

HHS Public Access

Author manuscript

Circ Heart Fail. Author manuscript; available in PMC 2015 September 09.

Published in final edited form as:

Circ Heart Fail. 2013 November; 6(6): 1116-1123. doi:10.1161/CIRCHEARTFAILURE.113.000495.

Mediterranean and DASH Diet Scores and Mortality in Women with Heart Failure: The Women's Health Initiative

Emily B. Levitan, ScD, Cora E. Lewis, MD, MSPH, Lesley F. Tinker, PhD, Charles B. Eaton, MD, MS, Ali Ahmed, MD, MPH, JoAnn E. Manson, MD, DrPH, Linda G. Snetselaar, RD, PhD, Lisa W. Martin, MD, Maurizio Trevisan, MD, MS, Barbara V. Howard, PhD, and James M. Shikany, DrPH

University of Alabama at Birmingham, Birmingham, AL (EBL, CEL, AA, JMS), Birmingham VA Medical Center, Birmingham, AL (AA), Fred Hutchinson Cancer Research Center, Seattle, WA (LFT), Brown University, Providence, RI (CBE), Brigham and Women's Hospital, Harvard Medical School, Boston, MA (JEM), University of Iowa, Iowa City, IA (LGS), George Washington University, Washington, DC (LWM), City College of New York, New York, NY (MT), MedStar Health Research Institute, Hyattsville, MD and Georgetown/Howard Universities Center for Clinical and Translational Sciences, Washington, DC (BVH)

Abstract

Background—Current dietary recommendations for heart failure (HF) patients are largely based on data from non-HF populations; evidence regarding associations of dietary patterns with outcomes in HF is limited. We therefore evaluated associations of Mediterranean and DASH diet scores with mortality among postmenopausal women with HF.

Methods and Results—Women's Health Initiative participants were followed from the date of HF hospitalization through the date of death or last participant contact prior to August 2009. Mediterranean and DASH diet scores were calculated from food-frequency questionnaires. Cox proportional hazards models adjusted for demographics, health behaviors, and health status were used to calculate hazard ratios (HR) and 95% confidence intervals (CI). Over a median of 4.6 years of follow-up, 1,385 of 3,215 (43.1%) participants who experienced a HF hospitalization died. Multivariable-adjusted HRs were 1 (reference), 1.05 (95% CI 0.89–1.24), 0.97 (95% CI 0.81–1.17), and 0.85 (95% CI 0.70–1.02) across quartiles of the Mediterranean diet score (p-trend = 0.08) and 1 (reference), 1.04 (95% CI 0.89–1.21), 0.83 (95% CI 0.70–0.98), and 0.84 (95% CI 0.70–1.00) across quartiles of the DASH diet score (p-trend = 0.01). Diet score components vegetables, must, and whole grain intake were inversely associated with mortality.

Conclusions—Higher DASH diet scores were associated with modestly lower mortality in women with HF, and there was a non-significant trend towards an inverse association with Mediterranean diet scores. These data provide support for the concept that dietary

Correspondence to Dr. Emily B. Levitan, University of Alabama at Birmingham Department of Epidemiology, 1530 3rd Ave S, RPHB 230K, Birmingham, AL 35924-0022, Telephone: 1-205-975-7680, Fax: 1-205-934-8665, elevitan@uab.edu. *Clinical Trial Registration*—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00000611.

Disclosures

None.

_

recommendations developed for other cardiovascular conditions or general populations may also be appropriate in HF patients.

Keywords

diet; heart failure; mortality; nutrition

Evidence regarding the effects of dietary patterns among people with heart failure (HF) is limited. Dietary intake, particularly high sodium, is thought to precipitate HF exacerbations, and HF management protocols with nutritional components can reduce rehospitalization. Current dietary recommendations for HF patients are largely based on data from populations without HF, and much of the focus is on sodium. Dietary patterns rich in fruits, vegetables, whole grains, nuts, and legumes and low in processed foods and red meats, such as the Mediterranean and DASH dietary patterns, can be palatable, relatively easy to adhere to, have demonstrated beneficial cardiovascular effects, and are consistent with many dietary recommendations. Although data are scarce, these dietary patterns may also reduce the rate of mortality in HF patients. The dietary patterns have many similarities but also distinctive characteristics. For example, the Mediterranean dietary pattern emphasizes intake of monounsaturated fat, largely from olive oil, and the DASH dietary pattern is moderately high in protein and low-fat dairy.

Trials have demonstrated that individuals with prior myocardial infarction (MI) type 2 diabetes, or multiple cardiovascular disease (CVD) risk factors who received advice on the Mediterranean dietary pattern and supplemental high monounsaturated fat foods have lower rates of CVD than control groups. ^{5,6} Mediterranean-style dietary patterns have been associated with lower rates of coronary heart disease (CHD), ^{7,8} sudden cardiac death, ⁹ and CVD mortality, ¹⁰ lower blood pressure ¹¹ and inflammatory markers, ^{11,12} and better endothelial, ¹² left ventricular, ¹³ and cardiac autonomic function. ¹⁴ The DASH dietary pattern effectively reduced blood pressure in trials. ^{15,16} In a single arm study, patients with HF had lower blood pressure, arterial stiffness, and oxidative stress after 3 weeks of the DASH dietary pattern. ¹⁷ Observational studies suggest that consistency with DASH may reduce the risk of developing HF ¹⁸ and CHD. ^{19,20}

To explore the relationship of dietary patterns with mortality among women with HF, we evaluated the associations of Mediterranean and DASH diet scores with mortality among Women's Health Initiative (WHI) participants following hospitalization for HF.

Methods

Study Population

The WHI has previously been described.^{21, 22} Between 1993 and 1998, postmenopausal women aged 50–79 were recruited at 40 US clinical centers. The WHI Clinical Trial (CT) component included 68,132 participants enrolled hormone therapy (HT), dietary modification (DM), and calcium plus vitamin D (CaD) trials, and the Observational Study (OS) component included 93,676 participants. The WHI CT and OS ended in 2004–2005;

participants were invited to continue in the WHI Extension Study (ES)-1 2005–2010 and ES-2 2010–2015.

During the WHI CT and OS (1993–2005), HF hospitalizations were adjudicated locally, with central adjudication for quality control. Adjudication of HF hospitalization was based on at least one of the following criteria: 1. diagnosis by a physician and receipt of medical treatment for HF during admission including diuretics, digitalis, vasodilators, and angiotensin-converting enzyme inhibitors; 2. HF diagnosed by a physician and receipt of medical treatment for HF during admission plus documented impaired systolic or diastolic left ventricular function; 3. pulmonary edema or congestion by chest X-ray on admission; or 4. dilated ventricles or poor left- or right-side ventricular function (e.g., wall motion abnormalities) by echocardiography, radionuclide ventriculogram/multigated acquisition, or other contrast ventriculography or evidence of left ventricular diastolic dysfunction. ²³ HF hospitalizations were not adjudicated during the WHI ES. We identified 4,043 WHI CT and OS participants who had a HF hospitalization between study entry and 2005 (Supplemental Figure 1). We excluded 29 participants who did not survive at least 1 day past HF hospitalization, 605 participants missing information on dietary intake or covariates, and 194 participants with implausible energy intake (< 600 kcal/d or > 5,000 kcal/d) calculated using a food-frequency questionnaire (FFQ), producing a final sample size of 3,215 women (Supplemental Table 1). Women who did not survive HF hospitalization were excluded because the outcome of interest was post-hospitalization mortality. Women with calculated energy intake < 600 kcal/d or > 5,000 kcal/d were excluded in accordance with the WHI analytic guidelines because the extreme energy intake suggests that the FFQ was not reliable. The WHI was approved by Institutional Review Boards at all participating centers and the Clinical Coordinating Center, and written informed consent was obtained from all participants.

Dietary intake measurement

Dietary intake was assessed using a modified Block FFQ.²⁴ The FFQ was administered during a baseline screening visit for all participants. Subsequently all participants in the DM trial completed FFQs at year 1, a proportion of the DM participants completed FFQs yearly thereafter, and OS participants completed FFQs at year 3. We selected the most recently completed FFQ prior to HF hospitalization for each participant. The FFQs were completed a median of 2.3 (interquartile range 1.2–3.8) years prior to HF hospitalization. We calculated Mediterranean and DASH diet scores as previously described.^{7, 20} Total energy intake was calculated using calibration equations derived from doubly-labeled water studies.²⁵ Details are reported in the Supplemental Methods.

Covariates

Covariates were assessed by questionnaires, pill-bottle reviews, and measurement of blood pressure, height, and weight. The most recent assessment of covariates prior to HF hospitalization was selected for each individual. Information on personal habits such as smoking was recorded a median of 2.5 (interquartile range 1.2–5.0) years prior to HF hospitalization. Women were considered to have comorbidities such as MI or

revascularization if they reported a history of the condition at the time of WHI enrollment or if they experienced the condition during WHI follow-up prior to HF hospitalization.

Mortality follow-up

Follow-up for mortality was conducted as part of the WHI OS, CT, and ES. For this study, follow-up began on the date of HF hospitalization and continued through the date of death or the last contact with the participant prior to August 2009. Deaths were ascertained through direct reports to the WHI by participants' family, friends, or health care providers; response to WHI mailings by participants' family, friends, or the US Postal Service; internet searches, including searches of obituaries; the Social Security Death Index; and the National Death Index. Deaths classified as definite CHD, possible CHD, cerebrovascular, other cardiovascular, and unknown cardiovascular were considered CVD deaths.

Statistical analysis

We summarized participant characteristics using means and standard deviations for continuous variables and percentages for categorical variables. We tested for differences in characteristics by mortality status using linear regression for continuous variables and χ^2 tests for categorical variables. We classified the participants by approximate quartile of diet score (groups had unequal numbers of participants because of the large number of ties in diet scores). Mean intake of food groups and nutrients was calculated within quartile of the diet scores. Tests of trend across category were conducted using linear regression models with the median value of the diet score in each quartile as the predictor. We calculated a Spearman correlation coefficient between the Mediterranean and DASH diet scores.

Cox proportional hazards models were used to estimate the hazard ratios (HR) of mortality associated with quartiles of the DASH and Mediterranean diet scores. To appropriately account for variability in the calibrated total energy estimate, we calculated standard errors for the regression coefficients using bootstrap resampling which were then used to calculate p-values and 95% confidence intervals (CIs) as previously described. ²⁵ To accommodate the bootstrap procedure, we excluded individuals missing data (i.e., a complete case analysis) instead of using multiple imputation Model 1 adjusted for age at HF hospitalization (linear) and total energy intake (linear). Model 2 further adjusted for race/ethnicity (white, black, or other), education (less than high school, high school graduate including some college, college graduate, or graduate school), income (<\$20,000, \$20,000-34,999, \$35,000-49,999, or >\$50,000), married (yes or no), current smoking (yes or no), total exercise (metabolic equivalent-hours/week, linear), physical function score (linear), use of off-study postmenopausal hormone therapy, and WHI study arm. In Model 3, we further adjusted for variables which may have been intermediates or confounders of the association of the dietary scores with mortality including systolic blood pressure (linear), diastolic blood pressure (linear), use of diuretics, beta-blockers, and angiotensin converting enzyme inhibitors or angiotensin receptor blockers, body mass index (linear), and history of high cholesterol, high blood pressure, diabetes, MI, coronary revascularization, and atrial fibrillation. Tests for linear trend across quartiles of the diet score were performed by including the median value in each quartile as a continuous variable in the models. In

addition, we calculated the HR for a 1 unit difference in the diet scores. We examined potential nonlinearity by including the square of the diet scores in the models.

In sensitivity analyses, we examined the associations between diet scores and mortality in the subgroup who did not report a history of HF at study entry because pre-existing HF may alter dietary intake (n = 2,922), the subgroup without a history of cancer at baseline or during follow-up because of the cardiotoxic effects of some chemotherapeutic agents (n = 2,583), the subgroup limited to those with a physician diagnosis of HF at the index hospitalization because of the potential for misclassification of disease in those without a physician diagnosis of HF (n = 2,955), and the subgroup who were not in the DM or CaD trials because DM and CaD participants may have altered their dietary intake in ways not captured by the FFQ (n = 2,039). We examined the associations of Mediterranean and DASH diet scores with CVD mortality and in subgroups defined by body mass index, history of diabetes, history of MI or revascularization, income, and cigarette smoking. Tests of whether the associations varied across subgroups were performed by entering interaction terms between indicators of subgroup membership and the median diet score in each quartile into the models. We examined the association of the components of the Mediterranean and DASH diet scores with mortality using Cox proportional hazards models adjusted as in Model 3 above. Because 60% of this population did not drink sweetened beverages, we examined intake in 3 rather than 4 categories for this component.

We tested the proportional hazards assumption by including the product of diet scores and the natural logarithm of time as a term in the models; there was no evidence of violation of this assumption. Statistical analyses were conducted using SAS version 9.3 (SAS Institute, Inc., Cary, NC). Two-sided p-values < 0.05 were considered statistically significant. No adjustments were made for multiple comparisons.

Results

Over a median of 4.6 years of follow-up, 1,385 of 3,215 (43.1%) WHI participants who experienced a HF hospitalization died; 694 deaths were due to CVD (Supplemental Table 2). Women who died were, on average, older, lower income, less likely to be married, more likely to smoke cigarettes, less physically active, and had slightly lower body mass index and were more likely to have a history of high cholesterol, diabetes, myocardial infarction, revascularization, and atrial fibrillation (Table 1). Compared to women in the lower quartiles, women in higher quartiles of the Mediterranean and DASH diet scores had higher average intake of fruit, vegetables, nuts, legumes, whole grains, low-fat dairy, fish, and lower intake of red and processed meats and sweetened beverages (Supplemental Table 3). Protein, carbohydrate, potassium, calcium, magnesium, and fiber were higher in the upper quartile of the diet scores and saturated, monounsaturated, and polyunsaturated fat were lower. Sodium intake was positively associated with the Mediterranean diet score and inversely associated with the DASH diet score. Women in the higher quartiles of the diet scores had higher alcohol consumption. The correlation between Mediterranean and DASH diet scores was 0.67.

Higher Mediterranean diet score was associated with a lower hazard rate of death among women with HF in the age- and energy-adjusted model (Table 2). After adjustment for demographics, health behaviors, comorbidities, and medications, women with Mediterranean diet scores in the top quartile had a 15% lower hazard rate of death than those in the bottom quartile, though the test of trend was not statistically significant (p = 0.08). In the fully adjusted models, the HR associated with a 1-unit higher Mediterranean diet score was 0.97 (95% CI 0.93–1.00, p = 0.06). We did not find evidence for a nonlinear association (p = 0.06).

Women with a higher DASH diet score had a lower hazard rate of death in models adjusted for age and energy intake and in more extensively adjusted models. In multivariable-adjusted models, women with HF who had DASH diet score in the top quartile had a 16% lower hazard rate of death than women with scores in the bottom quartile (p for linear trend = 0.01). In the fully adjusted models, the HR associated with a 1-unit higher DASH diet score was 0.98 (95% CI 0.97–0.99, p = 0.003). We did not find evidence for a nonlinear association (p for test of quadratic trend = 0.29).

Results were consistent in sensitivity analyses in subgroups of women without self-reported HF at baseline, women without cancer, and women who had physician diagnosis of HF at the index hospitalization (Supplemental Table 4). The associations were also consistent when we excluded women in the DM and CaD trials. Women in the top quartiles of the Mediterranean and DASH diet scores had a 12% and 18% lower hazard rate, respectively, of CVD mortality then women in the bottom quartiles, but the associations were not statistically significant (Supplemental Table 5). There was no statistically significant variation in the associations of Mediterranean or DASH diet scores with mortality across strata of body mass index, history of diabetes, history of CHD, income, or smoking status (Supplemental Table 6). Vegetables, nuts or nuts and legumes, and whole grains were inversely associated with mortality following HF (Table 3). Other components of the diet scores did not appear to be associated with mortality.

Discussion

In this population with HF, women in the top quartile of the DASH diet score had a 16% lower hazard rate of death than those in the bottom quartile (p for linear trend = 0.01). The association of the Mediterranean diet score with mortality was not statistically significant (p for linear trend = 0.08), but there was a trend towards lower hazard of mortality with higher Mediterranean diet score. These results suggest that dietary patterns recommended for the general population may also be beneficial in people with HF. Currently, few HF patients meet general nutritional recommendations. $^{27-29}$ Trials of controlled diets or dietary counseling among HF patients are needed to conclusively determine whether Mediterranean or DASH dietary patterns reduce mortality.

Both the Mediterranean and DASH dietary patterns can improve cardiovascular health. In trials with controlled diets, the DASH dietary pattern produced a substantial decrease in blood pressure, ^{15, 16} reduced total and LDL cholesterol, ³⁰ and decreased markers of inflammation, liver dysfunction, and coagulation abnormalities. ³¹ Additionally, in

observational studies, higher DASH diet scores were associated with lower rates of incident CHD ^{19, 20} and HF. ¹⁸ In a single arm study of HF patients with preserved ejection fraction, 3 weeks of the DASH dietary pattern resulted in lower blood pressure, arterial stiffness, and oxidative stress ¹⁷.

Advice to follow the Mediterranean dietary pattern combined with provision supplemental extra virgin olive oil or nuts reduced first CVD events as compared to advice to follow a low-fat diet in high risk individuals with type 2 diabetes or multiple risk factors for CVD in the PREDIMED randomized trial.⁵ Post-MI patients in the Lyon Heart Study who were randomized to receive advice on following a Mediterranean dietary pattern had a lower rate of CVD mortality and nonfatal MI than the control group who did not receive specific dietary advice.⁶ Higher Mediterranean diet scores have been associated with lower rates of CVD and better CVD risk profiles.^{7–12, 14} In HF patients, the Mediterranean diet score was associated with better systolic and diastolic function.¹³ The Alternative Healthy Eating Index and the WHI Dietary Modification Index, including some of the same components as the Mediterranean and DASH scores, were inversely associated with incident HF in the WHI population.³²

Dietary patterns are complex mixtures of foods and nutrients, and benefits may represent effects of specific foods or nutrients, interactions between foods and nutrients, displacement of other foods and nutrients, or combinations of these mechanisms. The aspect or aspects of the Mediterranean or DASH dietary patterns which affect CVD have not yet been determined. In this study, higher intake of vegetables, nuts and legumes, and whole grains were associated with lower mortality rates, but other dietary components including sodium and alcohol were not. In a prior study of HF patients, intake of sodium was positively associated with mortality and acute decompensation. However, FFQs like the one used in this study are not well-suited for capturing sodium intake as sodium was not a targeted nutrient for assessment. Other nutrients correlated with, but not included in, the diet scores such as magnesium, potassium, and calcium may also contribute to the associations. However, magnesium, potassium, and calcium intake were not associated with mortality in this population. While identifying specific nutrients which could prolong life among people with HF is of scientific interest, for patients, dietary advice focused on foods may be more relevant.

The racially and ethnically diverse study population, extensive covariate information available, large number of adjudicated HF hospitalizations, and relatively long follow-up for post-HF hospitalization mortality are strengths of this study. There are also limitations. HF is a progressive clinical syndrome with heterogeneous etiologies and anatomic and physiologic disturbances. The effect of dietary patterns may vary across HF subtypes and disease severity. Neither HF etiology nor severity was available in this population. However, HF hospitalization was an entry criterion in this study, excluding individuals with mild HF treated exclusively on an outpatient basis. FFQs are known to have substantial errors. Sodium and fluid intake, which are thought to be important in HF patients, were not targeted in the design of the FFQ. We were not able to specifically study intake of olive oil, a characteristic of the Mediterranean dietary pattern, because it was not distinguished from other cooking oils with high monounsaturated fat content in the FFQ. We used dietary

assessments made prior to HF hospitalization, and we have not detected possible changes in dietary intake or adherence to sodium or fluid restriction following HF hospitalization. This could lead to misclassification of dietary intake during the relevant time-period. We used previous described Mediterranean and DASH diet scores calculated from the FFQs which may not fully capture the dietary patterns. ^{12, 20} In particular, the Mediterranean diet score has a small range (0–9 points), and more than half of this population had scores of 3, 4, or 5 suggesting that it may not be able to distinguish between individuals with different patterns of dietary intake. This may partially explain why the association of the Mediterranean diet score did not reach statistical significance despite the large number of deaths. Additionally, we were not able to rule out unmeasured or residual confounding, for example by severity of HF or comorbidities or by the trial interventions.

In summary, higher DASH diet scores were modestly associated with lower mortality in women with HF; there was a trend toward an association with the Mediterranean diet score that did not reach statistical significance. These data provide support for the idea that diet recommendations developed for the general population or those with other cardiovascular conditions may also be appropriate for HF patients. Randomized trials of diets including fruits, vegetables, whole grains, nuts, and legumes and low in processed foods and red meats in HF patients are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors thank the WHI investigators and staff for their dedication, and the study participants for making the program possible.

Program Office: (National Heart, Lung, and Blood Institute, Bethesda, Maryland) Jacques Rossouw, Shari Ludlam, Dale Burwen, Joan McGowan, Leslie Ford, and Nancy Geller

Clinical Coordinating Center: Clinical Coordinating Center: (Fred Hutchinson Cancer Research Center, Seattle, WA) Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg

Investigators and Academic Centers: (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) JoAnn E. Manson; (MedStar Health Research Institute/Howard University, Washington, DC) Barbara V. Howard; (Stanford Prevention Research Center, Stanford, CA) Marcia L. Stefanick; (The Ohio State University, Columbus, OH) Rebecca Jackson; (University of Arizona, Tucson/Phoenix, AZ) Cynthia A. Thomson; (University at Buffalo, Buffalo, NY) Jean Wactawski-Wende; (University of Florida, Gainesville/Jacksonville, FL) Marian Limacher; (University of Iowa, Iowa City/Davenport, IA) Robert Wallace; (University of Pittsburgh, Pittsburgh, PA) Lewis Kuller; (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker

Women's Health Initiative Memory Study: (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker

Sources of Funding

The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts HHSN268201100046C, HHSN268201100001C, HHSN268201100002C, HHSN268201100003C, HHSN268201100004C, and HHSN271201100004C.

References

 Ghali JK, Kadakia S, Cooper R, Ferlinz J. Precipitating factors leading to decompensation of heart failure. Traits among urban blacks. Arch Intern Med. 1988; 148:2013–2016. [PubMed: 3046541]

- 2. Ershow AG, Costello RB. Dietary guidance in heart failure: A perspective on needs for prevention and management. Heart Fail Rev. 2006; 11:7–12. [PubMed: 16819572]
- Vogt TM, Appel LJ, Obarzanek E, Moore TJ, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Cutler JA, Windhauser MM, Lin PH, Karanja NM. Dietary Approaches to Stop Hypertension: Rationale, design, and methods. DASH collaborative research group. J Am Diet Assoc. 1999; 99:S12–S18. [PubMed: 10450289]
- Willett WC, Sacks F, Trichopoulou A, Drescher G, Ferro-Luzzi A, Helsing E, Trichopoulos D. Mediterranean diet pyramid: A cultural model for healthy eating. Am J Clin Nutr. 1995; 61:1402S–1406S. [PubMed: 7754995]
- Estruch R, Ros E, Salas-Salvado J, Covas MI, Pharm D, Corella D, Aros F, Gomez-Gracia E, Ruiz-Gutierrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pinto X, Basora J, Munoz MA, Sorli JV, Martinez JA, Martinez-Gonzalez MA. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med. 2013; 368:1279–1290. [PubMed: 23432189]
- 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; 343:1454–1459. [PubMed: 7911176]
- Fung TT, Rexrode KM, Mantzoros CS, Manson JE, Willett WC, Hu FB. Mediterranean diet and incidence of and mortality from coronary heart disease and stroke in women. Circulation. 2009; 119:1093–1100. [PubMed: 19221219]
- Buckland G, Gonzalez CA, Agudo A, Vilardell M, Berenguer A, Amiano P, Ardanaz E, Arriola L, Barricarte A, Basterretxea M, Chirlaque MD, Cirera L, Dorronsoro M, Egues N, Huerta JM, Larranaga N, Marin P, Martinez C, Molina E, Navarro C, Quiros JR, Rodriguez L, Sanchez MJ, Tormo MJ, Moreno-Iribas C. Adherence to the Mediterranean diet and risk of coronary heart disease in the Spanish EPIC cohort study. Am J Epidemiol. 2009; 170:1518–1529. [PubMed: 19903723]
- 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; 306:62–69. [PubMed: 21730242]
- Knoops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, van Staveren WA. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: The Hale project. JAMA. 2004; 292:1433–1439. [PubMed: 15383513]
- 11. Nordmann AJ, Suter-Zimmermann K, Bucher HC, Shai I, Tuttle KR, Estruch R, Briel M. Meta-analysis comparing Mediterranean to low-fat diets for modification of cardiovascular risk factors. Am J Med. 2011; 124:841–851. e842. [PubMed: 21854893]
- 12. Fung TT, McCullough ML, Newby PK, Manson JE, Meigs JB, Rifai N, Willett WC, Hu FB. Dietquality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr. 2005; 82:163–173. [PubMed: 16002815]
- 13. Chrysohoou C, Panagiotakos DB, Aggelopoulos P, Kastorini CM, Kehagia I, Pitsavos C, Stefanadis C. The Mediterranean diet contributes to the preservation of left ventricular systolic function and to the long-term favorable prognosis of patients who have had an acute coronary event. Am J Clin Nutr. 2010; 92:47–54. [PubMed: 20484450]
- 14. Dai J, Lampert R, Wilson PW, Goldberg J, Ziegler TR, Vaccarino V. Mediterranean dietary pattern is associated with improved cardiac autonomic function among middle-aged men: A twin study. Circ Cardiovasc Qual Outcomes. 2010; 3:366–373. [PubMed: 20551372]
- Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. A clinical trial of the effects of dietary patterns on blood pressure. DASH collaborative research group. N Engl J Med. 1997; 336:1117–1124. [PubMed: 9099655]
- Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller ER 3rd, Simons-Morton DG, Karanja N, Lin PH. 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. [PubMed: 11136953]
- 17. Hummel SL, Seymour EM, Brook RD, Kolias TJ, Sheth SS, Rosenblum HR, Wells JM, Weder AB. Low-sodium Dietary Approaches to Stop Hypertension diet reduces blood pressure, arterial stiffness, and oxidative stress in hypertensive heart failure with preserved ejection fraction. Hypertension. 2012; 60:1200–1206. [PubMed: 23033371]
- 18. Levitan EB, Wolk A, Mittleman MA. Consistency with the DASH diet and incidence of heart failure. Arch Intern Med. 2009; 169:851–857. [PubMed: 19433696]
- Fitzgerald KC, Chiuve SE, Buring JE, Ridker PM, Glynn RJ. Comparison of associations of adherence to a Dietary Approaches to Stop Hypertension (DASH)-style diet with risks of cardiovascular disease and venous thromboembolism. J Thromb Haemost. 2012; 10:189–198. [PubMed: 22151600]
- 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; 168:713–720. [PubMed: 18413553]
- 21. Hays J, Hunt JR, Hubbell FA, Anderson GL, Limacher M, Allen C, Rossouw JE. The Women's Health Initiative recruitment methods and results. Ann Epidemiol. 2003; 13:S18–S77. [PubMed: 14575939]
- 22. Langer RD, White E, Lewis CE, Kotchen JM, Hendrix SL, Trevisan M. The Women's Health Initiative observational study: Baseline characteristics of participants and reliability of baseline measures. Ann Epidemiol. 2003; 13:S107–S121. [PubMed: 14575943]
- 23. Curb JD, McTiernan A, Heckbert SR, Kooperberg C, Stanford J, Nevitt M, Johnson KC, Proulx-Burns L, Pastore L, Criqui M, Daugherty S. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. Ann Epidemiol. 2003; 13:S122–S128. [PubMed: 14575944]
- 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; 9:178–187. [PubMed: 10192650]
- 25. Tinker LF, Sarto GE, Howard BV, Huang Y, Neuhouser ML, Mossavar-Rahmani Y, Beasley JM, Margolis KL, Eaton CB, Phillips LS, Prentice RL. Biomarker-calibrated dietary energy and protein intake associations with diabetes risk among postmenopausal women from the Women's Health Initiative. Am J Clin Nutr. 2011; 94:1600–1606. [PubMed: 22071707]
- WHI Clinical Coordinating Center. [Accessed January 20, 2010] Women's Health Initiative scientific resources website. http://www.whiscience.org/
- 27. Lemon SC, Olendzki B, Magner R, Li W, Culver AL, Ockene I, Goldberg RJ. The dietary quality of persons with heart failure in NHANES 1999–2006. J Gen Intern Med. 2010; 25:135–140. [PubMed: 19882192]
- 28. Arcand J, Floras V, Ahmed M, Al-Hesayen A, Ivanov J, Allard JP, Newton GE. Nutritional inadequacies in patients with stable heart failure. J Am Diet Assoc. 2009; 109:1909–1913. [PubMed: 19857633]
- 29. Grossniklaus DA, O'Brien MC, Clark PC, Dunbar SB. Nutrient intake in heart failure patients. J Cardiovasc Nurs. 2008; 23:357–363. [PubMed: 18596500]
- 30. Obarzanek E, Sacks FM, Vollmer WM, Bray GA, Miller ER 3rd, Lin PH, Karanja NM, Most-Windhauser MM, Moore TJ, Swain JF, Bales CW, Proschan MA. Effects on blood lipids of a blood pressure-lowering diet: The Dietary Approaches to Stop Hypertension (DASH) trial. Am J Clin Nutr. 2001; 74:80–89. [PubMed: 11451721]
- 31. Azadbakht L, Surkan PJ, Esmaillzadeh A, Willett WC. The Dietary Approaches to Stop Hypertension eating plan affects c-reactive protein, coagulation abnormalities, and hepatic function tests among type 2 diabetic patients. J Nutr. 2011; 141:1083–1088. [PubMed: 21525259]
- 32. Belin RJ, Greenland P, Allison M, Martin L, Shikany JM, Larson J, Tinker L, Howard BV, Lloyd-Jones D, Van Horn L. Diet quality and the risk of cardiovascular disease: The Women's Health Initiative (WHI). Am J Clin Nutr. 2011; 94:49–57. [PubMed: 21613562]
- 33. Arcand J, Ivanov J, Sasson A, Floras V, Al-Hesayen A, Azevedo ER, Mak S, Allard JP, Newton GE. A high-sodium diet is associated with acute decompensated heart failure in ambulatory heart

- failure patients: A prospective follow-up study. Am J Clin Nutr. 2011; 93:332–337. [PubMed: $21084647]\,$
- 34. Willett, WC. Nutritional epidemiology. New York: Oxford University Press; 1998.
- 35. Levitan EB, Shikany JM, Ahmed A, Snetselaar LG, Martin LW, Curb JD, Lewis CE. Calcium, magnesium, and potassium intake and mortality in women with heart failure: The Women's Health Initiative. Br J Nutr. 2013; 110:179–185. [PubMed: 23199414]

Table 1 Characteristics of 3,215 Women's Health Initiative participants with heart failure hospitalization by mortality status*

	Died during follow-up (n = 1,385)	Survived follow-up (n = 1,830)	P
Age at heart failure hospitalization (y)	73.8 (6.7)	71.9 (7.1)	< 0.001
Race/ethnicity (%)			0.06
American Indian/Alaskan Native	0.8	0.3	
Asian/Pacific Islander	1.4	0.7	
Black	10.0	10.8	
Hispanic	1.3	2.1	
White not of Hispanic origin	85.6	85.2	
Not one of above	0.9	1.0	
Education (%)			0.27
Less than high school	9.0	7.5	
High school graduate/some college	62.0	61.0	
College graduate	8.2	8.3	
Graduate school	20.9	23.3	
Income (%)			< 0.001
<\$20,000	36.0	28.3	
\$20,000–34,999	29.2	31.5	
\$35,000–49,999	17.6	17.7	
\$50,000	17.2	22.5	
Married (%)	47.7	54.5	< 0.001
Current cigarette smoking (%)	11.0	7.3	< 0.001
Body mass index (kg/m²)	30.0 (7.4)	30.9 (7.4)	< 0.001
Physical activity (MET-hr/wk)	8.1 (11.0)	9.4 (11.4)	0.002
Rand-36 Physical function score	54.3 (27.0)	63.4 (25.8)	< 0.001
Systolic blood pressure (mm Hg)	135 (21)	134 (19)	0.07
Diastolic blood pressure (mm Hg)	71 (11)	73 (11)	< 0.001
History of high cholesterol (%)	24.2	21.3	0.05
History of hypertension (%)	59.7	57.5	0.20
History of diabetes (%)	31.8	24.9	< 0.001
History of myocardial infarction (%)	21.6	14.6	< 0.001
History of revascularization (%)	18.6	16.1	0.06
History of atrial fibrillation (%)	16.6	12.5	< 0.001
Off-study postmenopausal hormone use (%)	22.0	29.1	< 0.001
Use of diuretics (%)	46.5	38.3	< 0.001
Use of β-blockers (%)	22.8	23.8	0.50
Use of ACE inhibitor or ARB (%)	33.7	30.8	0.08
WHI hormone arm (%)			0.88
Estrogen alone intervention	5.1	5.1	

Levitan et al.

	Died during follow-up (n = 1,385)	Survived follow-up (n = 1,830)	P
Estrogen alone control	4.8	5.5	
Estrogen plus progestin intervention	4.3	4.8	
Estrogen plus progestin control	4.6	4.8	
WHI diet modification arm (%)			< 0.001
Diet modification intervention	10.6	12.7	
Diet modification control	15.2	19.3	
WHI calcium/vitamin D arm (%)			0.001
Calcium/vitamin D intervention	8.6	11.7	
Calcium/vitamin D control	9.1	11.3	

Page 13

^{*} Numbers are mean (standard deviation) or percent

Levitan et al. Page 14

 Table 2

 Mediterranean and DASH diet scores and mortality among women with heart failure

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p-trend
Mediterranean diet score					
Z	572	1,305	589	749	
Median (Range)	2 (0-2)	4 (3-4)	5 (5–5)	(6-9) 9	
Deaths	260	587	248	290	
Person-years	2,582	5,772	2,741	3,639	
Mortality rate per 100 person-years	10.1	10.2	0.6	8.0	
Model 1 HR (95% CI)*	1	1.00 (0.86–1.17)	0.88 (0.74–1.04)	0.75 (0.63–0.89)	<0.001
Model 2 HR (95% CI) †	1	1.09 (0.93–1.28)	1.02 (0.85–1.22)	0.91 (0.75–1.09)	0.29
Model 3 HR (95% CI) [‡]	1	1.05 (0.89–1.24)	0.97 (0.81–1.17) 0.85 (0.70–1.02)	0.85 (0.70–1.02)	0.08
DASH diet score					
Z	892	704	956	787	
Median (Range)	19 (9–21)	23 (22–24)	26 (25–28)	31 (29–40)	
Deaths	345	329	386	325	
Person-years	3,440	3,120	4,477	3,698	
Mortality rate per 100 person-years	10.0	10.5	8.6	8.8	
Model 1 HR (95% CI)*	1	1.00 (0.85–1.16)	0.77 (0.66–0.90)	0.75 (0.64–0.89)	<0.001
Model 2 HR (95% CI) †	1	1.05 (0.90–1.23)	0.86 (0.73–1.02)	0.89 (0.75–1.05)	0.07
Model 3 HR (95% CI) [‡]	1	1.04 (0.89–1.21)	0.83 (0.70-0.98)	0.84 (0.70-1.00)	0.01

Adjusted for age at heart failure hospitalization and total energy intake

[†] Adjusted for variables in Model 1 and race/ethnicity, education, income, married, current smoking, total exercise, physical function, use of off-study postmenopausal hormone therapy, and WHI study arm

^{*}Adjusted for variables in Model 2 and systolic blood pressure, diastolic blood pressure, use of diuretics, beta-blockers, and angiotensin converting enzyme inhibitors or angiotensin receptor blockers, body mass index, and history of high cholesterol, high blood pressure, diabetes, myocardial infarction, coronary revascularization, and atrial fibrillation.

Author Manuscript

Author Manuscript

Table 3

Components of the Mediterranean and DASH diet scores and mortality among women with heart failure*

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p-trend
Mediterranean diet score					
Fruits	1	1.06 (0.89–1.25)	1.06 (0.89–1.25) 1.06 (0.90–1.26)	1.05 (0.89–1.25)	0.67
Vegetables	1	0.95 (0.81–1.12)	0.97 (0.82–1.14)	0.81 (0.68-0.96)	0.01
Nuts	1	0.97 (0.83–1.14)	0.92 (0.81–1.06)	0.86 (0.74-0.96)	0.049
Legumes	1	1.01 (0.87–1.17)	0.98 (0.85-1.13)	0.95 (0.81-1.12)	0.49
Whole grains	1	0.91 (0.78–1.05)	0.82 (0.70-0.96)	0.79 (0.67–0.94)	0.005
Fish	1	1.00 (0.86–1.17)	1.01 (0.86–1.18)	1.00 (0.85-1.18)	86.0
Ratio of monounsaturated to saturated fat	1	0.91 (0.78–1.06)	1.06 (0.91–1.23)	0.91 (0.78–1.07)	0.51
Red and processed meat	1	0.97 (0.83–1.13)	0.95 (0.81-1.11)	1.13 (0.93–1.36)	0.16
Alcohol	1	1.02 (0.87–1.20)		0.99 (0.85–1.16) 0.94 (0.80–1.10)	0.32
DASH diet score					
Fruits	1	1.06 (0.89–1.25)	1.06 (0.90–1.26)	1.05 (0.89–1.25)	0.67
Vegetables	1	0.95 (0.81–1.12)	0.97 (0.82–1.14)	0.81 (0.68-0.96)	0.01
Nuts and legumes	1	0.87 (0.75–1.01)	0.90 (0.77–1.05)	0.81 (0.69-0.95)	0.03
Low-fat dairy	1	0.81(0.70-0.95)	0.84 (0.73–0.98)	0.83 (0.71–0.98)	0.11
Whole grains	1	0.91 (0.78–1.05)	0.82 (0.70-0.96)	0.79 (0.67–0.94)	0.005
Sodium	1	0.96 (0.82–1.12)	0.98 (0.84–1.14)	1.09 (0.94–1.28)	0.23
Sweetened beverages†		1.00 (0.85–1.18)	0.98 (0.85–1.13)		08.0
Red and processed meat	1	0.97 (0.83–1.13)	0.95 (0.81–1.11)	0.95 (0.81–1.11) 1.13 (0.93–1.36)	0.16

function, use of off-study postmenopausal hormone therapy, WHI study arm, systolic blood pressure, diastolic blood pressure, use of diuretics, beta-blockers, and angiotensin converting enzyme inhibitors Hazard ratios and 95% confidence intervals adjusted for age at heart failure hospitalization, total energy intake, race/ethnicity, education, income, married, current smoking, total exercise, physical or angiotensin receptor blockers, body mass index, and history of high cholesterol, high blood pressure, diabetes, myocardial infarction, coronary revascularization, and atrial fibrillation.

 $^{^{\}dagger}$ Divided into tertiles because of limited range of intake.