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HEART FAILURE PREVENTION (W TANG, SECTION EDITOR)

Diet and Risk of Heart Failure: an Update

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Abstract Congestive heart failure (HF) remains one of the leading causes of morbidity and mortality in the USA, and its prevalence continues to rise with an aging population. Few nutritional guidelines exist for the prevention of HF, but recent evidence demonstrating beneficial effects of dietary interventions in the prevention and treatment of cardiovascular disease (CVD) offers promise for their role in HF. The current review summarizes pertinent data from both clinical trials and observational studies focused on the potential contribution of individual food items, supplements, and dietary patterns to the primary and secondary prevention of HF. We further highlight gaps in our understanding of the role of diet in HF and future directions to help bridge important areas of need.

Keywords Congestive heart failure · Nutrition · Nutrients · Sodium · Mediterranean · DASH · Dietary pattern · Risk factors

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Introduction

The growing heart failure (HF) epidemic is a major public health burden in the USA, with more than 5.7 million Americans affected by clinically manifest disease [1]. The lifetime risk of HF for US adults ≥40 years of age is approximately 20 %, and with over 825,000 new cases diagnosed each year, HF prevalence is projected to reach more than 8 million people by 2030 [2, 3]. Despite advances in drug and device therapies, mortality rates after HF diagnosis remain >50 % within 5 years of diagnosis, and effective strategies for HF prevention are sorely needed [4, 5].

An expanding body of evidence has demonstrated that diet quality strongly influences health and, in particular, the risk of cardiometabolic disease. New insights have taught us that overall dietary pattern is more relevant to health than individual food items and nutrients because people seldom consume a single food item or a single nutrient [6]. Randomized controlled trials (RCTs) of dietary patterns on the risk of hypertension [7–9], coronary heart disease (CHD) [9, 10••], and diabetes mellitus [11] have validated these lessons and generated interest in the impact of diet on HF.

Both observational studies and RCTs focusing on the role of diet in the prevention and management of HF have yielded important insights into specific food items, supplements, and dietary patterns. In subsequent paragraphs, we will discuss (a) the basis for current HF guidelines, (b) RCT and observational studies focused on diet and HF, (c) remaining gaps, and (d) future directions of research emphasizing the role of nutrition on the risk and management of HF.

Dietary Guidelines for HF

Although diet undoubtedly plays an important role in the wellness of people with HF, few nutritional guidelines exist for

patients at risk for HF or with known HF. While the American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) clinical practice guidelines for HF have issued a recommendation for sodium restriction to 1500 mg/day as a reasonable practice in patients with ACCF/AHA stage A or B HF in order to prevent HF and reduce its progression, there is insufficient evidence to endorse specific sodium recommendations for patients with more advanced disease (stage C or D HF) [12•]. Disparate sodium recommendations within the spectrum of HF may be explained by the fact that (1) much of the data supporting these recommendations come from studies demonstrating a strong association between sodium intake and HF risk factors such as hypertension [13, 14], structural heart disease [15], and CHD [14, 16] and (2) recent evidence raises concern about potential harm in subjects with symptomatic HF undergoing substantial sodium restriction [17, 18].

Omega-3 polyunsaturated fatty acid (PUFA) supplementation also received a class IIa recommendation to reduce hospitalizations and mortality in patients with New York Heart Association (NYHA) functional class II–IV symptoms based on data from the GISSI-HF (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico) trial [19]. Results from this trial demonstrated a 9 % risk reduction in mortality among subjects with chronic HF randomized to omega-3 PUFAs compared to those receiving placebo (95 % CI 2 to 17 %, p=0.04). Conversely, the 2012 European Society of Cardiology's HF guidelines [20] make no specific dietary recommendations beyond fluid restriction, preventing malnutrition, and maintaining a healthy weight. Despite limited dietary guidelines for HF, a foundation of evidence is emerging from new clinical trials investigating the effects of dietary patterns on HF risk and observational studies relating diet with incident HF or HF severity.

Nutritional Trials and HF Risk

Several trials have yielded important information about the effects of specific foods, supplements, and dietary patterns on the risk of HF. The Lyon Diet Heart Study demonstrated a decrease in recurrent coronary events (HR 0.28, 95 % CI 0.15–0.53) and a composite of major cardiovascular events, including HF (HR 0.29, 95 % CI 0.12–0.59) in patients with previous myocardial infarction (MI) that were advised to adhere to a Mediterranean-type diet plus alpha-linolenic acid, a plant-based n-3 PUFA, compared to a group receiving advice to follow the AHA step I diet [21]. Despite the presence of some methodological shortcomings in this study [22], this seminal finding that dietary patterns could confer cardiovascular protection opened the door for further nutritional investigations in subjects with or at risk for CVD.

The GISSI-HF trial demonstrated a benefit of 1 g/day of n-3 PUFAs [850–882 mg eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in an average ratio of 1:1.2] on both all-cause mortality (HR 0.91, 95 % CI 0.83–0.99) and hospitalization for cardiovascular events (HR 0.93, 95 % CI 0.87–0.99) in ~7000 subjects with chronic, systolic HF compared to placebo [19]. This finding came after the Japan EPA Lipid Intervention Study (JELIS) trial demonstrated that EPA supplementation reduced the risk of CHD events in dyslipidemic subjects treated with HMG-CoA reductase inhibitors (statins) compared to placebo (HR 0.81, 95 % CI 0.69–0.95) [23].

Recently, the Spanish PREDIMED (Prevención con Dieta Mediterránea) trial showed an approximately 30 % risk reduction in a composite of CVD events, including MI, stroke, and death from CVD, when participants were advised to follow a traditional Mediterranean-type diet supplemented with either nuts or extra-virgin olive oil [10••]. This study differed from the Lyon Diet Heart Study in that (1) it was a primary prevention study, albeit in subjects at high risk for cardiovascular disease, and (2) subjects in the intervention arms were supplied with either extra-virgin olive oil or nuts rather than alpha-linolenic acid. The latter feature is notable because there is debate about which components of the Mediterranean diet pattern confer cardiovascular protection, with some arguing that the supplemented extra-virgin olive oil and/or nuts may have driven the findings from the PREDIMED trial [24] while others believe that alpha-linolenic acid may be the major influence [21]. Nonetheless, findings from the studies described above illustrate the beneficial effects of both alpha-linolenic acid and marine omega-3 fatty acids (EPA and DHA) in subjects at high risk for or with prevalent HF.

Other dietary patterns and supplements have been investigated in RCTs for the treatment and prevention of HF. Recently, Hummel et al. conducted a novel mechanistic study focused on the effects of the Dietary Approaches to Stop Hypertension (DASH) diet in a single-arm of subjects with treated hypertension and HF with preserved ejection fraction (HFpEF) [25••]. The authors fed a salt-restricted (1150 mg/2100 kcal) version of the DASH diet to 13 patients over a period of 21 days and evaluated cardiac function, including measurement of diastolic dysfunction using a parametrized diastolic filling (PDF) formalism that has previously been validated [26, 27]. Improvement in left ventricular diastolic function, arterial elastance, and ventricular-arterial coupling were seen at the end of the trial, suggesting more efficient loading conditions and transfer of blood between the heart and the circulatory system. Despite shortcomings of this study, including the lack of a control arm and small sample size, its findings are nonetheless important.

RCTs of vitamin D on HF risk or in subjects with prevalent HF have yielded mixed results. In 36,000 postmenopausal women from the Women's Health Initiative (WHI), Hsia

et al. showed that an intervention with 400 IU of vitamin D_3 plus calcium did not influence the risk of HF hospitalization compared to placebo (HR 0.95, 95 % CI 0.83–1.10) after an average of 7 years of follow-up [28]. Recently, Donneyong et al. re-analyzed data from the WHI excluding subjects with prevalent HF and found that vitamin D and calcium supplementation reduced the risk for incident HF by 37 % (HR 0.63, 95 % CI 0.46 to 0.87) in post-menopausal women with a "low cardiovascular risk" profile (defined as the absence of hypertension, diabetes mellitus, CHD, or CVD) compared to those with a "high-risk" profile [29•]. In 5292 older women with a mean age of 77.5 years, Ford et al. also demonstrated that supplementation with 800 IU of vitamin D_3 plus 1000 mg of calcium carbonate reduced the risk of incident HF by 25 % (HR 0.75; 95 % CI 0.58 to 0.97) after a median follow-up period of approximately 6 years [30••].

RCTs evaluating the efficacy of vitamin D in the treatment of HF have largely been inconclusive. In a double-blinded RCT of elderly subjects (mean age, 66 years old) with NYHA class II–IV HF, Boxer et al. did not find improvements in aerobic capacity and skeletal muscle strength after 6 months in those receiving weekly supplementation with 50,000 IU of vitamin D_3 compared to placebo [31•]. These findings were consistent with those of prior RCTs that did not demonstrate improvement in functional performance of subjects with systolic HF receiving either daily vitamin D_3 or two loading doses of vitamin D_2 [32, 33]. While some investigators have demonstrated improvements in serum cytokine [32] and aldosterone levels [34•] in subjects with HF receiving vitamin D supplementation, beneficial effects on cardiovascular structure and function and clinical outcomes have yet to be demonstrated in that population. We anticipate that results for the ongoing vitamin D and omega-3 trial (VITAL) trial will provide future answers on the role of vitamin D on the risk of HF [35].

Observational Studies and HF Risk

Table 1 summarizes published observational data on the relationship between diet and HF risk. Several groups prospectively studied the relation between dietary patterns and HF risk and mortality in the Women's Health Initiative (WHI) [36] cohort of over 48,000 post-menopausal women. Levitan et al. reported that HF subjects with the highest dietary approaches to stop hypertension (DASH) and Mediterranean diet scores had 16 % (HR 0.84, 95 % CI 0.7–1.0) and 15 % (HR 0.85, 95 % CI 0.7–1.02) lower rates of death, respectively, compared to those with the lowest scores [37••]. In Swedish subjects, Levitan et al. also found that higher DASH scores were associated with a 22 % lower risk of incident HF in men [38] (highest to lowest quartile score: HR 0.78, 95 % CI 0.65–0.95) and 37 % lower risk of HF in women (HR 0.63, 95 % CI 0.48–0.81) [39].

Further support for the role of healthy dietary patterns for HF prevention comes from a prospective analysis of two combined RCTs of either angiotensin-converting enzyme inhibitor (ACE-I) or aldosterone receptor blocking (ARB) or both therapies on a composite end point including CVD death, non-fatal MI or stroke, or CHF hospitalization in participants with CVD or diabetes mellitus. In this study, Dehghan et al. created a modified version of the alternative healthy eating index (AHEI) [40], and demonstrated that those in the highest AHEI quintile had a 28 % lower risk of incident HF compared to subjects in the lowest quintile of AHEI (95 % CI 0.58–0.88, $p<0.05$) [41••].

How might diet protect against HF? Strong evidence exists for the reduction of blood pressure through adherence to a DASH diet [8, 9], including data demonstrating blood pressure reduction throughout a range of sodium restriction [7]. Similar to the Mediterranean dietary pattern, the DASH diet may also protect against HF through reduction in CHD risk. Indeed, a pooled analysis of over 144,000 adults from six prospective cohorts showed a 21 % (95 % CI 0.71–0.88, $p<0.001$) lower risk of CHD among subjects following a DASH diet [42]. Less well established is the DASH diet's impact on diabetes mellitus [43]. In a recent secondary analysis of the PREDIMED trial, Fitó et al. demonstrated a significant reduction in N-terminal pro-brain natriuretic peptide (NT-proBNP) among subjects advised to follow a Mediterranean diet compared to those advised to follow a low-fat diet [44•].

Results from the studies above have fostered renewed attention on the features of dietary patterns that may contribute to their beneficial effects in HF. While there is no single "Mediterranean diet" given the diversity of cultures in the Mediterranean region, common features include the following: high consumption of fruits and nuts, vegetables, legumes, and whole grain cereals; low consumption of dairy products and processed meats; and moderate alcohol (e.g., red wine) intake [45]. Similarly, several iterations of the DASH diet exist [8, 46]; however, universal features include a diet rich in fruits, vegetables, and whole grains and low in sodium, processed foods, and red meats.

Many of the shared components of the DASH and Mediterranean diet have been investigated in prospective cohort studies. Data from the Physicians' Health Study (PHS) [47, 48] showed that higher consumption of whole grain breakfast cereals [49], fruits, and vegetables [50], chocolate [51•], and moderate alcohol intake [52] was associated with a lower risk of incident HF. Conversely, consumption of >1 egg/day [53] and higher consumption of red meat [54] has been associated with a higher risk of HF while nut consumption was not associated with incident HF in this cohort [55]. Increased consumption of baked or broiled fish has been

Table 1 Relationship of different foods and dietary patterns with the risk of HF or mortality in HF subjects in prospective cohort studies

	Authors	Study design	No. of subjects	Exposure and units	End point	HR (95 % CI)	Adjustment
Breakfast cereal	Djoussé et al. 2007 [49]	Prospective cohort (PC)	21,376	Whole grain breakfast cereal (servings in cups): ≥7 servings vs. 0	Incident HF	0.71 (0.60–0.85)	Age, smoking, alcohol, exercise, MVI, CVD
Fish	Mozaffarian et al. 2011 [56]	PC	4738	Broiled or baked fish (servings in ounces): 1–2/week vs. <1/month	Incident HF	0.78 (0.63–0.97)	Age, sex, race, BMI, education, DM, CVD, energy
	Belin et al. 2011 [57]	PC	84,493	Broiled/baked fish (servings in ounces): ≥5/week vs. <1/month; fried fish: ≥1/week vs. <1/month	Incident HF	0.70 (0.51–0.95) for baked/broiled 1.48 (1.19–1.84) for fried fish	Age, race, exercise, BMI, education, DM, CVD, diet
Red meat	Kaluza et al. 2014 [59•]	PC	37,035	Processed red meat (gram/day): ≥75 vs. <25 g/day	Incident HF	1.28 (1.10–1.48)	Age, education, exercise, smoking, alcohol, diet, energy, FH of MI
	Ashaye et al. 2011 [54]	PC	21,120	Total red meat (processed and unprocessed): highest vs. lowest quintile	Incident HF	1.24 (1.03–1.48)	Age, exercise, smoking, alcohol, BMI, diet, FH of MI
Chocolate	Petrone et al. 2014 [51•]	PC	20,278	Chocolate (1 oz servings): 1/week vs. <1/month	Incident HF	0.80 (0.66–0.98)	Age, BMI, smoking, alcohol, exercise, energy, AF
Alcohol	Goncalves et al. 2015 [60•]	PC	14,629	Alcohol intake (drinks in 14 g equivalents): ≤7 vs. 0/week	Incident HF	0.80 (0.68–0.94) in men 0.84 (0.71–1.0) in women	Age, education, exercise, smoking, BMI, DM, CVD
	Djoussé et al. 2007 [61]	PC	21,601	Alcohol intake (drinks): >7 vs. <1/week	Incident HF	0.62 (0.41–0.96)	Age, smoking, BMI, valvular heart disease
Egg	Djoussé et al. 2008 [53]	PC	21,275	Egg consumption: ≥1/day vs. <1/week	Incident HF	1.28 (1.02–1.61)	Age, smoking, BMI, alcohol, CVD, dyslipidemia
Fruits and vegetables	Rautiainen et al. 2015 [62•]	PC	34,319	Fruits and vegetables (servings): highest to lowest quintile	Incident HF	0.80 (0.70–0.90)	Age, education, smoking, exercise, energy, CVD, DM
	Djoussé et al. 2009 [50]	PC	20,900	Fruits and vegetables (servings): ≥4 and <4/day	Lifetime risk of HF after age 40	0.85[a]	
DASH diet	Levitan et al. 2009 [39]	PC	36,019	DASH diet score: highest vs. lowest quartile score	Incident HF	0.63 (0.48–0.81)	Age, exercise, smoking, alcohol, BMI, CVD, high cholesterol
	Levitan et al. 2009 [38]	PC	38,987	DASH diet score: highest vs. lowest quartile	Incident HF	0.78 (0.65–0.95)	Age, smoking, energy, BMI, CVD, high cholesterol
	Levitan et al. 2013 [37••]	PC	3215	DASH diet score: highest vs. lowest quartile	Mortality in subjects with HF	0.84 (0.70–1.0)	Demographics, health behaviors, comorbidities, medications

Table 1 (continued)

	Authors	Study design	No. of subjects	Exposure and units	End point	HR (95 % CI)	Adjustment
Mediterranean diet	Levitan et al. 2013 [37••]	PC	3215	Mediterranean diet score: highest to lowest quartile	Mortality in subjects with HF	0.85 (0.70–1.02)	Demographics, health behaviors, comorbidities, medications
	Fitó et al. 2014 [44•]	PC	930	Mediterranean diet + virgin olive oil (VOO) or nuts vs. low-fat diet	HF biomarker (NT-proBNP pg/mL)	−70[b] (−133 to −7.4) for VOO group −85 (−145 to −25) for nuts group	Age, gender, study center, exercise, systolic blood pressure, creatinine
Alternative healthy eating index (AHEI)	Belin et al. 2011	PC	83,183	AHEI score: highest to lowest quartile	Incident HF	0.70 (0.59–0.82)	Age, race, exercise, smoking, education, BMI, medications

[a] 95 % CIs reported for subjects consuming ≥4 (9.5–14.4) and <4 servings/day (13.0–15.1), $p<0.05$

[b] Mean difference in NT-proBNP between groups at 1 year

inversely associated with HF risk [56, 57], whereas higher consumption of fried fish is associated with a higher risk of incident HF [57].

Current Gaps and Future Directions

While new evidence continues to emerge in support of a beneficial role of diet in the development and/or management of HF, key questions remain unanswered. Results from observational studies have been limited by the following: (1) diet assessment that still relies heavily on food frequency questionnaires with inherent limitations (often lack details on macro- and micronutrients, supplements, and types of fats and carbohydrates consumed), (2) the lack of specificity in the identification of the type of HF [HFpEF vs. heart failure with reduced ejection fraction (HFrEF)], (3) the difficulty in making comparisons across studies because of the heterogeneity of diet assessment and HF assessment, and (4) and differential sociodemographic characteristics of cohorts that limit their generalizability. Future prospective studies could help bridge these knowledge gaps by addressing these methodological issues.

Compelling findings from DASH and Mediterranean feeding trials highlight the fact that despite the many shared features of each dietary pattern, key differences exist. The Mediterranean diet includes significant fat intake (mainly mono- or polyunsaturated fats) whereas the DASH diet features low-sodium, more fruits and vegetables, and low-fat dairy. It is unclear what features of each diet may impact the primary or secondary prevention of individuals with HF. Additional clinical trials are needed to help elucidate the specific beneficial factors of these dietary patterns. These areas of need have been highlighted in the strategic plan of a joint National Institute of Health (NIH) and National Heart, Lung, and Blood Institute (NHLBI) working group [58].

Conclusions

A lack of nutritional guidelines for HF beyond sodium restriction highlights the need for additional research on diet to help bridge such gaps in HF prevention and management. While omega-3 PUFAs have received AHA/ACC expert endorsement for people with systolic HF, recommendations for HFpEF are lacking. Data for other dietary supplements including vitamin D are inconclusive. We anticipate that findings from the ongoing VITAL study with vitamin D_3 as one of the interventions in middle-aged US men and women will help answer additional questions about the role of dietary supplements in HF prevention. Observational studies have shown that higher consumption of individual foods including fruits and vegetables, whole grains, breakfast cereals, and baked/

broiled fish; moderate chocolate and alcohol intake; and lower consumption of processed meats and eggs may provide some benefits against HF.

Findings from individual foods are consistent with results from RCTs demonstrating that healthy dietary patterns, including the DASH and Mediterranean diets, may reduce HF risk factors and improve cardiovascular function in people with prevalent HF. Prospective HF studies further suggest that consumption of these diet patterns may be associated with a reduced risk of incident HF in men and women and death in women with known HF.

Nonetheless, improvements are needed in the methodology of future prospective studies of diet and HF risk, including better dietary assessment tools that capture micro- and macronutrient quantity and quality, and routine collection tools for the assessment of HF phenotypes (HFpEF vs. HFrEF). RCTs focused on identifying the important features of dietary patterns on the risk and management of HF are sorely needed to help reduce future HF risk.

Compliance with Ethics Guidelines

Conflict of Interest Jeremy Robbins declares that he has no conflict of interest.

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Human and Animal Rights and Informed Consent As a review paper, the authors relied on published data on human subjects in the literature to prepare this article. To the best of our knowledge, those publications met ethical requirements for human research.

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