1 **Review Article**

2 **Dietary management of heart failure: room for improvement?**

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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.

78   The evolving knowledge of substrate usage in the failing heart has prompted several

79   investigators to re-examine the importance of dietary modification in this patient group. This

80   manipulation has extended further than preventing uncontrolled weight loss, itself shown to

81   be linked with greater incidence of mortality[7], to diet patterns linked with improvements in

82   cardiac function and delayed mortality. It may be suggested that the window for nutritional

83   intervention becomes narrower as HF progresses, with prevention of unintentional weight

84   loss potentially more important in end-stage disease. Indeed, management of malnutrition and

85   cachexia in HF patients is a key priority and has been reviewed extensively[8].

86   There is a substantial gap in clinical guidance for the dietetic management of patients

87   with HF, despite widely recognised nutritional deficiencies[9]. Sodium restriction has been the

88   significant nutritional recommendation by the American College of Cardiology

89   Foundation/American Heart Association (ACCF/AHA) for the reduction of congestive

90   symptoms[10] however this is not mirrored by European guidance[1], itself providing limited

91   advice other than of fluid restriction, maintenance of healthy weight and prevention of

92   malnutrition. Irrespective of sodium, both guidelines provide little information into additional

93   dietary changes that may be of benefit to the patient. The aim of this review is to present

94   current developments in the understanding of nutrition in HF and to highlight the areas that

95   need crucial development.

96

Ventricular remodelling

98   Left ventricular hypertrophy (LVH) is an important step in the development of HF.

99   LVH may initially be beneficial in normalising wall stress and haemodynamic function[11]

100   and several animal models have suggested that inhibiting the initial hypertrophic process is

101   detrimental[12,13]. Pathological ventricular remodelling patterns have recently been shown to

102   be associated with the incidence of HF and interestingly display differential risk for HF with

103   HFpEF and HFrEF[13]. Specifically, individuals with eccentric remodelling have a greater

104   than 2-fold risk of developing HFrEF, whereas those with concentric changes showed

105   increased risk of HFpEF. These statistics are of significance given the high prevalence of

106   HTN and IHD in HF patients[3].

107

108

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

141   the provision of a diet containing 60% lipid (25% palmitic acid, 33% stearic acid, and 33%

142   oleic acid)[25]. This study also demonstrated that the high-fat diet had no impact upon cardiac

143   performance in response to a dobutamine stress test, suggesting no additional impairment to

144   contractile reserve. Equally when failing hearts from rats fed a high-fat diet are perfused *ex*

145   *vivo* they demonstrate an improvement in cardiac FAO which is similar to that of non-

146   infarcted controls[26]. The authors of this study raise an important argument in that following

147   a MI, providing sufficient fuel for the non-infarcted myocardium is vitally important as the

148   burden of function is often shifted to healthy tissue. This is further compounded by the

149   observation that acutely limiting the availability circulating FAs in patients with

150   cardiomyopathic HF depresses cardiac function suggesting an important role of FAs in HF[27]

151   (table 1).

152

Cardiac triacylglycerol and lipotoxicity

154   The ability to store and utilise endogenous triacylglycerol (TAG) has been shown to

155   be important for cardiac function[28] and the role of endogenous TAG is particularly

156   important in the context of cardiac lipotoxicity. The traditional view of lipotoxicity relies

157   upon the concept that a reduced capacity of the cardiomyocyte to oxidise FAs coupled with

158   normal or increased FA delivery leads to progressive lipid accumulation, the shuttling of FA

159   species into the formation of biologically active intermediates such as diacylglycerol and

160   ceramide, and ultimately cellular and organ dysfunction [29]. An excellent review on the role

161   of FAs and their derivatives as signalling molecules can be found in van Bilsen and

162   Planavila[30].

163   Traditional view of lipotoxicity being a pathology solely attributable to lipid

164   accumulation is not completely accurate, and endogenous TAG accumulation may actually

165   protect against biologically active intermediate formation with a specific role of various FAs

166   in this process. Indeed previous research suggested that excessive supply of palmitate leads to

167   increased apoptosis, and that provision of oleate in addition to palmitate can attenuate this by

168   channelling palmitate into the formation of endogenous TAG and away from ceramide

169   synthesis[31]. Whislt impressive, this study was performed in a cell culture model and may not

170   reflect the chronic nature of lipid accumulation in disease or the consequences of prolonged

171   accumulation (table 1). Nonetheless, it reflects the complexity of lipid dynamics[32] and rasies

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

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

186

187 **Omega 3 intake in heart failure**

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

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

203   To draw further attention to the requirement of more research into diets specific to HF

204   patients, the results of two recent systematic reviews and meta-analyses have provided. The

205   first meta-analysis by Rizos et al.[37] considered randomised controlled trials whereby n-3s

206   were administered to participants by supplementation or diet with outcomes being all-cause

207   mortality, cardiac death, sudden death, MI, and stroke. The authors found no significant

208   relationship between n-3 supplementation and measured outcomes although a substantial

209   limitation is evident when examining the dose of n-3 intake used in studies. Indeed, studies

210   using a higher dose of n-3 supplement tended to show benefit yet they themselves were

211   limited by small sample size and therefore did not carry weight in the analysis. A more recent

212   meta-analysis[38] has also examined the relationship between n-3s and coronary risk as part of

213   larger review of the relationship between all FAs and coronary risk. The authors showed that

214   n-3 supplementation was found not to be significantly associated with a reduced risk of

215   coronary event in randomised controlled trials, whereas dietary n-3 intake was inversely

216   associated with coronary outcomes in prospective studies. Indeed this latter point is

217   reinforced by the observation that a higher marine or dietary n-3 (EPA and DHA) intake is

218   inversely associated with the development of HF[39]. It may be argued that if there is

219   discrepancy in the dietary evidence base for the general population, is it safe and justifiable to

220   offer the same advice to HF patients.

221   Considering all studies above regarding FAs and it is clear that the role of fat in HF is

222   not as simple as once thought. Rather than focusing solely on the calorie content of lipid, we

223   should consider the biological and metabolic effects various FAs may have, and use these to a

224   potential therapeutic advantage. N-3 supplementation may be of some benefit in HF patients

225   although it remains to be determined if such benefits could be gained from increasing intake

226   from dietary sources. At present there are no recommendations for HF patients in terms of

227   omega-9 (n-9) FAs and so it would be of use if appropriate studies were performed to

228   examine the effects of increasing n-9 FA consumption in addition to n-3s in this patient

229   group.

230

231   **Sodium and fluid restrictions in heart failure**

232   HF is characterised by altered renal perfusion which itself leads to increased

233   sympathetic activation and stimulation of the renin-angiotensin-aldosterone system (RAAS).

234   Sodium and fluid are retained leading to increased circulating volume in an attempt to

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

248   Several studies have shown little clinical benefit in restricting sodium and/or fluid,
249 although these may be confounded by their acute setting[42-44] (table 2). Compared to acute
250 decompensated HF patients managed with a free-fluid regimen, acute decompensated HF
251 patients managed with fluid restriction showed no improvement in time to clinical stability or
252 time spent receiving intravenous HF therapy[42]. An important limitation of this study is the
253 difference in achieved fluid intake in both groups. In the free-fluid group, total daily fluid
254 intake was 1466.6 mL versus 1074.3 mL in the fluid-restricted group. Although statistically
255 significant, clinically a greater restriction may have led to potential improvements however as
256 the authors note, this may have increased thirst and reduced compliance. Similarly, a
257 restriction of sodium (800 mg/day) and fluid intake (800 mL/d) in acute decompensated HF
258 patients increased thirst and led to no improvement in 30-day hospital readmission rates when
259 compared to a control group receiving no such restriction[43]. Furthermore, levels of brain-
260 type natriuretic peptide (BNP) were significantly higher in the restricted group at the end of
261 the study. A very real confounding factor in these trials examining sodium restriction is their
262 acute setting. Indeed, a low-sodium (1500 mg/d) diet proved to be more effective at reducing
263 BNP in ambulatory HF patients with NYHA II/III when compared to a moderate sodium
264 (2300 mg/d) diet[44]. An important aspect of this study is the use of ambulatory HF patients as
265 opposed to acute decompensated patients as described by references 39 and 40.

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

268 twice daily intravenous furosemide and 1000 mL fluid restriction in patients with HFrEF

269 produced a greater improvement in diuresis and natriuresis when compared to a group of HF

270 patients receiving a greater sodium restriction (1800 mg/day) and no hypertonic saline

271 solution. These patients were discharged on their in-hospital sodium and fluid restrictions in

272 addition to 50 – 125 mg twice daily furosemide. Those who maintained the moderate sodium

273 intake showed reduction in the occurrence of the combined endpoint of mortality and hospital

274 readmission in comparison to the restricted group[45]. The authors of this study speculate that

275 the greater sodium intake during the hospital admission and discharge may improve serum

276 sodium levels, chronically reduce neuro-hormonal activation and improve delivery of

277 diuretics to the loop of Henle, thus increasing their action of diuresis (table 2).

278 It is also relevant to consider in the context of sodium restriction that salt taste

279 diminishes with age[46], and that restricting sodium in hospitalised HF patients may lead to an

280 increased desire to satisfy the salt taste on discharge, further compounding difficulties of

281 adhering to a low-sodium diet. This concept would support the observations of Aliti et al.[43].

282 As such consideration needs to be given to the different HF populations (ambulatory or

283 hospitalised) in addition to the support required for patients to adhere to such a diet upon

284 discharge. Without support, we are expecting a great deal from the elderly HF population

285 which may be an additional reason why low-sodium diets are so difficult to follow. It would

286 also be prudent to note that restricting sodium intake in HF patients has been shown to be

287 associated with reduced intake of other important nutrients such as calcium, phosphate,

288 thiamine and folate[47] and therefore it would be advisable that patients discharged from

289 hospital with low-sodium advice receive regular follow-up to ensure compliance and also so

290 that dietary adequacy can be reviewed (table 2).

291 A recent Cochrane meta-analysis[48] has suggested that sodium restriction leads to

292 increased plasma renin, aldosterone, adrenaline and noradrenaline, irrespective of whether the

293 individual is hypertensive or not, and as such may aggravate features of decompensated HF

294 and explain the outcomes in previously mentioned studies. Furthermore elevated levels

295 plasma renin activity have been linked with increased mortality in patients with stable

296 symptomatic HF NYHA class III-IV, irrespective of pharmacotherapy[49]. In the analysis by

297 Graudal et al.[48] the authors report that restriction of sodium to a sub-normal level resulted in

298 a 1% and 3.5% decrease in systolic blood pressure (SBP) in normotensive and hypertensive

299 individuals, respectively. They also suggested that in normotensives a greater duration of

300 sodium restriction produced a larger reduction in SBP (estimated mean difference of 0.4

301 mmHg), however the reduction in SBP following sodium restriction in hypertensive

302 individuals did not appear to be time-dependent. It may be inferred from these observations

303 that sodium-restriction may have a greater impact upon afterload in those HF patients with

304 co-existing HTN who are salt-sensitive. Although HTN is more common in those individuals

305 with HFpEF, it is not exclusive to this group and therefore examining the specific benefits of

306 low-sodium diets in both hypertensive and non-hypertensive HFrEF and HFpEF populations

307 would be of use.

308   Considering different responses to sodium restriction between acute decompensated

309 and compensated HF patients, in addition to those who may be more salt-sensitive, a well-

310 designed clinical trial comparing short and long term effects of sodium restriction is required

311 not solely on the outcome of mortality but on additional clinically relevant factors such as

312 quality of life and hospital re-admission. A key recommendation should be that any sodium

313 and fluid sodium restrictions need be individualised based on the severity of HF, dose of

314 diuretic, degree of fluid accumulation and the clinical setting.

315

Dietary patterns and disease progression in heart failure

317   Discussion of the dietary management of each individual comorbidity experienced by

318 HF patients is beyond the scope of this review. However, is the author's opinion that through

319 appropriate nutritional education there is no reason why dietary patterns such as the

320 Mediterranean or Dietary Approaches to Stop Hypertension (DASH) cannot be modified to

321 account for comorbidities such as diabetes, COPD or gout, and act as an adjunct to traditional

322 pharmacotherapy for these conditions in HF patients.

323

DASH and Mediterranean Diet

325   Cohort studies have identified several dietary patterns as cardioprotective. Famous

326 examples include the Mediterranean and DASH diets[50]. A dietary pattern approach is

327 important as they acknowledge the synergistic effects of different foods, rather than focussing

328 on a single nutrient and recently studies have examined diet patterns in relation to specific

329 outcomes in HF[51]. Higher intakes of salty foods are associated with a shortened time to

330 transplantation in patients with advanced HF and increasing the intake of foods rich in

331 monounsaturated and polyunsaturated fatty acids (MUFA and PUFA, respectively) from

332 "occasionally" to "several times a week" was associated with approximately 50% reduction

333 in risk of death/deterioration[51]. Other interesting results from this study include the

334 association between different foods groups. Saturated fat (SFA) was significantly associated

335 with increased consumption of salty food, and inversely associated with MUFA and PUFA.

336 Similarly, both MUFA and PUFA also positively correlated with fruits/vegetables/legume

337 intake, thus suggesting that the consumption of one nutrient may predict other dietary

338 components. This observation may be important for the clinician or dietitian when taking a

339 diet history, and may allow a more rapid determination of diet quality. However, whilst

340 interesting this study is limited by the use of the food frequency questionnaire (FFQ) and

341 does not provide information on the amount of such nutrients consumed by the participants.

342 The DASH diet has a recognised beneficial effect in delaying the incidence of HF[52]

343 and should be examined for use in HF patients. Such a diet is typically low in SFA, with

344 increased consumption of low-fat dairy, complex carbohydrate, fish and vegetables[50]. This

345 dietary pattern is in contrast to that of the UK population which typically consume a diet

346 higher in refined carbohydrate and SFA, and lower in vegetables[53]. If individuals with HF

347 are required to change their diet, support and guidance to the most appropriate way of

348 achieving an optimal nutrient intake should be provided.

349 Hummel et al.[54] demonstrated a significant improvement in ventricular diastolic

350 function in 13 patients with HFpEF when these patients were provided with a sodium-

351 restricted DASH diet (DASH/SRD; 50 mmol/2100 kcal). Specifically, adherence to this

352 dietary pattern improved EF by 8% and increased stroke volume by approximately 11%.

353 Whilst impressive, the relatively small sample size and feeding protocol (controlled feeding

354 with prepared meals) mean that such a finding may not be observed in free-living individuals

355 with HF. Also, the nature of the population studied means that this finding may also be only

356 linked to those with HTN and HFpEF (table 3). The Geriatric Out of Hospital Randomised

357 Meal Trial in Heart Failure (GOURMET-HF) is one such study that will address if such

358 findings can be reproduced using a home-delivered low-sodium meal, examining quality of

359 life and cardiac functional parameters, although this study itself is still limited by the

360 provision of meals[55].

361 Levitan et al.[56] studied women enrolled in the Women's Health Initiative who were

362 admitted to hospital with HF to identify if adherence to a Mediterranean or DASH diet

363 pattern influenced CVD mortality. Following a median of 4.6 years of follow-up there were

364   1,385/3,215 deaths following HF hospitalisation. When stratified into quartiles, greater

365   adherence to either the Mediterranean or DASH diet was associated with a substantial

366   reduction in the hazard rate (HR) associated with mortality. Specifically, the HR for death

367   was 16% and 15% lower in the DASH and Mediterranean diet group, respectively, although

368   only reaching significance in the DASH group. Further analysis of the dietary intake of either

369   Mediterranean or DASH patients revealed that greater adherence to each diet was associated

370   with increased consumption of fruit and vegetables, nuts, legumes, whole grains and fish, and

371   reduced intake of sweetened beverages and red and processed meat. However important

372   limitations of this study were acknowledged by the authors, including difficulty in recording

373   sodium, fluid and olive oil intake, in addition to the group being of those diagnosed with

374   HFpEF. Whilst the results may be promising for the DASH diet, they do not support the

375   advocacy for the Mediterranean-style diet, despite a favourable trend. However, previous

376   cross-sectional data have shown that adherence to a Mediterranean Diet is associated with

377   improved diastolic function in individuals with congestive HF (CHF)[57] (table 3) and

378   subsequent studies have shown the Mediterranean Diet to reduce HF biomarkers in

379   individuals at high risk CVD[58]. Therefore at present, the role of the Mediterranean Diet in

380   the management of HF remains to be fully examined. There is a clear need for large,

381   randomised trials investigating if the improvement in mortality rate observed in the DASH

382   group is driven by the restriction in sodium or a rather combined effect of diet and sodium

383   restriction, and whether the Mediterranean diet has a role in the management of HF.

384

385   **Low carbohydrate and high protein**

386   There are several interesting reports regarding the use of low-carbohydrate diets in

387   humans with HF. However, an important limitation of some of these studies cited is that they

388   are almost exclusively conference abstracts and so caution should be exercised when

389   interpreting them. Nonetheless, in patients with HF and right-ventricular dysfunction a diet

390   classified as low in carbohydrate (40% carbohydrate, 40% fat, 20% protein) has been shown

391   to be effective at increasing weight loss and improving oxygen saturated when compared to a

392   conventional diet containing 50% of energy as carbohydrate[59]. In addition the authors report

393   an improvement in HF functional class. Like many HF trials, the study suffered from a

394   relatively small sample size and short duration, including 21 individuals studied for a

395   duration of 2 months. Therefore the long-term consequences of such a pattern remain

396 unknown in HF patients. Importantly, this study highlights a key issue facing nutritional

397 interventions: how diets are defined. Forty percent energy as carbohydrate may be regarded

398 by many as not being 'low carbohydrate' and is consistent with that achieved in the

399 PREDIMED study[60] (widely defined as a Mediterranean Diet). It would be appropriate for

400 the The National Heart, Lung, and Blood Institute (NHLBI) and NIH Office of Dietary

401 Supplements (ODS) working group[61] to also consider a standard protocol for reporting the

402 nutritional composition of experimental diets in HF studies to facilitate greater comparison of

403 dietary interventions, in addition to their other current recommendations (table 3).

404 Modifying protein intake has been shown to be effective in reducing weight in obese

405 patients (mean BMI 37.3 kg/m^2) with NYHA class II-III HF. Evangelista et al.[62] compared a

406 12-week hypocaloric diet (1200-1500 kcal/d) containing (as percentage of energy) 30%

407 protein, 40% carbohydrate and 30% fat to a standard protein, hypocaloric diet (55% total

408 energy from carbohydrates, 15% from protein, and 30% from fat) or the recommendations by

409 the AHA. The authors noted that the high protein hypocaloric diet led to a greater reduction

410 in % body fat and improved the patient's quality of life (assessed by the Minnesota Living

411 with Heart Failure Questionnaire). However, this study was performed in 5 individuals and is

412 therefore severely limited by the small sample size (table 3). At present, there are no

413 available large-scale dietary trails investigating protein intake and cardiac structure and

414 function, functional status, and quality of life in HF patients although these are in

415 development[63].

416

417 **The obesity paradox**

418 Studies 58 and 61 suggest a beneficial effect of weight loss in HF patients however it is

419 important to recognise that uncontrolled weight loss in HF is linked with increased incidence

420 of mortality[3]. The importance of weight in HF patients has frequently been examined as part

421 of the obesity paradox. The obesity paradox refers to observations that link the presence of

422 obesity (and in some instances overweight) in HF patients with improved survival in

423 comparison to lean counterparts. Horwich et al.[64] was one of the first groups to demonstrate

424 the inverse relationship between weight and mortality in patients with HF. In this study, the

425 majority of participants were of NYHA class IV, had an EF of 22% with obese patients more

426 likely to have diabetes and HTN. Following multivariate analysis overweight and obesity

427 were found to be associated with a significant survival benefit at 2 years with the worst

428   prognosis seen in those who were underweight, followed by those who were classified as

429   recommended weight. Importantly, whilst this study is used to draw evidence to the

430   protective nature of obesity, the survival benefit was not evident at 5 years follow-up. In

431   addition, categorisation of patients as underweight at baseline may not have accounted for

432   unintentional weight loss prior to the study. Importantly this study was only performed in

433   individuals with HFrEF and therefore may not apply to those with HFpEF. Despite this,

434   subsequently larger meta-analysis studies have further reinforced this observation.

435   Oreopoulus et al.[65] analysed a total of nine observational studies demonstrating that both

436   overweight and obesity were associated with a reduced relative risk of all-cause and

437   cardiovascular mortality when compared to patients with normal BMI levels. Regrettably the

438   authors of this study did not extract data on EF however a more-recent a meta-analysis

439   examined if HF subtype (HFrEF vs. HFpEF) impacted upon the obesity paradox. Using

440   individual patient data Padwal et al.[66] demonstrated the existence of a U-shaped relationship

441   between BMI and all-cause death in both HFrEF and HFpEF patients. In patients with HFrEF

442   or HFpEF, the lowest hazard ratio for all-cause mortality was observed when comparing

443   those individuals with a BMI between 30-34.9 kg/m^2 against the reference BMI range of

444   22.5-24.9 kg/m^2. In both subtypes a BMI less than 22.5 kg/m^2 was associated with a higher

445   risk of all-cause death.

446   There may be several mechanisms behind the proposed obesity paradox in HF. It is

447   well-known that advanced HF is associated with cachexia[8] and in this regard, greater

448   adiposity may simply reflect greater body energy stores and hence greater resistance to the

449   metabolic changes associated with the cachexic state. As shown by Padwal et al.[66]

450   individuals who were obese were also more likely to be receiving cardiovascular medication,

451   potentially suggesting greater clinical input and therefore greater clinical management of

452   their condition. It should however be noted that this was adjusted for in their study with no

453   effect upon their findings. Also the use of BMI as a marker of fatness in HF has been

454   questioned, with more accurate measurements of body composition being proposed[67]. The

455   presence of the obesity paradox means we may need to re-examine advice to achieve a

456   healthy weight in HF patients and raises important questions regarding the role of weight loss

457   (as described in Olvera et al.[59] and Evangelista et al.[62]) on the outcome of mortality. There

458   may be a point where excess weight is not associated with any additional benefit but

459   conversely increases risk. Indeed, in morbidly obese (BMI ≥40 kg/m^2) HF patients the

460   obesity paradox is absent[68]. Therefore one may conclude that in those individuals with

461 morbid obesity, intentional weight loss may be beneficial in terms of reducing mortality rate

462 however this should be carefully monitored and controlled. In lower BMI categories a

463 reduction in weight may improve clinical symptoms and disease classification, but may

464 impact negatively on long-term survival. It would be useful for future studies examining the

465 relationship between bodyweight and HF mortality to assess adipose tissues deposits (both

466 visceral and subcutaneous) and lean mass, in additional to cardiorespiratory fitness following

467 weight loss.

468

469 **Nutritional Messages – the role of the dietitian**

470 A key aspect of implementing a dietary strategy is addressing pre-conceived ideas and

471 beliefs regarding nutrition. A tailored nutritional message to patients with HF is sufficient to

472 alter patients' views and attitudes towards medications, adherence to a sodium-restricted diet

473 and self-monitoring[69]. Further support for the importance of nutritional input can be derived

474 from Arcand et al.[70]. In this 3 month study, HF patients randomised to a dietitian-led

475 education group showed greater improvements in salt reduction in comparison to usual care

476 (self-help literature). Whilst such a frequent dietetic input may be unlikely in the current

477 health-care setting, clinicians reviewing their patients may wish to follow-up nutritional

478 advice and reinforce nutritional messages at every opportunity. Indeed, frequent nutritional

479 counselling with HF patients may improve knowledge surrounding foods and reduce

480 admissions. In HF patients a low level of sodium knowledge has been shown to be associated

481 with a significantly greater odds ratio for hospital readmission for HF[71]. Using the Test of

482 Functional Health Literacy in Adults (TOFHLA) tool, sodium knowledge was associated

483 with a low health literacy score. When nutritional interventions are combined with

484 appropriate educational session substantial improvement in quality of life and disease score

485 can be seen. For example, a nutritional intervention consisting of 2000-2400 mg/d sodium,

486 50-55% (as % energy) carbohydrate, 15% protein, <10% SFA, 15% MUFA and 10% PUFA

487 coupled with written and oral instruction from a dietitian led to a significant improvement in

488 HF classification and quality of life when compared to a control group receiving general

489 nutritional advice[72]. Indeed the improvement in HF classification was reflected by a

490 significant reduction in the number of individuals with NYHA class II and III and an increase

491 in the number of those with class I by the end of the study (table 4).

492

493   As such, this would suggest that by using appropriate methods of patient education

494   and trained individuals it is never too late to make important and significant dietary changes

495   that may improve quality of life.

496

497   **Discussion and conclusions**

498   HF remains a chronic and debilitating condition. Whilst the value of dietary

499   manipulation is well-known in the primary, secondary and tertiary prevention of CVD it is

500   undervalued in patients with HF and is reflected by the paucity of data in guidelines. Despite

501   a large body of experimental data produced from animal models of HF examining the effect

502   of different diet compositions, this has not translated into human trials. From animal trials it

503   is clear that the traditional demonisation of fat may not be justified in HF, and human studies

504   should be designed to evaluate the therapeutic effectiveness of cardioprotective fats in HF.

505   Within this, consideration should be given to the underlying HF aetiology in addition to other

506   comorbidities. Indeed by manipulating dietary nutrient composition it is possible for those

507   individuals with other comorbidities to benefit from the potential therapeutic nature of food.

508   Studies that have been published in this field – albeit largely observational – now

509   suggest that diet advice in this area may need to be re-examined, with the traditional

510   cardioprotective diets such as the Mediterranean and DASH potentially being of benefit.

511   Such diet patterns have been shown to increase the consumption of cardioprotective food

512   items such as fruit and vegetables, nuts, legumes, whole grains and fish and are likely to have

513   additional health effects beyond HF.

514   It is simple to decide what foods an individual should consume, yet much more

515   difficult to actually achieve this. Regular nutritional education has been shown to lead to

516   better adoption of a prescribed diet and may lead to improved overall nutritional status. In

517   some studies, this has also translated to improvements in quality of life and reduced severity

518   of symptoms when delivered by nutritionally-trained individuals. The feasibility of such a

519   means of improving nutritional knowledge is clearly in need of evaluation, given the potential

520   cost such a service may incur.

521   Although the studies presented in this review are promising, many are limited by

522   small sample sizes, short duration and observational study design. It is therefore a

523   requirement that in order to progress towards better evidence-based dietary advice for

524   patients with HF, larger, longer, randomised clinical trials are needed. Such studies should

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

530

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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

Study	Population	Study design	Measurements	Results
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.