Published in final edited form as:

Am Heart J. 2015 March ; 169(3): 342–348.e4. doi:10.1016/j.ahj.2014.11.021.

Evaluating the Safety and Efficacy of Sodium-Restricted/Dietary Approaches to Stop Hypertension Diet After Acute Decompensated Heart Failure Hospitalization: Design and Rationale for the Geriatric Out of hospital Randomized MEal Trial in Heart Failure (GOURMET-HF)

Jeffrey D. Wessler, MD MPhil¹, Mathew S. Maurer, MD¹, and Scott S. Hummel, MD MS^{2,3}

¹Department of Medicine / Division of Cardiology Columbia University Medical Center New York, NY

²Department of Medicine / Division of Cardiovascular Medicine University of Michigan Ann Arbor, MI

³Ann Arbor Veterans Affairs Health System Ann Arbor, MI

Abstract

Background—Heart Failure (HF) is a major public health problem affecting predominantly older adults. Non-adherence to diet remains a significant contributor to acute decompensated HF (ADHF). The sodium-restricted Dietary Approaches to Stop Hypertension (DASH/SRD) eating plan reduces cardiovascular dysfunction that can lead to ADHF and is consistent with current HF guidelines. We propose that an intervention that promotes adherence to the DASH/SRD by home-delivering meals will be safe and improve health-related quality of life (QOL) in older adults following hospitalization for ADHF.

Methods/Design—This is a three center, randomized, single-blind, controlled trial of 12 weeks duration designed to determine the safety and efficacy of home-delivered DASH/SRD-compliant meals in older adults following discharge from ADHF hospitalization. 66 subjects will be randomized in a 1:1 stratified fashion by gender and left ventricular ejection fraction (< vs. ≥ 50%). Study subjects will receive either pre-prepared, home-delivered DASH/SRD-compliant meals or usual dietary advice for 4 weeks after hospital discharge. Investigators will be blinded to group assignment, food diaries, and urinary electrolyte measurements until study completion. The primary efficacy endpoint is the change in the Kansas City Cardiomyopathy Questionnaire (KCCQ) summary scores for health-related QOL from study enrollment to 4 weeks post-discharge. Safety evaluation will focus on hypotension, renal insufficiency, and hyperkalemia.

Address for correspondence: Scott L. Hummel Division of Cardiovascular Medicine Department of Internal Medicine University of Michigan 1500 East Medical Center Dr CVC Room 2383, SPC 5853 Ann Arbor, MI 48109 scothumm@med.umich.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Exploratory endpoints include echocardiography, non-invasive vascular testing, markers of oxidative stress, and salt taste sensitivity.

Conclusion—This randomized controlled trial will test the efficacy, feasibility and safety of 4 weeks of DASH/SRD after ADHF hospitalization. By testing a novel dietary intervention supported by multiple levels of evidence including preliminary data in outpatients with stable HF, we will address a critical evidence gap in the care of older patients with ADHF. If effective and safe, this intervention could be scaled to assess effects on readmission and healthcare costs in older adults following ADHF.

Keywords

Heart failure; sodium restriction; quality of life; dietary intervention

Background

Acute decompensated heart failure (ADHF) is the leading cause of hospitalization in older persons, and expenditures in the U.S. for this diagnosis exceed \$15 billion/year.¹ Rehospitalizations, the most frequent adverse outcome following ADHF, markedly worsen quality of life (QOL) and result in increased mortality and cost.² Poor or worsening QOL following ADHF hospitalization is an independent risk factor for mortality and readmission.³ Older patients are at specific risk for persistently poor QOL following ADHF hospitalization, in part due to challenges in managing the complexity of HF self-care.⁴ While some recent advances have been made in outpatient treatment for HF⁵ and novel pharmaceutical agents hold promise in ADHF,⁶ current management strategies have only modestly improved ADHF outcomes.² Other recent trials of telemedicine⁷, diuretics⁸ and newer pharmacologic agents⁹ have been disappointing, suggesting that outcomes in ADHF patients are driven by mechanisms not addressed by current approaches.

Dietary sodium restriction is associated with reduced risk for ADHF in observational studies,¹⁰ and has been described as a ‘cornerstone of HF disease management.’¹¹ However, several randomized studies suggest that this strategy may be ineffective or even harmful in recently discharged ADHF patients.¹² Dietary sodium restriction is the most frequently recommended self-care behavior for HF patients,¹³ and additional understanding of its efficacy and safety is critically important. The provision of ‘therapeutically-designed’ meals cost-effectively improves QOL in otherwise healthy older hypertensives,¹⁴ but has not been studied in older adults following ADHF hospitalization, a much more vulnerable population. The principle underlying this proposal is that non-adherence to dietary recommendations is one of the most common preventable causes of ADHF hospitalization, and meal provision following hospital discharge may reduce this risk.^{15,16}

The sodium-restricted/Dietary Approaches to Stop Hypertension (DASH/SRD) eating plan is recommended by current hypertension guidelines and lowers blood pressure (BP) more than sodium restriction alone. In ‘salt-sensitive’ animal models of hypertensive HF, dietary patterns similar to DASH/SRD reduce BP, ventricular and arterial stiffness, and vascular dysfunction by decreasing oxidative stress and inflammation.¹⁷ Predictors of a similar phenotype in humans include hypertension, renal insufficiency, diabetes, central obesity,

and chronic inflammation, all independent HF risk factors in older adults.¹⁸ The DASH/SRD reduces BP and improves vascular function in salt-sensitive humans without HF.¹⁹ In older outpatients with hypertension-associated HF, 21 days of DASH/SRD can improve BP, oxidative stress, ventricular diastolic function, ventricular-arterial coupling, and submaximal exercise capacity.^{20,21}

Aims and Hypotheses (Table)

Aim 1—To assess the feasibility and efficacy of providing DASH/SRD-compliant meals in older adults with hypertension following discharge from a hospital admission for ADHF. Efficacy will be assessed by improvement in health-related QOL and feasibility will be assessed by adherence to DASH/SRD.

Aim 2—To investigate the dietary, mechanistic, and safety effects of DASH/SRD in older adults with hypertension following discharge from a hospital admission for ADHF. Dietary effects will be assessed through salt taste affinity reduction; mechanistic effects will be assessed through echocardiography, functional improvement, systemic inflammation and oxidative stress reduction, and reduction in plasma volume; safety will be assessed through adverse effects including death, all-cause hospitalization, worsening renal function, hyperkalemia, and symptomatic hypotension or syncope.

The primary hypothesis is that providing 4 weeks of home-delivered DASH/SRD-compliant meals will improve health-related QOL in older adults after discharge from hospitalization for ADHF. The primary efficacy endpoint will be the change in the Kansas City Cardiomyopathy Questionnaire (KCCQ) summary scores for health-related QOL in patients with chronic HF from study enrollment to 4 weeks post-discharge. The KCCQ, a self-administered 23-item instrument, assesses physical limitations, symptoms, self-efficacy, social interference, and overall QOL in HF patients. The KCCQ summary score ranges from 0-100, with higher scores indicating better QOL. The KCCQ summary score independently predicts clinical outcomes such as hospitalization and mortality in outpatients with HF, including those recently hospitalized for ADHF.²² It is a reliable and valid measure in HF patients that is more sensitive to change than other measures of QOL, and is especially responsive in patients with multiple comorbidities.²³ A change in KCCQ score of 5 points correlates with changes in clinical status, physical function, and risk of all-cause mortality, cardiovascular death and hospitalization.^{3,24} Secondary hypotheses are: a) salt taste affinity reduction is greater; b) cardiovascular and sub-maximal functional measures are improved; c) systemic and gene expression markers of systemic inflammation and oxidative stress are reduced, and d) plasma volume is lower in the DASH/SRD group at 4 weeks when compared with the control group.

The secondary endpoints for this study are divided into three domains: safety, dietary, and mechanistic parameters. Safety will be assessed by tracking adverse events including death, all-cause hospitalization, new or worsening renal dysfunction, hyperkalemia, symptomatic hypotension, or syncope with specific responses to these events detailed below. Dietary endpoints will include long-term DASH/SRD adherence as measured by 3-day food diary, Food Frequency Questionnaire (FFQ), and urinary electrolyte measures at 12 weeks²⁵ as

well as salt taste affinity at 4 and 12 weeks.²⁶ Mechanism-related endpoints will include changes from baseline to 4 weeks in BP, noninvasive measures of ventricular function and ventricular-arterial coupling, blood/urine measures of neurohormonal activation, oxidative stress, systemic inflammation, and plasma volume measurements (the latter measured in a subset n=20 at Columbia University Medical Center).

Methods/Design

Trial registration and Funding

This trial is registered at ClinicalTrials.gov (NCT02148679, received 23 May 2014) and is funded by PurFoods, LLC (Des Moines, IA) and the National Institute of Aging (R21 AG047939-01). Dr. Hummel is supported by the National Heart, Lung, and Blood Institute (K23 HL109176) and the University of Michigan's Clinical and Translational Science Award (2UL1TR000433-06), and Dr. Maurer is supported by the National Institute of Aging (K24 AG036778). The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

General Design

This is a three-center, randomized, single-blind, trial of 12 weeks total duration designed to determine the safety and efficacy of home-delivered DASH/SRD-compliant meals in older adults following discharge from ADHF hospitalization. 66 subjects will be randomized in a 1:1 stratified fashion by gender and left ventricular ejection fraction (< vs. ≥ 50%). Study subjects will receive either pre-prepared, home-delivered DASH/SRD-compliant meals or usual dietary advice for 4 weeks after hospital discharge. The three study sites will be Columbia University Medical Center/NewYork Presbyterian Hospital, the University of Michigan Health System, and the Ann Arbor Veterans Affairs Health System. Investigators will be blinded to group assignment, food diaries, and urinary electrolyte measurements until the completion of the study. See Figure 1 for general study outline.

Study Subjects

66 patients aged ≥ 65 years with history of systemic hypertension and ADHF (primary diagnosis for admission or secondary diagnosis after hospitalization for another reason). ADHF will be confirmed by the study physician and require that all four of the following conditions are met: 1) 1 symptom of HF (dyspnea, fatigue, orthopnea, paroxysmal nocturnal dyspnea) has worsened from baseline, 2) 2 signs of HF (pulmonary congestion on exam and/or chest X-ray, elevated jugular venous pressure, peripheral edema or rapid weight gain, and/or increased B-type natriuretic peptide (BNP; ≥ 100 pg/ml), 3) change in medical treatment specifically targeting HF (diuretics, vasodilators, and/or neurohormonal modulating agents), and 4) no other cause of the patient's symptoms and signs is apparent.

Patients will be excluded based on the following criteria: persistent hypotension during hospitalization or excessive risk of hypotension from the study diet as judged by the investigators, use of inotropic therapy at hospital discharge, severe valvular heart disease as the primary etiology of HF, uncontrolled hypertension (systolic BP >180 mmHg or diastolic BP >100 mmHg) at discharge, serum potassium >5.0 mmol/L during hospitalization or

history of serum potassium >6.0 mmol/L, severe renal insufficiency (estimated glomerular filtration rate, eGFR, <30 ml/min/1.73m² at discharge), diabetes mellitus type 1 or non-adherence to routine diabetic monitoring, severe anemia (hemoglobin <9 gm/dl), length of stay <48 hours or >14 days, co-morbidity with expected survival <12 months, active alcohol or substance abuse, and/or a history of persistent noncompliance with treatment recommendations as judged by the investigators.

Intervention

Study food will be designed and prepared by PurFoods, LLC (Des Moines, IA) in consultation with research dietitians at the University of Michigan and Columbia University. Study patients randomized to food delivery will select from an available menu of meal options that adhere to nutritional targets as above. Study food will be pre-packaged for storage with preparation (typically microwave heating) to be completed at home by the subject, and will be delivered every 1 to 2 weeks under the direction of PurFoods.

The study diet will have goal daily sodium intake of 1500 mg/2100 kilocalories²⁷ and energy intake to maintain lean body mass while meeting DASH diet nutritional targets.²⁸ In patients with eGFR 45-60 ml/min/1.73m² and serum potassium >4.5 mmol/L at hospital discharge and in patients with eGFR <45 ml/min/1.73m², the potassium content of the DASH/SRD will be reduced to 3000 mg/d as recommended by the National Kidney Foundation.²⁹ The potassium content will also be reduced to 3000 mg/d in patients prescribed potassium-sparing diuretics (e.g. spironolactone) with serum potassium greater than 4.5 mmol/L at hospital discharge, regardless of renal function.

Upon study enrollment, both groups will receive a standardized pamphlet containing instructions on following a 2000 mg/d sodium restriction, the standard discharge recommendation at the three enrolling centers; the recommendations in this material are also generally consistent with the DASH diet pattern. In both groups, study personnel will solicit and answer questions related to dietary concerns at the safety visit and during scripted telephone calls at weeks 2 and 3. Specific dietary consumption will be assessed by 3-day food diaries and urinary sodium and potassium during weeks 1 and 4 post-discharge.

Procedures

In total, subjects will have the following number of procedures (see Figure 2 for study timeline): Up to 4 physical examinations; Up to 4 blood draws for assessment of renal function, electrolyte levels, and hemoglobin/hematocrits; 4 urine collections for urinary studies (3 $\times$ 24-hour collections, 1 $\times$ spot urine); 4 salt affinity taste strip tests; up to 5 supine/standing brachial blood pressure and pulse rate measurements (done at each visit); 3 ECGs; 2 two-dimensional (2D) echocardiograms; 2 non-invasive arterial tonometry tests; 3 six-minute walk tests; 4 Quality of Life Questionnaires; up to 3 Food Frequency/food diary questionnaires.

A description of the procedures follows

Medical history and brief physical exam: Demographic information, medical and food allergy history, medications, height, weight, vitals including supine and standing blood pressure, and a HF-focused physical examination will be obtained and recorded.

Blood tests: Total blood volume ~140ml, to be obtained in intervals at baseline, 1, and 4 weeks. Screening: basic metabolic panel, liver function test, lipid panel, hematocrit, BNP, troponin I; Safety: basic metabolic panel, cystatin C, phosphorus; Efficacy: BNP, lipid panel, IL-6, hs-CRP, TNF- α . In addition, blood will be collected in PaxGene tubes at hospital discharge and 4 weeks post-discharge. These samples will be analyzed with real-time PCR to explore inflammation-related gene response in peripheral blood mononuclear cells (Open Array Human Inflammation Panel, Applied Biosystems, Foster City, CA). At the Columbia site, 2 additional blood samples will be collected for the analysis of blood volume components (i.e. plasma and red cell volume);

Urine Tests: 24-hour urine specimens will be obtained at baseline, 4, and 12 weeks and will be used to measure sodium, potassium, creatinine, protein, aldosterone, and F2-isoprostanes.

Salt taste threshold testing: Salsave test strips (Advantech Toyo Co., Fukuoka, Japan) will be used to evaluate a patient's salt taste threshold. In this method 7 test strips containing salt (NaCl) concentrations ranging from 0 to 1.6 mg/cm² make up each set. Each test strip is sequentially placed on the tongue, and the strip whose salt concentration is detected determines the salt taste threshold.³⁰

Six-minute walk test: The six minute walk test will be conducted as described by Guyatt.³¹ The total distance walked after six minutes to the nearest meter will be recorded as well as patient's symptoms (angina, dyspnea, fatigue, dizziness).

Arterial tonometry: Central end-systolic BP and carotid-femoral pulse wave velocity will be non-invasively obtained at the radial artery with a Sphygmocor tonometer (AtCor Medical, Itasca, IL) as described.³² Carotid-femoral pulse wave velocity, a measure of central arterial stiffness, will also be obtained.

2D echocardiography: Using a commercially available GE Vivid-9 echocardiography system or equivalent, a complete 2D imaging protocol will be performed. Cardiac chamber dimensions, left ventricular (LV) ejection fraction, mitral inflow velocities (E:A ratio), deceleration time of early filling velocity and LV isovolumic relaxation time, and mitral annular tissue Doppler velocities (e', a', s') will be measured as per published procedures.³³ Speckle-tracking analysis will be performed on short-axis and 4-chamber views to derive radial, circumferential, and longitudinal strain and strain rate. Arterial and single-beat end-systolic ventricular elastance and Parametrized Diastolic Formalism analyses will be performed as previously described.³⁴

Plasma volume measurement: Twenty five microcuries of ¹³¹I labeled albumin (Megatope, IsoTex Diagnostics, Inc., TX) will be injected from a prefilled syringe provided by Daxor Corporation. A 20 gauge butterfly needle will be placed in an antecubital arm vein

for venous blood sampling. 5 cc of blood will be collected before isotope injection, and at 12, 18, 24, 30 and 36 minutes after isotope injection (total 30 cc). Specimens will be analyzed with an automated system (BVA100 Blood Volume Analyzer, Daxor Corp., NY).³⁵

QOL questionnaires: The KCCQ is a self-administered, 23-item questionnaire developed to describe health-related QOL in HF patients. It quantifies disease-specific physical limitations, symptoms, self-efficacy, social interference and quality of life with well-defined psychometric properties.²³ The 12-item Short-Form Survey (SF-12), previously validated in HF patients,³⁶ and the Visual Analog Scale will be administered to investigate the effects of home food delivery on general quality of life.

Dietary assessment: The Block Food Frequency Questionnaire will be used to analyze nutrient intake, and subjects' responses at baseline and 12 weeks will be scored for adherence to DASH/SRD.²⁵ Three-day food diaries will be performed during weeks 1, 4, and 12 post-discharge. The Dietary Sodium Restriction Questionnaire (DSRQ) was developed and validated in HF patients to assess patient-specific barriers to following low sodium diet recommendations.³⁷ We will administer a modified version that also investigates barriers to following the DASH dietary pattern (e.g. fruit and vegetable, fiber intakes).

Statistical Approach

In a large ADHF clinical trial, marked gains in QOL occurred during hospitalization but smaller gains were noted following hospital discharge (mean KCCQ scores among survivors: 32 ± 19 upon admission, 53 ± 22 at 1 week post-discharge, 58 ± 24 at 24 weeks).³⁸ Prior studies have shown a change in KCCQ scores from 60 ± 22 to 75 ± 17 over a 6-month dietary intervention,³⁹ and from 64 ± 23 to 70 ± 25 over 1-2 years for patients with good adherence to HF self-care recommendations compared to poor adherence.⁴⁰ While KCCQ scores vary across groups of patients, they are reproducible over time within stable individuals (e.g., in 811 stable HF patients, the intra-class coefficient of serial KCCQ over three months was 0.89)²³ and highly responsive to clinical change. We will use paired t-testing to compare within-group change in KCCQ summary score (KCCQ) between hospital discharge and week 4, and two-sample t-testing to compare between-group KCCQ at these two time points (primary endpoint). Randomizing 33 patients in the DASH/SRD and control arms (conservatively anticipating three post-discharge deaths or dropouts in each group for a total of 30 analyzed in each arm)⁴¹ and assuming SD of KCCQ = 8, this study will have 80% power to detect a between-group KCCQ difference of 5 points. Analysis will be by intention to treat, regardless of the location and status of the patient at the end of the intervention (i.e., QOL questionnaires will be administered even if the patient is currently rehospitalized and not currently consuming study food).

Other quantitative measures will be summarized with descriptive statistics and graphical representations of variance, then evaluated with t-testing as above. Correlation and regression techniques will be used to explore physiological relationships (e.g., the relationship between plasma volume and oxidative stress).

This study is not intended or powered to determine the impact of providing DASH/SRD on HF readmissions. However, we will explore 30-day and 90-day all-cause readmissions using logistic regression and Poisson regression methods (with count data days out of the hospital and alive within the interval), adjusted for a previously validated risk model that includes KCCQ summary score as the strongest predictor.³⁸

Data and safety monitoring

A data monitoring committee (DMC) composed of two independent clinicians and one statistician will be established to evaluate safety. Adverse events will be recorded from the day of the first study related procedure and reported on a monthly basis to the IRB and DMC; serious adverse events will be recorded until 30 days after the patient's last study visit, and reported to the IRB and DMC within 24 hours of knowledge of the event. The trial will be stopped for harm if there is in the judgment of the DMC, a large disparity in serious events in the DASH/SRD study arm. The Principal Investigators at each site and their study personnel will collect and manage the data provided to the DMC.

Renal function and electrolytes will be assessed at baseline and 1 week post-discharge during a safety visit, during which targeted physical examination for volume status will allow adjustment of diuretics by the investigators as clinically indicated. The dietary intervention will be stopped in any patient who develops new or worsened renal impairment as defined by eGFR decrease of $\geq 50\%$, hyperkalemia ($K > 5.7$ mmol/L), syncope, or other serious adverse event deemed by the investigators to be related to study participation. Note that study participants with recent ADHF hospitalization are inherently at high risk for rehospitalization and mortality (combined $\sim 25\%$ over the 4-week intervention period of the study, $\sim 35\%$ over the total 12-week term of the study) regardless of study participation. Patients randomized to food delivery will have delivery suspended if hospitalized; food delivery will be resumed after hospital discharge if the investigators have not determined contraindications to continued participation (e.g. hypotension, hyperkalemia).

Other design considerations/limitations

Our trial design does not adjust for habitual baseline variation in sodium intake. As in many North American hospitals, all ADHF inpatients at the three trial sites receive a 2000 mg/day sodium-restricted diet while hospitalized.⁴² This standardized intervention prior to randomization should minimize the impact of pre-hospitalization diets on our findings. The 1500 mg/d sodium threshold for the study diet was selected to match current American Heart Association recommendations, and is supported by our pilot study in which meals with 1500mg/d sodium were provided to older HF outpatients without adjustment for baseline dietary practices.^{20,21} We acknowledge that the effects of meal home-delivery on QOL may be challenging to separate from the effects specifically related to the DASH/SRD. In addition to the KCCQ we will obtain the SF-12, a well-validated measure of general QOL,³⁶ in order to evaluate changes in QOL related to food delivery alone.

Conclusion

The purpose of this randomized controlled trial is to test the efficacy and safety of 4 weeks of DASH/SRD after ADHF hospitalization. Hypothesized mechanisms of DASH/SRD benefits include improvements in ventricular function, ventricular-arterial coupling, and reduced plasma volume as well as reductions in systemic oxidative stress and inflammation and a shift in salt taste affinity. By testing a novel dietary intervention supported by multiple levels of evidence including preliminary data in outpatients with stable HF, we will address a critical evidence gap in the care of older patients with ADHF. If effective and safe, this intervention could then be scaled to assess effects on readmission and healthcare costs in older adults following ADHF hospitalization.

Acknowledgments

The authors gratefully acknowledge the assistance of Wahida Karmally, MS, RD, CDE (Columbia University), Theresa Han-Markey, MS, RD, and Debra Peterman, RD (University of Michigan).

References

1. Lloyd-Jones D, Adams RJ, Brown TM, et al. Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation*. 2010; 121:948–54. [PubMed: 20177011]
2. Ross JS, Chen J, Lin Z, et al. Recent national trends in readmission rates after heart failure hospitalization. *Circ Heart Fail*. 2010; 3:97–103. [PubMed: 19903931]
3. Kosiborod M, Soto GE, Jones PG, et al. Identifying heart failure patients at high risk for near-term cardiovascular events with serial health status assessments. *Circulation*. 2007; 115:1975–81. [PubMed: 17420346]
4. Wong CY, Chaudhry SI, Desai MM, Krumholz HM. Trends in Comorbidity, Disability, and Polypharmacy in Heart Failure. *Am J Med*. 2011; 124:136–43. [PubMed: 21295193]
5. McMurray JJ, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med*. 2014; 371:993–1004. [PubMed: 25176015]
6. Teerlink JR, Cotter G, Davison BA, et al. Serelaxin, recombinant human relaxin-2, for treatment of acute heart failure (RELAX-AHF): a randomised, placebo-controlled trial. *Lancet*. 2013; 381:29–39. [PubMed: 23141816]
7. Chaudhry SI, Mattera JA, Curtis JP, et al. Telemonitoring in patients with heart failure. *N Engl J Med*. 2010; 363:2301–9. [PubMed: 21080835]
8. Felker GM, Lee KL, Bull DA, et al. Diuretic strategies in patients with acute decompensated heart failure. *N Engl J Med*. 2011; 364:797–805. [PubMed: 21366472]
9. O'Connor CM, Starling RC, Hernandez AF, et al. Effect of nesiritide in patients with acute decompensated heart failure. *N Engl J Med*. 2011; 365:32–43. [PubMed: 21732835]
10. Hummel SL, DeFranco AC, Skorcz S, Montoye CK, Koelling TM. Recommendation of Low-Salt Diet and Short-term Outcomes in Heart Failure with Preserved Systolic Function. *Am J Med*. 2009; 122:1029–36. [PubMed: 19854331]
11. Fonarow G, Abraham W, Albert N, et al. Factors identified as precipitating hospital admissions for heart failure and clinical outcomes: findings from OPTIMIZE-HF. *Arch Intern Med*. 2008; 168:847–54. [PubMed: 18443260]
12. Paterna S, Gaspere P, Fasullo S, Sarullo FM, Di Pasquale P. Normal-sodium diet compared with low-sodium diet in compensated congestive heart failure: is sodium an old enemy or a new friend? *Clin Sci (Lond)*. 2008; 114:221–30. [PubMed: 17688420]
13. Gupta D, Georgiopoulou VV, Kalogeropoulos AP, et al. Dietary Sodium Intake in Heart Failure. *Circulation*. 2012; 126:479–85. [PubMed: 22825409]

14. Troyer JL, McAuley WJ, McCutcheon ME. Cost-Effectiveness of Medical Nutrition Therapy and Therapeutically Designed Meals for Older Adults with Cardiovascular Disease. *J Am Diet Assoc.* 2010; 110:1840–51. [PubMed: 21111094]
15. Fonarow GC, Abraham WT, Albert NM, et al. Factors identified as precipitating hospital admissions for heart failure and clinical outcomes: findings from OPTIMIZE-HF. *Arch Intern Med.* 2008; 168:847–54. [PubMed: 18443260]
16. Opasich C, Rapezzi C, Lucci D, et al. Precipitating factors and decision-making processes of short-term worsening heart failure despite “optimal” treatment (from the IN-CHF Registry). *Am J Cardiol.* 2001; 88:382–7. [PubMed: 11545758]
17. Klotz S, Hay I, Zhang G, Maurer M, Wang J, Burkhoff D. Development of heart failure in chronic hypertensive Dahl rats: focus on heart failure with preserved ejection fraction. *Hypertension.* 2006; 47:901–11. [PubMed: 16585423]
18. Gottdiener JS, Arnold AM, Aurigemma GP, et al. Predictors of congestive heart failure in the elderly: the cardiovascular health study. *J Am Coll Cardiol.* 2000; 35:1628–37. [PubMed: 10807470]
19. Jablonski KL, Racine ML, Geolfos CJ, et al. Dietary Sodium Restriction Reverses Vascular Endothelial Dysfunction in Middle-Aged/Older Adults With Moderately Elevated Systolic Blood Pressure. *J Am Coll Cardiol.* 2013; 61:335–43. [PubMed: 23141486]
20. Hummel SL, Seymour EM, Brook RD, et al. 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; 60:1200–6. [PubMed: 23033371]
21. Hummel SL, Seymour EM, Brook RD, et al. Low-Sodium DASH Diet Improves Diastolic Function and Ventricular-Arterial Coupling in Hypertensive Heart Failure with Preserved Ejection Fraction. *Circ Heart Fail.* 6:1165–71. [PubMed: 23985432]
22. Green CP, Porter CB, Bresnahan DR, Spertus JA. Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. *J Am Coll Cardiol.* 2000; 35:1245–55. [PubMed: 10758967]
23. Spertus JA, Jones PG, Kim J, Globe D. Validity, reliability, and responsiveness of the Kansas City Cardiomyopathy Questionnaire in anemic heart failure patients. *Qual Life Res.* 2008; 17:291–8. [PubMed: 18165909]
24. Flynn KE, Pina IL, Whellan DJ, et al. Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA.* 2009; 301:1451–9. [PubMed: 19351942]
25. Mellen PB, Gao SK, Vitolins MZ, Goff DC Jr. Deteriorating dietary habits among adults with hypertension: DASH dietary concordance, NHANES 1988-1994 and 1999-2004. *Arch Intern Med.* 2008; 168:308–14. [PubMed: 18268173]
26. Nishimoto K, Hirota R, Egawa M, Furuta S. Clinical evaluation of taste dysfunction using a salt-impregnated taste strip. *ORL J Otorhinolaryngol Relat Spec.* 1996; 58:258–61. [PubMed: 8936475]
27. Appel L, Frohlich E, Hall J, et al. The importance of population-wide sodium reduction as a means to prevent cardiovascular disease and stroke: a call to action from the American Heart Association. *Circulation.* 2011; 123:1138–43. [PubMed: 21233236]
28. Karanja NM, Obarzanek E, Lin PH, et al. Descriptive characteristics of the dietary patterns used in the Dietary Approaches to Stop Hypertension Trial. DASH Collaborative Research Group. *J Am Diet Assoc.* 1999; 99:S19–27. [PubMed: 10450290]
29. National Kidney Foundation. K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. *Am J Kidney Dis.* 2004; 43(suppl 1):S1–S290. [PubMed: 15114537]
30. Kusaba T, Mori Y, Masami O, et al. Sodium restriction improves the gustatory threshold for salty taste in patients with chronic kidney disease. *Kidney Int.* 2009; 76:638–43. [PubMed: 19516246]
31. Guyatt GH, Sullivan MJ, Thompson PJ, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. *Can Med Assoc J.* 1985; 132:919–23. [PubMed: 3978515]

32. Ott C, Haetinger S, Schneider MP, Pauschinger M, Schmieder RE. Comparison of two noninvasive devices for measurement of central systolic blood pressure with invasive measurement during cardiac catheterization. *J Clin Hypertens (Greenwich)*. 2012; 14:575–9. [PubMed: 22947354]
33. Gottdiener J, Bednarz J, Devereux R, et al. American Society of Echocardiography recommendations for use of echocardiography in clinical trials. *J Am Soc Echocardiogr*. 2004; 17:1086–119. [PubMed: 15452478]
34. Maurer MS, King DL, El-Khoury Rumbarger L, Packer M, Burkhoff D. Left heart failure with a normal ejection fraction: identification of different pathophysiologic mechanisms. *J Card Fail*. 2005; 11:177–87. [PubMed: 15812744]
35. Noumi B, Teruya S, Salomon S, Helmke S, Maurer MS. Blood volume measurements in patients with heart failure and a preserved ejection fraction: implications for diagnosing anemia. *Congest Heart Fail*. 2011; 17:14–8. [PubMed: 21272222]
36. Bennet SJ, Oldridge NB, Eckert GJ, et al. Discriminant properties of commonly used quality of life measures in heart failure. *Qual Life Res*. 2002; 11:349–59. [PubMed: 12086120]
37. Chung ML, Moser DK, Lennie TA, et al. Gender differences in adherence to the sodium-restricted diet in patients with heart failure. *J Card Fail*. 2006; 12:628–34. [PubMed: 17045182]
38. Allen LA, Gheorghiade M, Reid KJ, et al. Identifying Patients Hospitalized With Heart Failure at Risk for Unfavorable Future Quality of Life. *Circ Cardiovasc Qual Outcomes*. 2011; 4:389–98. [PubMed: 21693723]
39. Mariotti R, Castrogiovanni F, Canale ML, Borelli G, Rondinini L. Weight loss and quality of life in chronic heart failure patients. *J Cardiovasc Med (Hagerstown)*. 2008; 9:576–80. [PubMed: 18475125]
40. Marti CN, Georgiopoulou VV, Giamouzis G, et al. Patient-reported selective adherence to heart failure self-care recommendations: a prospective cohort study: the Atlanta Cardiomyopathy Consortium. *Congest Heart Fail*. 2013; 19:16–24. [PubMed: 22958604]
41. Gheorghiade M, Abraham WT, Albert NM, et al. Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure. *JAMA*. 2006; 296:2217–26. [PubMed: 17090768]
42. Arcand J, Steckham K, Tzianetas R, L'Abbe MR, Newton GE. Evaluation of sodium levels in hospital patient menus. *Arch Intern Med*. 2012; 172:1261–2. [PubMed: 22801878]

Highlights

- Older ADHF patients may have difficulty with self-care and are often rehospitalized
- This trial tests home-delivered DASH/SRD meals post-ADHF discharge in older adults
- The primary study outcome is health-related quality of life
- Feasibility outcomes include safety and dietary adherence
- Exploratory endpoints include plasma volume and oxidative stress

Figure 1.
General Study Design

Visit Type	During Hospitalization	Discharge	Week 1	Week 4	Week 12
Day	D -14 to -2	D0	D7	D28	D84
Window			±3D	±5D	±7D
Consent/enrollment	x				
DASH/SRD vs. control		x	x	x	
History, physical exam	x	x	x	x	
QOL questionnaires	x	x		x	x
3-day food diary			x	x	x
Food frequency, DSRQ questionnaires	x				x
Blood studies	x	x	x	x	
Urinary studies		x	x	x	x
Na Taste affinity	x	x	x	x	x
6-minute walk testing		x		x	x
Electrocardiogram		x	x	x	
Echocardiogram, tonometry		x		x	
Blood volume (Columbia site)		x		x	
PaxGene tube collection		x		x	

DASH/SRD, sodium-restricted Dietary Approaches to Stop Hypertension Diet ; DSRQ, dietary sodium restriction questionnaire; QOL, quality of life

Figure 2.
Study Procedures Timeline

Table

Aims and Hypotheses for GOURMET-HF

Protocol Term	Endpoint
Specific Aim 1:	Feasibility and efficacy
Primary hypothesis	Improvement in Health-Related QOL
Feasibility	Adherence to DASH/SRD
Specific Aim 2:	Dietary, mechanistic, and safety
Secondary hypothesis	
Dietary	Salt taste affinity reduction
Mechanistic	Echocardiography
	Functional improvement
	Systemic inflammation and oxidative stress reduction
	Reduced plasma volume
Safety	Adverse events
	Salt taste affinity testing; Food Frequency Questionnaire
	Cardiac chamber dimensions; LV ejection fraction; mitral E:A ratio; Mitral annular tissue
	Doppler velocities; Ventricular-arterial coupling; 6 minute hall walk distance
	IL-6, hs-CRP, TNF- α , urine F2-isoprostanes; inflammation-related gene response in PBMC
	Plasma volume measured by I-131
	Death, all-cause hospitalization, new or worsening renal dysfunction, hyperkalemia, symptomatic hypotension, syncope

QOL, Quality of Life; DASH/SRD, sodium-restricted Dietary Approaches to Stop Hypertension diet ; LV = Left Ventricle; PBMC, peripheral blood mononuclear cells