Mediterranean and Dietary Approaches to Stop Hypertension dietary patterns and risk of sudden cardiac death in postmenopausal women[1–3]

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ABSTRACT

Background: The Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets are characterized by higher intake of fruit, vegetables, whole grains, and unsaturated fatty acids. All of these foods and nutrients may affect cholesterol, inflammation, the development of atherosclerosis, and, therefore, risk of cardiac death.

Objective: Our objective was to examine the association between the Mediterranean and DASH dietary patterns and risk of sudden cardiac death (SCD) in women.

Design: We used a prospective cohort of 93,122 postmenopausal women enrolled in the Women's Health Initiative study between 1993 and 1998 and followed for an average of 10.5 y. Women completed a food-frequency questionnaire (FFQ) twice during follow-up. We scored their diets according to how closely the reported diet resembled each dietary pattern. SCD was defined as death that occurred within 1 h of symptom onset.

Results: A higher Mediterranean diet score was associated with lower risk of SCD (HR: 0.64; 95% CI: 0.43, 0.94) when women in the highest quintile were compared with women in the lowest quintile after adjustment for age, total energy, race, income, smoking, and physical activity. After adjustment for potential mediators, the association was similar (HR: 0.67; 95% CI: 0.46, 0.99). A higher DASH diet score was not associated with risk of SCD. However, sodium intake, which is a crucial component of the DASH dietary pattern, was not well characterized by the FFQ.

Conclusion: The Mediterranean dietary pattern may be associated with lower risk of SCD in women. This trial was registered at clinicaltrials.gov as NCT00000611. *Am J Clin Nutr* 2014;99:344–51.

INTRODUCTION

Because of its low incidence [0.1–0.2% annually (1)], less is known about sudden cardiac death (SCD)[4] than other cardiovascular events such as myocardial infarction, especially in women who have a lower incidence rate of SCD than men. Despite its low incidence, SCDs account for ~50% of all cardiovascular deaths (2), the leading cause of death in Americans (3). SCD occurs within minutes; therefore, there is little or no time to intervene, and primary prevention is essential. One potential focus of primary prevention efforts is diet, which is modifiable and associated with risk of several types of cardiovascular disease.

Dietary patterns or combinations of higher intakes of beneficial foods and nutrients and lower intakes of harmful foods and nutrients may have a larger impact on disease than do single nutrients in isolation (4). The Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets include high fruit, vegetable, whole grain, and unsaturated fatty acid intakes. All of these foods and nutrients may affect cholesterol, inflammation, the development of atherosclerosis, and, therefore, risk of cardiac death.

Besides higher intakes of fruit, vegetables, whole grains and unsaturated fat, the Mediterranean diet (5) is also characterized by high intakes of nuts, fish, and moderate alcohol, all of which may improve cardiovascular health through reduced inflammation (6), insulin resistance (7, 8), blood pressure (9), weight gain (10), arrhythmia (11), atherosclerosis (12), and improved lipid profiles (8, 13). Furthermore, the Mediterranean diet is typically characterized by low intakes of red and processed meats and high-fat dairy products, both of which are high in saturated fat and thought to negatively affect cardiovascular

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[4] Abbreviations used: CAD, coronary artery disease; CHF, congestive heart failure; DASH, Dietary Approaches to Stop Hypertension; FFQ, food-frequency questionnaire; OS, observational study; SCD, sudden cardiac death; WHI, Women's Health Initiative; WHR, waist-to-hip ratio.

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health (14, 15). The recent Prevención con Dieta Mediterránea study showed that a Mediterranean diet supplemented with either olive oil or nuts reduced risk of a major cardiovascular disease event by ~30% (16).

The DASH (17) diet similarly encourages intakes of fruit, vegetables, nuts, and whole grains and discourages intakes of red and processed meats and saturated fat. Unlike the Mediterranean diet, the DASH diet has no specific alcohol recommendations, and in addition, it discourages sodium and sugar-sweetened beverages and encourages the intake of low-fat dairy. Sugar-sweetened beverages are positively associated with risk of coronary artery disease (CAD) (18), and higher sodium intake is associated with hypertension, which is a major risk factor for SCD (19).

Two studies have examined the association between the Mediterranean diet and risk of SCD. The Lyon Diet Heart Study randomly assigned participants either to receive or not receive advice to adhere to a Mediterranean-style diet and showed that participants in the intervention arm had significantly reduced risk of SCD (20). However, SCD was not the primary endpoint of this study, and only 8 SCD events occurred. Chiuve et al (21) showed that a higher alternate Mediterranean diet score, which indicated a diet that closely resembled the Mediterranean diet, was associated with lower risk of SCD in a prospective study of 81,700 nurses; however, the study population was almost entirely white, whereas in our Women's Health Initiative (WHI) cohort, 18% of SCDs were in women of nonwhite race. Besides lowering blood pressure, adherence to the DASH diet appears to reduce risk of some acute cardiovascular events including heart failure (22) and possibly death from cardiovascular disease or stroke, although findings have been mixed (23, 24). To our knowledge, no studies have examined adherence to the DASH diet and risk of SCD.

The WHI cohort provides a unique opportunity to study dietary patterns and risk of SCD because comprehensive dietary intake data were collected at baseline and a relatively large number of SCD events occurred during follow-up. Goals of this study were to examine the association between *1*) a Mediterranean diet and *2*) the DASH diet and risk of SCD.

SUBJECTS AND METHODS

Study participants

A total of 161,808 postmenopausal women participated in the WHI including 93,676 postmenopausal women in the WHI observational study (OS) and 68,133 postmenopausal women in one or more of the following 3 clinical trials: the hormone therapy, calcium and vitamin D, or dietary modification trials (25). These women enrolled at 40 study sites across the United States and were aged 50–79 y at baseline (1993–1998). Women were excluded if they planned to move out of the study recruitment area within 3 y, had a predicted survival time <3 y, were participating in another clinical trial, had characteristics that would compromise study compliance (dementia, drug dependency, or mental illness alcoholism), or did not provide written informed consent. Each of the trials had additional exclusion criteria as described previously (25).

All women (OS and clinical trial participants) completed the WHI food-frequency questionnaire (FFQ) at baseline, and OS participants completed a second FFQ at year 3. Because OS participants changed their diets during follow-up (≥10% of participants moved to a different quartile or category of intake between baseline and year 3), we felt that the baseline diet was not representative of a long-term diet during follow-up. Therefore, we restricted our analysis to women in the OS so that we could conduct a time-dependent exposure analysis that uses diet intake from both baseline and year 3. After the exclusion of 96 women with missing baseline dietary pattern data, 265 women with missing race data, and 196 women with missing pulse data, our analytic sample consisted of 93,122 women.

Exposure measurement

The WHI used a validated, semiquantitative FFQ designed specifically for postmenopausal women to measure dietary intake (26). The WHI FFQ asks participants to recall diet over the past 3 mo and includes 122 line items and >350 unique foods. We scored women according to how closely their reported diets resembled the Mediterranean and DASH dietary patterns at baseline and year 3.

We adjusted each dietary pattern food group for total energy by using the residual method (27, 28). The residual method computes energy-adjusted nutrient intake as the residuals of a regression model of total energy intake (independent variable) and absolute nutrient intake (dependent variable). This approach isolates the variation in nutrient intake attributed to the composition of the diet from the variation in nutrient intake attributed to the total amount of energy consumed. An additional strength of the residual method is that it removes the problem of collinearity that can occur when the multivariable approach is used if total energy intake is correlated with the nutrient of interest.

A Mediterranean diet score was created with use of the rules developed by Trichopoulou et al (5). This score ranged from 0 to 40, where 40 indicated perfect agreement between the reported diet and the Mediterranean diet pattern. The score was created by categorizing the following food groups and nutrients into quintiles: fruit, vegetables, nuts and legumes, whole grains, fish, monounsaturated and polyunsaturated fats, red and processed meats, poultry, high-fat dairy, and alcohol. All food groups except alcohol intake and the percentage of total fat from monounsaturated and polyunsaturated fats were adjusted for energy with the use of the residual method, described previously, before categorizing intake into quintiles. Individuals received a score from 0 to 4 for being in the lowest to highest quintiles of intake for the following food groups and nutrients: fruit, vegetables, nuts and legumes, whole grains, fish, and percentage of fat from monounsaturated and polyunsaturated fats. Scores were reversed (4–0 for lowest to highest quintiles) for the following food groups: red and processed meats, poultry, and high-fat dairy. Individuals received a score of 0 if they were in the lowest quintile of alcohol intake, 4 if they were in the second quintile, 3 if they were in the third quintile, 2 if they were in the fourth quintile, and 1 if they were in the fifth quintile. All food group and nutrient scores were summed to create a total Mediterranean diet score, which was then categorized into quintiles for our analysis. Baseline score quintile cutoffs were used to categorize both year 3 and average Mediterranean diet scores into quintiles.

With the use of the same dietary data, a DASH diet score was created by using National Heart, Lung, and Blood Institute guidelines developed from DASH studies (29). The score ranged

TABLE 1
Selected baseline characteristics by sudden cardiac death status[1]

	Sudden cardiac death (n = 237)	No sudden cardiac death (n = 92,885)	P
Age (y)	69.0 ± 6.4[2]	63.6 ± 7.4	<0.01
Daily energy intake (kcal)	1648 ± 1591	1550 ± 694	0.35
Race (%)			<0.01
White (non-Hispanic)	81.4	83.5	
African American	13.1	8.2	
Hispanic/Latino	0.8	3.9	
Asian/Pacific Islander	2.5	2.9	
American Indian/Alaska Native	1.3	0.5	
Family income (%)			<0.01
<$20,000	32.7	16.1	
$20,000–$74,999	57.0	63.6	
≥$75,000	10.3	20.3	
Smoking status (%)			<0.01
Never smoker	44.4	50.9	
Former smoker	44.0	42.8	
Current smoker	11.5	6.3	
Physical activity (MET-h[3]/wk)	10.3 ± 12.6	13.7 ± 14.4	<0.01
BMI (kg/m^2)	28.5 ± 6.2	27.3 ± 5.9	<0.01
Waist-to-hip ratio (%)			<0.01
Quartile 1 (0.28–0.76)	15.2	27.8	
Quartile 2 (0.77–0.80)	16.0	25.6	
Quartile 3 (0.81–0.86)	22.8	24.1	
Quartile 4 (0.87–2.88)	46.0	22.5	
Resting pulse (beats/min)	71.5 ± 14.2	69.3 ± 12.1	0.02
Self-reported disease history (%)			
Coronary artery disease	27.0	7.4	<0.01
Diabetes	18.1	3.2	<0.01
Hypertension	87.8	67.4	<0.01
Congestive heart failure	6.8	0.9	<0.01
Coronary bypass surgery	7.3	0.9	<0.01
Angioplasty of coronary arteries	6.5	1.2	<0.01
Carotid endarterectomy/angioplasty	4.3	0.4	<0.01
Atrial fibrillation	13.1	4.7	<0.01
Angina	21.2	5.9	<0.01

[1] P values were calculated with t tests for continuous variables and chi-square tests for categorical variables.
[2] Mean ± SD (all such values).
[3] MET-h, metabolic equivalent task hours.

from 8 to 40, where 40 represented perfect agreement between the reported diet and the DASH diet. The score was created by categorizing intakes of the following food groups and nutrients into quintiles: fruit, vegetables, nuts and legumes, low-fat dairy, red and processed meat, sugar-sweetened beverages, whole grains, and sodium. All food groups were adjusted for energy before categorizing intake into quintiles. Individuals received a score from 1 to 5 for being in the lowest to highest quintiles of intake for the following food groups: fruit, vegetables, nuts and legumes, low-fat dairy, and whole grains. Scores were reversed (5–1 for lowest to highest quintiles) for the following food groups and nutrients: sodium, red and processed meats, and sugar-sweetened beverages. All food group and nutrient scores were summed to create a total DASH diet score that was categorized into quintiles for our analysis. Baseline-score quintile cutoffs were used to categorize year 3 and average DASH diet scores into quintiles.

Outcome measurement

SCD was defined as death that occurred within 1 h of symptom onset. Deaths that were the result of a potentially lethal non-coronary disease process were excluded. For unobserved deaths, documentation that a relative or observer found the patient unresponsive ≤60 min from a previous direct observation of stable clinical status was required. Trained physician adjudicators reviewed medical records to determine cases of SCD including death records, overnight hospital stays, and outpatient coronary revascularization procedures (30). Death certificates, autopsy reports, circumstances of death, electrocardiograms, laboratory test results, and reports from all relevant procedures were used to confirm deaths caused by coronary disease.

Covariates

Age, race, income, education, smoking status, physical activity (metabolic equivalents per week from recreational activity), and disease history were self-reported at baseline using standardized questionnaires. Trained, certified staff measured height, weight, BMI, waist-to-hip ratio (WHR), and pulse at the baseline exam. Height was measured with the use of a stadiometer, weight was measured with participants wearing light clothing, and BMI was calculated as weight divided by the square of height (kg/m^2).

Waist circumference was measured at the natural waist after an exhale, and hip circumference was measured at the maximal circumference, both to the nearest 0.1 cm (31). The WHR was calculated as the ratio of these 2 measures.

Participants reported any new medical conditions annually during follow-up in the OS. Trained physicians confirmed self-reported outcomes by reviewing medical records as described previously for SCD (30). Participants were asked to bring all of their prescription medications to their baseline visit. A history of diabetes was defined as a self-report of a physician diagnosis at baseline and the use of diabetes medication. Hypertension was defined as measured systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or the use of antihypertension medication during follow-up. After women sat quietly for 5 min, blood pressure was measured with a mercury manometer twice and 30 s apart. We used the average of the 2 measurements for this analysis.

Statistical analysis

We computed HRs for SCD according to the quintile of dietary pattern score by using Cox proportional hazards models with time-dependent exposure and covariates [CAD, congestive heart failure (CHF), diabetes, and hypertension] (32). Briefly, this approach used baseline diet scores for women who experienced SCD or were censored before year 3 and diet scores calculated from the year 3 FFQ for all other women in our analysis. Person-years of follow up were calculated from the date of return of the baseline FFQ to the first of the following variables: SCD, death from other causes, or August 2009.

In multivariable model 2, we adjusted for potential confounders, including age, total energy, race, income, smoking status, and physical activity. In addition, we adjusted for potential mediators in model 3 including pulse, WHR, BMI, CAD, CHF, diabetes, and hypertension. We used missing indicators for women with missing data for the following covariates: physical activity ($n = 1051$), BMI ($n = 1105$), income ($n = 6907$), and smoking status ($n = 1351$). Tests for linear trend assigned the quintile number to each participant and modeled this variable in separate proportional hazards models. In addition, we ran sensitivity analyses by using quartiles instead of quintiles and the cumulative average diet instead of the most recent diet. Rather than using the most recent diet (ie, diet reported at year 3 for all events that occurred after year 3), the cumulative average method used the average of baseline and year 3 diet scores. All analyses were conducted with SAS statistical software (version 9.3; SAS Institute Inc). All

TABLE 2
Selected baseline characteristics according to quintile of the Mediterranean diet score[1]

	Mediterranean diet quintile					
	1	2	3	4	5	*P*
n	21,154	12,845	21,648	18,397	19,078	
Age (y)	62.9 ± 7[2]	63.4 ± 7	63.8 ± 7	63.9 ± 7	64.0 ± 7	<0.01
Daily energy (kcal)	1468 ± 805	1446 ± 693	1508 ± 685	1574 ± 623	1737 ± 609	<0.01
Race (%)						<0.01
White (non-Hispanic)	80.1	82.1	84.2	85.3	85.7	<0.01
African American	10.4	9.0	7.9	7.0	6.6	
Hispanic/Latino	5.7	4.8	3.7	3.0	2.2	
Family income (%)						<0.01
<$20,000	20.6	17.4	15.6	14.0	13.0	
$20,000–$74,999	63.1	63.4	63.8	63.7	63.9	
≥$75,000	16.3	19.2	20.6	22.4	23.2	
Smoking status (%)						<0.01
Never smoker	47.6	49.8	51.0	52.4	53.8	
Former smoker	42.0	42.9	43.1	43.2	42.9	
Current smoker	10.4	7.3	5.9	4.4	3.3	
Physical activity (MET-h[3]/wk)	10.3 ± 13	12.1 ± 13	13.5 ± 14	14.9 ± 15	17.5 ± 16	<0.01
BMI (kg/m^2)	28.1 ± 6	27.6 ± 6	27.2 ± 6	27.0 ± 6	26.4 ± 6	<0.01
Waist-to-hip ratio (%)						<0.01
Quartile 1 (0.28–0.76)	23.3	26.4	27.9	29.4	31.8	
Quartile 2 (0.77–0.80)	24.2	24.7	25.8	26.5	26.8	
Quartile 3 (0.81–0.86)	25.3	25.3	24.1	23.5	22.4	
Quartile 4 (0.87–2.88)	27.2	23.6	22.2	20.6	19.0	
Resting pulse (beats/min)	70.2 ± 12	69.7 ± 12	69.2 ± 12	68.9 ± 12	68.5 ± 12	<0.01
Self-reported disease history (%)						
Coronary artery disease	7.7	7.4	7.5	7.3	7.2	0.08
Diabetes	3.6	3.5	3.1	3.2	3.1	<0.01
Hypertension	69.3	68.3	67.4	66.4	65.6	<0.01
Congestive heart failure	1.2	0.8	0.9	0.9	0.8	<0.01

[1] A higher score indicates greater similarity between the reported diet and Mediterranean diet. *P* values were calculated with the chi-square test for comparisons when at least one categorical variable was nominal or a test for linear trend using ANOVA for continuous variables, or the Mantel-Haenszel chi-square test if both categorical variables were ordinal.

[2] Mean ± SD (all such values).

[3] MET-h, metabolic equivalent task hours.

participants gave informed consent, and review boards of all collaborating institutions approved the study.

RESULTS

Of the 93,122 women included in our analysis, 237 women experienced SCD over an average of 10.5 y follow-up. Women who experienced SCD were older, more likely to smoke, and more likely to have a history of CAD, diabetes, hypertension, CHF, and carotid artery disease (**Table 1**).

Women with higher Mediterranean diet scores were more likely to be non-Hispanic white, had higher incomes, and were less likely to smoke (**Table 2**). They also had a lower WHR and a lower pulse and were less likely to have a history of diabetes, hypertension, and CHF. Similarly, women with a higher DASH diet score were more likely to be non-Hispanic white, had higher incomes, and were less likely to smoke (**Table 3**). Women with a higher DASH score were also more active, had a lower WHR, and were less likely to have a history of CAD, diabetes, hypertension, and CHF.

As expected, women with a higher Mediterranean diet score had higher intakes of fruit, vegetable, nuts and legumes, whole grain, and fish and lower intakes of red and processed meats, poultry, and high-fat dairy (**Table 4**). However, women with a higher Mediterranean diet score also had slightly lower intakes (percentage of total fat) of monounsaturated and polyunsaturated fat. Women with a higher DASH score had higher intakes of fruit, vegetable, nuts and legumes, low-fat dairy, and whole grains and lower intakes of red and processed meats and sugar-sweetened beverages (Table 4).

Women in the third and fifth quintiles of the Mediterranean diet score had a statistically significant reduced risk of SCD compared with women in the lowest quintile after adjustment for age, total energy intake, race, income, smoking status, and physical activity (**Table 5**). These differences were very similar after further adjusting for potential mediators or mechanisms through which the Mediterranean diet could potentially lower risk of SCD including pulse, WHR, BMI, CAD, CHF, diabetes, and hypertension. With the use of the cumulative average method, we saw a similar association between the Mediterranean diet score and risk of SCD with HRs (95% CIs) of 0.77 (0.50, 1.17), 0.65 (0.45, 0.93), 0.81 (0.56, 1.18), and 0.63 (0.41, 0.96) for quintiles 2, 3, 4, and 5, respectively, compared with quintile 1 and adjusted for all covariates in model 2. There was no evidence of a dose-response relation between the Mediterranean diet score and risk of SCD ($P > 0.05$).

TABLE 3
Selected baseline characteristics according to quintile of DASH diet score[1]

	DASH diet quintile					
	1	2	3	4	5	*P*
n	18,465	18,216	20,220	17,808	18,413	
Age (y)	62.5 ± 7[2]	63.4 ± 7	63.8 ± 7	64.1 ± 7	64.2 ± 7	<0.01
Daily energy (kcal)	1524 ± 914	1432 ± 719	1482 ± 625	1567 ± 577	1753 ± 546	<0.01
Race (%)						<0.01
White (non-Hispanic)	72.6	81.1	85.2	88.0	90.6	
African American	15.2	9.3	6.7	5.4	4.4	
Hispanic/Latino	6.3	4.7	3.4	2.8	2.1	
Family income (%)						<0.01
<$20,000	23.9	18.2	14.5	13.0	11.2	
$20,000–$74,999	61.6	63.6	64.1	64.1	64.4	
≥$75,000	14.5	18.2	21.3	22.9	24.4	
Smoking status (%)						<0.01
Never smoker	49.2	49.9	51.9	51.6	51.9	
Former smoker	38.4	42.3	43.0	44.7	45.6	
Current smoker	12.4	7.7	5.1	3.7	2.5	
Physical activity (MET-h/wk)	8.8 ± 12	11.5 ± 13	13.7 ± 14	15.8 ± 15	18.7 ± 16	<0.01
BMI (kg/m^2)	28.8 ± 7	27.7 ± 6	27.1 ± 6	26.6 ± 5	26.1 ± 5	<0.01
Waist-to-hip ratio (%)						<0.01
Quartile 1 (0.28–0.76)	21.0	24.8	28.6	30.1	34.1	
Quartile 2 (0.77–0.80)	23.0	24.9	26.2	26.6	27.2	
Quartile 3 (0.81–0.86)	26.2	25.3	23.8	23.4	21.7	
Quartile 4 (0.87–2.88)	29.8	25.0	21.5	19.7	17.0	
Resting pulse (beats/min)	70.5 ± 12	69.8 ± 12	69.1 ± 12	68.8 ± 12	68.3 ± 12	<0.01
Self-reported disease history (%)						
Coronary artery disease	8.5	7.9	7.4	7.2	6.2	<0.01
Diabetes	4.2	3.5	3.3	2.9	2.4	<0.01
Hypertension	71.7	69.2	66.8	66.0	63.5	<0.01
Congestive heart failure	1.2	1.2	0.8	0.9	0.7	<0.01

[1] A higher score indicates greater similarity between the reported diet and DASH diet. *P* values were calculated with the chi-square test for comparisons when at least one categorical variable was nominal or a test for linear trend using ANOVA for continuous variables, or the Mantel-Haenszel chi-square test if both categorical variables were ordinal. DASH, Dietary Approaches to Stop Hypertension; MET-h, metabolic equivalent task hours.

[2] Mean ± SD (all such values).

TABLE 4
Mean baseline intake of each food group (energy adjusted) according to quintile of dietary pattern score[1]

	Quintile				
	1	2	3	4	5
Mediterranean diet					
n	21,154	12,845	21,648	18,397	19,078
Pattern score (range)	3–16	17–18	19–21	22–24	25–40
Total energy (kcal/d)	1468 ± 805[2]	1446 ± 693	1508 ± 685	1574 ± 623	1737 ± 609
Fruit (servings/d)	0.8 ± 0.8	1.1 ± 0.9	1.4 ± 1.0	1.7 ± 1.0	2.2 ± 1.1
Vegetables (servings/d)	1.3 ± 0.8	1.6 ± 0.9	2.0 ± 1.1	2.4 ± 1.2	3.0 ± 1.3
Nuts and legumes (servings/d)	0.4 ± 0.3	0.5 ± 0.4	0.6 ± 0.4	0.7 ± 0.5	1.0 ± 0.6
Whole grains (servings/d)	0.5 ± 0.4	0.7 ± 0.5	0.7 ± 0.5	0.8 ± 0.5	1.0 ± 0.6
Red and processed meat (servings/d)	1.1 ± 0.5	0.9 ± 0.5	0.8 ± 0.5	0.7 ± 0.4	0.5 ± 0.4
High-fat dairy (servings/d)	0.6 ± 0.5	0.5 ± 0.4	0.4 ± 0.4	0.3 ± 0.3	0.2 ± 0.3
Fish (servings/d)	0.2 ± 0.2	0.2 ± 0.2	0.3 ± 0.2	0.3 ± 0.3	0.4 ± 0.3
Monounsaturated and polyunsaturated fat (percentage of total fat)[3]	18.6	18.4	17.9	17.3	16.8
Poultry (servings/d)	0.4 ± 0.3	0.4 ± 0.3	0.4 ± 0.3	0.4 ± 0.3	0.3 ± 0.2
Alcohol (%)[3]					
Nondrinker	46.0	42.4	40.7	40.1	40.2
Moderate drinker (0.1–15 g/d)	37.1	43.8	46.5	49.5	51.3
Heavy drinker (≥15 g/d)	16.9	13.9	12.8	10.9	8.5
DASH[4] diet					
n	18,465	18,216	20,220	17,808	18,413
Pattern score (range)	8–19	20–22	23–25	26–28	29–40
Total energy (kcal/d)	1524 ± 914	1432 ± 719	1482 ± 625	1567 ± 577	1753 ± 546
Fruit (servings/d)	0.6 ± 0.5	1.0 ± 0.7	1.4 ± 0.9	1.8 ± 1.0	2.4 ± 1.0
Vegetables (servings/d)	1.2 ± 0.7	1.6 ± 0.9	2.0 ± 1.1	2.5 ± 1.3	3.0 ± 1.3
Nuts and legumes (servings/d)	0.4 ± 0.3	0.6 ± 0.4	0.6 ± 0.4	0.7 ± 0.5	0.9 ± 0.6
Whole grains (servings/d)	0.5 ± 0.4	0.6 ± 0.5	0.7 ± 0.5	0.8 ± 0.5	1.1 ± 0.6
Red and processed meat (servings/d)	1.2 ± 0.6	0.9 ± 0.4	0.8 ± 0.4	0.6 ± 0.4	0.4 ± 0.4
Low-fat dairy (servings/d)	0.6 ± 0.7	0.9 ± 0.9	1.2 ± 1.0	1.4 ± 1.1	1.9 ± 1.3
Sugar beverages (servings/d)	0.7 ± 0.9	0.4 ± 0.7	0.4 ± 0.6	0.3 ± 0.5	0.1 ± 0.4
Sodium (mg/d)	2749 ± 523	2725 ± 480	2738 ± 470	2742 ± 483	2725 ± 527

[1] Women in the fifth quintile reported diets that were most similar to the dietary pattern of interest. A test for linear trend was calculated using ANOVA for continuous variables or the Mantel-Haenszel chi-square test for categorical variables. All P-trend < 0.01.

[2] Mean ± SD (all such values).

[3] Not energy adjusted.

[4] DASH, Dietary Approaches to Stop Hypertension.

Women in the fourth and fifth quintiles of the DASH diet score had 35% and 52% lower risk, respectively, of SCD than did women in the lowest quintile after adjustment for age and total energy (Table 5). After adjustment for potential confounders and mediators, the association between the DASH diet score and risk of SCD was no longer statistically significant. Similarly, after adjustment for the same set of potential confounders and mediators, we showed no association between the DASH diet score and risk of SCD when using the cumulative average method (data not shown). There was no evidence of a dose-response relation between the DASH diet score and risk of SCD ($P > 0.05$). No women met all of the DASH diet goals, and therefore, we were not able to examine the effect of complete adherence to the DASH diet (total fat: ≤27% of energy; saturated fat: ≤ 6% of energy; cholesterol: ≤150 mg; sodium, ≤2300 mg; potassium: ≥4700 mg; calcium: ≥1250 mg; magnesium: ≥500 mg; fiber: ≥30g; protein: 18% of energy; and carbohydrate: 55% of energy; nutrient goals for a 2100-kcal eating plan). We examined low-fat dairy, sodium, and sugar-sweetened beverages separately and saw no association with risk of SCD (data not shown). Finally, results were similar for both DASH diet and Mediterranean diet scores when we used quartiles rather than quintiles (data not shown).

DISCUSSION

We found that a higher Mediterranean diet score was associated with a lower risk of SCD, especially in women in the highest quintile of the Mediterranean diet score. Although a higher DASH diet score was associated with a lower risk of SCD, this association appeared to be explained by a healthy lifestyle and other CAD risk factors. The DASH diet is known to reduce risk of hypertension (17), which is a major risk factor for SCD in this cohort (19); however, even when we did not adjust for hypertension, we still found no association between the DASH diet score and risk of SCD.

Reduced sodium intake is a central goal of the DASH diet, and sodium is an extremely challenging nutrient to measure with validity with an FFQ. Sodium was not one of the primary nutrients that the WHI FFQ was designed to assess; the FFQ did not ask about salt added during cooking or at the table or about reduced or low-sodium foods. Therefore, our results for the DASH diet

TABLE 5
HRs (95% CIs) for sudden cardiac death according to quintile of dietary pattern score by using a simple time-varying analysis[1]

	Mediterranean diet score quintile						DASH[2] diet score quintile					
	1	2	3	4	5	*P*-trend	1	2	3	4	5	*P*-trend
No. of events	59	37	49	47	45		52	56	57	41	31	
Model 1	1.0 (reference)	0.50 (0.33, 0.75)	0.70 (0.49, 0.98)	0.56 (0.38, 0.83)	0.49 (0.33, 0.73)	<0.01	1.0 (reference)	0.91 (0.63, 1.33)	0.79 (0.54, 1.15)	0.65 (0.43, 0.99)	0.48 (0.31, 0.75)	<0.01
Model 2	1.0 (reference)	0.80 (0.53, 1.20)	0.62 (0.43, 0.90)	0.70 (0.48, 1.03)	0.64 (0.43, 0.94)	0.18	1.0 (reference)	1.04 (0.71, 1.52)	1.00 (0.68, 1.46)	0.88 (0.57, 1.34)	0.69 (0.43, 1.10)	0.09
Model 3	1.0 (reference)	0.81 (0.54, 1.23)	0.69 (0.47, 1.00)	0.76 (0.52, 1.11)	0.67 (0.46, 0.99)	0.21	1.0 (reference)	1.09 (0.75, 1.60)	1.11 (0.75, 1.63)	0.95 (0.62, 1.45)	0.86 (0.54, 1.38)	0.46

[1] Model 1 was adjusted for age and energy. Model 2 was adjusted as for model 1 and for race, income, smoking status, and physical activity. Model 3 was adjusted as for model 2 and for the following potential mediators: pulse in 60 s, waist-to-hip ratio, BMI, coronary artery disease, heart failure, diabetes, and hypertension. All quintile cutoffs were based on the baseline.
[2] DASH, Dietary Approaches to Stop Hypertension.

could have been biased toward the null because of likely nondifferential measurement error of sodium intake.

Both dietary patterns include higher intakes of fruit, vegetables, nuts and legumes, and whole grains and lower intakes of red and processed meats (5, 29). Main differences between the 2 diets are that the DASH diet additionally recommends reducing intakes of sugar-sweetened beverages and sodium and recommends increasing the intake of low-fat dairy. These nutrients and food groups were not individually associated with risk of SCD in this population. The Mediterranean diet pattern, as described by Trichopoulou et al (5), further emphasizes increasing fish and unsaturated fat intakes and reducing intake of poultry and high-fat dairy. The Mediterranean diet pattern also recommends moderate alcohol intake. Total fish and, especially, dark fish intakes were individually associated with lower risk of SCD (HR 0.63; 95% CI: 0.42, 0.95) for quintiles 5 compared with 1 of total fish intake, with adjustment for model 2 covariates; however unsaturated fat, poultry, and high-fat dairy were not individually associated with risk of SCD. A meta-analysis of observational and experimental studies also showed an inverse association between fish or fish-oil intake and risk of coronary death, whereby moderate compared with low consumption was associated with 36% lower risk of CAD death including SCD (11).

To our knowledge, 2 previous studies have examined the association between a Mediterranean diet score and risk of SCD in women. The Lyon Diet Heart Study trial randomly assigned 605 men and women who had recently survived a myocardial infarction either to receive or not receive advice to adhere to a Mediterranean style diet (20). Although it was shown that participants in the intervention arm had a statistically significant reduced risk of SCD, SCD was not the primary endpoint of this study, and only 8 SCD events occurred. Chiuve et al (21) examined the association between an alternate Mediterranean Diet Score that did not include the traditional components of poultry and high-fat dairy and risk of SCD in the Nurses' Health Study, which is another large, prospective cohort of women. Chiuve et al (21) showed a similar inverse association whereby a higher alternate Mediterranean Diet Score was associated with reduced risk of SCD (RR: 0.60; 95% CI 0.43, 0.84) for subjects in the highest compared with lowest quintiles.

Our study had several strengths including its prospective design, the inclusion women of multiple ethnicities, recruitment of women from all over the US, physician-adjudicated cardiac death, and an FFQ designed specifically for the WHI, which was administered twice during follow-up. Correlation coefficients between the WHI FFQ and 8 d dietary intake (a 4-d food record and four 24-h recalls) were 0.89 for alcohol, 0.64 for monounsaturated fat, and 0.59 for total EPA, which suggested good agreement (26).

A potential weakness of our study was the use of an FFQ to measure diet. Although FFQs are cost effective and considered satisfactory for the assessment of long-term dietary intake in a large population, they have several limitations. First, FFQs collected only once or twice during follow-up may not represent the average diet across the entire period relevant to risk of SCD. Second, dietary variables measured at a single point in time are subject to measurement error, but other researchers have shown that such classification measures are adequate to find etiologic associations (14, 15, 18, 21). The presumably nondifferential (random) misclassification in FFQ data, especially for sodium,

could have potentially biased our estimates toward the null, especially if the true associations were modest. Third, although FFQs typically underestimate nutrient intakes (33), they can categorize participants into lower and higher nutrient intakes fairly well. Finally, no women completely adhered to the DASH diet eating plan in our study, but most women were not prescribed this diet or the Mediterranean diet by their physicians.

Another possible weakness of the study was the lack of data on SCD subtypes, such as whether the death was arrhythmic, which would have given more insight about underlying mechanisms. In addition, all population studies of SCD may incorrectly classify some deaths attributable to noncoronary causes and SCDs, such as those from cerebral hemorrhage, acute pulmonary embolism, or aortic rupture. Finally, our study may have been subject to residual confounding because of its observational nature, and our results are not necessarily generalizable to men and premenopausal women.

In conclusion, we showed that a higher Mediterranean diet score may be associated with a lower risk of SCD in postmenopausal women. We did not show an association between the DASH diet score and SCD in this population. Future research should try to replicate our findings in other populations as well as investigate the association between individual components of these dietary patterns and risk of SCD.

See "Supplemental data" in the online issue for a list of WHI investigators we acknowledge.

The authors' responsibilities were as follows—CBE: conducted research; MLB: performed statistical analyses; MLB and CBE: had primary responsibility for final content of the manuscript; and all authors: wrote the manuscript and read and approved the final manuscript. None of the authors had any conflicts of interest to disclose.

REFERENCES

1. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, Gregoratos G, Klein G, Moss AJ, Myerburg RJ, et al. ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (writing committee to develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation 2006; 114:e385–484.
2. Zipes DP, Wellens HJ. Sudden cardiac death. Circulation 1998;98: 2334–51.
3. Centers for Disease Control and Prevention. Deaths and mortality. 2009. Available from: http://www.cdc.gov/nchs/FASTATS/deaths.htm (cited18 September 2009).
4. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol 2002;13:3–9.
5. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med 2003;348:2599–608.
6. Li JM, Mukamal KJ. An update on alcohol and atherosclerosis. Curr Opin Lipidol 2004;15:673–80.
7. Babio N, Bullo M, Salas-Salvado J. Mediterranean diet and metabolic syndrome: the evidence. Public Health Nutr 2009;12:1607–17.
8. Harris KA, Kris-Etherton PM. Effects of whole grains on coronary heart disease risk. Curr Atheroscler Rep 2010;12:368–76.
9. Schwingshackl L, Strasser B, Hoffmann G. Effects of monounsaturated fatty acids on cardiovascular risk factors: a systematic review and meta-analysis. Ann Nutr Metab 2011;59:176–86.
10. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in diet and lifestyle and long-term weight gain in women and men. N Engl J Med 2011;364:2392–404.
11. Mozaffarian D. Fish and n−3 fatty acids for the prevention of fatal coronary heart disease and sudden cardiac death. Am J Clin Nutr 2008; 87:1991S–6S.
12. de Lorgeril M, Salen P. The Mediterranean diet: rationale and evidence for its benefit. Curr Atheroscler Rep 2008;10:518–22.
13. Brinton EA. Effects of ethanol intake on lipoproteins. Curr Atheroscler Rep 2012;14:108–14.
14. Pan A, Sun Q, Bernstein AM, Schulze MB, Manson JE, Stampfer MJ, Willett WC, Hu FB. Red meat consumption and mortality: results from 2 prospective cohort studies. Arch Intern Med 2012;172:555–63.
15. van Aerde MA, Soedamah-Muthu SS, Geleijnse JM, Snijder MB, Nijpels G, Stehouwer CD, Dekker JM. Dairy intake in relation to cardiovascular disease mortality and all-cause mortality: the Hoorn Study. Eur J Nutr 2013;52:609–16.
16. Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella D, Aros F, Gomez-Gracia E, Ruiz-Gutierrez V, Fiol M, Lapetra J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med 2013;368:1279–90.
17. Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller ER 3rd, Simons-Morton DG, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med 2001;344:3–10.
18. de Koning L, Malik VS, Kellogg MD, Rimm EB, Willett WC, and Hu FB. Sweetened beverage consumption, incident coronary heart disease, and biomarkers of risk in men. Circulation 2012; 125:1735–41, S1.
19. Bertoia ML, Allison MA, Manson JE, Freiberg MS, Kuller LH, Solomon AJ, Limacher MC, Johnson KC, Curb JD, Wassertheil-Smoller S, et al. Risk factors for sudden cardiac death in post-menopausal women. J Am Coll Cardiol 2012;60:2674–82.
20. de Lorgeril M, Renaud S, Mamelle N, Salen P, Martin JL, Monjaud I, Guidollet J, Touboul P, Delaye J. Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. Lancet 1994;343:1454–9.
21. Chiuve SE, Fung TT, Rexrode KM, Spiegelman D, Manson JE, Stampfer MJ, Albert CM. Adherence to a low-risk, healthy lifestyle and risk of sudden cardiac death among women. JAMA 2011;306:62–9.
22. Levitan EB, Wolk A, Mittleman MA. Consistency with the DASH diet and incidence of heart failure. Arch Intern Med 2009;169:851–7.
23. Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. Arch Intern Med 2008;168:713–20.
24. Parikh A, Lipsitz SR, Natarajan S. Association between a DASH-like diet and mortality in adults with hypertension: findings from a population-based follow-up study. Am J Hypertens 2009;22:409–16.
25. The Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. Control Clin Trials 1998;19:61–109.
26. Patterson RE, Kristal AR, Tinker LF, Carter RA, Bolton MP, Agurs-Collins T. Measurement characteristics of the Women's Health Initiative food frequency questionnaire. Ann Epidemiol 1999;9:178–87.
27. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol 1986;124:17–27.
28. Kannel WB, Gagnon DR, Cupples LA. Epidemiology of sudden coronary death: population at risk. Can J Cardiol 1990;6:439–44.
29. United States Department of Health and Human Services, National Institutes of Health, and National Heart Lung aBI. Your guide to lowering your blood pressure with DASH. 2009. Available from: http://www.nhlbi.nih.gov/health/public/heart/hbp/dash/how_plan.html (cited 22 September 2009).
30. Curb JD, McTiernan A, Heckbert SR, Kooperberg C, Stanford J, Nevitt M, Johnson KC, Proulx-Burns L, Pastore L, Criqui M, et al. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. Ann Epidemiol 2003;13:S122–8.
31. The Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study Control Clin Trials 1998;19:61–109.
32. Hu FB, Stampfer MJ, Rimm E, Ascherio A, Rosner BA, Spiegelman D, Willett WC. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. Am J Epidemiol 1999;149:531–40.
33. Kristal AR, Peters U, Potter JD. Is it time to abandon the food frequency questionnaire? Cancer Epidemiol Biomarkers Prev 2005;14: 2826–8.