Review Article

Dietary management of heart failure: room for improvement?

Thomas Butler

Department of Clinical Sciences and Nutrition
University of Chester
Chester
CH1 4BJ
United Kingdom
Telephone: +44 (0) 1244 511312
Email: t.butler@chester.ac.uk
Fax: +44 (0) 1244 511310

Short title: Diet and heart failure
Keywords: Heart failure; Diet; Remodelling; cardiac function

Abstract

There is growing awareness of the role of diet in both health and disease management. Much data is available on the cardioprotective diet in the primary and secondary prevention of cardiovascular disease (CVD). However, there is limited information on the role of diet in the management of heart failure (HF). Animal models of HF have provided interesting insight and potential mechanisms by which dietary manipulation may improve cardiac performance and delay the progression of the disease, and small-scale human studies have highlighted beneficial diet patterns. The aim of this review is to summarise the current data available on the role of diet in the management of human HF and to demonstrate that dietary manipulation needs to progress further than the simple recommendation of salt and fluid restriction.

Introduction

Heart failure (HF) represents a clinically defined end point that can be the result of many different cardiac diseases which impair ventricular function. Impaired ventricular function results in clinical signs of disease such as dyspnoea, fatigue and oedema. HF can be classified based upon the time course of events, the side of the heart affected, whether systolic or diastolic function is impaired, ejection fraction (EF), and the severity of symptoms[1]. Mortality still remains high with HF, although data from the UK National Heart Failure audit shows in-hospital mortality has fallen from 11.1% to 9.5% between 2011/12 to 2013/14[2,3]. However, 6.2% of patients who survive to discharge die in the 30-days following discharge, and overall one-year mortality stands at 27%[3].

In the UK, the most common New York Heart Association (NYHA) classification at time of first hospital admission is class III or IV, representing a total of 80% of those diagnosed with HF[3]. Ischaemic heart disease (IHD) and hypertension (HTN) are observed in 46% and 54% of HF patients, respectively[3] suggesting that both conditions are important risk factors for the development of HF. Indeed, a medical history of IHD is more likely to result in the diagnosis of left ventricular systolic dysfunction (LVSD) and hence reduced ejection fraction (EF) whereas HTN or valvular disease is associated with non-systolic HF with a preserved or normal EF (HFpEF)[3]. This latter form of HF is more frequently observed in obese women with pre-existing diabetes[4] whereas male sex, smoking and prior MI are associated more strongly with HF with reduced EF (HFrEF)[5]. Recognised comorbidities present in the HF population include anaemia, cachexia, cancer, chronic obstructive pulmonary disease (COPD), depression, diabetes, gout, hyperlipidaemia, HTN, iron-deficiency anaemia and renal dysfunction, all of which may require careful management in addition the condition of HF[1]. Interestingly those patients with HFpEF tend to have a higher non-cardiac comorbidity burden when compared to patients with HFrEF[6], potentially identifying them as a unique patient group.

In addition to the known medical causes, HF has important socioeconomically determinants. Individuals with HF living in the most deprived areas of the UK are more likely to present at a younger age when compared to those living is less deprived areas[3], suggesting additional factors – rather than just medical comorbidities – may influence prognosis. Such factors may include access to care, educational level but also lifestyle choices, including dietary habits.

The evolving knowledge of substrate usage in the failing heart has prompted several investigators to re-examine the importance of dietary modification in this patient group. This manipulation has extended further than preventing uncontrolled weight loss, itself shown to be linked with greater incidence of mortality[7], to diet patterns linked with improvements in cardiac function and delayed mortality. It may be suggested that the window for nutritional intervention becomes narrower as HF progresses, with prevention of unintentional weight loss potentially more important in end-stage disease. Indeed, management of malnutrition and cachexia in HF patients is a key priority and has been reviewed extensively[8].

There is a substantial gap in clinical guidance for the dietetic management of patients with HF, despite widely recognised nutritional deficiencies[9]. Sodium restriction has been the significant nutritional recommendation by the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) for the reduction of congestive symptoms[10] however this is not mirrored by European guidance[1], itself providing limited advice other than of fluid restriction, maintenance of healthy weight and prevention of malnutrition. Irrespective of sodium, both guidelines provide little information into additional dietary changes that may be of benefit to the patient. The aim of this review is to present current developments in the understanding of nutrition in HF and to highlight the areas that need crucial development.

Ventricular remodelling

Left ventricular hypertrophy (LVH) is an important step in the development of HF. LVH may initially be beneficial in normalising wall stress and haemodynamic function[11] and several animal models have suggested that inhibiting the initial hypertrophic process is detrimental[12,13]. Pathological ventricular remodelling patterns have recently been shown to be associated with the incidence of HF and interestingly display differential risk for HF with HFpEF and HFrEF[13]. Specifically, individuals with eccentric remodelling have a greater than 2-fold risk of developing HFrEF, whereas those with concentric changes showed increased risk of HFpEF. These statistics are of significance given the high prevalence of HTN and IHD in HF patients[3].

Metabolic remodelling

Ventricular remodelling processes also extend to metabolism and have been extensively reviewed[14-16]. Classically the predominance of fatty acid (FA) oxidation (FAO) in the healthy heart is replaced by glycolytic substrate usage and reduced ability to utilise FAs in the failing heart[16,17] although this concept has been challenged[18]. Indeed, the conflicting changes observed in anmial models may represent confounding factors such as the method used to induce HF, the strain of animal and duration of the intervention giving rise to different cardiac responses when challenged with varying diets[19]. Nonetheless, in patients with NYHA Class IV HF the mRNA and protein levels for key enzymes associated with FAO are reduced, supporting the metabolic change[20]. In addition to altered FAO there is evidence that mitochondrial oxidation of glucose may be diminished in HF[17] leading to a scenario where the heart cannot process sufficient FAs or glucose to maintain adequate energy supply. As such there is reduced ability to synthesise ATP leading to impaired contractile function. This concept of the failing heart being energy-starved is not new and is why the failing heart has been likened to "an engine out of fuel" [21]. Many groups have used this concept to suggest that manipulation of the diet to facilitate sufficient ATP production may be important in regulating function in the failing heart.

The role of lipid in heart failure

Much of the work on dietary manipulation has been performed in experimental models of LVH and/or HF, and has been reviewed extensively[22,23]. A limitation of such models is that whilst providing useful mechanistic insight, they do little to represent benefits in quality of life and reduced rates of hospital admission. However from these mechanistic studies there is evidence to suggest manipulation of nutrient intake – predominantly carbohydrate and fat content – has an important role in regulating cardiac structure and function in HF[24]. The importance of fat is often overshadowed by its high energy content per gram, however in HF patients this same parameter may be beneficial in increasing an individual's calorie intake and preventing unintentional weight loss and cachexia[8]. Several animal studies have also shown a potential beneficial role of dietary fat that extends beyond calories, forcing us to question if we should be encouraging a greater intake of this macronutrient in the HF population. For example, coronary artery ligation in Wistar rats has shown to reduce stroke volume and EF, although this finding can be partially attenuated by

the provision of a diet containing 60% lipid (25% palmitic acid, 33% stearic acid, and 33% oleic acid)[25]. This study also demonstrated that the high-fat diet had no impact upon cardiac performance in response to a dobutamine stress test, suggesting no additional impairment to contractile reserve. Equally when failing hearts from rats fed a high-fat diet are perfused *ex vivo* they demonstrate an improvement in cardiac FAO which is similar to that of non-infarcted controls[26]. The authors of this study raise an important argument in that following a MI, providing sufficient fuel for the non-infarcted myocardium is vitally important as the burden of function is often shifted to healthy tissue. This is further compounded by the observation that acutely limiting the availability circulating FAs in patients with cardiomyopathic HF depresses cardiac function suggesting an important role of FAs in HF[27] (table 1).

Cardiac triacylglycerol and lipotoxicity

The ability to store and utilise endogenous triacylglycerol (TAG) has been shown to be important for cardiac function[28] and the role of endogenous TAG is particularly important in the context of cardiac lipotoxicity. The traditional view of lipotoxicity relies upon the concept that a reduced capacity of the cardiomyocyte to oxidise FAs coupled with normal or increased FA delivery leads to progressive lipid accumulation, the shuttling of FA species into the formation of biologically active intermediates such as diacylglycerol and ceramide, and ultimately cellular and organ dysfunction [29]. An excellent review on the role of FAs and their derivatives as signalling molecules can be found in van Bilsen and Planavila[30].

Traditional view of lipotoxicity being a pathology solely attributable to lipid accumulation is not completely accurate, and endogenous TAG accumulation may actually protect against biologically active intermediate formation with a specific role of various FAs in this process. Indeed previous research suggested that excessive supply of palmitate leads to increased apoptosis, and that provision of oleate in addition to palmitate can attenuate this by channelling palmitate into the formation of endogenous TAG and away from ceramide synthesis[31]. Whislt impressive, this study was performed in a cell culture model and may not reflect the chronic nature of lipid accumulation in disease or the consequences of prolonged accumulation (table 1). Nonetheless, it reflects the complexity of lipid dynamics[32] and rasies

questions over whether lipid accumulation per se is damaging, or wherther impairment to the dynamic nature of this enrgy store is more important.

In HF endogenous TAG may be an important yet inaccessible source of substrate. The induction of HF in rats leads to a significant reduction in TAG turnover suggesting impaired access to this energy store[33]. An inability to utilise stored TAG through decreased oxidation may lead to reduced energy provision in the setting of HF. Consequently improving the heart's access to its own endogenous energy supply may have a significant impact upon cardiac function. In support of this theory, provision of oleate to failing hearts of Sprague Dawley rats maintains the myocardial TAG pool and increases TAG turnover when compared to palmitate[34]. This finding was associated with improved cardiac contractility, augmentation of target genes associated with FAO and a reduction in the reactive intermediate C16 ceramide[34]. Although performed in rodents, the significance of this study is that that via manipulating the exposure of the failing heart to different FA species, mechanical performance can be improved (table 1).

Omega 3 intake in heart failure

Omega-3 (n-3) supplementation is currently listed as a class IIb recommendation and level B evidence in patients with systolic HF in European guidance[1], with similar recommendations present in ACCF/AHA guidance[10].

The Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico-Heart Failure (GISSI-HF) study demonstrated the advantageous method of supplementing stage II-IV HF patients with 1g daily of an eicosapentaenoic acid (EPA)/docosahexaenoic acid (DHA) mix, however only producing a small yet significant reduction in hazard ratio for mortality compared to the placebo group[35] (table 2). A recent meta-analysis[36] has also confirmed the beneficial effect of n-3s on cardiac health and function in HF patients. In this study, pooled results of 4 studies totaling 350 participants showed fish oil supplementation to significantly reduce left ventricular LV end-systolic volume (LVESV) compared with placebo. Similarly analysis also suggested fish oil to be associated with improved LVEF[36]. Whilst this meta-analysis supports the notion that fish oil supplementation may have a beneficial effect in patients with HF, it remains to be determined if similar effects can be observed by dietary sources alone.

To draw further attention to the requirement of more research into diets specific to HF patients, the results of two recent systematic reviews and meta-analyses have provided. The first meta-analysis by Rizos et al.[37] considered randomised controlled trials whereby n-3s were administered to participants by supplementation or diet with outcomes being all-cause mortality, cardiac death, sudden death, MI, and stroke. The authors found no significant relationship between n-3 supplementation and measured outcomes although a substantial limitation is evident when examining the dose of n-3 intake used in studies. Indeed, studies using a higher dose of n-3 supplement tended to show benefit yet they themselves were limited by small sample size and therefore did not carry weight in the analysis. A more recent meta-analysis[38] has also examined the relationship between n-3s and coronary risk as part of larger review of the relationship between all FAs and coronary risk. The authors showed that n-3 supplementation was found not to be significantly associated with a reduced risk of coronary event in randomised controlled trials, whereas dietary n-3 intake was inversely associated with coronary outcomes in prospective studies. Indeed this latter point is reinforced by the observation that a higher marine or dietary n-3 (EPA and DHA) intake is inversely associated with the development of HF[39]. It may be argued that if there is discrepancy in the dietary evidence base for the general population, is it safe and justifiable to offer the same advice to HF patients.

Considering all studies above regarding FAs and it is clear that the role of fat in HF is not as simple as once thought. Rather than focusing solely on the calorie content of lipid, we should consider the biological and metabolic effects various FAs may have, and use these to a potential therapeutic advantage. N-3 supplementation may be of some benefit in HF patients although it remains to be determined if such benefits could be gained from increasing intake from dietary sources. At present there are no recommendations for HF patients in terms of omega-9 (n-9) FAs and so it would be of use if appropriate studies were performed to examine the effects of increasing n-9 FA consumption in addition to n-3s in this patient group.

Sodium and fluid restrictions in heart failure

HF is characterised by altered renal perfusion which itself leads to increased sympathetic activation and stimulation of the renin-angiotensin-aldosterone system (RAAS). Sodium and fluid are retained leading to increased circulating volume in an attempt to

preserve cardiac output. However combined with fluid expansion, vasoconstriction caused by increased sympathetic activity raises blood pressure. Whilst initially beneficial, chronic activation of the RAAS and augmented sodium and fluid retention increases both afterload and preload, contributing to oedema formation and congestive symptoms[40]. Reflecting the potential link between sodium intake and fluid accumulation, the ACCF/AHA advise sodium restriction in patients with symptomatic HF although this class of recommendation is IIa and carries a C level of evidence[10]. Fluid restriction to 1.5 to 2.5 L/day is also suggested by the ACCF/AHA in those patients with NYHA class IV[10], in particular patients with hyponatraemia, with a similar recommendation by European guidance (although the latter carries no class or recommendation or level of evidence)[1]. This is concerning given that sodium and fluid restriction are viewed as a mainstay of dietary intervention in HF and is further complicated by the presence of "salt-sensitive" phenotype, itself associated with increased mortality independent of blood pressure[41].

Several studies have shown little clinical benefit in restricting sodium and/or fluid, although these may be confounded by their acute setting[42-44] (table 2). Compared to acute decompensated HF patients managed with a free-fluid regimen, acute decompensated HF patients managed with fluid restriction showed no improvement in time to clinical stability or time spent receiving intravenous HF therapy[42]. An important limitation of this study is the difference in achieved fluid intake in both groups. In the free-fluid group, total daily fluid intake was 1466.6 mL versus 1074.3 mL in the fluid-restricted group. Although statistically significant, clinically a greater restriction may have led to potential improvements however as the authors note, this may have increased thirst and reduced compliance. Similarly, a restriction of sodium (800 mg/day) and fluid intake (800 mL/d) in acute decompensated HF patients increased thirst and led to no improvement in 30-day hospital readmission rates when compared to a control group receiving no such restriction[43]. Furthermore, levels of brain-type natriuretic peptide (BNP) were significantly higher in the restricted group at the end of the study. A very real confounding factor in these trials examining sodium restriction is their acute setting. Indeed, a low-sodium (1500 mg/d) diet proved to be more effective at reducing BNP in ambulatory HF patients with NYHA II/III when compared to a moderate sodium (2300 mg/d) diet[44]. An important aspect of this study is the use of ambulatory HF patients as opposed to acute decompensated patients as described by references 39 and 40.

To further complicate the issue of sodium restriction in HF patients a moderate in-hospital sodium restriction (2800 mg/day) combined with hypertonic saline solution, 250 mg

twice daily intravenous furosemide and 1000 mL fluid restriction in patients with HFrEF produced a greater improvement in diuresis and natriuresis when compared to a group of HF patients receiving a greater sodium restriction (1800 mg/day) and no hypertonic saline solution. These patients were discharged on their in-hospital sodium and fluid restrictions in addition to 50 – 125 mg twice daily furosemide. Those who maintained the moderate sodium intake showed reduction in the occurrence of the combined endpoint of mortality and hospital readmission in comparison to the restricted group[45]. The authors of this study speculate that the greater sodium intake during the hospital admission and discharge may improve serum sodium levels, chronically reduce neuro-hormonal activation and improve delivery of diuretics to the loop of Henle, thus increasing their action of diuresis (table 2).

It is also relevant to consider in the context of sodium restriction that salt taste diminishes with age[46], and that restricting sodium in hospitalised HF patients may lead to an increased desire to satisfy the salt taste on discharge, further compounding difficulties of adhering to a low-sodium diet. This concept would support the observations of Aliti et al.[43]. As such consideration needs to be given to the different HF populations (ambulatory or hospitalised) in addition to the support required for patients to adhere to such a diet upon discharge. Without support, we are expecting a great deal from the elderly HF population which may be an additional reason why low-sodium diets are so difficult to follow. It would also be prudent to note that restricting sodium intake in HF patients has been shown to be associated with reduced intake of other important nutrients such as calcium, phosphate, thiamine and folate[47] and therefore it would be advisable that patients discharged from hospital with low-sodium advice receive regular follow-up to ensure compliance and also so that dietary adequacy can be reviewed (table 2).

A recent Cochrane meta-analysis[48] has suggested that sodium restriction leads to increased plasma renin, aldosterone, adrenaline and noradrenaline, irrespective of whether the individual is hypertensive or not, and as such may aggravate features of decompensated HF and explain the outcomes in previously mentioned studies. Furthermore elevated levels plasma renin activity have been linked with increased mortality in patients with stable symptomatic HF NYHA class III-IV, irrespective of pharmacotherapy[49]. In the analysis by Graudal et al.[48] the authors report that restriction of sodium to a sub-normal level resulted in a 1% and 3.5% decrease in systolic blood pressure (SBP) in normotensive and hypertensive individuals, respectively. They also suggested that in normotensives a greater duration of sodium restriction produced a larger reduction in SBP (estimated mean difference of 0.4

mmHg), however the reduction in SBP following sodium restriction in hypertensive individuals did not appear to be time-dependent. It may be inferred from these observations that sodium-restriction may have a greater impact upon afterload in those HF patients with co-existing HTN who are salt-sensitive. Although HTN is more common in those individuals with HFpEF, it is not exclusive to this group and therefore examining the specific benefits of low-sodium diets in both hypertensive and non-hypertensive HFrEF and HFpEF populations would be of use.

Considering different responses to sodium restriction between acute decompensated and compensated HF patients, in addition to those who may be more salt-sensitive, a well-designed clinical trial comparing short and long term effects of sodium restriction is required not solely on the outcome of mortality but on additional clinically relevant factors such as quality of life and hospital re-admission. A key recommendation should be that any sodium and fluid sodium restrictions need be individualised based on the severity of HF, dose of diuretic, degree of fluid accumulation and the clinical setting.

Dietary patterns and disease progression in heart failure

Discussion of the dietary management of each individual comorbidity experienced by HF patients is beyond the scope of this review. However, is the author's opinion that through appropriate nutritional education there is no reason why dietary patterns such as the Mediterranean or Dietary Approaches to Stop Hypertension (DASH) cannot be modified to account for comorbidities such as diabetes, COPD or gout, and act as an adjunct to traditional pharmacotherapy for these conditions in HF patients.

DASH and Mediterranean Diet

Cohort studies have identified several dietary patterns as cardioprotective. Famous examples include the Mediterranean and DASH diets[50]. A dietary pattern approach is important as they acknowledge the synergistic effects of different foods, rather than focussing on a single nutrient and recently studies have examined diet patterns in relation to specific outcomes in HF[51]. Higher intakes of salty foods are associated with a shortened time to transplantation in patients with advanced HF and increasing the intake of foods rich in monounsaturated and polyunsaturated fatty acids (MUFA and PUFA, respectively) from

"occasionally" to "several times a week" was associated with approximately 50% reduction in risk of death/deterioration[51]. Other interesting results from this study include the association between different foods groups. Saturated fat (SFA) was significantly associated with increased consumption of salty food, and inversely associated with MUFA and PUFA. Similarly, both MUFA and PUFA also positively correlated with fruits/vegetables/legume intake, thus suggesting that the consumption of one nutrient may predict other dietary components. This observation may be important for the clinician or dietitian when taking a diet history, and may allow a more rapid determination of diet quality. However, whilst interesting this study is limited by the use of the food frequency questionnaire (FFQ) and does not provide information on the amount of such nutrients consumed by the participants.

The DASH diet has a recognised beneficial effect in delaying the incidence of HF[52] and should be examined for use in HF patients. Such a diet is typically low in SFA, with increased consumption of low-fat dairy, complex carbohydrate, fish and vegetables[50]. This dietary pattern is in contrast to that of the UK population which typically consume a diet higher in refined carbohydrate and SFA, and lower in vegetables[53]. If individuals with HF are required to change their diet, support and guidance to the most appropriate way of achieving an optimal nutrient intake should be provided.

Hummel et al.[54] demonstrated a significant improvement in ventricular diastolic function in 13 patients with HFpEF when these patients were provided with a sodium-restricted DASH diet (DASH/SRD; 50 mmol/2100 kcal). Specifically, adherence to this dietary pattern improved EF by 8% and increased stroke volume by approximately 11%. Whilst impressive, the relatively small sample size and feeding protocol (controlled feeding with prepared meals) mean that such a finding may not be observed in free-living individuals with HF. Also, the nature of the population studied means that this finding may also be only linked to those with HTN and HFpEF (table 3). The Geriatric Out of Hospital Randomised Meal Trial in Heart Failure (GOURMET-HF) is one such study that will address if such findings can be reproduced using a home-delivered low-sodium meal, examining quality of life and cardiac functional parameters, although this study itself is still limited by the provision of meals[55].

Levitan et al.[56] studied women enrolled in the Women's Health Initiative who were admitted to hospital with HF to identify if adherence to a Mediterranean or DASH diet pattern influenced CVD mortality. Following a median of 4.6 years of follow-up there were

1,385/3,215 deaths following HF hospitalisation. When stratified into quartiles, greater adherence to either the Mediterranean or DASH diet was associated with a substantial reduction in the hazard rate (HR) associated with mortality. Specifically, the HR for death was 16% and 15% lower in the DASH and Mediterranean diet group, respectively, although only reaching significance in the DASH group. Further analysis of the dietary intake of either Mediterranean or DASH patients revealed that greater adherence to each diet was associated with increased consumption of fruit and vegetables, nuts, legumes, whole grains and fish, and reduced intake of sweetened beverages and red and processed meat. However important limitations of this study were acknowledged by the authors, including difficulty in recording sodium, fluid and olive oil intake, in addition to the group being of those diagnosed with HFpEF. Whilst the results may be promising for the DASH diet, they do not support the advocacy for the Mediterranean-style diet, despite a favourable trend. However, previous cross-sectional data have shown that adherence to a Mediterranean Diet is associated with improved diastolic function in individuals with congestive HF (CHF)[57] (table 3) and subsequent studies have shown the Mediterranean Diet to reduce HF biomarkers in individuals at high risk CVD[58]. Therefore at present, the role of the Mediterranean Diet in the management of HF remains to be fully examined. There is a clear need for large, randomised trials investigating if the improvement in mortality rate observed in the DASH group is driven by the restriction in sodium or a rather combined effect of diet and sodium restriction, and whether the Mediterranean diet has a role in the management of HF.

Low carbohydrate and high protein

There are several interesting reports regarding the use of low-carbohydrate diets in humans with HF. However, an important limitation of some of these studies cited is that they are almost exclusively conference abstracts and so caution should be exercised when interpreting them. Nonetheless, in patients with HF and right-ventricular dysfunction a diet classified as low in carbohydrate (40% carbohydrate, 40% fat, 20% protein) has been shown to be effective at increasing weight loss and improving oxygen saturated when compared to a conventional diet containing 50% of energy as carbohydrate[59]. In addition the authors report an improvement in HF functional class. Like many HF trials, the study suffered from a relatively small sample size and short duration, including 21 individuals studied for a duration of 2 months. Therefore the long-term consequences of such a pattern remain

unknown in HF patients. Importantly, this study highlights a key issue facing nutritional interventions: how diets are defined. Forty percent energy as carbohydrate may be regarded by many as not being 'low carbohydrate' and is consistent with that achieved in the PREDIMED study[60] (widely defined as a Mediterranean Diet). It would be appropriate for the The National Heart, Lung, and Blood Institute (NHLBI) and NIH Office of Dietary Supplements (ODS) working group[61] to also consider a standard protocol for reporting the nutritional composition of experimental diets in HF studies to facilitate greater comparison of dietary interventions, in addition to their other current recommendations (table 3).

Modifying protein intake has been shown to be effective in reducing weight in obese patients (mean BMI 37.3 kg/m^2) with NYHA class II-III HF. Evangelista et al.[62] compared a 12-week hypocaloric diet (1200-1500 kcal/d) containing (as percentage of energy) 30% protein, 40% carbohydrate and 30% fat to a standard protein, hypocaloric diet (55% total energy from carbohydrates, 15% from protein, and 30% from fat) or the recommendations by the AHA. The authors noted that the high protein hypocaloric diet led to a greater reduction in % body fat and improved the patient's quality of life (assessed by the Minnesota Living with Heart Failure Questionnaire). However, this study was performed in 5 individuals and is therefore severely limited by the small sample size (table 3). At present, there are no available large-scale dietary trails investigating protein intake and cardiac structure and function, functional status, and quality of life in HF patients although these are in development[63].

The obesity paradox

Studies 58 and 61 suggest a beneficial effect of weight loss in HF patients however it is important to recognise that uncontrolled weight loss in HF is linked with increased incidence of mortality[3]. The importance of weight in HF patients has frequently been examined as part of the obesity paradox. The obesity paradox refers to observations that link the presence of obesity (and in some instances overweight) in HF patients with improved survival in comparison to lean counterparts. Horwich et al.[64] was one of the first groups to demonstrate the inverse relationship between weight and mortality in patients with HF. In this study, the majority of participants were of NYHA class IV, had an EF of 22% with obese patients more likely to have diabetes and HTN. Following multivariate analysis overweight and obesity were found to be associated with a significant survival benefit at 2 years with the worst

prognosis seen in those who were underweight, followed by those who were classified as recommended weight. Importantly, whilst this study is used to draw evidence to the protective nature of obesity, the survival benefit was not evident at 5 years follow-up. In addition, categorisation of patients as underweight at baseline may not have accounted for unintentional weight loss prior to the study. Importantly this study was only performed in individuals with HFrEF and therefore may not apply to those with HFpEF. Despite this, subsequently larger meta-analysis studies have further reinforced this observation. Oreopoulus et al.[65] analysed a total of nine observational studies demonstrating that both overweight and obesity were associated with a reduced relative risk of all-cause and cardiovascular mortality when compared to patients with normal BMI levels. Regrettably the authors of this study did not extract data on EF however a more-recent a meta-analysis examined if HF subtype (HFrEF vs. HFpEF) impacted upon the obesity paradox. Using individual patient data Padwal et al.[66] demonstrated the existence of a U-shaped relationship between BMI and all-cause death in both HFrEF and HFpEF patients. In patients with HFrEF or HFpEF, the lowest hazard ratio for all-cause mortality was observed when comparing those individuals with a BMI between 30-34.9 kg/m^2 against the reference BMI range of 22.5-24.9 kg/m^2. In both subtypes a BMI less than 22.5 kg/m^2 was associated with a higher risk of all-cause death.

There may be several mechanisms behind the proposed obesity paradox in HF. It is well-known that advanced HF is associated with cachexia[8] and in this regard, greater adiposity may simply reflect greater body energy stores and hence greater resistance to the metabolic changes associated with the cachexic state. As shown by Padwal et al.[66] individuals who were obese were also more likely to be receiving cardiovascular medication, potentially suggesting greater clinical input and therefore greater clinical management of their condition. It should however be noted that this was adjusted for in their study with no effect upon their findings. Also the use of BMI as a marker of fatness in HF has been questioned, with more accurate measurements of body composition being proposed[67]. The presence of the obesity paradox means we may need to re-examine advice to achieve a healthy weight in HF patients and raises important questions regarding the role of weight loss (as described in Olvera et al.[59] and Evangelista et al.[62]) on the outcome of mortality. There may be a point where excess weight is not associated with any additional benefit but conversely increases risk. Indeed, in morbidly obese (BMI $\geq$40 kg/m^2) HF patients the obesity paradox is absent[68]. Therefore one may conclude that in those individuals with

morbid obesity, intentional weight loss may be beneficial in terms of reducing mortality rate however this should be carefully monitored and controlled. In lower BMI categories a reduction in weight may improve clinical symptoms and disease classification, but may impact negatively on long-term survival. It would be useful for future studies examining the relationship between bodyweight and HF mortality to assess adipose tissues deposits (both visceral and subcutaneous) and lean mass, in additional to cardiorespiratory fitness following weight loss.

Nutritional Messages – the role of the dietitian

A key aspect of implementing a dietary strategy is addressing pre-conceived ideas and beliefs regarding nutrition. A tailored nutritional message to patients with HF is sufficient to alter patients' views and attitudes towards medications, adherence to a sodium-restricted diet and self-monitoring[69]. Further support for the importance of nutritional input can be derived from Arcand et al.[70]. In this 3 month study, HF patients randomised to a dietitian-led education group showed greater improvements in salt reduction in comparison to usual care (self-help literature). Whilst such a frequent dietetic input may be unlikely in the current health-care setting, clinicians reviewing their patients may wish to follow-up nutritional advice and reinforce nutritional messages at every opportunity. Indeed, frequent nutritional counselling with HF patients may improve knowledge surrounding foods and reduce admissions. In HF patients a low level of sodium knowledge has been shown to be associated with a significantly greater odds ratio for hospital readmission for HF[71]. Using the Test of Functional Health Literacy in Adults (TOFHLA) tool, sodium knowledge was associated with a low health literacy score. When nutritional interventions are combined with appropriate educational session substantial improvement in quality of life and disease score can be seen. For example, a nutritional intervention consisting of 2000-2400 mg/d sodium, 50-55% (as % energy) carbohydrate, 15% protein, <10% SFA, 15% MUFA and 10% PUFA coupled with written and oral instruction from a dietitian led to a significant improvement in HF classification and quality of life when compared to a control group receiving general nutritional advice[72]. Indeed the improvement in HF classification was reflected by a significant reduction in the number of individuals with NYHA class II and III and an increase in the number of those with class I by the end of the study (table 4).

As such, this would suggest that by using appropriate methods of patient education and trained individuals it is never too late to make important and significant dietary changes that may improve quality of life.

Discussion and conclusions

HF remains a chronic and debilitating condition. Whilst the value of dietary manipulation is well-known in the primary, secondary and tertiary prevention of CVD it is undervalued in patients with HF and is reflected by the paucity of data in guidelines. Despite a large body of experimental data produced from animal models of HF examining the effect of different diet compositions, this has not translated into human trials. From animal trials it is clear that the traditional demonisation of fat may not be justified in HF, and human studies should be designed to evaluate the therapeutic effectiveness of cardioprotective fats in HF. Within this, consideration should be given to the underlying HF aetiology in addition to other comorbidities. Indeed by manipulating dietary nutrient composition it is possible for those individuals with other comorbidities to benefit from the potential therapeutic nature of food.

Studies that have been published in this field – albeit largely observational – now suggest that diet advice in this area may need to be re-examined, with the traditional cardioprotective diets such as the Mediterranean and DASH potentially being of benefit. Such diet patterns have been shown to increase the consumption of cardioprotective food items such as fruit and vegetables, nuts, legumes, whole grains and fish and are likely to have additional health effects beyond HF.

It is simple to decide what foods an individual should consume, yet much more difficult to actually achieve this. Regular nutritional education has been shown to lead to better adoption of a prescribed diet and may lead to improved overall nutritional status. In some studies, this has also translated to improvements in quality of life and reduced severity of symptoms when delivered by nutritionally-trained individuals. The feasibility of such a means of improving nutritional knowledge is clearly in need of evaluation, given the potential cost such a service may incur.

Although the studies presented in this review are promising, many are limited by small sample sizes, short duration and observational study design. It is therefore a requirement that in order to progress towards better evidence-based dietary advice for patients with HF, larger, longer, randomised clinical trials are needed. Such studies should

account for differences in HF subtype (HFrEF versus HFpEF) and have clearly defined clinical endpoints. In addition, there is a requirement for standardisation of dietary reporting. The studies highlighted in this review provide a potential starting point for the development of future trials, and fundamentally demonstrate that in addition to fluid and sodium, consideration should be given to other dietary components.

Acknowledgments

The author thanks their colleagues for interesting and stimulating discussions. The present review received no financial support. All literature was searched for, analysed and revisions made by the author. The author declares no conflict of interest that may undermine the validity of the conclusions made by this work.

1. McMurray JJ, Adamopoulos S, Anker SD *et al*. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur Heart J* **33**, 787-847.

2. Cleland J, Dargie H, Hardman S *et al.* (2013) National Heart Failure Audit April 2012 - March 2013. http://www.ucl.ac.uk/nicor/audits/heartfailure/documents/annualreports/hfannual12-13.pdf (accessed May 2015).

3. Mitchell P, Marle, D, Donkor A *et al*. (2015) National Heart Failure Audit April 2013 - March 2014. http://www.ucl.ac.uk/nicor/audits/heartfailure/documents/annualreports/hfannual13-14.pdf (accessed November 2015).

4. Lam CSP, Donal E, Kraigher-Krainer E *et al*. (2011) Epidemiology and clinical course of heart failure with preserved ejection fraction. *Eur J Heart Fail* **13**, 18-28.

5. Borlaug BA. (2013) Heart failure with preserved and reduced ejection fraction: different risk profiles for different diseases. *Euro Heart J* **34**, 1393-1395.

6. Ather S, Chan W, Bozkurt B, *et al*. (2012) Impact of Noncardiac Comorbidities on Morbidity and Mortality in a Predominantly Male Population With Heart Failure and Preserved Versus Reduced Ejection Fraction. *J Am Coll Cardiol* **59**, 998-1005.

7. Rossignol P, Masson S, Barlera S *et al*. (2015) Loss in body weight is an independent prognostic factor for mortality in chronic heart failure: insights from the GISSI-HF and Val-HeFT trials. *Eur J Heart Fail* **17**, 424-433.

8. Rahman A, Jafry S, Jeejeebhoy K *et al*. Malnutrition and cachexia in heart failure *J Parenter Enteral Nutr*. Published online 29 January 2015. doi: 10.1177/0148607114566854.

9. Witte KKA, Clark AL, Cleland JGF (2001) Chronic heart failure and micronutrients. *J Am Coll Cardiol* **37**, 1765-1774.

10. Yancy CW, Jessup M, Bozkurt B *et al.* (2013) 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. *Circulation* **62**, 1495-1539.

11. Grossman W (1980) Cardiac hypertrophy: useful adaptation or pathologic process? *Am J Med* **69**, 576-584.

12. Oie E, Bjornerheim R, Clausen OP *et al.* (2000) Cyclosporin A inhibits cardiac hypertrophy and enhances cardiac dysfunction during postinfarction failure in rats. *Am J Physiol Heart Circ Physiol* **278**, H2115-H2123.

13. Shiojima I, Sato K, Izumiya Y *et al*. (2005) Disruption of coordinated cardiac hypertrophy and angiogenesis contributes to the transition to heart failure. *J Clin Invest* **115**, 2108-2118.

13. Velagaleti RS, Gona P, Pencina MJ *et al*. (2014) Left Ventricular Hypertrophy Patterns and Incidence of Heart Failure With Preserved Versus Reduced Ejection Fraction. *J Am Coll Cardiol* **113**, 117-122.

14. Stanley WC, Recchia FA, Lopaschuk GD (2005) Myocardial Substrate Metabolism in the Normal and Failing Heart. *Physiol Rev* **85**, 1093-1129.

15. Kolwicz SC, Jr., Purohit S, Tian R (2013) Cardiac metabolism and its interactions with contraction, growth, and survival of cardiomyocytes. *Circ Res* **113**, 603-616.

16. Doenst T, Nguyen TD, Abel ED (2013) Cardiac Metabolism in Heart Failure: Implications Beyond ATP Production. *Circ Res* **113**, 709-724.

17. Kato T, Niizuma S, Inuzuka Y *et al*. (2010). Analysis of Metabolic Remodeling in Compensated Left Ventricular Hypertrophy and Heart Failure. *Circ Heart Fail* **3**, 420-430.

18. de Brouwer KF, Degens H, Aartsen WM *et al*. (2006) Specific and sustained down-regulation of genes involved in fatty acid metabolism is not a hallmark of progression to cardiac failure in mice. *J Mol Cell Cardiol* **40**, 838-845.

19. Abdurrachim D, Luiken JJ, Nicolay, K *et al*. (2015). Good and bad consequences of altered fatty acid metabolism in heart failure: evidence from mouse models. *Cardiovasc Res* **106**, 194-205.

20. Sack MN, Rader TA, Park S *et al*. (1996) Fatty Acid Oxidation Enzyme Gene Expression Is Downregulated in the Failing Heart. *Circulation* **94**, 2837-2842.

21. Neubauer S (2007) The Failing Heart — An Engine Out of Fuel. *N Engl J Med* **356**, 1140-1151.

22. Patten RD, Hall-Porter MR (2009) Small Animal Models of Heart Failure. *Circ Heart Fail* **2**, 138-144.

23. Berry JM, Naseem RH, Rothermel BA *et al*. (2007) Models of cardiac hypertrophy and transition to heart failure. *Drug Discov Today Dis Models* **4**, 197-206.

24. Stanley WC, Dabkowski ER, Ribeiro RF *et al*. (2012) Dietary Fat and Heart Failure: Moving From Lipotoxicity to Lipoprotection. *Circ Res* **110**, 764-776.

25. Berthiaume JM, Bray MS, McElfresh TA *et al*. (2010) The myocardial contractile response to physiological stress improves with high saturated fat feeding in heart failure. *Am J Physiol Heart Circ Physiol* **299**, H410-H421.

26. Berthiaume JM, Young ME, Chen X *et al*. (2012) Normalizing the metabolic phenotype after myocardial infarction: impact of subchronic high fat feeding. *J Mol Cell Cardiol* **53**, 125-133.

27. Tuunanen H, Engblom E, Naum A *et al*. (2006) Free fatty acid depletion acutely decreases cardiac work and efficiency in cardiomyopathic heart failure. *Circulation* **114**, 2130-2137.

28. Banke NH, Wende AR, Leone TC *et al*. (2010) Preferential oxidation of triacylglyceride-derived fatty acids in heart is augmented by the nuclear receptor PPARalpha. *Circ Res* **107**, 233-241.

29. Wende AR, Symons JD, & Abel ED (2012) Mechanisms of lipotoxicity in the cardiovascular system. *Curr Hypertens Rep* **14**, 517-531.

30. van Bilsen M & Planavila A (2014). Fatty acids and cardiac disease: fuel carrying a message. *Acta Physiol* **211**, 476-490.

31. Listenberger LL, Han X, Lewis SE *et al*. (2003) Triglyceride accumulation protects against fatty acid-induced lipotoxicity. *Proc Natl Acad Sci USA* **100**, 3077-3082.

32. Greenberg AS, Coleman RA, Kraemer FB *et al.* (2011) The role of lipid droplets in metabolic disease in rodents and humans. *J Clin Invest* **121**, 2102-2110.

33. O'Donnell JM, Fields AD, Sorokina N *et al*. (2008) The absence of endogenous lipid oxidation in early stage heart failure exposes limits in lipid storage and turnover. *J Mol Cell Cardiol* **44**, 315-322

34. Lahey R, Wang X, Carley AN *et al*. (2014) Dietary fat supply to failing hearts determines dynamic lipid signaling for nuclear receptor activation and oxidation of stored triglyceride. *Circulation* **130**, 1790-1799.

35. Tavazzi L, Maggioni AP, Marchioli R *et al*. (2008) Effect of n-3 polyunsaturated fatty acids in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. *Lancet* **372**, 1223-1230.

36. Xin W, Wei W, Li X (2012) Effects of fish oil supplementation on cardiac function in chronic heart failure: a meta-analysis of randomised controlled trials. *Heart* **98**, 1620-1625.

37. Rizos EC, Ntzani EE, Bika E *et al*. (2012) Association between omega-3 fatty acid supplementation and risk of major cardiovascular disease events: a systematic review and meta-analysis. *JAMA* **308**, 1024-1033.

38. Chowdhury R, Warnakula S, Kunutsor, S *et al.* (2014) Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. *Ann Intern Med* **160**, 398-406.

39. Djoussé L, Akinkuolie AO, Wu JH *et al.* (2012) Fish consumption, omega-3 fatty acids and risk of heart failure: a meta-analysis. *Clin Nutr* **31**, 846-853.

40. Bansal S, Lindenfeld J, & Schrier, RW (2009) Sodium Retention in Heart Failure and Cirrhosis Potential Role of Natriuretic Doses of Mineralocorticoid Antagonist? *Circ heart Fail* **2**, 370-376.

41. Weinberger MH, Fineberg, NS, Fineberg SE *et al*. (2001) Salt sensitivity, pulse pressure, and death in normal and hypertensive humans. *Hypertension* **37**, 429-432.

42. Travers B, O'Loughlin C, Murphy NF *et al.* (2007) Fluid restriction in the management of decompensated heart failure: no impact on time to clinical stability. *J Card Fail* **13**, 128-132.

43. Aliti GB, Rabelo ER, Clausell N *et al.* (2013) Aggressive fluid and sodium restriction in acute decompensated heart failure: a randomized clinical trial. *JAMA Intern Med* **173**, 1058-1064.

44. Colin-Ramirez E, McAlister FA, Zheng Y *et al.* (2015). The long-term effects of dietary sodium restriction on clinical outcomes in patients with heart failure. The SODIUM-HF (Study of Dietary Intervention Under 100 mmol in Heart Failure): A pilot study. *Am Heart J* **169**, 274-281.

45. Paterna S, Fasullo S, Parrinello G, *et al*. (2011). Short-term effects of hypertonic saline solution in acute heart failure and long-term effects of a moderate sodium restriction in patients with compensated heart failure with New York Heart Association class III (Class C)(SMAC-HF Study). *Am J Med Sci* **342**, 27-37.

46. Wessler JD, Hummel SL, & Maurer MS (2014) Dietary Interventions for Heart Failure in Older Adults: Re-Emergence of the Hedonic Shift. *Prog Cardiovasc Dis* **57**, 160-167.

47. Jefferson K, Ahmed M, Choleva M *et al.* (2015). Effect of a sodium-restricted diet on intake of other nutrients in heart failure: Implications for research and clinical practice. *J Card Fail*. Published online: 20 October 2015. doi: 10.1016/j.cardfail.2015.10.002

48. Graudal NA, Hubeck-Graudal T, & Jürgens G (2012). Effects of low-sodium diet vs. high-sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Cochrane Review). *Am J Hypertens* **25**, 1-15.

49. Masson S, Solomon S, Angelici L *et al.* (2010). Elevated plasma renin activity predicts adverse outcome in chronic heart failure, independently of pharmacologic therapy: data from the Valsartan Heart Failure Trial (Val-HeFT). *J Card Fail* **16**, 964-970.
50. Appel LJ, Moore TJ, Obarzanek E *et al*. (1997) A Clinical Trial of the Effects of Dietary Patterns on Blood Pressure. *N Engl J Med* **336**, 1117-1124.
51. Spaderna H, Zahn D, Pretsch J *et al*. (2013) Dietary Habits are Related to Outcomes in Patients With Advanced Heart Failure Awaiting Heart Transplantation. *J Card Fail* **19**, 240-250.
52. Levitan EB, Wolk A, Mittleman MA (2009) Relation of consistency with the dietary approaches to stop hypertension diet and incidence of heart failure in men aged 45 to 79 years. *Am J Cardiol* **104**,1416-1420.
53. Bates B, Lennox A, Prentice A *et al.* (2014) National Diet and Nutrition Survey. Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009 – 2011/2012). Crown Copyright. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/310995/NDNS_Y1_to_4_UK_report.pdf (accessed May 2015).
54. Hummel SL, Seymour EM, Brook RD *et al*. (2013) Low-Sodium DASH Diet Improves Diastolic Function and Ventricular–Arterial Coupling in Hypertensive Heart Failure With Preserved Ejection Fraction. *Circ Heart Fail* **6**, 1165-1171.
55. University of Michigan (2014). Effects of Home-delivered Low-sodium Meals in Older Adults Following Heart Failure Hospitalization. https://clinicaltrials.gov/ct2/show/NCT02148679: NML Identifier NCT02148679 (accessed June 2015).
56. Levitan EB, Lewis CE, Tinker LF *et al*. (2013) Mediterranean and DASH Diet Scores and Mortality in Women with Heart Failure: The Women's Health Initiative. *Circ Heart Fail* **6**, 1116-1123.
57. Chrysohoou C, Pitsavos C, Metallinos G *et al*. (2012) Cross-sectional relationship of a Mediterranean type diet to diastolic heart function in chronic heart failure patients. *Heart Vessels* **27**, 576-584.
58. Fitó M, Estruch R, Salas-Salvadó J *et al*. (2014) Effect of the Mediterranean diet on heart failure biomarkers: a randomized sample from the PREDIMED trial. *Eur J Heart Fail* **16**, 543-550.

59. Olvera G, Castillo L, Orea A *et al*. (2014) PP125-SUN: Effect of a Low Carbohydrate Diet on the Clinical Status of Patients with Heart Failure and Right Ventricular Dysfunction. *Clin Nutr* **33**, S66.
60. Estruch R, Ros E, Salas-Salvadó J *et al*. (2013) Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. *N Engl J Med* **368**, 1279-1290.
61. NIH Heart, Lung and Blood Institute. NHLBI Working Group. Designing clinical studies to evaluate the role of nutrition and diet in heart failure management (2013) http://www.nhlbi.nih.gov/research/reports/2013-heart-failure-management (accessed June 2015).
62. Evangelista LS, Heber D, Li Z *et al*. (2009) Reduced body weight and adiposity with a high-protein diet improves functional status, lipid profiles, glycemic control, and quality of life in patients with heart failure: a feasibility study. *Eur J Cardiovasc Nurs* **24**, 207-215.
63. Motie M, Evangelista LS, Horwich T *et al*. (2013) Pro-HEART - a randomized clinical trial to test the effectiveness of a high protein diet targeting obese individuals with heart failure: rationale, design and baseline characteristics. *Contemp Clin Trials* **36**, 371-381.
64. Horwich TB, Fonarow GC, Hamilton MA *et al.* (2001). The relationship between obesity and mortality in patients with heart failure. *J Am Coll Cardiol* **38**, 789-795.
65. Oreopoulos A, Padwal R, Kalantar-Zadeh K, *et al.* (2008). Body mass index and mortality in heart failure: a meta-analysis. *Am Heart J* **156**, 13-22.
66. Padwal R, McAlister FA, McMurray JJV *et al*. (2014). The obesity paradox in heart failure patients with preserved versus reduced ejection fraction: a meta-analysis of individual patient data. *Int J Obesity* **38**, 1110-1114.
67. Oreopoulos A, Fonarow GC, Ezekowitz JA *et al*. (2011). Do anthropometric indices accurately reflect directly measured body composition in men and women with chronic heart failure? *Congest Heart Fail* **17**, 89-91.
68. Nagarajan V, Cauthen CA, Starling RC *et al*. (2013). Prognosis of morbid obesity patients with advanced heart failure. *Congest Heart Fail* **19**, 160-164.
69. Sethares KA, Elliott K (2004) The effect of a tailored message intervention on heart failure readmission rates, quality of life, and benefit and barrier beliefs in persons with heart failure. *Heart Lung* **33**, 249-260.
70. Arcand JA, Brazel S, Joliffe C *et al*. (2005) Education by a dietitian in patients with heart failure results in improved adherence with a sodium-restricted diet: a randomized trial. *Am Heart J* **150**, 716.e1-716.e5.

71. Kollipara UK, Jaffer O, Amin A *et al*. (2008) Relation of Lack of Knowledge About Dietary Sodium to Hospital Readmission in Patients With Heart Failure. *Am J Cardiol* **102**, 1212-1215.

72. Colín-Ramirez E, Castillo ML, Orea TA *et al*. (2004) Effects of a nutritional intervention on body composition, clinical status, and quality of life in patients with heart failure. *Nutrition* **20**, 890-895.

Table 1 abbreviations

SFA, saturated fat; TAG, triacylglycerol; PET, positron emission tomography; EF, ejection fraction; NYHA, New York Heart Association; BMI, body mass index; FBS, foetal bovine serum; BSA, bovine serum albumin; FA, fatty acid; MS, mass spectrometry; DNA, deoxyribonucleic acid SCD, stearoyl-CoA desaturase; TAC, transverse aortic constriction; NMR, nuclear magnetic resonance; HF, heart failure; DAG, diacylglycerol; PPAR-α, peroxisome proliferator activated receptor alpha; mRNA messenger RNA; PUFA, polyunsaturated fatty acid; EPA, eicosapentaenoic acid; DHA docosahexaenoic acid; MI, myocardial infarction.

Table 2 abbreviation

BNP, brain natriuretic peptide; EF, ejection fraction; HF, heart failure; NYHA, New York Heart Association; BMI, body mass index; KCCQ, Kansas City Cardiomyopathy Questionnaire.

Table 3 abbreviations

EF, ejection fraction; NYHA, New York Heart Association; BMI, body mass index; VO_2, maximal oxygen consumption; HFpEF, heart failure with preserved ejection fraction; DASH; dietary approaches to stop hypertension; CVD, cardiovascular disease; HFrEF, heart failure with reduced ejection fraction; AHA, American heart association; LHFQ, Minnesota Living With Heart Failure Questionnaire.

Table 4 abbreviations

EF, ejection fraction; NYHA, New York Heart Association; BMI, body mass index; KCCQ, Kansas City Cardiomyopathy Questionnaire; LHFQ, Minnesota Living With Heart Failure Questionnaire; TOFHLA, Test of Functional Health Literacy in Adults; SFA, saturated fat.

Table 1 Summary of studies presented in this review investigating the role of fatty acids in HF patients and experimental models

Study	Participant characteristics	Study Design	Measures and time points	Key observations
Berthiaume et al. (25)	Male Wistar rats Control + standard diet: *n* = 9-10 Control + high SFA: *n* = 9-10 Intervention + standard diet: *n* = 9-10 Intervention + high SFA: *n* = 9-10	Control: sham procedure followed by 8 weeks normal diet (10% kcal fat) or a high SFA diet with 60% kcal from fat (25% palmitic acid, 33% stearic acid, and 33% oleic acid) Intervention: Coronary artery ligation followed by 8 weeks normal diet or high SFA diet as above	Cardiac function using echocardiography and pressure-volume catheter, plasma and metabolic parameters, and genomic expression Diet intervention for 8-weeks	High SFA diet did not exacerbate ventricular remodelling associated with coronary artery ligation High SFA diet prevented decline in stroke volume associated with coronary artery ligation and improved function during stress tests Greater transcription of nuclear material in failing hearts from the high SFA diet compared to respective surgical controls
Berthiaume et al. (26)	Male Wistar rats Control + standard diet: *n* = 13-16 Control + high SFA: *n* = 13-16 Intervention + standard diet: *n* = 13-16 Intervention + high SFA: *n* = 13-16	Control: sham procedure followed by 8 weeks normal diet (10% kcal fat) or a high SFA diet with 60% kcal from fat (25% palmitic acid, 33% stearic acid, and 33% oleic acid) Intervention: Coronary artery ligation followed by 8 weeks normal diet or high SFA diet as above	Cardiac function using echocardiography, pressure-volume catheter and working-heart perfusions, plasma and tissue metabolite analysis, and genomic expression Diet intervention for 8-weeks	Cardiac TAG significantly increased following high-SFA diet High SFA diet prevented decline in EF and stroke work observed in dietary control Failing hearts from rats fed the high SFA diet showed normalisation of glucose and oleate oxidation compared to dietary controls
Tuunanen et al. (27)	Total participants: *n* = 24 Control group: *n* = 8 Intervention group: *n* = 18 Control group: 75.0% men Intervention group: 77.7% men Control group EF: 66.0% Intervention group EF: 33.0% Control group NYHA class: 0.0 Intervention group NYHA class: 2.2 Control group BMI: 26.0 kg/m^2 Intervention group BMI: 28.0 kg/m^2 Race and weight not reported	Prospective study Both groups received Acipimox (250 mg orally twice daily)	Myocardial perfusion and oxidative metabolism via PET, cardiac dimensions and function, and insulin sensitivity Baseline and after treatment	Comparable levels of β-oxidation at baseline between groups Acipimox reduced cardiac work and cardiac efficiency in the intervention group only

	Of note is that all patients had idiopathic dilated cardiomyopathy			
Listenberger et al. (31)	CHO and 25RA cells, and *Dgat1*$^{-/-}$ fibroblasts	Cells cultured in knockout Dulbecco's modified Eagle's medium supplemented with 10% FBS, 1 mM/L-glutamine, 50 units/ml penicillin G sodium, and 50 units/ml streptomycin sulphate. Cell culture incubated with palmitate and/or oleate bound to BSA at 6.6:1 molar ratio Cells supplemented with FA media for 6 hours with ^{14}C-labelled palmitate	Apoptosis, uptake and accumulation of palmitate, lipid accumulation palmitate incorporation into triacylglycerol, MS for ceramide and TAG, enzyme activity DNA laddering measured after 26* hours Palmitate, neutral lipid accumulation, alterations in lipid composition and lipotoxicity measured after 6 hours of incubation with different FAs *SCD activity measured at 0, 18, 24 and 28 hours	Palmitate-associated apoptosis and DNA laddering was prevented with co-incubation with oleate Oleate prevented increase in ceramide associated with palmitate Increased activity of SCD associated TAG synthesis and resistance to palmitate-induced apoptosis Oleate promoted neutral lipid accumulation and led to greater incorporation of palmitate into TAG Failure of *Dgat1*$^{-/-}$ fibroblasts to accumulate TAG was associated with cell death
O'Donnell et al. (33)	3-week old male Sprague Dawley rats Control group: *n* = 16 Intervention group: *n* = 18	Control: sham procedure Intervention: pressure overload model of cardiac failure via TAC	Substrate metabolism using NMR, cardiac function, lipid content and turnover Hearts excised 10-12 weeks post-banding and perfused	Oxidation of TAG was not evident in failing hearts yet was observable in control rats TAG turnover significantly reduced in HF compared to control hearts TAG turnover uncoupled from workload in failing hearts Reduced ability to oxidise endogenous TAG was not matched by increase in exogenous oxidation of palmitate
Lahey et al. (34)	3-week old male Sprague Dawley rats Control oleate: *n* = 10-15 Control palmitate: *n* = 10-15 Intervention oleate: *n* = 10-15 Intervention palmitate: *n* = 10-15	Control: sham procedure Intervention: pressure overload model of cardiac failure via TAC	*Ex vivo* cardiac function and metabolism measured following ^{13}C-labelled palmitate and oleate perfusion, TAG dynamics, DAG and ceramide content, and protein expression Hearts excised 12 weeks post-banding and perfused	TAC + oleate prevented decline in contractility seen in TAC + palmitate TAC + oleate preserved normal TAG turnover and had greater TAG enrichment TAC + palmitate hearts had lower levels of DAG and increased C16 ceramide TAC + oleate leads to preservation of PPAR-α target gene mRNA

Tavazzi et al. (35)	Randomised 7046 patients Excluded 71 Total participants: *n* = 6975 Control group: *n* = 3481 Intervention group: *n* = 3494 Control group: 78.8% men Intervention group: 77.8% men Control group EF: 33.2% Intervention group EF: 33.0% Control group NYHA class: 63.2% II, 34.1% III, 2.7% IV Intervention group NYHA class: 63.7% II, 33.7% III, 2.9% IV Control group BMI: 27.0 kg/m^2 Intervention group BMI: 27.0 kg/m^2 Race and weight not reported	Randomised control trail Control group: placebo Intervention group: 1 g/d n-3 PUFA (850-882 mg EPA and DHA ratio 1:1.2) All participants were also randomly assigned to 10 mg/d oral rosuvastatin Study power of 90%	Cardiovascular examination, vital signs, 12-lead electrocardiogram, compliance with study protocol, assessment of adverse events and blood biochemistry Primary outcome(s); time to death, and time to death or admission to hospital for cardiovascular reasons Secondary outcome(s): cardiovascular mortality or admission for any reason, sudden cardiac death, admission for cardiovascular reasons, admission for HF, MI and stroke Baseline, 1, 3, 6, and 12 months and then every 6 months until the end of the trial Median follow-up of 3.9 years	Significantly greater all-cause mortality observed in control group Fewer deaths or hospital admissions attributable to cardiovascular reasons in intervention group Significant reduction in plasma TAG in intervention group

SFA, saturated fat; TAG, triacylglycerol; PET, positron emission tomography; EF, ejection fraction; NYHA, New York Heart Association; BMI, body mass index; FBS, foetal bovine serum; BSA, bovine serum albumin; FA, fatty acid; MS, mass spectrometry; DNA, deoxyribonucleic acid SCD, stearoyl-CoA desaturase; TAC, transverse aortic constriction; NMR, nuclear magnetic resonance; HF, heart failure; DAG, diacylglycerol; PPAR-α, peroxisome proliferator activated receptor alpha; mRNA messenger RNA; PUFA, polyunsaturated fatty acid; EPA, eicosapentaenoic acid; DHA docosahexaenoic acid; MI, myocardial infarction.

Table 2 Summary dietary sodium studies in HF patients presented in the current review

Study	Participant characteristics	Study Design	Measures and time points	Key observations
Travers et al.(42)	Total participants: *n* = 67 Control group: *n* = 33 Intervention group: *n* = 34 Control group: 48.4 % men Intervention group: 58.8 % men Control group EF: 40.2% Intervention group EF: 37.4% All patients had diagnosis of NYHA class IV HF Control group weight: 72.1 kg Intervention group weight: 76.2 kg Number screened, race and BMI not reported	Randomised control trial Control group: free fluid Intervention: fluid restriction to 1 L/d free fluid	Renal profile measured for the duration of experiment. BNP assayed for first 7 days and alternative days following this until stability. Daily weight, HF status and medication review Primary end point: time in days to clinical stability Secondary endpoints: changes in renal parameters, BNP, duration of intravenous HF therapy and compliance with fluid restriction Followed until clinical stability	Significant reduction in fluid intake in intervention group No significant difference in average weight loss, time to clinical stability, duration of intravenous HF therapy, BNP or renal profile at time of clinical stability between groups
Aliti et al.(43)	813 individuals screened 738 excluded Total participants: *n* = 75 Control group: *n* = 37 Intervention group: *n* = 38 Control group: 64.8 % men Intervention group: 73.6 % men Control group EF: 24.6% Intervention group EF: 27.4% Control group NYHA class: 45.9% III, 48.6% IV Intervention group NYHA class: 47.3% III, 42.1% IV Control group weight: 82.4.0 kg Intervention group weight: 78.0 kg Race and BMI not reported	Randomised control trial Control group: 3-5 g/d sodium intake, minimum fluid intake of 2.5 L/d Intervention group: 800 mg/d sodium and 800 mL/d fluid	Daily assessment of perceived thirst, weight, use of intravenous diuretics, vasodilators and inotropes and clinical congestion score Serum biochemical analysis Primary outcome: weight loss and clinical stability during hospital stay (measured at 3 days) Secondary outcomes: assessment of thirst and hospital readmission within 30 days of discharge 30-day follow-up	No statistical difference in length of stay, weight loss clinical congestion score, intravenous medications, laboratory tests or 30-day readmission score. Rating of thirst was significantly increased in intervention group compared with control. Intervention group showed significantly greater congestion at 30-day follow-up

Colín-Ramirez et al.(44)	451 individuals screened 413 excluded Total participants: *n* = 38 Control group: *n* = 19 Intervention group: *n* = 19 Control group: 38.9% men Intervention group: 36.8 % men Control group EF: 46.5% Intervention group EF: 34.5% Control group NYHA class: 84.2 % II, 15.8 % IV Intervention group NYHA class: 94.7% II, 5.3% IV Control group BMI categories: 0.0% <18.5 kg/m^2, 21.1% 18.5-24.9 kg/m^2, 26.3% 25.0-29.9 kg/m^2, 52.6% ≥ 30 kg/m^2 Intervention group BMI categories: 0.0% <18.5 kg/m^2, 10.5% 18.5-24.9 kg/m^2, 26.3% 25.0-29.9 kg/m^2, 63.2% ≥ 30 kg/m^2 Population 95% white, 3% Afro-American and 3% South Asian Weight not reported	Randomised control trial Control group: moderate sodium intake (<2300 mg/d) Intervention group: low sodium intake (<1500 mg/d) Both groups were prescribed 50-55% dietary kcal from carbohydrate, 15-20% protein and 25-30% lipids, and were provided with a sample of 6 daily menus according to their energy requirements	3-day food record during week prior to clinical visit (2 weekdays + 1 weekend day) Serum biochemical analysis, BNP Quality of life using KCCQ Baseline, 3 months and 6 months follow-up	2 patients dropped-out and 1 died Both groups significantly reduced sodium intake compared to baseline values At 6 months median BNP significantly reduced in the intervention group but did not differ between groups Median quality of life scores improved significantly in the intervention group and trended to improve in the control group. No change in NYHA classification between groups was observed
Paterna et al.(45)	2 phases Phase 1 4728 screened. 1927 participants met entry criteria Total participants: *n* = 1927 Control group: *n* = 974 Intervention group: *n* = 953 Control group: 37.1% men Intervention group: 36.9 % men Control group EF: 34.4% Intervention group EF: 33.7% Control group weight: 84.5 kg Intervention group weight: 82.7 kg	Randomised control trial Phase 1 Control group: Intravenous infusion of furosemide (250mg) twice daily, low-sodium diet (1.8 g/day), and 1000 mL/d fluid restriction Intervention group: Hypertonic saline solution (150 mL of 1.4%-4.6%) twice daily, intravenous infusion of furosemide (250 mg) twice daily, moderate-sodium diet (2.8 g/day), 1000 mL/d fluid restriction Phase 2	Serum biochemical analysis, BNP, 24 hour natriuresis and diuresis, clinical and pharmacological assessment and cardiac function Primary outcomes: death or first hospitalisation for worsening HF Secondary outcomes: death from cardiac cause, hospitalisation for cardiac causes and combined end point of death from cardiac cause or hospitalisation for a change for a cardiac cause and change in NYHA classification Phase 1 Baseline and discharge Phase 2 Every week for first month, every month for first 6 months and 3 monthly thereafter	Phase 1 Significant increase in diuresis observed in both group from admission to discharge although was significantly greater in the intervention group Natriuresis was significantly greater in the intervention group Significant increase in serum sodium concentration in intervention group. No increase in control group Significantly lower BNP in intervention group at discharge when compared to control group

	All participants were NYHA class III at entry Phase 2 Total participants: *n* = 1927 Control group: *n* = 974 Intervention group: *n* = 953 Control group: 36.4% men Intervention group: 37.3 % men Control group NYHA: 83.4 % I, 16.8 % II Intervention group NYHA: 77.2% I, 22.8% II BMI and race not reported	Groups from phase 1 were continued on respective sodium-restricted diets as out-patients		Greater number of patients moving from NYHA class III to class I following intervention Phase 2 156 subjects from phase 1 did not complete phase 2, leaving 1771 subjects who completed the study (control group *n* = 890; intervention group *n* = 881) BNP significantly lower in intervention group when compared to control group. Greater weight stability and diuresis in the intervention group Significant reduction in mortality and combined mortality + readmissions in the intervention group at 57 months follow-up
Jefferson et al. (47)	Total participants: *n* = 18 77.7% men EF: 28.0% NYHA class: 22.2% I, 61.1 % II, 16.6% III BMI: 31.1 kg/m^2 Weight and race not reported	Prospective study All participants received a <2,000 mg/d sodium-restricted diet + individualised counselling from a dietitian before discharge and during study period (1 week)	3-day food record collected prior to baseline and daily food record during study Baseline and 1 week follow-up	2 subjects were excluded due to missing data. Final data based on N = 6 Significant reduction in sodium and kcal intake at 1 week compared to baseline values Calcium, phosphate, thiamine and folate intakes were significantly reduced at 1 week

BNP, brain natriuretic peptide; EF, ejection fraction; HF, heart failure; NYHA, New York Heart Association; BMI, body mass index; KCCQ, Kansas City Cardiomyopathy Questionnaire.

Table 3 Summary dietary studies in HF patients presented in the current review

Study	Participant characteristics	Study Design	Measures and time points	Key observations
Spaderna et al. (51)	380 participants met inclusion criteria 340 consented. 22 did not complete questionnaire Total participants: *n* = 318 72.8% men EF: 21.5% NYHA class(N=316): 39.6% II, II-III, III, 36.1% III-IV, 24.4% IV BMI: 25.9 kg/m^2 Race and weight, not reported	Prospective study Participants recruited from The Waiting for a New Heart Study were mailed a food frequency questionnaire	Food frequency questionnaire and fluid intake Resting heart rate, EF, mean blood pressure, peak VO_2, serum sodium, interventricular conduction delay, ischaemic diagnosis (used to calculate Heart Failure Survival Score) Death on waiting list, high-urgency transplantation, elective transplantation, delisting due to clinical deterioration or improvement Baseline and occurrence of outcome listed above (mean follow-up of 462.8 days)	6 participants were lost to follow-up Fluid intake > 2 L/d associated with hyponatraemia Greater intake of salty food significantly associated with shortened time to transplantation Consumption of foods high in MUFA+PUFA associated with reduced hazard ratio for death/deterioration
Hummel et al. (54)	Screened 22 participants Total participants: *n* = 14 7.1% men EF: 66.0% NYHA class: 14.3% II, 85.7% III Weight: 94.0 kg BMI: 35.5 kg/m^2 Race not reported Total population classed as displaying HFpEF	Prospective study Participants randomised to a DASH diet with a goal of 1150 mg sodium/2100 kcal	3 day food diary, 24-hour urinary sodium and potassium, blood pressure and cardiac function Day 1 (blood pressure) and 2 (cardiac function), and 25 days follow-up (21 days of diet)	1 participant withdrawn due to hyperkalaemia Significant decrease in systolic blood pressure following diet Arterial elastance, stroke volume and EF all improved significantly following dietary intervention
Levitan et al. (56)	Identified 4043 participants Excluded 828 Total participants: *n* = 3215 0.0 % men BMI: 30.5 kg/m^2 85.4% White not of Hispanic origin, 10.5% Black, 1.7% Hispanic, 1.0% Asian/Pacific Islander, 0.5% American Indian/Alaskan Native No measures of cardiac function or NYHA classification or weight	Prospective study Participants were taken from the Women's Health Initiative dietary modification and observational study and were followed from HF hospitalisation to date of death or last contact with participant prior to August 2009	Modified block food frequency questionnaire, Mediterranean and DASH diet scores Median follow-up of 4.6 years	1385 deaths occurred, of which 694 attributable to CVD. Women who died were older, more likely to smoke, were less active and had a lower BMI Highest quartile* of Mediterranean and DASH scores had greater intake of fruit and vegetables, nuts, legumes, whole-grains, low-fat dairy, fish and lower intakes of red and processed meat, in addition to sugar-sweetened beverages

				Higher DASH score associated with significantly lower hazard rate of death. Non-significant trend for lower hazard rate for death following Mediterranean diet Vegetables, nuts, nuts and legumes and wholegrain inversely associated with mortality post hospitalisation from HF *tertitles for sugar-sweetened beverages due to limited range of intake
Chrysohoou et al. (57)	Total participants: *n* = 372 84.4 % men BMI: 28.0 kg/m^2 All participants were of HFrEF (EF <40%). Race, NYHA class and EF were not reported	Cross-sectional Statistical power of 87%	Semi-quantitative food frequency questionnaire and Mediterranean diet score, cardiac function	Greater adherence to Mediterranean diet associated with a significant improvement diastolic function and flow propagation Greater intake of fish, olive oil and vegetables associated with improvements in diastolic indices
Olvera et al. (59)	Total participants: *n* = 39 Control group: *n* = 18 Intervention group: *n* = 21 Number randomised, sex, race, BMI, EF, and NYHA class not reported Note study performed in patients with HF and right ventricular dysfunction	Randomised control trial Control group: standard diet with 50% energy from carbohydrate, 30% from fat and 20% from protein Intervention group: 40% energy from carbohydrate, 40% from fat and 20% from protein Sodium and fluid intake not available	Bioelectrical impedance and anthropometry, stress test and laboratory assessments Baseline and 2 months follow-up	Significant reduction in weight in intervention group Significantly greater number of individuals with improved symptoms in intervention group compared to control group Improvement in oxygen saturated following intervention
Evangelista et al. (62)	Total participants: *n* = 14 Control group: *n* = 4 Intervention group 1: *n* = 5 Intervention group 2: *n* = 5 Control group: 75.0% men Intervention group 1: 80.0% men Intervention group 2: 80.0% men Control group EF: 26.6% Intervention group 1 EF: 27.8% Intervention group 2 EF: 23.8%	Randomised control trial Control group: AHA recommendations for healthy adults. No energy restrictions Intervention group 1: high protein hypoenergetic diet (40% total energy from carbohydrates, 30% from fat and 30% from protein)	Anthropometry, functional status, biochemical measurements, LHFQ and 3-day food diary Baseline and 12 weeks follow-up	Significantly greater weight loss in intervention group 1 compared to intervention group 2 and control group Trend toward increased lean mass in intervention group 1 Greater improvement in LHFQ in intervention group 1 than in intervention group 2

Control group NYHA class: 25.0% II, 75.0% III Intervention group 1 NYHA class: 40.0% II, 60.0% III Intervention group 2 NYHA class: 40.0% II, 60.0% III Control group weight: 109.8 kg Intervention group 1 weight: 110.8 kg Intervention group 2 weight: 99.5 kg Control group BMI: 40.7 kg/m^2 Intervention group 1 BMI: 37.3 kg/m^2 Intervention group 2 BMI: 35.9 kg/m^2 kg/m^2 Control group LHFQ: 70.9 Intervention group 1 LHFQ: 68.5 Intervention group 2 LHFQ: 73.0 Control group peak VO_2: 10. 9 mL/kg/min Intervention group 1 peak VO_2: 13.5 mL/kg/min Intervention group 2 peak VO_2: 12.7 mL/kg/min Race not reported	Intervention group 2: standard protein, hypoenergetic (55% total energy from carbohydrates, 30% from fat and 15% from protein) Both intervention groups participated in intensive 12-week supervised weight-loss intervention Meals plans designed to incorporate 500-800 kcal/d deficit		Significant improvement in VO_2 peak in intervention group 1

EF, ejection fraction; NYHA, New York Heart Association; BMI, body mass index; VO_2, maximal oxygen consumption; HFpEF, heart failure with preserved ejection fraction; DASH; dietary approaches to stop hypertension; CVD, cardiovascular disease; HFrEF, heart failure with reduced ejection fraction; AHA, American heart association; LHFQ, Minnesota Living With Heart Failure Questionnaire

Table 4 Summary of nutritional education studies in HF patients presented in the current review

Study	Participant characteristics	Study Design	Measures and time points	Key observations
Sethares et al. (69)	Recruited 88 participants 8 withdrew and 10 died before follow-up Total participants: *n* = 67 Control group: *n* = 37 Intervention group: *n* = 33 Control group: 43.2% men Intervention group: 51.5% men Control group: 89.2% white Intervention group: 93.9% white Control group EF: 38.8% Intervention group EF: 41.5% Control group NYHA class: 3 Intervention group NYHA class: 3 BMI and weight not reported	Randomised control trial Control group: received usual care Intervention: received tailored message during hospitalisation, 1 week and 1 month post-discharge.	Health belief scales, LHFQ, medication and hospital readmission rates LHFQ determined at 1 month post-discharge Change in benefit and barriers towards medications, diet and self-monitoring at 1 week and 1 month Readmission rate at 3 months	No significant change in hospital readmissions between groups No change in quality of life scores Intervention led to a significant improvement in understanding benefits and barriers towards diet and self-monitoring. No change to perceived benefit of medication between groups
Arcand et al. (70)	Recruited 50 patients 3 excluded Total participants: *n*= 47 Control group: *n* = 23 Intervention group: *n* = 24 Control group: 73.9% men Intervention group: 75.0% men Control group EF: 23.0% Intervention group EF: 22.0% Control group mean furosemide: 82 mg/d Intervention group mean furosemide: 90 mg/d Weight, BMI, race or NYHA class not reported	Randomised control trial Control group: Prescribed 2 g/day sodium diet and provided with self-help low-sodium literature Intervention: Prescribed 2 g/d sodium diet, low sodium literature plus two education sessions with a dietitian	3 day food record (including 2 weekdays + 1 weekend) Primary outcome: change in sodium intake Secondary outcomes weight, medication fluid Baseline and 3 month follow-up	Significant reduction in dietary sodium intake following the intervention No change in dietary macronutrients between groups
Kollipara et al. (71)	Recruited 105 patients 7 excluded Total participants: *n* = 97	Prospective Participants grouped based on dietary sodium score	Sodium knowledge assessed by Parkland Dietary Sodium Knowledge Test, TOFHLA 90-day hospital readmission	90-day hospital readmission inversely associated with sodium knowledge

	Very low dietary sodium knowledge: *n* = 40 Not very low dietary sodium knowledge: *n* = 57 Very low dietary sodium knowledge: 63.0% men Not very low dietary sodium knowledge: 70.0% men Very low dietary sodium knowledge: 78.0% African American Not very low dietary sodium knowledge: 82.0% African American BMI, weight, EF and NYHA class	≤3: Very low dietary sodium knowledge ≥4: Not very low dietary sodium knowledge		Significant association between TOFHLA and dietary sodium knowledge following intervention
Colín-Ramirez et al. (72)	Randomised 65 patients 8 excluded or lost to follow-up Total participants: *n*= 58 Control group: *n* = 31 Intervention group: *n* = 27 Control group: 61.3% men Intervention group: 33.3% men Control group EF: 42.3% Intervention group EF: 40.0% Control group NYHA class: 56.7% I, 30.0% II. 13.3% III Intervention group NYHA class: 59.3% I, 22.2% II, 18.5% III Control group BMI: 27.3 kg/m^2 Intervention group BMI: 27.5 kg/m^2 Control group weight: 67.6 kg Intervention group weight: 63.9 kg Race not reported	Randomised control trial Control group: traditional dietary advice regarding sodium and fluid intake Intervention: Prescribed 2-2.4 g/day sodium, 50-55% dietary kcal from carbohydrate, 15% protein and 30-35% lipids. Fluids limited to 1.5 L/d. Received written and oral advice from a dietitian	Serum biochemical analysis, adapted KCCQ score and LHFQ, physical activity and 3-day food questionnaire (2 weekdays + 1 weekend) Baseline and 6 month follow-up	Significant reduction total fat and SFA following intervention Intervention led to significant reduction in sodium and fluid Significant reduction in number of NYHA class II and II and increase in class I in the intervention group.

EF, ejection fraction; NYHA, New York Heart Association; BMI, body mass index; KCCQ, Kansas City Cardiomyopathy Questionnaire; LHFQ, Minnesota Living With Heart Failure Questionnaire; TOFHLA, Test of Functional Health Literacy in Adults; SFA, saturated fat.