JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 72, NO. 19, 2018

PUBLISHED BY ELSEVIER

COUNCIL PERSPECTIVES

Lifestyle Modifications for Preventing and Treating Heart Failure

Monica Aggarwal, MD,[a] Biykem Bozkurt, MD,[b] Gurusher Panjrath, MD,[c,d] Brooke Aggarwal, EdD, MS,[e] Robert J. Ostfeld, MD, MSc,[f] Neal D. Barnard, MD,[g] Hanna Gaggin, MD,[h] Andrew M. Freeman, MD,[i] Kathleen Allen, BA,[j] Shivank Madan, MD,[f] Daniele Massera, MD, MSc,[f] Sheldon E. Litwin, MD,[k] on behalf of American College of Cardiology's Nutrition and Lifestyle Committee of the Prevention of Cardiovascular Disease Council

JACC JOURNAL CME/MOC/ECME

This article has been selected as the month's *JACC* CME/MOC/ECME activity, available online at http://www.acc.org/jacc-journals-cme by selecting the *JACC* Journals CME/MOC/ECME tab.

Accreditation and Designation Statement

The American College of Cardiology Foundation (ACCF) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The ACCF designates this Journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1 Medical Knowledge MOC point in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Lifestyle Modifications for Preventing and Treating Heart Failure will be accredited by the European Board for Accreditation in Cardiology (EBAC) for 1 hour of External CME credits. Each participant should claim only those hours of credit that have actually been spent in the educational activity. The Accreditation Council for Continuing Medical Education (ACCME) and the European Board for Accreditation in Cardiology (EBAC) have recognized each other's accreditation systems as substantially equivalent. Apply for credit through the post-course evaluation. While offering the credits noted above, this program is not intended to provide extensive training or certification in the field.

Method of Participation and Receipt of CME/MOC/ECME Certificate

To obtain credit for *JACC* CME/MOC/ECME, you must:

1. Be an ACC member or *JACC* subscriber.
2. Carefully read the CME/MOC/ECME-designated article available online and in this issue of the *Journal*.
3. Answer the post-test questions. A passing score of at least 70% must be achieved to obtain credit.
4. Complete a brief evaluation.
5. Claim your CME/MOC/ECME credit and receive your certificate electronically by following the instructions given at the conclusion of the activity.

CME/MOC/ECME Objective for This Article: Upon completion of this activity, the learner should be able to: 1) describe the impact of obesity on congestive heart failure and role of weight management; 2) discuss the American College of Cardiology Foundation/American Heart Association lifestyle guidelines associated with congestive heart failure; 3) recommend exercise to patients with congestive heart failure by discussing mortality benefits; 4) recognize which supplements show promise in treatment of congestive heart failure and which have not shown benefit; 5) consider the benefits of yoga and meditation in congestive heart failure; and 6) understand the negative impact of unintended weight loss.

CME/MOC/ECME Editor Disclosure: *JACC* CME/MOC/ECME Editor Ragavendra R. Baliga, MD, FACC, has reported that he has no financial relationships or interests to disclose.

Author Disclosures: Dr. B. Aggarwal has received research funding from an American Heart Association Go Red for Women Strategically Focused Research Network Award (grant 16SFRN27960011). Dr. Ostfeld has served as a consultant for Better Therapeutics. Dr. Barnard has served, without financial compensation, as president of the Physicians Committee for Responsible Medicine and Barnard Medical Center, a nonprofit organization providing education, research, and medical care related to nutrition. Dr. Gaggin is supported in part by the Clark Fund for Cardiac Research Innovation; has received research grant support from Roche Diagnostics and Portola; has served as a consultant for Amgen, Boston Heart Diagnostics, and Ortho Clinical; and has served on the clinical endpoint committee for EchoSense and Radiometer. Dr. Freeman has done nonpromotional speaking for Boehringer Ingelheim. Dr. Litwin has served on the event adjudication committee for CVRx (Beat HF Trial). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Medium of Participation: Print (article only); online (article and quiz).

CME/MOC/ECME Term of Approval

Issue Date: November 6, 2018
Expiration Date: November 5, 2019

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

ISSN 0735-1097/$36.00
https://doi.org/10.1016/j.jacc.2018.08.2160

JACC VOL. 72, NO. 19, 2018
NOVEMBER 6, 2018:2391–405

Lifestyle Modifications for Preventing and Treating Heart Failure

Monica Aggarwal, MD,[a] Biykem Bozkurt, MD,[b] Gurusher Panjrath, MD,[c,d] Brooke Aggarwal, EdD, MS,[e] Robert J. Ostfeld, MD, MSc,[f] Neal D. Barnard, MD,[g] Hanna Gaggin, MD,[h] Andrew M. Freeman, MD,[i] Kathleen Allen, BA,[j] Shivank Madan, MD,[f] Daniele Massera, MD, MSc,[f] Sheldon E. Litwin, MD,[k] on behalf of American College of Cardiology's Nutrition and Lifestyle Committee of the Prevention of Cardiovascular Disease Council

ABSTRACT

Continued improvement in medical and device therapy for heart failure (HF) has led to better survival with this disease. Longer survival and increasing numbers of unhealthy lifestyle factors and behaviors leading to occurrence of HF at younger ages are both contributors to an increase in the overall prevalence of HF. Clinicians treating this complex disease tend to focus on pharmacological and device therapies, but often fail to capitalize on the significant opportunities to prevent or treat HF through lifestyle modification. Herein, the authors review the evidence behind weight management, exercise, nutrition, dietary composition, supplements, and mindfulness and their potential to influence the epidemiology, pathophysiology, etiology, and management of stage A HF. (J Am Coll Cardiol 2018;72:2391–405)

The prevalence of heart failure (HF) appears to be increasing in the United States (1). Other countries have also seen increases, particularly in patients <50 years of age (2). The onset of heart failure with preserved ejection fraction (HFpEF) is rising faster than heart failure with reduced ejection fraction (HFrEF) (3,4). The appearance of HF in younger patients has been attributed to a larger burden of risk factors, most notably obesity and its attendant comorbidities (2,5). Management of adverse lifestyles and related comorbidities is most important in stage A HF, when patients are at high risk of developing left ventricular (LV) dysfunction (Stage B HF) or symptomatic HF (stages C to D). Poor dietary quality, including excess caloric intake and unhealthy food choices, low physical activity, and mental stress, are major, modifiable lifestyle factors that are likely contributing to the rapidly changing epidemiology of HF (6). Fortunately, the potentially favorable effects of lifestyle measures are similar in HFpEF and HFrEF. There is stronger evidence that HF can be prevented by favorable lifestyle choices, compared with treatment of existing HF. Nonetheless, it is likely that lifestyle therapies can be effective through the various stages of the disease.

Although favorable lifestyle changes are widely endorsed, the evidence supporting the utility of such

The views expressed in this paper are from the American College of Cardiology's Nutrition and Lifestyle Committee as part of the Prevention of Cardiovascular Disease Council and do not necessarily reflect the position of the American College of Cardiology.

From the [a]Division of Cardiology, University of Florida, Gainesville, Florida; [b]Division of Cardiology, Baylor College of Medicine, Houston, Texas; [c]Division of Cardiology, George Washington University School of Medicine and Health Sciences, Washington, DC; [d]Inova Heart and Vascular Institute, Fairfax, Virginia; [e]Division of Cardiology, Columbia University Medical Center, New York, New York; [f]Division of Cardiology, Montefiore Health System, Bronx, New York; [g]George Washington University School of Medicine, Washington, DC; [h]Division of Cardiology, Massachusetts General Hospital, Boston, Massachusetts; [i]Division of Cardiology, Department of Medicine, National Jewish Health, Denver, Colorado; [j]Department of Food and Nutrition, New York-Presbyterian, New York, New York; and the [k]Division of Cardiology, Medical University of South Carolina and Ralph H. Johnson Veterans Affairs Medical Center, Charleston, South Carolina. Dr. B. Aggarwal has received research funding from an American Heart Association Go Red for Women Strategically Focused Research Network Award (grant 16SFRN27960011). Dr. Ostfeld has served as a consultant for Better Therapeutics. Dr. Barnard has served, without financial compensation, as president of the Physicians Committee for Responsible Medicine and Barnard Medical Center, a nonprofit organization providing education, research, and medical care related to nutrition. Dr. Gaggin is supported in part by the Clark Fund for Cardiac Research Innovation; has received research grant support from Roche Diagnostics and Portola; has served as a consultant for Amgen, Boston Heart Diagnostics, and Ortho Clinical; and has served on the clinical endpoint committee for EchoSense and Radiometer. Dr. Freeman has done nonpromotional speaking for Boehringer Ingelheim. Dr. Litwin has served on the event adjudication committee for CVRx (Beat HF Trial). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received November 9, 2017; revised manuscript received August 7, 2018, accepted August 12, 2018.

changes is limited. Further, there are multiple barriers to implementation of lifestyle changes in "real-world" clinical practice. The goal of this review is to familiarize health care practitioners with a broad overview of lifestyle measures, specifically as they relate to HF, so that they can engage in more informed, shared decision-making with their patients. In this paper, the evidence for lifestyle-based treatment approaches as preventive strategies for patients with stage A HF will be reviewed.

PREVENTIVE STRATEGIES IN PATIENTS WITH STAGE A HF

Stage A HF, or "pre-HF," as it is commonly referred to, is defined as those patients who are at high risk for developing symptomatic HF (7). The risk factors that define stage A HF include atherosclerotic heart disease, hypertension, and diabetes. Despite vigorous efforts to achieve aggressive blood pressure, glucose, and lipid goals using effective pharmacological approaches, the prevalence of HF continues to increase, suggesting that a focus on the upstream drivers (i.e., lifestyle factors) of the individual risk factors might produce incremental benefit.

OBESITY AS A MODIFIABLE RISK FACTOR FOR HF DEVELOPMENT

Multiple large, observational studies have shown associations between obesity and incident HF (8–10). There is a dose-dependent relationship between increasing body mass index (BMI) and risk of HF, supporting a causal role (9,11). Conversely, long-term avoidance of obesity along with higher physical activity, modest alcohol intake, and not smoking have been independently associated with a markedly lower risk of HF (12,13). Keeping BMI <30.0 kg/m^2 over an average period of 21.5 years in older adults was associated with an adjusted hazard ratio of 0.70 for HF development (12).

Multiple mechanisms, including inflammation, myocardial injury (14), hypertension, impaired glucose homeostasis, dyslipidemia, sleep-disordered breathing, and LV hypertrophy (15–18), are hypothesized to contribute to the association between obesity and new-onset HF (**Central Illustration**) (18). Adjustment for obesity-related comorbidities (8) or fitness levels (9) attenuated or eliminated the association between obesity and HF in some studies.

Although obesity is widely recognized as a disease, prospective research on the management of obesity has lagged behind that of other risk factors for HF. Most current strategies for management of obesity have limited effectiveness or lack of broad applicability. Loss of at least 10% body weight is likely necessary to favorably affect the subsequent risk of developing HF or reducing hospitalizations (19). Unfortunately, this magnitude of weight loss is infrequently realized or maintained with lifestyle changes alone (20). Large amounts of sustained weight loss achieved through bariatric surgery have been associated with reductions in both LV mass (21) and in new cases of HF (22,23). Although it is not a lifestyle intervention per se, the data from several large bariatric surgery registries provides important proof of concept that weight loss can be effective for prevention of HF (22,23). Weight management achieved through adoption of healthy eating and exercise habits likely has similar benefits for preventing incident HF. This, however, is difficult to prove, mostly due to the lack of resiliency of lifestyle interventions in the long-term (19,20,24).

Weight management for treatment of existing HF is controversial due to the presence of an "obesity paradox" (25) in which overweight and/or obesity appears to be a risk factor for the development of HF, but is paradoxically associated with better survival in those with stage C to D HF. Conversely, low body weight and unintentional weight loss are known harbingers of poor prognosis in HF. Whether intentional weight loss carries any adverse effects in patients with HF is uncertain. Several retrospective studies suggest that severely obese patients with higher stages of HFrEF have increases in left ventricular ejection fraction (LVEF) (26) and lower rates of HF-related hospitalizations (27) following bariatric surgery. A single randomized controlled trial (RCT) of exercise and hypocaloric diet in patients with HFpEF showed beneficial effects of diet-induced weight loss on exercise capacity (28), but the trial was not powered for other clinical endpoints.

BOTTOM LINE: OBESITY MANAGEMENT FOR HF PREVENTION AND TREATMENT

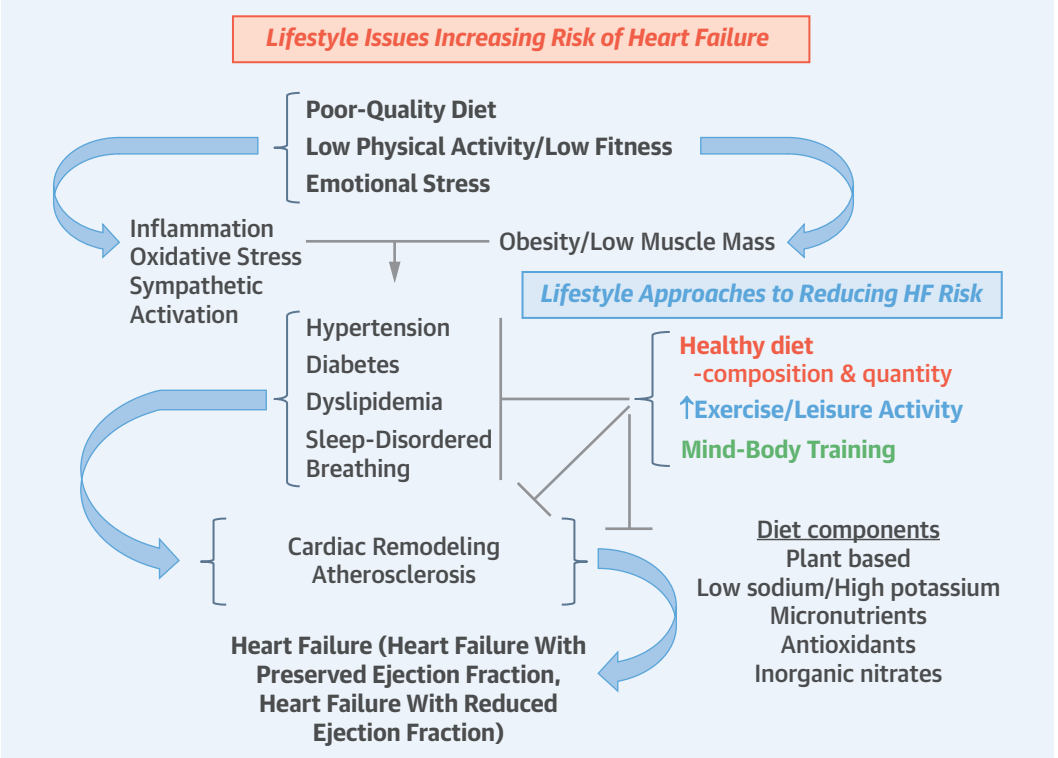
MAINTENANCE OF NORMAL BODY WEIGHT THROUGHOUT ADULT LIFE IS STRONGLY PROTECTIVE AGAINST HF. Weight management achieved through bariatric surgery has relatively large, favorable effects in protection against progression in stage A HF and

ABBREVIATIONS AND ACRONYMS

BMI = body mass index
CHD = coronary heart disease
CoQ10 = coenzyme Q10
CRF = cardiorespiratory fitness
ET = exercise training
HF = heart failure
HFpEF = heart failure with preserved ejection fraction
HFrEF = heart failure with reduced ejection fraction
TM = transcendental meditation

JACC VOL. 72, NO. 19, 2018
NOVEMBER 6, 2018:2391–405

CENTRAL ILLUSTRATION **Overview of Lifestyle Factors That May Contribute to the Risk of Heart Failure and Opportunities for Therapeutic Interventions**



Aggarwal, M. et al. J Am Coll Cardiol. 2018;72(19):2391–405.

Poor diet quality, low physical activity, and emotional stress can cause inflammation, oxidative stress, and sympathetic activation, and contribute to obesity **(top curved arrows)**. Together, these factors can trigger or exacerbate hypertension, diabetes, dyslipidemia, and sleep-disordered breathing **(middle curved arrows)**, which can lead to left ventricular (LV) remodeling, atherosclerosis, and ultimately, heart failure **(bottom curved arrows)**. Healthy diet, exercise, and mind-body training can work against all of these processes **(T lines)**.

also appears to have some benefit in stage C to D HF, although this is much less firmly established. Unfortunately, long-term success with lifestyle changes directed at weight management in patients with all stages of HF is challenging.

DIETARY COMPOSITION IN HF PREVENTION

Dietary composition may affect HF risk through mechanisms other than effects on weight. Only 1.5% of the U.S. population follows all of the dietary recommendations of the American Heart Association (AHA) (1). Diets containing greater amounts of plant-based foods including fruits, vegetables, nuts, seeds, and legumes and fewer animal-derived foods and processed foods appear to be beneficial for both atherosclerosis and HF prevention (29-34) (**Table 1**). In the Physician's Health Study, men who consumed more fruits and vegetables had a lower risk of HF (35). Similar results were obtained in populations from Finland (36), Sweden (37), and the United Kingdom (38). Conversely, diets higher in phosphatidyl choline (contained in red meat, cheese, and eggs) appear to promote an increase in the intestinal metabolite trimethylamine-N-oxide, a risk factor for myocardial infarction, stroke, HF, and death (39,40).

In prospective studies and RCTs, higher fruit and vegetable intake have consistently been linked to improved cardiovascular outcomes (41-43). Better adherence to the Dietary Approaches to Stop Hypertension (DASH) diet, which is low in saturated fat and high in fruits and vegetables, whole grains, beans, and legumes, was associated with lower blood pressures and reduced incidence of HF in men and women in 2 large prospective Swedish cohorts (44) and with decreased mortality among women with HF (45). Consumption of a DASH diet was associated

TABLE 1 Benefits of a Plant-Based Diet on Risk Factors for Heart Failure

Risk Factor	Benefit
Blood pressure	Diets rich in plant-based foods, particularly vegetarian and vegan diets, reduce systolic and diastolic blood pressure, presumably due, in part, to their high potassium content and their tendency to reduce blood viscosity and improve endothelial function (33,157,158). The DASH (Dietary Approaches to Stop Hypertension) study, which was in large part inspired by the blood pressure–lowering effect of vegetarian diets, was successful in lowering blood pressure (159), and was associated with favorable changes in diastolic and arterial function among individuals with heart failure with preserved ejection fraction (47).
Body weight	Diets rich in plant-based foods are consistently associated with reduced body weight in observational studies and clinical trials, apparently due to their low energy density and tendency to increase postprandial energy expenditure. Those following entirely plant-based (vegan) diets have demonstrably healthier body weights, on average, compared with other groups (31,42,160).
Lipid control	Elevated LDL cholesterol (161) concentrations and atherosclerotic cardiovascular disease (162) contribute to endothelial dysfunction, which is associated with systolic and diastolic heart failure (163). Because most plants are extremely low in saturated fat and devoid of cholesterol, and many are rich in soluble fiber or other lipid-lowering ingredients, plant-based diets improve plasma lipid concentrations (32). Vegetarian diets may also render LDL cholesterol more resistant to oxidation (164).
Glycemic control	Diabetes and insulin resistance are associated with altered energy metabolism, adverse cardiac remodeling, and incident heart failure (165,166). Vegan diets are associated with a particularly low prevalence of type 2 diabetes (167) and improve glucose metabolism in individuals with diabetes (42). Moreover, a Mediterranean diet versus control has been associated with lower incident diabetes (168).
Inflammation	Incident heart failure is associated with inflammation (169). Diets rich in plant-based foods may reduce inflammation (170–172) adding a measure of protection against heart failure (35–38). In contrast, meats, particularly processed red meat, may increase inflammation, as shown by increasing serum levels of C-reactive protein (173,174). Furthermore, a Mediterranean diet vs. control is associated with reduced serum markers of inflammation (175). MMPs participate in inflammation: higher levels are associated with increased atherosclerosis and heart failure risk (176,177). A vegetarian diet is associated with decreased levels of MMP compared with an omnivorous diet, and hence may be protective (178).
Reactive oxygen species	Reactive oxygen species may induce interstitial fibrosis, myocyte hypertrophy, and aortic stiffness and contribute to the development of heart failure (179,180). Plant-based diets, with their high antioxidant content, may reduce oxidative stress and provide greater amounts of antioxidants than do non-plant-based foods (70). Accordingly, both a Mediterranean diet and a DASH diet were associated with greater serum antioxidant capacity vs. control (181,182). Furthermore, a vegetarian diet may be protective as it is associated with lower serum myeloperoxidase levels, a promoter of reactive oxygen species formation, vs. an omnivorous diet (178,183).
TMAO	TMAO is produced by intestinal bacteria as a byproduct of choline and L-carnitine metabolism (184). Increased TMAO levels are associated with vascular inflammation (185), platelet reactivity, decreased reverse cholesterol transport (184), cardiovascular disease (184,185), and heart failure severity (186,187). Plant-based diets reduce TMAO formation through favorable effects on gut microbiota, whereas animal-based foods may raise TMAO levels (184,188).

LDL = low-density lipoprotein; MMP = metalloproteinase; TMAO = trimethylamine N-oxide.

with improved indexes of LV function in a multiethnic population without overt cardiovascular disease (46) and was associated with favorable changes in diastolic and arterial function among individuals with HFpEF (47). In a population cohort of 32,921 women, greater adherence to a Mediterranean style diet, which emphasizes vegetables, fruits, nuts, whole grains, legumes, fish, fermented dairy, monounsaturated fat, and low amounts of red meat, was also associated with a lower HF risk (48) and lower N-terminal pro-brain natriuretic peptide level (49). However, not all studies of a Mediterranean diet found a clear association. Although a pre-specified secondary analysis of the PREDIMED (Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Study) was strongly in favor of Mediterranean diet in patients with HFrEF, this diet did not result in a lower HF incidence. Importantly, this analysis was underpowered to prove this hypothesis, so the question of whether a Mediterranean style diet can prevent HF remains open (50). In a recent study looking at diet quality (DASH-style diet, Mediterranean diet, and the Alternate Healthy Index), a 20% increase in diet quality scores was associated with an 8% to 17% decrease of death from any cause (51).

BOTTOM LINE: DIETARY APPROACHES TO HF PREVENTION

Population-based samples and limited data from RCTs provide modest support for dietary approaches to reduce HF. Healthful eating patterns, particularly those that are based more on consumption of foods derived from plants, such as the Mediterranean, whole grain, plant-based diet and DASH diets, may offer some protection against HF development.

SODIUM RESTRICTION

Population-based cohort studies have demonstrated an association between higher salt intake and an increased incidence of HF (52). In a cohort of overweight and obese participants, increased dietary sodium intake was associated with increased relative risk for incident HF by 26% (52). Adherence to the DASH diet, which advocates salt reduction, was inversely proportional to HF incidence (44). Clinical trials and meta-analyses provide strong scientific support for salt restriction to prevent hypertension (44,53,54), stroke, and cardiovascular disease (53,55,56). However, prospective studies examining whether sodium restriction specifically reduces the

incidence of HF are lacking. If it is to be advocated, the amount of sodium restriction that is optimal for patients who are at high risk for cardiovascular disease or HF is uncertain. The AHA recommends limiting dietary sodium intake to <1,500 mg/day (53). Because of the data linking sodium intake with blood pressure, these recommendations for sodium appear to be applicable to patients with stage A and B HF, many of whom have hypertension (7).

In patients with known HF, the 2010 Heart Failure Society of America guidelines recommend dietary sodium restriction to 2 to 3 g daily (57). Although widely accepted, it should however be noted that the data supporting these recommendations are limited, inconsistent, and controversial (58–60). The relationship between sodium intake and outcomes may be nonlinear, as suggested by recent data on salt consumption and hypertension (61). Some studies suggest a worsening neurohormonal profile with sodium restriction in patients with HF (62–64), and observational studies suggested that sodium restriction might be associated with increased risk of death or HF hospitalization (65). Sodium restriction may be most appropriate for patients in New York Heart Association (NYHA) functional class III and IV (66). In the 2013 AHA/American College of Cardiology Foundation (ACCF) guidelines for the management of HF, sodium restriction is considered reasonable (Class IIa recommendation) for patients with symptomatic HF to reduce congestive symptoms, but the guideline also emphasized that there is lack of evidence for a stronger recommendation (7).

Despite guideline recommendations, patient adherence to dietary sodium restriction is poor. In an analysis of survey data from patients with self-reported HF, the mean sodium intake was 2,719 mg/day, with only 34% consuming <2,000 mg/day (67). There is a strong need for well-designed, prospective trials on the effects of sodium restriction in HF patients.

BOTTOM LINE: SODIUM RESTRICTION

Strong evidence is available to support restriction of salt/sodium intake to prevent hypertension, stroke, and cardiovascular disease. Given the strong link between hypertension and HF, it is reasonable to recommend limitation of sodium intake in stage A HF. The optimal amount of dietary sodium is uncertain, although most professional societies advocate for 1,500 to 2,400 mg (68). Although widely advocated, the role of sodium restriction in established HF is less definitive, and ongoing studies are addressing this controversy.

ANTIOXIDANTS (DIETARY AND SUPPLEMENTAL) AND OTHER NUTRITION SUPPLEMENTS

Among 33,713 women from the Swedish Mammography Cohort, the total antioxidant capacity of participants' diets was estimated from a food questionnaire and intake of antioxidants was inversely associated with the development of HF over 11.3 years of follow-up (69). Antioxidants such as vitamin C, vitamin E, beta-carotene, lycopene, lutein, zeaxanthin, and anthocyanins are found in a number of different plant-based foods (70). Deficiencies of zinc (71) and selenium (72) have been reported in patients with HF. Despite the associations, the use of antioxidant supplements has not been effective in prevention of coronary heart disease (CHD) and has not been well studied for HF.

COENZYME Q10

Coenzyme Q10 (CoQ10) is hypothesized to reduce harmful effects of reactive oxygen species that are increased in patients with HF and thus function as an antioxidant. CoQ10 is present in food, including red meat, plants, and fish, but the quantities are thought to be insufficient to affect HF incidence or progression. Reduced myocardial tissue content of CoQ10 has been demonstrated in patients with HF. CoQ10 deficiency correlates with the severity of HF symptoms and the degree of LV dysfunction (73,74), and is associated with mortality in HF (75). Published meta-analyses of RCTs with CoQ10 in HF have mostly indicated a positive effect on LVEF, with or without improvement of NYHA functional class (76,77). Most of these studies were small and heterogeneous, and lacked information on clinically relevant major endpoints such as mortality (76,78). In 2 systematic reviews, there was either a nonsignificant trend toward reduced mortality (79) or no effect on total mortality from CoQ10 supplementation (78). The recently published Q-SYMBIO RCT reported that in 420 patients with NYHA functional class III or IV HF, CoQ10 supplementation over 2 years was associated with a significantly lower incidence of major adverse cardiovascular events, cardiovascular death, urgent cardiac transplantation, mechanical circulatory support, total mortality, cardiovascular mortality, HF hospitalizations, and improvement in NYHA functional class (80). The evidence for CoQ10 supplementation is stronger than that for other supplements, and it is one of the few dietary therapies that has been directly studied in stage C to D HF. Nonetheless, the level of evidence for CoQ10

supplementation is still only moderate due to the relatively small size of the study.

L-CARNITINE AND TAURINE

L-carnitine is an amino acid derivative that plays a critical role in fatty acid transport into the mitochondria. Genetic causes of carnitine deficiency are associated with cardiomyopathy, and reduced L-carnitine content has been documented in the failing heart (81). Small studies have shown benefits of L-carnitine dietary supplements on cardiac remodeling after myocardial infarction (82), increases in exercise capacity (83), increases in peak oxygen consumption (VO_2), improvement in LVEF, cardiac remodeling (84), and improved clinical outcomes in patients with HF (85). Doses of L-carnitine in the studies ranged from 1.5 to 6 g/day, and follow-up periods lasted from 7 days to 3 years. Taurine, a related amino acid, has also been studied as a cardioprotective dietary supplement (86). Taurine administered orally (3 g/day) for 6 weeks, compared with CoQ10 (30 g/day), in a double-blind trial of 17 patients with HF and ejection fraction <50% resulted in significant improvements in LV systolic function, whereas no effects were observed for CoQ10 (87). There is little to no evidence for the use of these supplements in the prevention of HF (Stage A).

THIAMINE (VITAMIN B1) AND OTHER B VITAMINS

B vitamins are water-soluble, and tissue levels are dependent on intake. Severe thiamine deficiency, or beriberi, can result in cardiomyopathy and HF. Thiamine deficiency is rare in areas with access to vitamin-enriched foods or whole grains. Prolonged and large doses of diuretic use can be associated with thiamine deficiency, especially in patients hospitalized with HF (88). Doses of 1.5 mg/day of oral thiamine may restore normal levels. Thiamine repletion has been associated with improvement in LV function in 1 study (89), but other studies show mixed results (90,91). High dietary intakes of folate and vitamin B6 have been associated with reduced risk of mortality from stroke, CHD, and HF in some cohorts (92), but the data are conflicting (93). Studies on the effects of B-vitamin supplementation in patients with HF or at risk for HF (Stage A) are currently lacking, although routine supplementation has not been found to be beneficial in other populations (94).

VITAMIN D, CALCIUM

Low vitamin D levels have been reported in HF patients (95), correlate with severity of HF (96), and have been hypothesized to contribute to cardiac dysfunction through both calcium-dependent and -independent processes (81). Small studies of vitamin D supplementation in patients with HF and vitamin D deficiency have reported improvement in LVEF in the elderly (97), decreases in aldosterone levels (98), and improvement in NYHA functional class and exercise capacity (98,99). Vitamin D plus calcium supplementation did not significantly reduce the incidence of HF in the overall cohort of 35,983 postmenopausal women enrolled in in the Women's Health Initiative randomized trial (100). There is little to no evidence for these supplements in the prevention of HF (Stage A).

TABLE 2 Vegetables According to Nitrate Concentration

Nitrate Content (mg/100 g) of Fresh Food	Vegetables
Very low, <20 mg	Asparagus, garlic, onion, green bean, pepper, potato, sweet potato, tomato, and watermelon
Low, 20–<50 mg	Broccoli, carrot, cauliflower, and chicory
Regular, 50–<100 mg	Cabbage, turnip, and dill
High, 100–<250 mg	Endive, sweet leaf, parsley, and leek
Very high, >250 mg	Celery, chard, lettuce, beetroot, spinach, arugula, and watercress

Reproduced with permission from d'El-Rei J, Cunha AR, Trindade M, Neves MF. Beneficial effects of dietary nitrate on endothelial function and blood pressure levels. Int J Hypertens 2016;2016:6791519.

DIETARY APPROACHES TO INCREASING NITRIC OXIDE AVAILABILITY

HF is associated with reduced nitric oxide bioavailability, which may contribute to endothelial dysfunction (101,102). Once viewed as toxic and potentially carcinogenic, inorganic nitrates are now regarded as potentially beneficial bioactive molecules with promising therapeutic effects on vascular health (103). Green leafy vegetables, such as arugula, lettuce, beet greens, and spinach, are the major sources of dietary nitrate (**Table 2**) (104). The Mediterranean diet, known for its high concentration of vegetables, contains an estimated 400 to 550 g of nitrate versus 77 g in the typical Western diet (105,106). Similarly, the high nitrate content of the fruit and vegetable-rich DASH diet has been proposed as 1 potential mechanism through which this dietary pattern helps to lower blood pressure (101,104).

Intake of dietary inorganic nitrate has been associated with improved exercise capacity, reduced blood pressure and inflammation, and increased browning of adipose tissue (103,107–111). In a double-blind crossover study, 13 patients with LVEF ≤40% received nitrate-rich or -depleted beetroot juice for

9 days. Active treatment had no significant effects on exercise time, central hemodynamics, resting or exercising blood pressure, pulmonary oxygen uptake kinetics, skeletal muscle oxygenation, or blood lactate (112). In 2 small studies of 17 and 20 subjects with HFpEF, doses of nitrate-rich beetroot juice were found to significantly increase exercise capacity and were both feasible and safe (108,109). Recent results from the INDIE (Inorganic Nitrite Delivery to Improve Exercise Capacity in Heart Failure With Preserved Ejection Fraction) trial, however, did not show any beneficial effects on exercise tolerance in patients with HFpEF (113). There is little to no evidence for these supplements in the prevention of HF (Stage A).

BOTTOM LINE: SUPPLEMENTS FOR STAGE A AND MORE ADVANCED HF

Higher dietary antioxidant content may be protective, although use of antioxidant supplements has not been found to be effective in CHD and data in HF are lacking. The 2013 ACCF/AHA guidelines for the management of HF (7) advise against the use of supplements in patients with current or prior symptoms of HF (Level of Evidence: B). Similarly, the 2010 HFSA guidelines advise against the use of nutraceutical agents for relief of symptomatic HF (57). Coenzyme Q10 has the most promising data for use in HF, but firm recommendations regarding use are limited by small trial size.

CARDIORESPIRATORY FITNESS

Physical inactivity and poor cardiorespiratory fitness (CRF) are independent and modifiable risks for development of HF (9,114). The mechanisms underlying the protective effects of exercise are probably multifactorial (115). A strong dose-dependent inverse risk has been shown to exist between level of physical activity and risk of incident HF. Improvement in CRF among middle-age subjects with low fitness (<8 metabolic equivalents) was associated with a lower risk of HF in older age, independent of BMI (116). Similarly, increased physical activity was associated with a lower risk of HF (117), whereas a slower decline in CRF was associated with favorable systolic and diastolic parameters independent of other risk factors (118). An inverse dose-response relationship was reported between moderate to vigorous physical activity and incident HF hospitalization. This was true among both black men and women with normal ejection fractions (119). There may, however, be upper limits to the protective dose of exercise (120). The dose-dependent inverse relationship between physical activity and incident HF likely exists in both HFrEF and HFpEF, although direct comparisons are lacking. A recent study looked at 61 healthy, sedentary men and placed them on a 2-year intensive supervised exercise program. A total of 53 people completed the study, and adherence to the exercise regimen was 88%. After 2 years, maximal oxygen uptake increased by 18%, and cardiac stiffness reduced (as measured by 3D echocardiography and right heart catheterization). These changes suggest that improved physical activity could have a potential role in reducing the risk of HFpEF (121). Current guidelines recommend 30 min of walking for at least 5 days/week or 2 h and 30 min/week of moderate intensity, 1 h and 15 min (75 min)/week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic physical activity for optimal cardiovascular health (122).

Exercise training (ET) has been proven to be efficacious as a treatment for HF of both phenotypes. In HFrEF, the HF-ACTION (Efficacy and Safety of Exercise Training in Patients With Chronic Heart Failure) trial was a prospective RCT of ET in 2,231 HFrEF patients with NYHA functional class II to IV symptoms. Patients were randomized to usual care plus aerobic ET, consisting of 36 supervised sessions followed by home-based training, or usual care alone. Exercise did not significantly affect all-cause mortality or all-cause hospitalization; however, there was a reduction in mortality seen after adjustment for covariates. Men and women undergoing ET had equal improvement of peak VO_2 at 3 months (123). In subanalysis, ET in women with HF was associated with a larger reduction in rate of the combined endpoint of all-cause mortality and hospital stay than in men (124). No interaction was found between race and ET with respect to outcomes (125). The study highlighted the challenges of long-term adherence to ET prescription with only a small number of patients maintaining adherence to training after the initial supervised sessions. Based on findings from the HF-ACTION trial, cardiac rehabilitation or exercise therapy is now covered by the Center for Medicare or Medicaid and strongly recommended by the ACC/AHA guidelines in HFrEF patients (7).

In HFpEF, ET has been proven to be efficacious for improving peak VO_2 (126–128). However, Centers for Medicare & Medicaid Services coverage for cardiac rehabilitation in HFpEF has been limited by the smaller sizes of the studies and lack of long-term outcomes in this HF phenotype. Recently, a small study suggested that HFpEF patients had greater

TABLE 3 Exercise Prescription: Essential Components

Factor	Considerations
Intensity	• % heart rate reserve: 70% • Borg RPE: >14 • Resistance training: elastic bands, weights
Duration	• 30 min minimum • Shorter duration for frail • Additional warm-up or cool down phase
Frequency	• Daily to 5 days a week
Progression	• Advance to HR/Borg RPE targets
Maintenance	• Use of behavioral and nontraditional strategies

Modified with permission from Piña IL. Cardiac rehabilitation in heart failure: a brief review and recommendations. Curr Cardiol Rep 2010;12:223–9.

RPE = rate of perceived exertion.

TABLE 4 Mind-Body Techniques and Associated Improvements in Randomized Controlled Trials

MBI Practice	Improved Variables
Tai chi	Depression Quality of life Exercise tolerance
Yoga	Exercise capacity Peak VO_2
Relaxation response training	Symptoms Quality of life
Meditation	6-min walk Depression Hospitalizations
Acupuncture	6-min walk test Quality of life
Biofeedback	Quality of life
Reflexology	Depression 6-min walk test

VO_2 = peak oxygen consumption.

peak VO_2 improvement in response to 16-week supervised moderate-intensity endurance training compared with those with HFrEF (129).

EXERCISE PRESCRIPTION IN HF

Based on current evidence, exercise should be prescribed in both HF phenotypes. A construct on exercise prescription considerations is shown in **Table 3**. Emphasis should be made on the intensity and components of exercise, and recommendations should include aerobic and resistance training. It is known that higher exercise intensity compared with recommended guidelines leads to a lower risk of incident HF compared with low exercise intensities (130). Consideration should be made to include inspiratory muscle training (to enhance functional capacity) and strength training (to reduce sarcopenia) especially in certain high-risk groups such as elderly, frail HF patients with multiple comorbidities and activity limiting symptoms. Novel approaches such as telemedicine, exergaming systems, and behavioral coaches may increase adherence (131). As comprehensive HF managements continue to gain acceptance, such programs and community-based approaches should be harnessed to reinforce maintenance of ET in these patients who may find it difficult to adhere to office-based programs.

BOTTOM LINE: PHYSICAL ACTIVITY TO PREVENT AND TREAT HF

Increased CRF is strongly associated with decreased incident HF and has benefit in both HFrEF and HFpEF. ET has functional benefits in HFpEF and HFrEF and survival benefits in HFrEF.

MIND/BODY INTERVENTIONS

Mind and body intervention is described as activities that focus on the interplay among social, spiritual, mental, and behavioral factors that affect overall health (**Table 4**) (132,133).

Yoga is an ancient practice that combines body movements, respiration, and mind control (134). It is postulated that the beneficial effects of yoga on the cardiovascular system are mediated via increased vagal tone, enhanced parasympathetic, and reduced sympathetic activity (135). Different types of yoga have been associated with improvements in anginal symptoms (136) and exercise capacity (136,137), reduction in inflammation (137) and atherosclerosis (138), and improvement in multiple additional cardiovascular risk factors (139). There have been 2 main studies looking at yoga in known HF. They included both sexes and NYHA functional classes I to III. One of the studies was limited to patients with HFrEF, and the other study included both HFrEF and HFpEF. Both studies utilized a warm-up that included breathing exercises, a 40-min session of standing or seated postures, and 15 to 20 min of relaxation or recovery. Both studies showed an improvement in VO_2 in the yoga intervention group and both had an improvement in quality-of-life scores. In meta-analysis, the change in VO_2 was 22% in the intervention group. Considering that any improvement in peak VO_2 of ≥10% is considered significant, this change appears to be compelling. The quality-of-life indexes also improved by 24% in the yoga group. This is likely an important marker in a population that has a high incidence of depression (140). Yoga should be considered as an option for cardiac rehabilitation of HF patients (140,141).

Transcendental meditation (TM) is chant-based meditation that has also been shown to have cardiovascular benefits and potential benefits in all stages

TABLE 5 Transmitting Measures into Clinical Practice

Practice Measure	Level of Evidence	Incorporating Into Practice
Whole grain, plant-based diets	Moderate benefit in stage A HF Potential Benefit in stages B–D HF	"Starting the Conversation Survey" is a good start to asking about daily intake. Websites: Physicians Committee for Responsible Medicine and Forks Over Knives are available with recipes and educational materials for patients
Sodium restriction	Strong for stage A HF Moderate for stages B–D HF	Focusing on avoidance of processed foods and restaurant foods; 1 teaspoon of salt is 2,000 mg of sodium; nutrition label education Website: American Heart Association regarding sodium and salt
Weight loss	Strong for bariatric surgery for stage A HF in severely obese patients. Moderate for improving symptoms or reducing hospitalizations in existing HF, stages B–D	Focus on diet education in terms of removing sugar-sweetened beverages, processed foods highlighting "instant" meals; education on nutrition labeling; establish a nutritionist in clinic
Supplements 1. Coenzyme q10 2. Taurine and carnitine 3. B vitamins 4. Vitamin D and calcium	Evidence on supplements is conflicting and weak, although several micronutrient deficiencies have been associated with HF	Coenzyme Q10 has slightly more compelling evidence for a role in stages B–D HF; dosing in Q-SYMBIO trial was 100 mg 3 times daily
Exercise: low, moderate, high	Strong in all stages of HF	In HF patients, starting with stationary bicycle, low level, no incline treadmill, pool walking is a good start
Mind-body 1. Yoga 2. Meditation 3. Tai chi	1. Weak in all stages of HF 2. Weak in all stages of HF 3. Moderate in stages B–D HF, but with low risk profile	1. Chair yoga, wall squats are reasonable first steps; community yoga programs are widely available 2. Transcendental meditation is widely available but can be expensive. Apps such as Headspace and Calm are reasonable to advocate 3. Tai-chi classes are widely available but will typically require a higher-functioning HF patient

of HF. An early study showed that during TM, practitioners experienced a decrease in heart rate and also lowered their oxygen consumption (142). Since then, TM has been associated with reduced mortality (143) and improvements in blood pressure (144) and insulin resistance (145). A pooled analysis of 202 subjects (mean age 72 years) with high blood pressure from 2 separate studies and with a mean follow-up of 7.6 years found that compared with the combined control subjects, TM and other behavioral interventions were associated with a 23% relative risk reduction in all-cause mortality and a 30% relative reduction in cardiovascular mortality (143). In a study of 23 African-American patients with EF <40%, the TM group showed significant improvement in 6-min walk, depression scores, and quality-of-life measures compared with patients who received standard health education at 6 months. In addition, the TM group had fewer rehospitalizations during the 6-month follow-up period (146). In another study, 19 HF patients were randomized to either usual care or usual care plus weekly meetings including meditation. At the end of 12 weeks, the meditation group showed improved measures of exercise performance, improved quality-of-life scores, and reduction in plasma norepinephrine (147). The Support, Education, and Research in Chronic Heart Failure study was an 8-week mindfulness-based psychoeducational intervention among patients with HF. Treatment reduced anxiety and depression compared with control subjects. Although this effect was attenuated at 1 year, those in the treatment arm had better HF symptom control at 12 months. There was no effect on death or hospitalization at 1 year (148). In response to this and other information, the AHA advocates TM as part of secondary prevention of CHD (149). Most of the studies on yoga and TM were of low quality and had a high risk of bias, thereby limiting the strength of conclusions that can be drawn from them (150). However, yoga classes are widely available in the community and are generally low risk.

TAI CHI. Tai-chi exercise may benefit patients in all stages of HF through improvements in their quality of life and capacity to exercise. In 1 study, 100 patients with systolic HF were randomized to either a tai-chi intervention for 60 min, twice per week for 4 to 16 weeks, or an education-only control. Tai chi reduced depressive scores, improved quality of life and increased exercise tolerance (151,152). The Compassionate Approach to Lifestyle and Mind-Body Skills for Patients with CHF enrolled patients who were hospitalized within the previous 12 months. Patients had 8 weekly visits focusing on education about medications, diet, exercise, sleep, and stress management and training in mind-body. In this pilot study, improvements were observed in depression, fatigue, and satisfaction with life (153). Recently, researchers randomized 16 patients with HFpEF to 12 weeks of tai chi or aerobic exercise and found improvements in the 6-min walk and depression scores with tai chi versus exercise (154).

BOTTOM LINE: MINDFULNESS APPROACHES FOR HF TREATMENT

In small studies, yoga and meditation have shown benefit in reduction of blood pressure and reduced cardiovascular mortality. They have also shown symptomatic benefit in more advanced HF in small studies. Although high-quality evidence is limited or absent, there is almost no harm in recommending these practices for stage A to D HF. Further research into these approaches is ongoing.

FUTURE TECHNOLOGICAL APPROACHES TO LIFESTYLE CHANGE

Given the difficulties in maintaining healthy lifestyle changes, there has been a great deal of interest in leveraging the widespread use of new technologies that may easily provide reminders, trackers (dietary intake and activity), and motivational tools to people attempting to adopt healthy habits (155,156). Evidence is currently limited in this arena.

PUTTING LIFESTYLE MEASURES INTO CLINICAL PRACTICE

HF incidence continues to rise despite overall improvements in HF mortality. Lifestyle factors such as poor diet, obesity, lack of physical activity, and increased levels of emotional stress have likely contributed to the changing epidemiology of HF (onset at younger ages, higher proportion of HFpEF). There are many opportunities to institute lifestyle changes that have the potential to decrease the risk of developing HF, which is particularly important for the emerging HFpEF phenotype that lacks beneficial medical or device therapies. A summary of the benefits of all of the lifestyle interventions is shown in **Table 5**. Many of these same approaches have potential utility in the management of more advanced HF. In summary, achieving and maintaining high levels of fitness (9,13,120) and maintenance of normal body weight (9,13,116) have the most compelling benefits for prevention, while ET has the strongest evidence for patients with established HF (123). Stress reduction through mind/body interventions has many health benefits, and the long-term efficacy on HF is not yet clearly defined. Supplements of all sorts have limited data or evidence for benefit in HF risk reduction at this time. Patients should be encouraged to enroll in cardiac rehabilitation programs and/or engage in home exercise options.

ADDRESS FOR CORRESPONDENCE: Dr. Monica Aggarwal, Division of Cardiovascular Medicine, Health Science Center, Room M-415, University of Florida, P.O. Box 100288, 1600 SW Archer Road, Gainesville, Florida 32610-0277. E-mail: Monica.aggarwal@medicine.ufl.edu. Twitter: @StrongHeartDoc, @UFHealth.

REFERENCES

1. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics—2017 update: a report from the American Heart Association. Circulation 2017;135:e146–603.

2. Christiansen MN, Kober L, Weeke P, et al. Age-specific trends in incidence, mortality, and comorbidities of heart failure in Denmark, 1995 to 2012. Circulation 2017;135:1214–23.

3. Oktay AA, Rich JD, Shah SJ. The emerging epidemic of heart failure with preserved ejection fraction. Curr Heart Fail Rep 2013;10:401–10.

4. Vasan RS, Xanthakis V, Lyass A, et al. Epidemiology of left ventricular systolic dysfunction and heart failure in the Framingham study: An echocardiographic study over 3 decades. J Am Coll Cardiol Img 2018;11:1–11.

5. Rosamond WD, Johnson A. Trends in heart failure incidence in the community: a gathering storm. Circulation 2017;135:1224–6.

6. Andersson C, Vasan RS. Epidemiology of cardiovascular disease in young individuals. Nat Rev Cardiol 2018;15:230–40.

7. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;62:e147–239.

8. Ebong IA, Goff DC, Rodriguez CJ, et al. The relationship between measures of obesity and incident heart failure: the Multi-Ethnic Study of Atherosclerosis. Obesity (Silver Spring) 2013;21:1915–22.

9. Pandey A, LaMonte M, Klein L, et al. Relationship between physical activity, body mass index, and risk of heart failure. J Am Coll Cardiol 2017;69:1129–42.

10. Larsson SC, Tektonidis TG, Gigante B, Akesson A, Wolk A. Healthy lifestyle and risk of heart failure: Results from 2 prospective cohort studies. Circ Heart Fail 2016;9:e002855.

11. Kenchaiah S, Evans JC, Levy D, et al. Obesity and the risk of heart failure. N Engl J Med 2002;347:305–13.

12. Del Gobbo LC, Kalantarian S, Imamura F, et al. Contribution of major lifestyle risk factors for incident heart failure in older adults: The Cardiovascular Health Study. J Am Coll Cardiol HF 2015;3:520–8.

13. Hu G, Jousilahti P, Antikainen R, Katzmarzyk PT, Tuomilehto J. Joint effects of physical activity, body mass index, waist circumference, and waist-to-hip ratio on the risk of heart failure. Circulation 2010;121:237–44.

14. Ndumele CE, Coresh J, Lazo M, et al. Obesity, subclinical myocardial injury, and incident heart failure. J Am Coll Cardiol HF 2014;2:600–7.

15. Alexander JK. The cardiomyopathy of obesity. Prog Cardiovasc Dis 1985;27:325–34.

16. Avelar E, Cloward TV, Walker JM, et al. Left ventricular hypertrophy in severe obesity: Interactions among blood pressure, nocturnal hypoxemia, and body mass. Hypertension 2007;49:34–9.

17. Turkbey EB, McClelland RL, Kronmal RA, et al. The impact of obesity on the left ventricle: The Multi-Ethnic Study of Atherosclerosis (MESA). J Am Coll Cardiol Img 2010;3:266–74.

18. Gadde KM, Martin CK, Berthoud HR, Heymsfield SB. Obesity: pathophysiology and management. J Am Coll Cardiol 2018;71:69–84.

19. Wing RR, Bolin P, Brancati FL, et al., for the Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. N Engl J Med 2013;369:145–54.

20. Fothergill E, Guo J, Howard L, et al. Persistent metabolic adaptation 6 years after "The Biggest Loser" competition. Obesity (Silver Spring) 2016; 24:1612–9.

21. Owan T, Avelar E, Morley K, et al. Favorable changes in cardiac geometry and function following gastric bypass surgery: 2-year follow-up in the Utah Obesity Study. J Am Coll Cardiol 2011; 57:732–9.

22. Sundstrom J, Bruze G, Ottosson J, Marcus C, Naslund I, Neovius M. Weight loss and heart failure: a nationwide study of gastric bypass surgery versus intensive lifestyle treatment. Circulation 2017;135:1577–85.

23. Benotti PN, Wood GC, Carey DJ, et al. Gastric bypass surgery produces a durable reduction in cardiovascular disease risk factors and reduces the long-term risks of congestive heart failure. J Am Heart Assoc 2017;6:e005126.

24. Knowler WC, Fowler SE, Hamman RF, et al., for the Diabetes Prevention Program Research Group. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009;374: 1677–86.

25. Clark AL, Fonarow GC, Horwich TB. Obesity and the obesity paradox in heart failure. Prog Cardiovasc Dis 2014;56:409–14.

26. Vest AR, Patel P, Schauer PR, et al. Clinical and echocardiographic outcomes after bariatric surgery in obese patients with left ventricular systolic dysfunction. Circ Heart Fail 2016;9:e002260.

27. Shimada YJ, Tsugawa Y, Brown DF, Hasegawa K. Bariatric surgery and emergency department visits and hospitalizations for heart failure exacerbation: Population-based, self-controlled series. J Am Coll Cardiol 2016;67: 895–903.

28. Kitzman DW, Brubaker P, Morgan T, et al. Effect of caloric restriction or aerobic exercise training on peak oxygen consumption and quality of life in obese older patients with heart failure and preserved ejection fraction: a randomized, controlled trial. JAMA 2016;315:36–46.

29. Lara KM, Levitan EB, Gutierrez OM, et al. Abstract 15448: dietary patterns and incident heart failure in adults with no known coronary disease or heart failure: The REGARDS cohort (abstr). Circulation 2017;136:A15448.

30. Micha R, Peñalvo JL, Cudhea F, Imamura F, Rehm CD, Mozaffarian D. Association between dietary factors and mortality from heart disease, stroke, and type 2 diabetes in the United States. JAMA 2017;317:912–24.

31. Barnard ND, Levin SM, Yokoyama Y. A systematic review and meta-analysis of changes in body weight in clinical trials of vegetarian diets. J Acad Nutr Diet 2015;115:954–69.

32. Wang F, Zheng J, Yang B, Jiang J, Fu Y, Li D. Effects of vegetarian diets on blood lipids: A systematic review and meta-analysis of randomized controlled trials. J Am Heart Assoc 2015;4: e002408.

33. Yokoyama Y, Nishimura K, Barnard ND, et al. Vegetarian diets and blood pressure: a meta-analysis. JAMA Intern Med 2014;174:577–87.

34. Ornish D, Scherwitz LW, Billings JH, et al. Intensive lifestyle changes for reversal of coronary heart disease. JAMA 1998;280:2001–7.

35. Djousse L, Driver JA, Gaziano JM. Relation between modifiable lifestyle factors and lifetime risk of heart failure. JAMA 2009;302:394–400.

36. Wang Y, Tuomilehto J, Jousilahti P, et al. Lifestyle factors in relation to heart failure among Finnish men and women. Circ Heart Fail 2011;4: 607–12.

37. Rautiainen S, Levitan EB, Mittleman MA, Wolk A. Fruit and vegetable intake and rate of heart failure: a population-based prospective cohort of women. Eur J Heart Fail 2015;17:20–6.

38. Pfister R, Sharp SJ, Luben R, Wareham NJ, Khaw KT. Plasma vitamin C predicts incident heart failure in men and women in European Prospective Investigation Into Cancer and Nutrition-Norfolk prospective study. Am Heart J 2011;162:246–53.

39. Suzuki T, Heaney LM, Bhandari SS, Jones DJL, Ng LL. Trimethylamine n-oxide and prognosis in acute heart failure. Heart 2016;102:841–8.

40. Tang WH, Hazen SL. The contributory role of gut microbiota in cardiovascular disease. J Clin Invest 2014;124:4204–11.

41. Martinez-Gonzalez MA, Sanchez-Tainta A, Corella D, et al. A provegetarian food pattern and reduction in total mortality in the Prevencion Con Dieta Mediterranea (PREDIMED) study. Am J Clin Nutr 2014;100 Suppl 1:320s–8s.

42. Barnard ND, Cohen J, Jenkins DJ, et al. A low-fat vegan diet improves glycemic control and cardiovascular risk factors in a randomized clinical trial in individuals with type 2 diabetes. Diabetes Care 2006;29:1777–83.

43. Miller V, Mente A, Dehghan M, et al. Fruit, vegetable, and legume intake, and cardiovascular disease and deaths in 18 countries (PURE): a prospective cohort study. Lancet 2017;100:320S–8S.

44. Levitan EB, Wolk A, Mittleman MA. Consistency with the DASH diet and incidence of heart failure. Arch Intern Med 2009;169:851–7.

45. Levitan EB, Lewis CE, Tinker LF, et al. Mediterranean and DASH diet scores and mortality in women with heart failure: The Women's Health Initiative. Circ Heart Fail 2013;6:1116–23.

46. Nguyen HT, Bertoni AG, Nettleton JA, Bluemke DA, Levitan EB, Burke GL. DASH eating pattern is associated with favorable left ventricular function in the Multi-Ethnic Study of Atherosclerosis. J Am Coll Nutr 2012;31:401–7.

47. 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 2013;6:1165–71.

48. Tektonidis TG, Akesson A, Gigante B, Wolk A, Larsson SC. A Mediterranean diet and risk of myocardial infarction, heart failure and stroke: a population-based cohort study. Atherosclerosis 2015;243:93–8.

49. Fito M, Estruch R, Salas-Salvado J, et al. Effect of the Mediterranean diet on heart failure biomarkers: A randomized sample from the PREDIMED trial. Eur J Heart Fail 2014;16:543–50.

50. Papadaki A, Martinez-Gonzalez MA, Alonso-Gomez A, et al. Mediterranean diet and risk of heart failure: results from the PREDIMED randomized controlled trial. Eur J Heart Fail 2017;19: 1179–85.

51. Sotos-Prieto M, Bhupathiraju SN, Mattei J, et al. Association of changes in diet quality with total and cause-specific mortality. N Engl J Med 2017;377:143–53.

52. He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton P. Dietary sodium intake and incidence of congestive heart failure in overweight us men and women: First National Health and Nutrition Examination Survey epidemiologic follow-up. Arch Intern Med 2002;162:1619–24.

53. Whelton PK, Appel LJ, Sacco RL, et al. Sodium, blood pressure, and cardiovascular disease: further evidence supporting the American Heart Association sodium reduction recommendations. Circulation 2012;126:2880–9.

54. Graudal NA, Hubeck-Graudal T, Jurgens G. Effects of low-sodium diet vs. high-sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Cochrane review). Am J Hypertens 2012;25:1–15.

55. He FJ, MacGregor GA. Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials. Lancet 2011;378:380–2.

56. Cook NR, Appel LJ, Whelton PK. Lower levels of sodium intake and reduced cardiovascular risk. Circulation 2014;129:981–9.

57. Lindenfeld J, Albert NM, Boehmer JP, et al., for the Heart Failure Society of America. HFSA 2010 comprehensive heart failure practice guideline. J Card Fail 2010;16:e1–194.

58. Gupta DGV, Kalogeropoulos AP, et al. Dietary sodium intake in heart failure. Circulation 2012; 126:479–85.

59. Van HL, Yancy C. Diet prevention and therapy for heart failure? Circ Heart Fail 2013;6:1109–11.

60. Yancy CW. The uncertainty of sodium restriction in heart failure: we can do better than this. J Am Coll Cardiol HF 2016;4:39–41.

61. Mente A, O'Donnell MJ, Rangarajan S, et al., for the PURE Investigators. Association of urinary sodium and potassium excretion with blood pressure. N Engl J Med 2014;371:601–11.

62. Aliti GB, Rabelo ER, Clausell N, Rohde LE, Biolo A, Beck-da-Silva L. Aggressive fluid and sodium restriction in acute decompensated heart failure: a randomized clinical trial. JAMA Intern Med 2013;173:1058–64.

63. Paterna S, Parrinello G, Cannizzaro S, et al. Medium term effects of different dosage of diuretic, sodium, and fluid administration on neurohormonal and clinical outcome in patients with recently compensated heart failure. Am J Cardiol 2009;103:93–102.

64. Parrinello G, Di Pasquale P, Licata G, et al. Long-term effects of dietary sodium intake on cytokines and neurohormonal activation in patients with recently compensated congestive heart failure. J Card Fail 2009;15:864–73.

65. Doukky R, Avery E, Mangla A, et al. Impact of dietary sodium restriction on heart failure outcomes. J Am Coll Cardiol HF 2016;4:24–35.

66. Lennie TA SE, Wu JR, et al. Three gram sodium intake is associated with longer event-free survival only in patients with advanced heart failure. J Card Fail 2011;17:325–30.

67. Lemon SC OB, Magner R, et al. The dietary quality of persons with heart failure in NHANES 1999–2006. J Gen Intern Med 2010;25:135–40.

68. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63 25 Pt B:2960–84.

69. Rautiainen S, Levitan EB, Mittleman MA, Wolk A. Total antioxidant capacity of diet and risk of heart failure: A population-based prospective cohort of women. Am J Med 2013;126:494–500.

70. Carlsen MH, Halvorsen BL, Holte K, et al. The total antioxidant content of more than 3100 foods, beverages, spices, herbs and supplements used worldwide. Nutr J 2010;9:3.

71. Ripa S, Ripa R, Giustiniani S. Are failured cardiomyopathies a zinc-deficit related disease? A study on Zn and Cu in patients with chronic failured dilated and hypertrophic cardiomyopathies. Minerva Med 1998;89:397–403.

72. Saliba W, Fakih RE, Shaheen W. Heart failure secondary to selenium deficiency, reversible after supplementation. Int J Cardiol 2010;141:e26–7.

73. Folkers K WJ, Simonsen R, Morishita M, Vadhanavikit S. Biochemical rationale and the cardiac response of patients with muscle disease to therapy with coenzyme q10. Proc Natl Acad Sci U S A 1985;82:4513–6.

74. Sander S, Coleman CI, Patel AA, Kluger J, White CM. The impact of coenzyme q10 on systolic function in patients with chronic heart failure. J Card Fail 2006;12:464–72.

75. Molyneux SL, Florkowski CM, George PM, et al. Coenzyme q10: an independent predictor of mortality in chronic heart failure. J Am Coll Cardiol 2008;52:1435–41.

76. Fotino AD, Thompson-Paul AM, Bazzano LA. Effect of coenzyme q10 supplementation on heart failure: A meta-analysis. Am J Clin Nutr 2013;97:268–75.

77. Sharma A, Fonarow GC, Butler J, Ezekowitz JA, Felker GM. Coenzyme q10 for heart failure. Cochrane Database Syst Rev 2014;6:e002639.

78. Madmani ME, Yusuf Solaiman A, Tamr Agha K, et al. Coenzyme q10 for heart failure. Cochrane Database Syst Rev 2014:CD008684.

79. Rosenfeldt F, Hilton D, Pepe S, Krum H. Systematic review of effect of coenzyme q10 in physical exercise, hypertension and heart failure. Biofactors 2003;18:91–100.

80. Mortensen SA, Rosenfeldt F, Kumar A, et al. The effect of coenzyme q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. J Am Coll Cardiol HF 2014;2:641–9.

81. Soukoulis V, Dihu JB, Sole M, et al. Micronutrient deficiencies an unmet need in heart failure. J Am Coll Cardiol 2009;54:1660–73.

82. Iliceto S, Scrutinio D, Bruzzi P, et al. Effects of l-carnitine administration on left ventricular remodeling after acute anterior myocardial infarction: the l-Carnitine Ecocardiografia Digitalizzata Infarto Miocardico (CEDIM) trial. J Am Coll Cardiol 1995;26:380–7.

83. Anand IS, Francis G, Maseri A, Milazzotto F, Pepine CJ, Yusuf S. Study on propionyl-l-carnitine in chronic heart failure. Eur Heart J 1999;20:70–6.

84. Anand I, Chandrashekhan Y, De Giuli F, et al. Acute and chronic effects of propionyl-l-carnitine on the hemodynamics, exercise capacity, and hormones in patients with congestive heart failure. Cardiovasc Drugs Ther 1998;12:291–9.

85. Rizos I. Three-year survival of patients with heart failure caused by dilated cardiomyopathy and l-carnitine administration. Am Heart J 2000;139:S20–3.

86. Xu YJ, Arneja AS, Tappia PS, Dhalla NS. The potential health benefits of taurine in cardiovascular disease. Exp Clin Cardiol 2008;13:57–65.

87. Azuma J, Sawamura A, Awata N. Usefulness of taurine in chronic congestive heart failure and its prospective application. Jpn Circ J 1992;56:95–9.

88. Hanninen SA, Darling PB, Sole MJ, Barr A, Keith ME. The prevalence of thiamin deficiency in hospitalized patients with congestive heart failure. J Am Coll Cardiol 2006;47:354–61.

89. Shimon I, Almog S, Vered Z, et al. Improved left ventricular function after thiamine supplementation in patients with congestive heart failure receiving long-term furosemide therapy. Am J Med 1995;98:485–90.

90. Pfitzenmeyer P, Guilland JC, d'Athis P, Petit-Marnier C, Gaudet M. Thiamine status of elderly patients with cardiac failure including the effects of supplementation. Int J Vitam Nutr Res 1994;64:113–8.

91. Smithline H. Thiamine for the treatment of acute decompensated heart failure. Am J Emerg Med 2007;25:124–6.

92. Cui R, Iso H, Date C, Kikuchi S, Tamakoshi A. Dietary folate and vitamin B6 and B12 intake in relation to mortality from cardiovascular diseases: Japan Collaborative Cohort Study. Stroke 2010;41:1285–9.

93. Marti-Carvajal AJ, Solà I, Lathyris D, Salanti G. Homocysteine lowering interventions for preventing cardiovascular events. Cochrane Database Syst Rev 2009:CD006612.

94. Lonn E, Yusuf S, Arnold MJ, et al. Homocysteine lowering with folic acid and b vitamins in vascular disease. N Engl J Med 2006;354:1567–77.

95. Zittermann A, Schleithoff SS, Tenderich G, Berthold HK, Körfer R, Stehle P. Low vitamin D status: a contributing factor in the pathogenesis of congestive heart failure? J Am Coll Cardiol 2003;41:105–12.

96. Belen E, Tipi FF, Aykan AÇ, et al. Clinical staging in chronic heart failure associated with low vitamin D and elevated parathormone levels. Acta Cardiol 2014;69:665–71.

97. Dalbeni ASG, Degan M, Minuz P, Delva P. Effects of six months of vitamin D supplementation in patients with heart failure: a randomized double-blind controlled trial. Nutr Metab Cardiovasc Dis 2014;24:861–8.

98. Boxer RS, Hoit BD, Schmotzer BJ, Stefano GT, Gomes A, Negrea L. The effect of vitamin D on aldosterone and health status in patients with heart failure. J Card Fail 2014;20:334–42.

99. Amin A, Minaee S, Chitsazan M, Naderi N, Taghavi S, Ardeshiri M. Can vitamin D supplementation improve the severity of congestive heart failure? Congest Heart Fail 2013;19:E22–8.

100. Donneyong MM, Hornung CA, Taylor KC, et al. Risk of heart failure among postmenopausal women: a secondary analysis of the randomized trial of vitamin D plus calcium of the Women's Health Initiative. Circ Heart Fail 2015;8:49–56.

101. Bauersachs J, Widder JD. Endothelial dysfunction in heart failure. Pharmacol Rep 2008;60:119–26.

102. Lundberg JO, Feelisch M, Björne H, Jansson EA, Weitzberg E. Cardioprotective effects of vegetables: Is nitrate the answer? Nitric Oxide 2006;15:359–62.

103. McNally B, Griffin JL, Roberts LD. Dietary inorganic nitrate: from villain to hero in metabolic disease? Mol Nutr Food Res 2016;60:67–78.

104. Hord NG, Tang Y, Bryan NS. Food sources of nitrates and nitrites: the physiologic context for potential health benefits. Am J Clin Nutr 2009;90:1–10.

105. Dich J, Järvinen R, Knekt P, Penttilä PL. Dietary intakes of nitrate, nitrite and NDMA in the Finnish Mobile Clinic Health Examination Survey. Food Addit Contam 1996;13:541–52.

106. Raat NJ, Noguchi AC, Liu VB, et al. Dietary nitrate and nitrite modulate blood and organ nitrite and the cellular ischemic stress response. Free Radic Biol Med 2009;47:510–7.

107. Kapil V, Weitzberg E, Lundberg JO, Ahluwalia A. Clinical evidence demonstrating the utility of inorganic nitrate in cardiovascular health. Nitric Oxide 2014;38:45–57.

108. Zamani P, Rawat D, Shiva-Kumar P, et al. Effect of inorganic nitrate on exercise capacity in heart failure with preserved ejection fraction. Circulation 2015;131:371–80.

109. Eggebeen J, Kim-Shapiro DB, Haykowsky M, et al. One week of daily dosing with beetroot juice improves submaximal endurance and blood pressure in older patients with heart failure and preserved ejection fraction. J Am Coll Cardiol HF 2016;4:428–37.

110. Yang T, Peleli M, Zollbrecht C, et al. Inorganic nitrite attenuates NADPH oxidase-derived superoxide generation in activated macrophages via a nitric oxide-dependent mechanism. Free Radic Biol Med 2015;83:159–66.

111. Roberts LD, Ashmore T, Kotwica AO, et al. Inorganic nitrate promotes the browning of white adipose tissue through the nitrate-nitrite-nitric oxide pathway. Diabetes 2015;64:471–84.

112. Hirai DM, Zelt JT, Jones JH, et al. Dietary nitrate supplementation and exercise tolerance in patients with heart failure with reduced ejection fraction. Am J Physiol Regul Integr Comp Physiol 2017;312:R13–22.

113. Borlaug BA. Inorganic nitrite delivery to improve exercise capacity in heart failure with preserved ejection fraction: The Indie Trial. Paper presented at: American College of Cardiology's 67th Annual Scientific Sessions; March 11, 2018; Orlando, FL.

114. Agha G, Loucks EB, Tinker LF, et al. Healthy lifestyle and decreasing risk of heart failure in women: The Women's Health Initiative observational study. J Am Coll Cardiol 2014;64:1777–85.

115. Florido R, Ndumele CE, Kwak L, et al. Physical activity, obesity, and subclinical myocardial damage. J Am Coll Cardiol HF 2017;5:377–84.

116. Farrell SW, Finley CE, Radford NB, Haskell WL. Cardiorespiratory fitness, body mass index, and heart failure mortality in men: Cooper Center Longitudinal Study. Circ Heart Fail 2013;6:898–905.

117. Kraigher-Krainer E, Lyass A, Massaro JM, et al. Association of physical activity and heart failure with preserved vs. reduced ejection fraction in the elderly: The Framingham Heart Study. Eur J Heart Fail 2013;15:742–6.

118. Pandey A, Allen NB, Ayers C, et al. Fitness in young adulthood and long-term cardiac structure and function: The CARDIA study. J Am Coll Cardiol HF 2017;5:347–55.

119. Koo P, Gjelsvik A, Choudhary G, et al. Prospective association of physical activity and heart failure hospitalizations among black adults with normal ejection fraction: The Jackson Heart Study. J Am Heart Assoc 2017;6:e006107.

120. Rahman I, Bellavia A, Wolk A, Orsini N. Physical activity and heart failure risk in a prospective study of men. J Am Coll Cardiol HF 2015;3:681–7.

121. Howden EJ, Sarma S, Lawley JS, et al. Reversing the cardiac effects of sedentary aging in middle age-a randomized controlled trial: implications for heart failure prevention. Circulation 2018;137:1549–60.

122. United States Department of Health and Human Services. 2008 physical activity guidelines for Americans. [serial online]. October 2008. Available at: https://health.gov/paguidelines/pdf/paguide.pdf. Accessed October 27, 2017.

123. O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. JAMA 2009;301:1439–50.

124. Pina IL, Bittner V, Clare RM, et al. Effects of exercise training on outcomes in women with heart failure: Analysis of HF-ACTION (Heart Failure-A Controlled Trial Investigating Outcomes Of Exercise Training) by sex. J Am Coll Cardiol HF 2014;2:180–6.

125. Mentz RJ, Bittner V, Schulte PJ, et al. Race, exercise training, and outcomes in chronic heart failure: findings from Heart Failure-A Controlled Trial Investigating Outcomes In Exercise Training (HF-ACTION). Am Heart J 2013;166:488–95.

126. Kitzman DW, Brubaker P, Morgan T, et al. Effect of caloric restriction or aerobic exercise training on peak oxygen consumption and quality of life in obese older patients with heart failure with preserved ejection fraction: a randomized clinical trial. JAMA 2016;315:36–46.

127. Pandey A, Parashar A, Kumbhani D, et al. Exercise training in patients with heart failure and preserved ejection fraction: meta-analysis of randomized control trials. Circ Heart Fail 2015;8:33–40.

128. Edelmann F, Gelbrich G, Dungen HD, et al. Exercise training improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction: Results of the EX-DHF (Exercise Training in Diastolic Heart Failure) pilot study. J Am Coll Cardiol 2011;58:1780–91.

129. Pandey A, Berry JD. Physical activity in heart failure with preserved ejection fraction: Moving toward a newer treatment paradigm. Circulation 2017;136:993–5.

130. Pandey A, Garg S, Khunger M, et al. Dose-response relationship between physical activity and risk of heart failure: a meta-analysis. Circulation 2015;132:1786–94.

131. Klompstra L, Jaarsma T, Stromberg A. Exergaming to increase the exercise capacity and daily physical activity in heart failure patients: a pilot study. BMC Geriatr 2014;14:119.

132. US Department of Health & Human Services. Mind-body medicine practices in complementary and alternative medicine [serial online]. March 2013. Available at: https://report.nih.gov/NIHfactsheets/ViewFactSheet.aspx?csid=102. Accessed October 27, 2017.

133. Metin ZG, Ejem D, Dionne-Odom JN, et al. Mind-body interventions for individuals with heart failure: a systematic review of randomized trials. J Card Fail 2018;24:186–201.

134. Gaiswinkler L, Unterrainer H. The relationship between yoga involvement, mindfulness and psychological well-being. Complement Ther Med 2016;26:123–7.

135. Krishna BH, Pal P, Pal G, et al. Effect of yoga therapy on heart rate, blood pressure and cardiac autonomic function in heart failure. J Clin Diagn Res 2014;8:14–6.

136. Manchanda S, Narang R, Reddy K, et al. Retardation of coronary atherosclerosis with yoga lifestyle intervention. J Assoc Physicians India 2000;48:687–94.

137. Pullen PR, Nagamia SH, Mehta PK, et al. Effects of yoga on inflammation and exercise capacity in patients with chronic heart failure. J Card Fail 2008;14:407–13.

138. Manchanda S, Mehrotra U, Makhija A, Mohanty A, Dhawan S, Sawhney J. Reversal of early atherosclerosis in metabolic syndrome by yoga-a randomized controlled trial. J Yoga Phys Ther 2013;3:132.

139. Pal A, Srivastava N, Narain V, Agrawal G, Rani M. Effect of yogic intervention on the autonomic nervous system in the patients with coronary artery disease: a randomized controlled trial. East Mediterr Health J 2013;19:452–8.

140. Gomes-Neto M, Rodrigues ES Jr., Silva WM Jr., Carvalho VO. Effects of yoga in patients with chronic heart failure: a meta-analysis. Arq Bras Cardiol 2014;103:433–9.

141. Cramer H, Lauche R, Haller H, Dobos G, Michalsen A. A systematic review of yoga for heart disease. Eur J Prev Cardiol 2015;22:284–95.

142. Wallace RK. Physiological effects of transcendental meditation. Science 1970;167:1751–4.

143. Schneider RH, Alexander CN, Staggers F, et al. Long-term effects of stress reduction on mortality in persons ≥ 55 years of age with systemic hypertension. Am J Cardiol 2005;95:1060–4.

144. Barnes VA, Treiber FA, Davis H. Impact of transcendental meditation® on cardiovascular function at rest and during acute stress in adolescents with high normal blood pressure. J Psychosom Res 2001;51:597–605.

145. Paul-Labrador M, Polk D, Dwyer JH, et al. Effects of a randomized controlled trial of transcendental meditation on components of the metabolic syndrome in subjects with coronary heart disease. Arch Intern Med 2006;166:1218–24.

146. Jayadevappa R, Johnson JC, Bloom BS, et al. Effectiveness of transcendental meditation on functional capacity and quality of life of African Americans with congestive heart failure: a randomized control study. Ethn Dis 2007;17:72–7.

147. Curiati JA, Bocchi E, Freire JO, et al. Meditation reduces sympathetic activation and improves the quality of life in elderly patients with optimally treated heart failure: a prospective randomized study. J Altern Complement Med 2005;11:465–72.

148. Sullivan MJ, Wood L, Terry J, et al. The support, education, and research in chronic heart failure study (search): a mindfulness-based psychoeducational intervention improves depression and clinical symptoms in patients with chronic heart failure. Am Heart J 2009;157:84–90.

149. Levine GN, Lange RA, Bairey-Merz CN, et al. Meditation and cardiovascular risk reduction: A scientific statement from the American Heart Association. J Am Heart Assoc 2017;6:e002218.

150. Hartley L, Dyakova M, Holmes J, et al. Yoga for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev 2014:CD010072.

151. Yeh GY, Wood MJ, Lorell BH, et al. Effects of tai chi mind-body movement therapy on functional status and exercise capacity in patients with chronic heart failure: a randomized controlled trial. Am J Med 2004;117:541–8.

152. Yeh GY, McCarthy EP, Wayne PM, et al. Tai chi exercise in patients with chronic heart failure: A randomized clinical trial. Arch Intern Med 2011;171:750–7.

153. Kemper KJ, Carmin C, Mehta B, Binkley P. Integrative medical care plus mindfulness training for patients with congestive heart failure: Proof of concept. J Evid Based Complementary Altern Med 2016;21:282–90.

154. Yeh GY, Wood MJ, Wayne PM, et al. Tai chi in patients with heart failure with preserved ejection fraction. Congest Heart Fail 2013;19:77–84.

155. Alharbi M, Straiton N, Gallagher R. Harnessing the potential of wearable activity trackers for heart failure self-care. Curr Heart Fail Rep 2017;14:23–9.

156. Nundy S, Razi RR, Dick JJ, et al. A text messaging intervention to improve heart failure self-management after hospital discharge in a largely African-American population: before-after study. J Med Internet Res 2013;15:e53.

157. McCall DO, McGartland CP, McKinley MC, et al. Dietary intake of fruits and vegetables improves microvascular function in hypertensive subjects in a dose-dependent manner. Circulation 2009;119:2153–60.

158. Dod HS, Bhardwaj R, Sajja V, et al. Effect of intensive lifestyle changes on endothelial function and on inflammatory markers of atherosclerosis. Am J Cardiol 2010;105:362–7.

159. Appel LJ, Moore TJ, Obarzanek E, et al., for the DASH Collaborative Research Group. A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med 1997;336:1117–24.

160. Le LT, Sabate J. Beyond meatless, the health effects of vegan diets: findings from the ADVENTIST cohorts. Nutrients 2014;6:2131–47.

161. Chin JH, Azhar S, Hoffman BB. Inactivation of endothelial derived relaxing factor by oxidized lipoproteins. J Clin Invest 1992;89:10–8.

162. Celermajer DS, Sorensen KE, Gooch VM, et al. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet 1992;340:1111–5.

163. Marti CN, Gheorghiade M, Kalogeropoulos AP, Georgiopoulou VV, Quyyumi AA, Butler J. Endothelial dysfunction, arterial stiffness, and heart failure. J Am Coll Cardiol 2012;60:1455–69.

164. Lu SC, Wu WH, Lee CA, Chou HF, Lee HR, Huang PC. LDL of Taiwanese vegetarians are less oxidizable than those of omnivores. J Nutr 2000;130:1591–6.

165. Banerjee D, Biggs ML, Mercer L, et al. Insulin resistance and risk of incident heart failure: Cardiovascular Health Study. Circ Heart Fail 2013;6:364–70.

166. Vardeny O, Gupta DK, Claggett B, et al. Insulin resistance and incident heart failure: the ARIC study (Atherosclerosis Risk In Communities). J Am Coll Cardiol HF 2013;1:531–6.

167. Tonstad S, Butler T, Yan R, Fraser GE. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. Diabetes Care 2009;32:791–6.

168. Salas-Salvadó J, Bulló M, Babio N, et al. Reduction in the incidence of type 2 diabetes with the Mediterranean diet. Diabetes Care 2011;34:14–9.

169. Anker SD, von Haehling S. Inflammatory mediators in chronic heart failure: an overview. Heart 2004;90:464–70.

170. Watzl B. Anti-inflammatory effects of plant-based foods and of their constituents. Int J Vitam Nutr Res 2008;78:293–8.

171. Turner-McGrievy GM, Wirth MD, Shivappa N, et al. Randomization to plant-based dietary approaches leads to larger short-term improvements in dietary inflammatory index scores and macronutrient intake compared with diets that contain meat. Nutr Res 2015;35:97–106.

172. Eichelmann F, Schwingshackl L, Fedirko V, Aleksandrova K. Effect of plant-based diets on obesity-related inflammatory profiles: a systematic review and meta-analysis of intervention trials. Obes Rev 2016;17:1067–79.

173. Chai W, Morimoto Y, Cooney RV, et al. Dietary red and processed meat intake and markers of adiposity and inflammation: the Multiethnic Cohort Study. J Am Coll Nutr 2017;36:378–85.

174. Azadbakht L, Esmaillzadeh A. Red meat intake is associated with metabolic syndrome and the plasma c-reactive protein concentration in women. J Nutr 2009;139:335–9.

175. Estruch R. Anti-inflammatory effects of the Mediterranean diet: the experience of the PREDIMED study. Proc Nutr Soc 2010;69:333–40.

176. Liu P, Sun M, Sader S. Matrix metalloproteinases in cardiovascular disease. Can J Cardiol 2006;22:25B–30B.

177. Gunasinghe SK, Ikonomidis J, Spinale FG. Contributory role of matrix metalloproteinases in cardiovascular remodeling. Curr Drug Targets Cardiovasc Haematol Disord 2001;1:75–91.

178. Navarro JA, de Gouveia LA, Rocha-Penha L, et al. Reduced levels of potential circulating biomarkers of cardiovascular diseases in apparently healthy vegetarian men. Clinica Chimica Acta 2016;461:110–3.

179. Munzel T, Gori T, Keaney JF Jr., Maack C, Daiber A. Pathophysiological role of oxidative stress in systolic and diastolic heart failure and its therapeutic implications. Eur Heart J 2015;36:2555–64.

180. Belch JJ, Bridges AB, Scott N, Chopra M. Oxygen free radicals and congestive heart failure. Br Heart J 1991;65:245–8.

181. Asemi Z, Samimi M, Tabassi Z, Shakeri H, Sabihi SS, Esmaillzadeh A. Effects of DASH diet on lipid profiles and biomarkers of oxidative stress in overweight and obese women with polycystic ovary syndrome: a randomized clinical trial. Nutrition 2014;30:1287–93.

182. Zamora-Ros R, Serafini M, Estruch R, et al. Mediterranean diet and non enzymatic antioxidant capacity in the PREDIMED study: evidence for a mechanism of antioxidant tuning. Nutr Metab Cardiovasc Dis 2013;23:1167–74.

183. Nicholls SJ, Hazen SL. Myeloperoxidase and cardiovascular disease. Arterioscler Thromb Vasc Biol 2005;25:1102–11.

184. Koeth RA, Wang Z, Levison BS, et al. Intestinal microbiota metabolism of l-carnitine, a nutrient in red meat, promotes atherosclerosis. Nat Med 2013;19:576–85.

185. Chen ML, Zhu XH, Ran L, Lang HD, Yi L, Mi MT. Trimethylamine-n-oxide induces vascular inflammation by activating the nlrp3 inflammasome through the sirt3-sod2-mtros signaling pathway. J Am Heart Assoc 2017;6:e006347.

186. Tang WH, Wang Z, Fan Y, et al. Prognostic value of elevated levels of intestinal microbe-generated metabolite trimethylamine-n-oxide in patients with heart failure: refining the gut hypothesis. J Am Coll Cardiol 2014;64:1908–14.

187. Troseid M, Ueland T, Hov JR, et al. Microbiota-dependent metabolite trimethylamine-n-oxide is associated with disease severity and survival of patients with chronic heart failure. J Intern Med 2015;277:717–26.

188. Tuso P, Stoll SR, Li WW. A plant-based diet, atherogenesis, and coronary artery disease prevention. Perm J 2015;19:62–7.

KEY WORDS coenzyme Q10, congestive heart failure, diet, diuretics, exercise, lifestyle, meditation, nitrates, nutrition, obesity, risk modification, sodium, supplements, weight management, yoga

Go to http://www.acc.org/jacc-journals-cme to take the CME/MOC/ECME quiz for this article.