	86.4 (85.6, 87.2)	87.1 (86.0, 88.2)	87.7 (86.8, 88.7)	<0.001	0.19	0.5 (0.2, 0.8)
Left ventricular ejection fraction, %	68.0 (67.5, 68.5)	69.1 (68.7, 69.5)	69.4 (68.9, 69.9)	69.4 (69.0, 69.8)	<0.001	0.55	0.3 (0.1, 0.4)
Model 1	68.3 (67.8, 68.8)	69.1 (68.8, 69.4)	69.2 (68.7, 69.6)	69.4 (68.9, 69.8)	0.001	0.64	0.2 (0.1, 0.3)
Model 2	68.4 (67.9, 68.8)	69.1 (68.8, 69.4)	69.1 (68.6, 69.6)	69.4 (68.9, 69.8)	0.004	0.55	0.2 (0.1, 0.3)

[1]All values are means (95% CIs). *P* values were calculated with the use of linear regression models. Model 1 was adjusted for age, sex, race-ethnicity, total energy intake, cigarette smoking, education, physical activity (intentional exercise metabolic-equivalent minutes/wk), height, and weight. Model 2 was adjusted as for model 1 and for history of diabetes, systolic blood pressure, use of antihypertensive medications, heart rate, HDL cholesterol, LDL cholesterol, use of lipid-lowering therapy, C-reactive protein, estimated glomerular filtration rate, and the albumin-to-creatinine ratio. MESA, Multi-Ethnic Study of Atherosclerosis.

[2]Calculated only when there was no evidence of a quadratic trend.

TABLE 4

Association of Mediterranean diet–score components (for the comparison of participants who received a point associated with the component with participants who did not) with left ventricular structure and function measured with the use of cardiac MRI in MESA participants[1]

	Fruit	Vegetables	Nuts	Legumes	Whole grains	Fish	Red meat	Monounsaturated fat:saturated fat	Alcohol
Left ventricular mass, g	0.1 (−1.5, 1.7)	-1.8 (−3.5, −0.1)[2]	1.1 (−0.5, 2.7)	1.6 (0.0, 3.3)[2]	0.8 (−0.7, 2.4)	1.1 (−0.5, 2.7)	0.1 (−1.5, 1.8)	−1.1 (−2.6, 0.5)	2.4 (0.4, 4.4)[2]
Left ventricular end diastolic volume, mL	−0.1 (−1.6, 1.4)	−0.7 (−2.3, 0.9)	0.7 (−0.8, 2.2)	0.9 (−0.6, 2.5)	0.6 (−0.9, 2.1)	0.7 (−0.8, 2.2)	2.1 (0.5, 3.6)[2]	−0.8 (−2.3, 0.7)	2.5 (0.6, 4.4)[2]
Left ventricular mass-to-volume ratio, g/mL	0.00 (−0.01, 0.01)	0.00 (−0.02, 0.01)	0.00 (−0.01, 0.01)	0.00 (−0.01, 0.02)	0.00 (−0.02, 0.01)	0.00 (−0.01, 0.01)	-0.02 (−0.04, −0.01)[2]	0.00 (−0.02, 0.01)	−0.01 (−0.02, 0.01)
Left ventricular stroke volume, mL	0.6 (−0.4, 1.6)	−0.4 (−1.5, 0.7)	0.3 (−0.7, 1.3)	0.7 (−0.4, 1.8)	0.4 (−0.6, 1.4)	0.6 (−0.5, 1.6)	1.8 (0.7, 2.9)[2]	0.1 (−0.9, 1.2)	2.0 (0.7, 3.3)[2]
Left ventricular ejection fraction, %	0.6 (0.1, 1.0)[2]	−0.1 (−0.6, 0.4)	−0.2 (−0.7, 0.2)	0.2 (−0.2, 0.7)	0.0 (−0.4, 0.4)	0.2 (−0.2, 0.6)	0.2 (−0.3, 0.6)	0.5 (0.0, 0.9)[2]	0.2 (−0.3, 0.8)

[1] All values are adjusted differences (95% CIs). Estimates were mutually adjusted for each diet component, age, sex, race-ethnicity, total energy intake, cigarette smoking, education, physical activity (intentional exercise metabolic-equivalent minutes/wk), height, weight, history of diabetes, systolic blood pressure, use of antihypertensive medications, heart rate, HDL cholesterol, LDL cholesterol, use of lipid-lowering therapy, C-reactive protein, estimated glomerular filtration rate, and albumin-to-creatinine ratio. In women, 1 point was awarded for fruit intake ≥1.8 servings/d, vegetable intake ≥2.4 servings/d, nut intake ≥0.1 serving/d, legume intake ≥0.2 servings/d, whole-grain intake ≥0.6 servings/d, fish intake ≥0.2 servings/d, red meat intake ≤0.4 servings/d, ratio of monounsaturated fat to saturated fat ≥1.2, and alcohol intake between 5 and 25 g/d. In men, 1 point was awarded for fruit intake ≥1.4 servings/d, vegetable intake ≥2.1 servings/d, nut intake ≥0.1 serving/d, legume intake ≥0.2 servings/d, whole-grain intake ≥0.6 servings/d, fish intake ≥0.2 servings/d, red meat intake ≤0.6 servings/d, ratio of monounsaturated fat to saturated fat ≥1.2, and alcohol intake between 10 and 50 g/d. MESA, Multi-Ethnic Study of Atherosclerosis.

[2] Significantly different from zero in linear regression models, $P < 0.05$.

DISCUSSION

We showed associations between the Mediterranean diet score and LV structure and function in participants in the MESA who are a multiethnic population of middle-aged and older US adults without known CVD. The higher average ejection fraction and average stroke volume in individuals with higher compared with lower Mediterranean diet scores were in the hypothesized direction (6). Higher compared with lower Mediterranean diet scores were also associated with a slightly higher LV volume, and there was a weak U-shaped relation with LV mass. The higher LV mass and higher volume associated the diet score were balanced and were not indicative of adverse remodeling because there was no association between the Mediterranean diet score and the LV mass-to-volume ratio. We showed no association of the Mediterranean diet score with LV hypertrophy, which was defined as the LV mass at or above the population-specific 95th percentile (4). Heart rate was lower in individuals in the highest quartile of the Mediterranean diet score than in individuals in the lower quartiles. This pattern was consistent with better ventricular filling that contributed to higher end-diastolic filling, slightly larger LV volumes, an increased stroke volume, and a better ejection fraction. In individuals without CVD, this pattern may represent physiologic responses to healthy behaviors that are similar to an adaptation to exercise (32, 33).

A previous study of a Mediterranean diet score and LV mass in participants without a history of ischemic stroke showed an inverse association between the Mediterranean diet score and LV mass (19). The previous study used echocardiograms to measure LV mass in contrast to the cardiac MRI that we used in the current study; in addition, it is not clear whether a nonlinear relation was considered. In a study of patients with acute coronary syndrome, a Mediterranean dietary pattern was associated with lower probability of a reduced ejection fraction at hospitalization and, in people with reduced ejection fraction at hospitalization, a higher likelihood of having an ejection fraction ≥50% at 3 mo of follow-up (34). In patients with systolic heart failure, a higher Mediterranean diet score was associated with better diastolic and systolic function (35).

In the MESA sample, a DASH-diet score, which also captured a prudent dietary pattern, had associations with the LV volume, stroke volume, and ejection fraction in the same direction as observed in the current study (20). Although the consistent results were not unexpected because of the similarities of the 2 dietary patterns, Mediterranean diet scores include moderate intake of alcohol and a high monounsaturated fat:saturated fat ratio, which are not components of DASH-diet scores (20). In addition, the DASH-diet score includes intake of salt and sweets, which the Mediterranean diet score does not. A data-derived dietary pattern that was characterized by high intakes of processed foods, high–glycemic index foods, and meat and low intakes of fruit and vegetables and seeds and nuts was associated with a higher LV mass and a lower stroke volume and ejection fraction in the MESA (21). A positive association between dietary phosphorous intake, which was largely from additives present in processed foods, and LV mass was also previously described in the MESA (36).

A number of CVD risk factors could mediate an association between a Mediterranean dietary pattern and LV structure and function. Dietary intake more concordant with a Mediterranean dietary pattern has previously been associated with lower blood pressure (18, 37), better insulin sensitivity (38), and lower fasting glucose (18), lower inflammation (39), and a more favorable lipid profile (18) in many but not all studies (40, 41). The studies included participants with and without clinically recognized CVD and controlled trials of Mediterranean-type diets as well as observational studies. In the current study, the results were consistent between models that did and did not control for diabetes, blood pressure, heart rate, C-reactive protein, and blood lipids.

We used a previously described method to create a Mediterranean diet score with components that were selected on the basis of a traditional Mediterranean dietary pattern (12, 23). However, the scoring system relied on the distribution of intake within a population rather than absolute intake, and few, if any, of the MESA participants had dietary patterns that resembled traditional dietary patterns in Mediterranean countries. For example, median intake of vegetables in the Greek component of the European Prospective Investigation into Cancer and Nutrition was 550 g/d in men and 500 g/d in women (∼5–7 servings/d) (23) compared with median vegetable intake of 2.1 servings/d in men and 2.4 servings/d in women in the MESA. We have chosen to examine a Mediterranean diet score in particular because it has the benefit of simplicity and because previous research has shown associations with a range of CVD risk factors and outcomes. We showed that diet-score components alcohol, monounsaturated fat-to-saturated fat ratio, red meat, vegetable, legumes, and fruit intakes were associated with LV-structure and -function measures. Moderate alcohol intake, compared with both light and heavy intakes, was the component that was most associated with a higher LV mass, volume, and stroke volume. The effects of alcohol on the cardiovascular system are complex and nonlinear (42). Although we showed associations with specific diet-score components, from a public health perspective, food-based dietary pattern guidance may be the most relevant. In addition, diet scores that are derived from FFQs have within-person correlations of 0.5–0.6 over 18–20 y, which are substantially higher than for individual foods and nutrients (43, 44).

Strengths of this study included the large multiethnic sample of women and men without clinical CVD. The cardiac MRI-based measures of LV structure and function were accurate and highly reproducible (4, 25). However, there were also a number of important limitations. Dietary intake was measured with the use of an FFQ, and reported intake was summarized in a dietary score. The validity of this questionnaire has been examined (26, 27), but FFQs have substantial errors, and these errors may not be uniform across all components of the diet score. Because of a programming error, we had to use imputed values for 16% of the food items in some participants. In this cross-sectional study, we could not exclude residual confounding, and the time course could not be established. Additional research will be needed to determine whether the associations we observed are causal. In this population, the Mediterranean diet score was positively associated with intentional physical activity and total energy intake and inversely associated with BM and heart rate, which suggested that the associations with LV structure and function may in part represent a beneficial cardiac response to exercise (32). However, the Mediterranean diet score showed significant associations with metrics of LV structure and function after adjustment for these covariates, and physical activity did not appear to modify the associations. Associations were also similar when we excluded participants with diabetes and antihypertensive use. Longitudinal studies are needed to verify whether the associations of the Mediterranean diet with cardiac structure and function will be maintained over time.

In conclusion, a Mediterranean diet score is associated with modestly higher LV volume, ejection fraction, and stroke volume in apparently healthy middle-aged and older US adults. The Mediterranean diet score has a weak U-shaped relation with LV mass; the lack of an association with the LV mass-to-volume ratio or the frankly elevated LV mass indicates an absence of adverse cardiac remodeling. This pattern suggests that a Mediterranean-type dietary pattern is cross-sectionally associated with modestly better LV structure and function in this healthy, multiethnic sample.

The authors' responsibilities were as follows—EBL: analyzed the data and had primary responsibility for the final content of the manuscript; EBL and JAN: wrote the manuscript; JFP, WGH, DAB, SRH, and DRJ: conducted the research; and all authors: designed the research and read and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

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