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A Mediterranean-style Diet and Left Ventricular Mass (From The Northern Manhattan Study)

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Abstract

One mechanism linking diet, specifically the Mediterranean-style diet (DT), with cardiovascular disease prevention may be an association between a DT and LV mass. However, there is little data on this relationship. We hypothesized that adherence to a DT would be inversely associated with left ventricular (LV) mass in the multi-ethnic population-based Northern Manhattan Study. The study included 1937 participants with diet assessments and LV mass measured using echocardiography (mean age=67±9years, 39% male, 58% Hispanic, 20% White, 20% Black). A DT adherence score (range=0-9, 9 representing maximal adherence) was examined continuously and categorically (score 6-9 representing the top quartile vs. 0-5). Multivariable-adjusted linear regression models were constructed to examine the cross-sectional association between DT and LV mass. An inverse association was observed between the DT score and LV mass. In a model controlling for demographics, behavioral risk factors, diabetes and blood pressure variables, LV mass was 1.98 g lower for each 1-point greater DT score, and those with scores of 6-9 had an average LV mass that was 7.30 g smaller than those with scores of 0-5. The association was attenuated but remained statistically significant after additionally adjusting for BMI. Results were similar when LV mass was corrected for height ($LVM/HT^{2.7}$). In conclusion, greater adherence to a DT is associated with decreased LV mass, an important risk factor for CVD, and this association may be partly mediated by obesity. The association with LV mass may be involved in the protective effect of a DT on clinical vascular outcomes.

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Keywords

diet; left ventricular mass; epidemiology; Mediterranean diet

Introduction

Left ventricular (LV) mass, as measured by echocardiography, is associated with morbidity and mortality due to cardiovascular disease (CVD), independently of associated demographic variables and vascular risk factors such as dyslipidemia, hypertension, and smoking[1]. One underlying mechanism linking diet, specifically the Mediterranean-style diet (DT), with CVD protection may be an association between a DT and LV mass. However, there is currently little data on this relationship. Elucidation of the potential impact of adherence to a DT on LV morphology and function is important to better understand how a DT may protect against clinical CVD events, identify patients at risk for CVD for whom dietary interventions may be particularly effective, and to identify a potential subclinical marker of disease risk that may be used as an intermediate endpoint in clinical trials of dietary interventions. Therefore, the goal of the current study is to examine the hypothesis that greater adherence to a DT is associated with lower LV mass in the race/ethnically diverse population-based Northern Manhattan Study (NOMAS). In this cohort, we have previously observed that adherence to a DT is inversely associated with the risk of clinical vascular events, including stroke and myocardial infarction (MI), and particularly vascular death[2].

Methods

NOMAS is a population-based cohort study designed to determine the incidence of and risk factors for stroke and other vascular outcomes in a multiethnic urban community. Details of the NOMAS design have been described previously[3]. Briefly, eligible participants: a) had never been diagnosed with ischemic stroke; b) were >40 years old; and c) resided in Northern Manhattan for ≥ 3 months, in a household with a telephone. Participants were identified by random-digit dialing, and interviews were conducted by trained bilingual research assistants. The telephone response rate was 91%. Participants were recruited from the telephone sample to have an in-person baseline interview and assessment. The enrollment response rate was 75%, the overall participation rate was 69%, and a total of 3298 participants were enrolled. Participants with a myocardial infarction prior to baseline (N=237) were excluded. Food frequency data sufficient to calculate a Mediterranean diet score were available for 2,568 participants, and of these participants measurement of LV mass was available for 1,937. This study was approved by the Institutional Review Boards of Columbia University Medical Center and the University of Miami and participants provided written informed consent.

Data were collected through interviews with trained research assistants in English or Spanish. Physical and neurological examinations were conducted by study neurologists. Race-ethnicity was based upon self-identification through a series of questions modeled after the US census and conforming to standard definitions outlined by Directive 15[4].

Standardized questions were adapted from the Behavioral Risk Factor Surveillance System by the Centers for Disease Control regarding hypertension, diabetes, smoking, and cardiac conditions[5]. Blood pressure was measured with mercury sphygmomanometers and appropriately-sized cuffs. Hypertension was defined as a blood pressure ≥140/90 mmHg (based on the average of two measurements during one sitting), the patient's self-reported hypertension, or use of anti-hypertensive medications. Diabetes mellitus was defined by the patient's self-reported diabetes, use of insulin or oral anti-diabetic medication, or fasting glucose ≥126 mg/dl. Body mass index (BMI) was calculated in kg/m^2. Smoking was categorized as never smoking, former smoking, and current (within the past year) smoking. Physical activity was defined as the frequency and duration of 14 recreational activities during the 2-week period before the interview, as described previously[6].

At baseline, participants were administered a comprehensive in-person diet assessment using a modified Block National Cancer Institute food frequency questionnaire (FFQ) by trained research assistants in English or Spanish depending on their primary language[7]. This FFQ listed 207 foods and was intended to represent typical food consumption over the previous year. The available food responses were modified to include specific dietary items frequently consumed by Hispanic populations.

Construction of the DT score has been described previously. Briefly, we regressed energy intake (kilocalories) and calculated the derived residuals of daily gram intake for the following food categories: dairy, meat, fruits and nut, vegetables (excluding potatoes), legumes, grains and cereals, and fish[8, 9]. Participants scored one point for each beneficial component (fruits and nuts, vegetables, legumes, grains and cereals, and fish) whose consumption was at or above the sex-specific median, one point for each component associated with increased CVD risk (meat and dairy products) whose consumption was below the median, and one point for a ratio of monounsaturated fats to saturated fats above the median, and for mild to moderate alcohol consumption (defined as >0 drinks/week but ≤2 drinks/day over the previous year)[5]. The DT score was the sum of the scores in the food categories (range 0-9) with a greater score indicating stricter adherence. The DT score, the primary exposure of interest, was analyzed categorically (the top quartile score 6-9 vs. the bottom 3 quartiles score 0-5) and as a continuous variable (per 1-point increment).

Transthoracic echocardiography was performed and measurements were taken by standard two-dimensional (2-D) protocols according to the guidelines of the American Society of Echocardiography. Left ventricular end-diastolic diameter (LVDD), left ventricular end-systolic diameter (LVSD), interventricular septum (IVS), and posterior wall thickness (PWT) at end diastole were measured. LV mass was calculated using the corrected American Society of Echocardiography method: $0.8\times(1.04\times[(IVS+LVDD+PWT)^3-LVDD^3]+0.6)$. For this analysis, LV mass was examined two ways, consistent with previous literature: (1) as a raw uncorrected value; and (2) indexed to body size by dividing raw LV mass by height to the allometric power of 2.7 ($LVM/HT^{2.7}$). Both LV mass indices were examined as continuous variables.

The cross-sectional associations between the DT score (assessed continuously and as a dichotomous variable) with the LV mass indices were examined using multivariable-

adjusted linear regression models after confirming the normal distributions of the LV mass variables. We used a sequence of four models: 1) unadjusted; 2) adjusted for age, sex, race-ethnicity, and education level; 3) adjusted for the variables in model 2 and physical activity, average total daily kilocalorie consumption, and smoking (never/past/current/never); 4) adjusting for potential mediators as well as confounders, including the covariates in model 3 and diabetes, systolic blood pressure (SBP), diastolic blood pressure (DBP), and use of anti-hypertensive medications. We also conducted an additional analysis that included BMI in addition to the variables in model 4. In a supplementary analysis we simultaneously entered the DT score components into model 3 as predictors of the LV mass variables. Because self-reported kcal <500 or >4000 might indicate inaccurate reporting of dietary information, we conducted sensitivity analyses excluding these participants. Lastly, we examined the potential for effect modification by age, sex, race/ethnicity, and hypertension by including interaction terms with the continuous DT score in model 4 for each of the LV mass dependent variables of interest.

Results

Twenty-five percent of participants had a DT score 6-9. The mean unadjusted LV mass was 186±59 g and the mean $LVM/HT^{2.7}$ was 50±16 g/m2.7. Table 1 provides a description of the sample included in this study in relation to the covariates of interest, overall and stratified by DT score. Male sex, Hispanic ethnicity, lower BMI, and moderate-heavy physical activity were associated with increased adherence to a DT, while current smokers had decreased adherence.

The association between DT score and LV mass indices is shown in Table 2. We found an inverse association between DT score and uncorrected LV mass in models 2-4. Those in the top quartile of DT adherence had an approximate 4% lower LV mass as compared to the rest of the study population. To provide some context for the magnitude of this association in our study population, in the same models used for the current analysis, this effect size was larger than the reduction in LV mass observed among those with moderate-heavy physical activity and those without diabetes (not shown).

The association was attenuated but remained statistically significant after additionally adjusting for BMI. Similar conclusions were made when LV mass was corrected for height ($LVM/HT^{2.7}$). In these models the inverse association with a DT was also strong in models 2-4, but was not significant in the analysis that included BMI. We observed no significant interactions between age, sex, race/ethnicity, or hypertension with the DT score in relation to either of the LV mass variables ($p>0.05$).

Table 3 shows the results of the analysis of the individual DT components, examined simultaneously in model 3, in relation to the LV mass indexed to body size. Greater consumption of cereals and grains and moderate alcohol use were independently associated with reduced $LVM/HT^{2.7}$. The association for cereals and grains remained significant after additionally adjusting for diabetes, blood pressure, anti-hypertensive medication use, and BMI ($p=0.001$).

The conclusions remained consistent in sensitivity analyses in which 77 participants with reported total daily kilocalorie consumption <500 or >4000 were excluded (not shown).

Discussion

The results of this study, although cross-sectional, raise the possibility that greater adherence to a DT may decrease the risk of elevated LV mass, an important risk factor for CVD. An effect on LV mass may be on a pathway linking increased adherence to a DT with a decreased risk of clinical vascular outcomes, an association that we have previously reported in the NOMAS cohort[2]. The observed association may be largely due to an inverse association between adherence to a DT and body size, but is not explained by a lower caloric intake.

Although the underlying mechanisms linking LV mass with clinical events remains poorly understood, diet remains a modifiable risk factor of interest for clinicians and researchers that could have a salutary effect on LV mass. Unfortunately, little research attention has been paid to a potential association between DT and cardiac morphology (including LV mass) and function. The only previous report is from a recent clinic-based study of 1,000 patients with acute coronary syndrome which suggested that those with greater adherence to a DT were more likely to have preserved LV systolic function, as measured by LV ejection fraction at hospitalization[10]. In that study, a DT diet was also associated with a lower likelihood of remodeling 3 months following hospitalization. The latter study is distinct from ours in its focus on LV function rather than mass, and having been conducted in a population that had suffered a cardiac event. We are not aware of any studies other than ours that has examined the relationship between adherence to a DT and LV mass in a population-based sample of adults without a prior stroke or MI, which allows for greater generalizability and inferences about potential primary prevention.

Few studies have also investigated other dietary patterns. A cross-sectional analysis in the Multi-Ethnic Study of Atherosclerosis (MESA) looked at a dietary pattern characterized by its ability to predict the metabolic syndrome in relation to LV mass and ejection fraction. This unhealthy dietary pattern included a relatively high consumption of foods with a high glycemic index, high-fat meats, cheeses, and processed foods, and a relatively low consumption of vegetables, soy, fruit, green and black tea, low-fat dairy desserts, seeds and nuts, and fish. They found that this unhealthy dietary index was positively associated with LV mass corrected for body size, and inversely associated with the ejection fraction[11]. The Dietary Approaches to Stop Hypertension (DASH) diet was associated with reduced LV mass, particularly in combination with weight management, in a randomized controlled trial of 144 overweight and obese unmedicated patients with high blood pressure[12].

As LV hypertrophy is often the result of chronic hypertension, it should be noted that in the current study an association between adherence to a DT and lower LV mass persisted after controlling for BP values and antihypertensive medication use. Adherence to a DT was also not significantly related to systolic or diastolic BP, antihypertensive medication use, nor history of hypertension. This may be due to residual confounding or the cross-sectional nature of this analysis if the effect of a DT on BP may occur at a younger age. Therefore, we

cannot rule out the possibility that effects on blood pressure may be on a pathway linking a DT to lower LV mass. Whether adoption of a DT may decrease the risk of developing LV hypertrophy, and whether its adoption by patients with LV hypertrophy may help reduce their chances of clinical CVD remains unknown, but our results underscore the need for further study. Our findings also suggest that LV mass indices have potential as surrogate intermediate markers in future randomized trials of a DT on vascular health.

The biological mechanisms underlying the inverse relationship between DT adherence and LV mass are not entirely clear. Inflammation is one possible link, as a DT has been shown to be associated with lower levels of inflammatory markers[13-15]. A prior study in this cohort found that levels of TNF receptor 1 were associated with LV mass and LV hypertrophy[16]. In the current study a DT was inversely associated with several important vascular risk factors associated with LV mass, most notably obesity. The association between a DT and LV mass as a raw variable was attenuated but remained statistically significant after adjusting for obesity, and the association for cereal and grains remained significant. However the association with LV mass indexed for height was no longer significant after controlling for obesity, suggesting that a correlation between a DT and body size may account for much of the relationship with LV mass. This potent vascular risk factor may be both a confounder and effect mediator in the current study due to the cross-sectional nature and single time point of dietary data collection.

Current nutritional epidemiological approaches emphasize overall dietary patterns rather than individual nutrients and foods in the etiology of cardiovascular outcomes. However, our secondary analysis of the independent associations of the individual DT components suggests that the consumption of cereals and grains and alcohol may be important components of a DT for the protection against LV hypertrophy. We previously found that the DT components independently associated with a reduced risk of vascular death were moderate alcohol use and high consumption of fish and legumes. One previous study suggested a U-shaped relationship between alcohol and LV mass[17], while another suggested a potential positive relationship in men, and differential effects based on alcohol type[18]. We recently reported that light alcohol consumption was associated with reduced BP variability on 24-hour ambulatory BP monitoring, a finding that could in turn be associated with a beneficial effect on LV mass[19]. The other DT components have not been examined on their own in relation to LV mass.

An important strength of this study is the use of a race/ethnically diverse, mostly Hispanic, population. Although Hispanics represent the fastest growing minority population in the US, they remain underrepresented in epidemiologic studies of novel risk factors for vascular health outcomes. We have previously shown that in our cohort Hispanics have greater adherence to a DT as compared to non-Hispanics blacks and whites[2]. Despite the differences in DT adherence across race/ethnic groups, we observed no race-ethnic differences in the association between a DT and LV mass, although the statistical power to detect effect modification was limited. Further research in other race/ethnically diverse cohorts is needed.

Some methodological limitations of the current study are important to note. The primary limitation of the current study is the cross-sectional design, which impedes inferences about

causality and temporality. Second, the dietary data was collected based on self-report and at a single point in time, resulting in possible misclassification of long-term dietary habits. Despite this potential issue, it is important to note that the FFQ is designed to measure relatively long-term dietary habits (over a year) as compared to diet records, and previous studies have suggested moderate stability of dietary habits over time. We tried to reduce the potential for misclassification of diet by conducting sensitivity analyses excluding those with improbably low or high total daily kilocalories. As in any observational cohort study, residual confounding remains a potential source of bias, although we did control for many vascular risk factors.

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Highlights

1. A Mediterranean-style diet was inversely associated with left ventricular mass.
2. The association between a MeDi and LV mass may be partly mediated by obesity.
3. Cereals and grains and moderate alcohol use were associated with reduced LV mass.

Table 1

Description of the study population

	Study Population N=1756	**DT score 0-5 N=1320**	**DT score 6-9 N=436**
Variables			
Male[a]	690 (39%)	499 (38%)	191 (44%)
Female[a]	1066 (61%)	821 (62%)	245 (56%)
Black[a]	355 (20%)	275 (21%)	80 (18%)
White[a]	351 (20%)	288 (22%)	63 (14%)
Hispanic[a]	1015 (58%)	735 (56%)	280 (64%)
Other race[a]	35 (2%)	22 (2%)	13 (3%)
High school completion	801 (46%)	612 (46%)	189 (43%)
Current smoker[a]	277 (16%)	220 (17%)	57 (13%)
Former smoker[a]	665 (38%)	506 (38%)	159 (36%)
Never smoker[a]	814 (46%)	594 (45%)	220 (50%)
Moderate-heavy physical activity[a]	159 (9%)	103 (8%)	56 (13%)
Diabetes mellitus	380 (22%)	298 (23%)	82 (19%)
Hypertension	899 (51%)	668 (51%)	231 (53%)
Hypertension Medication	755 (43%)	562 (43%)	193 (44%)
Continuous Covariates	**Mean ± standard deviation**		
Age (years)	67.49±9.49	67.70±9.57	66.82±9.21
Total daily kilocalories	1579.39±746.08	1574.03±773.18	1595.61±657.80
Body mass index (kg/m2)[a]	27.98±5.51	28.16±5.64	27.42±4.58
Systolic blood pressure (mmHg)	143.78±20.80	143.74±21.14	143.88±19.74
Diastolic blood pressure (mmHg)	83.41±10.91	83.27±10.97	83.82±10.72

[a] $p<0.05$ across DT categories

Table 2

Association between the Mediterranean-style diet score and left ventricular mass indices (N=1756)

	Change in LV mass (grams): beta, p-value	Change in LVM/HT$^{2.7}$: beta, p-value
DT continuous (per 1-point increase)		
Model 1[a]	−1.49, 0.08	−0.44, 0.06
Model 2[b]	−2.14, 0.01	−0.48, 0.04
Model 3[c]	−1.93, 0.02	−1.09, 0.03
Model 4[d]	−1.98, 0.01	−1.11, 0.02
Model 4+Body mass index	−1.53, 0.05	−0.25, 0.27
Score 6-9 vs. score 0-5		
Model 1[a]	−6.24, 0.03	−1.89, 0.03
Model 2[b]	−6.97, 0.02	−1.86, 0.03
Model 3[c]	−6.32, 0.04	−3.79, 0.04
Model 4 [d]	−7.30, 0.01	−4.35, 0.01
Model 4+Body mass index	−5.82, 0.04	−1.36, 0.09

[a] Model 1: univariate

[b] Model 2: controlling for age, sex, race/ethnicity (black, white, Hispanic, other), education

[c] Model 3: model 2 + smoking, physical activity, total daily calories

[d] Model 4: model 3 + diabetes, systolic blood pressure, diastolic blood pressure, use of anti-hypertensive medications

Table 3

Association between the individual Mediterranean-style diet components and left ventricular mass

Mediterranean Diet Component	LVM/HT$^{2.7}$: beta, p-value[a]
Alcohol	−4.06, 0.02
Fish	−0.30, 0.85
Legumes	−1.69, 0.32
Vegetables	0.79, 0.64
Fruit and nuts	−1.59, 0.34
Cereal and grains	−5.55, 0.001
Meat	−1.33, 0.41
Dairy	0.67, 0.69
Monounsaturated: saturated fat	1.01, 0.55

[a]Calculated using linear regression models controlling for all DT score components, age, sex, race/ethnicity, education, smoking, physical activity, total daily calories