Current Heart Failure Reports (2018) 15:131–140
https://doi.org/10.1007/s11897-018-0388-6

PHARMACOLOGIC THERAPY (W.H.W. TANG, SECTION EDITOR)

Nutritional Interventions in Heart Failure: Challenges and Opportunities

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Published online: 6 April 2018

Abstract

Purpose of Review There is a growing body of evidence that nutritional factors influence the incidence of heart failure (HF). The current manuscript aims to collate evidence relating to nutritional intervention in the treatment of HF as well as to provide context regarding challenges and opportunities in the field.

Recent Findings Despite the accepted importance of nutritional factors relating to cardiovascular disease severity, there is surprisingly little human intervention research regarding dietary intake and HF. Further, existing nutritional interventions in HF were mostly pilot studies with small samples and short follow-up.

Summary There is consistent evidence that nutritional factors majorly influence HF. Despite limited research, there is evidence that nutritional modification can rapidly and profoundly influence multiple aspects of HF. There is an urgent need for well-conducted research to ascertain if nutritional modification can alter the long-term course of HF.

Keywords Nutrition · Diet · Food · Intervention · Heart failure

Abbreviations

CVD	Cardiovascular disease
CVEs	Cardiovascular events
DART	Diet And Reinfarction Trial
DASH	Dietary Approaches to Stop Hypertension
DASH-DHF	DASH-Diastolic Heart Failure
HF	Heart failure
MedDiet	Mediterranean diet
MI	Myocardial infarction
PREDIMED	Prevención con Dieta Mediterránea

Introduction

Heart failure (HF) is a leading and increasing cause of hospitalization, morbidity, and mortality worldwide. Medical advances have improved HF survival, yet mortality rates remain high. Therefore, feasible and cost-effective interventions to help prevent and treat HF are crucial.

This article is part of the Topical Collection on *Pharmacologic Therapy*

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The majority of HF research to date has focused on pharmacology and devices. The potential of nutritional intervention has received little attention, and therefore the role of nutritional factors in the pathogenesis and treatment of HF remains underexplored and underappreciated [1–3]. Guidelines regarding nutrition in HF are modest and unspecific with a focus on restriction of sodium (salt) and fluid. However, specific dietary patterns may have superior effects. Being relatively cheap and safe, nutritional modification represents an attractive strategy to prevent and treat HF.

Nutrition and Heart Failure

Multiple metabolic derangements (obesity, dyslipidemia, insulin resistance, systemic inflammation) and certain pathologies (hypertension, diabetes) are associated with HF incidence/severity. Nutritional factors are major contributors to these risk factors and to cardiovascular disease (CVD) itself. There is robust evidence from several landmark trials that nutritional intake has a profound influence on CVD including Diet And Reinfarction Trial (DART) [4], Dietary Approaches to Stop Hypertension (DASH) [5], and Prevención con Dieta Mediterránea (PREDIMED) [6•].

Specific to HF, several epidemiological studies have demonstrated marked reductions (45–81%) in HF incidence with adherence to a healthy lifestyle (regular physical activity,

healthy dietary pattern, normal body mass index, no/moderate alcohol, not smoking) incidence [7–15]. Although these large studies are consistent, they are limited by observational nature. Further, the inclusion of several lifestyle factors means the specific effect of nutrition cannot be elucidated.

However, there is observational evidence specifically relating to a number of dietary patterns or scores and HF (Table 1). Healthy dietary patterns have been associated with improved cardiac function and decreased HF incidence in healthy adults [12, 18, 23] including males [19, 24•] and females [16, 20, 25] as well as in those with pre-existing CVD [17, 26] including atrial fibrillation [27•] and diabetes [17]. Further, a beneficial and synergistic effect regarding primary prevention of HF has been observed in those receiving proven medications (ACE inhibitors or angiotensin II receptor antagonists) [17, 29].

Interestingly, observational studies suggest a dose-response relationship whereby greater adherence to healthy behaviors [7–15], dietary patterns [23, 24•, 25, 27•], or specific dietary components [30–32] displays a graded relationship towards HF incidence. Further, separate systematic reviews and meta-analysis reported decreased CVD, and particularly decreased HF, associated with adherence to either DASH [33] or Mediterranean diet [34•]. These reviews suggest that the profound effect of nutrition in non-HF CVD may be present in HF and may even be magnified. Finally, additional observational evidence among those with pre-existing HF suggests a protective association between a healthy DASH/Mediterranean diet pattern and improved cardiac function [28] and even decreased mortality [21••, 24•].

Nutritional Interventions in Heart Failure

Despite the accepted importance of nutritional factors relating to CVD regression or progression, there is surprisingly little human intervention research regarding dietary intake and HF. In the context of the suggestive effect of nutritional intervention for HF prevention/treatment, it is puzzling that nutritional modification has not been explored further to date. Nutritional interventions specific to HF are detailed briefly below as well as in Table 2.

The Rice Diet

One of the first documented nutritional interventions for HF was from Dr. Walter Kempner at Duke University and his "Rice Diet" from the 1940s [35]. The protocol consisted of white rice, sugar, fruit, fruit juices, and supplemental vitamins and iron, providing ~2000 cal, 20 g protein, 2–3% fat, 1000 ml liquid, and 150–250 mg sodium daily. Blood pressure

Table 1 Observational nutrition research specific to HF

Diet	Description	Adherence associated with:	References
Alternative Healthy Eating Index	A 9-component index including vegetables, fruit nuts and soy protein, cereal fiber, multivitamin use, low in trans-fat and alcohol, and high ratios of polyunsaturated to saturated fatty acids and of white to red meat	-Decreased HF risk	[12, 16, 17]
Dietary Approaches to Stop Hypertension (DASH)	Plant-based diet, rich in carbohydrates, and low fat that emphasizes consumption of fruits, vegetables, whole grains, and nuts with addition of some fish, poultry, and low-fat dairy products and minimization of red meat, sugar, and processed foods	-Favorable heart function -Decreased HF risk -Decreased mortality	[18–20, 21••]
Dietary inflammatory index	Developed to characterize dietary intake from maximally anti- to pro-inflammatory	-Decreased HF risk	[22]
Dietary modification index	Based on percentage of total energy intake from fat, vegetables, and fruit servings, grain servings, percentage of energy intake from saturated fat, percentage of energy intake from trans-fat and dietary cholesterol intake	-Decreased HF risk	[16]
Dietary risk score	Based on food items that are considered predictive (meat, salty snacks, and fried foods) or protective (fruits and green leafy vegetables, other cooked vegetables, and other raw vegetables) of CVD	-Decreased HF risk	[17]
Mediterranean diet	Plant-based, carbohydrate-rich, moderate-fat diet characterized by high intake of vegetables, fruits, whole grains, and nuts with a moderate intake of extra virgin olive oil (EVOO), fish, and sometimes wine and a low intake of dairy products, poultry, processed meat, red meat, sugar, and processed foods	-Favorable heart function -Decreased cardiac remodeling -Decreased CVD events -Decreased HF risk -Decreased HF mortality	[23, 24•, 25, 26, 27•, 28]

Table 2 Nutrition intervention research specific to HF

Diet	Subjects	Randomized	Blinded?	Controlled?	Duration	Weight loss	Effect	Comment	Ref
Rice Diet	?	N	N	N	?	Y	Marked and rapid improvements in BP and related symptoms	Profound reported effect but outdated evidence, potentially difficult to adhere to	[35]
MedDiet	202 first MI survivors	?	?	Y—usual-care group, matched for age, gender, presence of DM/HTN. MI type/treatment	46 months	?	better primary outcome-free survival (84%) than usual-care controls (60%)	Diet was low in saturated fat and cholesterol with or without addition of omega-3	[36]
DASH diet	13 primarily obese, postmenopausal women with HFpEF	N	N	N	21d	Y—mean weight loss of 1.7 kg	Significant improvement in biomarkers and in cardiac function with trend towards increased exercise capacity	All foods were prepared and served under observation by dietitians in a metabolic kitchen	[37, 38••, 39]
DASH diet	48 patients with mild-moderate HF	Y	N	Y—general HF recommendations	12 weeks	N	Significant improvements in biomarkers, cardiac function, exercise capacity, and QoL	–	[40••]
Low-carbohydrate diet - high-protein, restricted energy diet	14 overweight/obese subjects with mild-moderate HF and DM	?	N	Y—standard protein, restricted energy diet or a normocaloric AHA diet	12 weeks	Y	Significantly greater reductions in total/LDL cholesterol and TAG as well greater improvements in exercise capacity, HDL, and QoL and a trend towards increased muscle mass	High-protein groups were encouraged to increase plant protein as opposed to animal protein	[41]
Low-carbohydrate diet - NNR diet to a high-protein "Paleo" diet	68 overweight postmenopausal women	Y	N	Y—standard protein, restricted energy diet or a normocaloric AHA diet	2 years	Y (NS)	Decreases in LVM and end-diastolic volume in both high-protein groups	There was weight loss despite diets being ad libitum (i.e., no energy restriction). However, apparent beneficial effect accompanied by decreased SV and CO	[42]
Low-carbohydrate diet	88 HF patients	Y	Y—single-blind	Y—standard diet	2 months	?	Significant improvement in arterial oxygen saturation	Deterioration in arterial oxygen saturation in the standard diet group	[43••]
Low-fat, plant based diet	Case report of a 79-year-old male with documented triple vessel disease (80–95% stenosis) and (EJ = 35%) with progressive dyspnea	N	N	N	2 months	Y	Improved cardiac biomarkers, exercise tolerance, and ejection fraction (+ 15%)	–	[44•]

AHA, American Heart Association; *CO*, cardiac output; *DM*, diabetes mellitus; *EJ*, ejection fraction; *LVEF*, left ventricular ejection fraction; *LVM*, left ventricular mass; *LVSD*, left ventricular systolic dysfunction; *NNR*, Nordic Nutrition Recommendation; *NS*, non-significant; *QoL*, quality of life; *SV*, stroke volume; *TAG*, triglycerides

and related symptoms reportedly improved markedly and rapidly. A 1949 editorial in the *New England Journal of Medicine* stated "results are little short of miraculous…practically speaking, there is probably no more effective diet for obese decompensated cardiac patients" [45]. Although there has been no original research regarding the Rice Diet since 1975 [46], two articles recounted this interesting concept in 2014 [47, 48].

Mediterranean Diet

The traditional Mediterranean diet (MedDiet) is a plant-based, carbohydrate-rich, moderate-fat diet characterized by high intake of vegetables, fruits, whole grains, and nuts with a moderate intake of extra virgin olive oil, fish, and sometimes wine, and a low intake of dairy products, poultry, processed meat, red meat, sugar, and processed foods. There is observational evidence that MedDiet is associated with benefit regarding HF (Table 1). In fact, a 2016 systematic review and meta-analysis involving 10,950 participants comparing randomized controlled trials of Mediterranean to control diets suggested a 70% reduction in HF incidence with MedDiet [34•].

One of the first reports of nutrition and HF in "modern literature" comes from the seminal Lyon Diet Heart Study. This randomized, single-blind trial tested the hypothesis that a MedDiet might reduce CVD complications compared to usual care + usual diet among myocardial infarction (MI) survivors. After 27 months, there were eight cases of non-fatal HF in 303 subjects in the usual-care group (1.35%), while there were two cases in 302 subjects following a MedDiet (0.33%) [49]. Follow-up at 46 months demonstrated that MedDiet significantly reduced the risk of a composite endpoint (including HF) by 67% ($p = 0.0001$) [29].

PREDIMED is a large randomized, controlled trial ($N = 7403$) to assess the impact of MedDiet with the addition of either additional virgin olive oil or nuts compared to low-moderate-fat diet among adults at high risk of CVD. Preliminary analysis reported decreased plasma NT-proBNP and oxidized LDL as well as prevention of lipoprotein(a) increase [50•]. However, there is only a single randomized, controlled trial assessing MedDiet and HF outcome. A 2008 controlled trial among subjects after a first MI demonstrated significantly increased survival at follow-up (84%) compared to usual care (60%) with a low saturated fat (≤ 7% calories) and low dietary cholesterol (≤ 200 mg/day) MedDiet [36].

Dietary Approaches to Stop Hypertension Diet

Similar to MedDiet, Dietary Approaches to Stop Hypertension (DASH) is a plant-based, carbohydrate-rich diet, characterized by high intake of vegetables, fruits, whole grains, and nuts with addition of some fish, poultry, and low-fat dairy products and minimization of processed/red meat, sugar, and processed foods. The DASH diet was designed to prevent and treat hypertension [5, 51]. Based on early studies of lower blood pressure in vegetarians, "the diet design goals were to create patterns that would have the blood pressure lowering benefits of a vegetarian diet, yet contain enough animal products to make them palatable to non-vegetarians" [51]. There is also observational evidence that DASH is associated with benefit regarding HF (Table 1). In fact, a 2013 systematic review and meta-analysis of observational prospective studies including > 144,000 adults reported that a DASH-like diet was associated with significant reductions in CVD incidence, including coronary heart disease and stroke (19 to 21%), but the greatest risk reduction was for HF (29%) [33].

Interventional evidence regarding the DASH diet and HF comes from the pilot, DASH-Diastolic Heart Failure (DASH-DHF) trial. DASH-DHF was a non-blinded, non-randomized, and non-controlled pilot study conducted among 13 primarily obese, postmenopausal women with HFpEF which led to three publications. Importantly, all foods were prepared and served under observation by dietitians in a metabolic kitchen to increase dietary compliance. There was a mean weight loss of 1.7 kg after 3 weeks which was accompanied by decreases in biomarkers (urinary sodium, BNP, and oxidative stress), dyspnea, 24-h blood pressure, arterial elastance, viscoelastic/relaxation, and chamber stiffness. In tandem, there were increases in stroke volume, ejection fraction, and cardiac contractility as well as alternate biomarkers (24-h urinary potassium and aldosterone) and a trend towards increased exercise capacity [37, 38••]. A third publication reported increases in short-chain acyl carnitines which correlated with improved left ventricular function [39] suggesting improved myocardial energy utilization. A separate, more recent randomized, controlled trial compared DASH to general HF recommendations in 48 patients with mild-moderate HF. Despite no weight loss after 12 weeks, there were significant increases in large artery elasticity, exercise capacity, and quality of life as well as a significant decrease in BNP [40••]. A limitation of both trials is the lack of investigator blinding.

Low-Carbohydrate Diets

Low-carbohydrate diets (e.g., Atkins, ketogenic) emphasize a combination of high-fat (e.g., butter, oils) and high-protein foods (e.g., meats, egg) with the addition of small amounts of non-starchy fruit and vegetables (e.g., avocado). This type of approach has gained popularity with the public and for select clinical conditions. Preliminary evidence suggests that low-carbohydrate diets may improve pre-HF metabolic derangements (obesity, dyslipidemia, insulin resistance, systemic inflammation). A 2017 review article suggested that weight loss either through energy restriction or through a low-

carbohydrate diet would improve glucose and lipid metabolism in HF, potentially providing clinical benefit [52].

There are three interventional trials which have utilized different low-carbohydrate diets in HF. The earliest comprised a small, three-arm trial comparing 12 weeks of high-protein, restricted energy diet to a standard protein, restricted energy diet or a normocaloric American Heart Association recommended diet among 14 overweight/obese subjects with mild-moderate HF and diabetes. There were significantly greater reductions in weight, body fat, total/LDL cholesterol, and triglycerides as well as significantly greater improvements in exercise capacity, HDL, and quality of life and a trend towards increased muscle mass with the higher protein diet [41]. Interestingly, patients in the high-protein group were encouraged to increase plant protein as opposed to animal protein. A subsequent randomized trial compared high-protein Nordic Nutrition Recommendation diet to a high-protein "Paleo" diet (both ad libitum) in 68 overweight postmenopausal women. After 2 years, there were non-significant decreases in weight but significant decreases in left ventricular mass and end-diastolic volume in both high-protein groups. However, this trial also reported a decrease in both stroke volume and cardiac output [42]. Again, a limitation of both trials is the lack of investigator blinding. A more recent single-blind, randomized controlled clinical trial assigned 88 HF patients to a low-carbohydrate or standard diet. After 2 months, there was an improvement in arterial oxygen saturation in the low-carbohydrate group and a deterioration in the standard-diet group [43••]. However, there was no effect on BP or handgrip strength. Importantly, there was a clinically significant weight loss of 5.9 kg in the low-carbohydrate group (2.3 kg as water) with weight gain of 2.6 kg in the standard diet group but this was no statistically significant [43••].

Low-Fat Diets

Low-fat diets advise the limitation of high-fat foods (e.g., butter) with the liberal consumption of low-fat products (e.g., whole grains) and remain the cornerstone of CVD dietary advice. There is interventional evidence from randomized, controlled trials that low-fat diets lead to weight loss and improved cardiac biomarkers as well as reductions in cardiovascular events (CVEs), including HF incidence, and total mortality [36, 53]. Additional controlled trials utilized a low-fat, plant-based diet (emphasizing fruits, vegetables, whole grains, legumes) with exercise and stress management in subjects with coronary artery disease or multiple risk factors. After only 24 days, there were significant increases in exercise capacity and left ventricular ejection fraction as well as significant decreases in total cholesterol and angina frequency compared to usual care [54]. These preliminary findings were reaffirmed in longer trials of 3 months and 3 years which demonstrated decreases in body mass index, body fat, total/LDL, inflammation (CRP), apolipoprotein B, blood pressure, resting heart rate, frequency/severity of physical limitation, CVEs, and revascularization in conjunction with increased exercise capacity and quality of life [55–57]. To date, low-fat diets have not been subjected to a trial specifically regarding HF outcome. However, a recent 2-month, case study demonstrating a marked improvement with a low-fat, plant-based 269 diet is detailed in Table 2.

Non-specific Trials Relating to Nutrition Knowledge

Additionally, there have been several randomized, controlled trials which focused on educational interventions to improve nutritional knowledge and compliance with dietary recommendations in HF. These trials noted increased nutritional knowledge, higher compliance with dietary guidelines, increased exercise tolerance [58], and even decreased HF hospitalization/death [59]. These educational trials are important because they suggest that simply improving the nutrition knowledge of HF patients may have broad clinical benefit.

Summary of Nutrition Interventions

There is consistent evidence that nutritional factors majorly influence HF incidence and severity. There is surprisingly little human intervention research regarding nutritional intake and HF. Nevertheless, there is evidence that nutritional modification can rapidly and profoundly influence multiple aspects of HF.

Perhaps the greatest benefit of nutritional modification regarding secondary prevention of HF has been demonstrated by the Rice Diet, but this evidence is limited by its historical nature. There is preliminary yet interesting evidence relating to both low-carbohydrate diets and low-fat diets (particularly plant-based). However, perhaps the most consistent evidence relates to MedDiet and DASH diets. This evidence is limited by its largely observational nature and focus on primary prevention. However, there is a single randomized, controlled trial of MedDiet compared to usual care among 202 MI survivors. After 46-month follow-up, there was significantly improved primary outcome-free survival in the intervention group (84%) than in the usual-care controls (60%). Similarly, there are only two intervention studies to date regarding the DASH diet: one small ($n = 13$) uncontrolled and unblinded feeding trial lasting 3 weeks [37, 38••, 39] and one small ($n = 48$) randomized, controlled trial lasting 12 weeks [40••]. Nevertheless, DASH has been called "an optimal dietary plan for symptomatic HF" [60]. Further, the DASH diet was formally adopted into the 2013 AHA/ACC CVD risk prevention guidelines (strong recommendation: 2013: level 1A) [61]. Ultimately, the lack of large-scale, well-designed human intervention

research regarding nutrition and HF brings many challenges but also opportunities.

Challenges

Challenges Relating to Interventional Nutrition Research

Nutrition is a powerful tool to modulate CVD incidence and outcome. However, research regarding interventional nutrition brings several challenges. Nutritional science has historically used a reductionist approach, focusing on single foods or nutrients. However, humans eat foods, not nutrients, and foods are consumed as part of an overall dietary pattern. Dietary patterns involve complex relationships between components of dietary intake, not just a single nutrient or foods. As such, overall diet assessment represents a broad picture of food and nutrient consumption and has been suggested to be more predictive of disease risk than individual foods/nutrients [62]. The gold standards for human intervention research are double-blind, randomized, placebo-controlled trials. Although it may be possible to conduct such research regarding a new drug or vitamin pill, it is impossible to double-blind a full nutrition intervention. For example, if a subject is asked to consume a Mediterranean diet, they will be aware and hence not blinded!. In contrast, it is possible for investigators to remain blinded, although this is not always utilized [35, 37, 38••, 39, 40••, 41, 42, 44•].

Nutritional trials should preferably be randomized and include a control group. It is important to select an appropriate control intervention. Usual care or standard dietary recommendations appear suitable for use as a control intervention. Importantly, randomization to a specific nutrition intervention does not ensure compliance, i.e., being asked to consume a Mediterranean does not mean the subject will actually eat a Mediterranean diet. For example, the PREDIMED trial used a low-fat diet in the control group. However, the authors acknowledge that "changes in total fat were small" in the low-fat group. To complicate adherence further, it is well known that a major limiting factor in nutrition research is accurately assessing long-term nutritional intake and adherence to a nutritional intervention [63].

Challenges Relating to Interventional Nutrition Research in HF

Interventional nutrition research specific to HF brings several additional challenges. HF can be right sided or left sided. Left-sided HF can be further characterized by preserved ejection fraction or reduced ejection fraction. The types of HF as well as the severity and any comorbidity are important contributors to pharmacological treatment and may be important factors influencing nutritional intervention. Regarding comorbidities, renal disease may present a particular consideration due to varying dietary alterations, such as sodium, potassium, phosphate, or protein restrictions. Additional comorbidities (e.g., depression, anxiety) and life circumstances (e.g., diminished mobility, financial limitations) may affect desire to eat, as well as ability to purchase and prepare food and hence dietary intake. Similarly, frequent clinical appointments and/or hospitalizations disrupt usual routine (including nutritional intake) and may lead to impaired nutritional intake.

Calorie and nutrient requirements may differ in HF and may be influenced by HF sub-type and/or comorbidities (e.g., diabetes). There is evidence that HF may decrease nutrient absorption including macronutrients (carbohydrate, protein, fat) and micronutrients (e.g., vitamins). Further, elevated oxidative stress and certain mediations routinely used therapeutically for those with HF (e.g., diuretics) may contribute to micronutrient depletion (e.g., potassium and magnesium, thiamine, vitamin D) [64–66].

It is accepted that overweight/obesity is a major predisposing factor for HF incidence. Indeed, weight loss achieved through various means, including surgery [67], exercise [68••, 69], or differing dietary regimens [35, 37, 38••, 39, 41, 42, 44•], is associated with diverse improvements in HF. In contrast, rapid and inappropriate weight loss is detrimental in HF, particularly in the setting of cardiac cachexia or sarcopenia. Indeed, poor nutritional status is associated with poor HF prognosis [70–72]. Therefore, it is important for clinical and research purposes that trained professionals, ideally dietitians, are involved in the nutritional assessment of HF patients to ensure appropriate advice regarding weight loss/maintenance/gain. Currently, appropriate ways to assess nutritional status in HF, and how best to interpret, are not well defined, and therefore a variety of methods in conjunction with clinical expertise would ideally be used.

The importance of nutritional status (under/overweight) with regard to HF prognosis is clear. In this context, broad nutritional interventions which would lead overweight patients to lose weight would theoretically improve HF associated with overweight. For example, most existing nutritional interventions in HF have led to weight loss (Table 2). Therefore, the question remains: would these interventions be successful in the absence of weight loss? This is particularly important because weight loss is difficult and the maintenance of weight loss is even more difficult. Further, weight loss may not always be indicated. The PREDIMED trial demonstrated that a MedDiet supplemented with EVOO or nuts could decrease important HF biomarkers in subjects at high risk of CVD, even in the absence of weight loss [50•]. Specific to pre-existing HF, there is currently only a single, small ($n = 48$) trial demonstrating benefit of a nutrition intervention in the absence of weight loss. A small ($n = 48$) 2015 randomized, controlled

trial reported that the DASH diet led to broad clinical benefit in 12 weeks [40••].

Existing nutritional interventions in HF have lasted from 21 days to 46 months. Diverse clinical benefit has been reported in the short term inferring a remarkable treatment effect. However, shorter term trials have reported markers of HF biomarkers (BP, symptoms, cardiac function) as opposed to hard clinical outcomes such as CVEs or mortality. To date, there is only a single nutrition intervention which examined the effect on clinical outcomes. Tuttle and colleagues reported significantly improved outcome-free survival (84%) with a low-fat, low-cholesterol Mediterranean-style diet compared to usual care (60%) [36]. Additionally, low-fat diets, with or without exercise and stress management, have been documented to decrease CVEs and HF incidence in those with pre-existing CVD [36, 53–57].

Opportunities

It is clear that nutritional intervention has much potential regarding multiple aspects of HF, including prevention as well as targeting relevant comorbidities, improving several aspects of quality of life in HF (e.g., exercise tolerance, dyspnea) and improving short- and possibly long-term prognosis.

Large-scale observational studies report a profound effect of nutritional intake on HF incidence, prognosis, and even mortality (Table 1). Further, large systematic reviews report a beneficial role of nutrition with regard to CVD and a pronounced benefit specifically relating to HF [33, 34•]. However, there is a disappointing and notable lack of human nutrition interventions specifically among those with pre-existing HF.

This provides clear opportunity for clinical and research teams to conduct well-designed interventions to further elucidate the effect, if any, of nutrition on HF pathogenesis. Further, there is ample opportunity to explore the mechanistic pathways via which nutritional modification may prove beneficial. Nutrition is only a single component of a healthy lifestyle. There is potential to explore the synergistic effect of nutrition and other lifestyle components regarding HF (e.g., exercise).

Regarding nutrition, the entire spectrum of HF manifestation, with or without comorbidities, needs to be considered. Recommendations may need to be defined in the context of each individual patient who may have concomitant disease (e.g., renal disease), which requires additional and even conflicting nutritional recommendations.

A seminal 1999 editorial [73] regarding the famous Lyon Diet Heart Study stated "relatively simple dietary changes achieved greater reductions in risk of all-cause and coronary heart disease mortality in a secondary prevention trial than any of the cholesterol-lowering studies to date." This editorial details the cost-effectiveness and high benefit to risk ratio of dietary manipulation compared to "drugs and invasive procedures" and concludes that "dietary factors must be very important." The current author agrees that diet does seem important and I quote a more recent, expert editorial: "in our search for the silver bullet, we have overlooked the silver plate. It is regrettable that we remain so imprecise and ill-informed about a cornerstone in patient care. Diet is important. We can and should know more" [3].

Conclusions and Future Perspective

Nutritional intervention appears promising as an adjunctive strategy in the treatment of HF. However, there is a clear lack of well-designed and relevant nutrition interventional research. Further, existing nutritional interventions in HF were typically pilot studies with small samples and short follow-up.

Existing research suggests a consistent benefit of MedDiet and DASH diet for HF. However, there is suggestive data regarding both low-fat (especially plant based) diets and low-carbohydrate diets. Overall, dietary patterns characterized by high intake of fruits, vegetables, whole grains, and legumes are high in micronutrients, antioxidants, and fiber and appear beneficial with regard to HF.

Well-designed clinical investigations are urgently needed to help resolve the many remaining issues in nutritional management of HF patients. These studies will require adequate statistical power and accurate stratification of patients in terms of HF sub-type, severity, and medication as well as adequate follow-up, suitable definition of endpoints, and rigorous characterization of diet and nutritional status. Further, these trials should aim to be randomized, investigator blinded and utilize a suitable control diet. So far, few studies meet all of these criteria, and essentially none meets the highest standards of evidence-based medicine.

Compliance with Ethical Standards

Conflict of Interest The author declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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