# Diet and Cardiovascular Disease: Heart Failure

## Part II: Red Meat, Micronutrients, Special Diets, and Obesity


## Abstract

Diet is a major modifiable factor in the prevention and management of cardiovascular diseases. Part I of this two-part manuscript on the relationship between diet and heart failure discussed several healthy dietary patterns. In general, a plant-based with seafood, lean meats, low-fat dairy products, and unsaturated fatty acid intake is helpful to prevent and manage heart failure. This part reviews several macronutrients that are harmful, the role of micronutrients and supplements in the pathogenesis and management of heart failure, and the impact of some special diets on this disease. Red meat and especially processed red meat is high in saturated fat and sodium which tend to worsen heart failure. Refined carbohydrates and sugar-sweetened beverages are also not good choices. Supplementation with some micronutrients such as iron and magnesium may be reasonable in these patients if clinically indicated. The role of Coenzyme Q10 is still unclear. Popular diets such as the Mediterranean, DASH, and vegetarian, are also reviewed in the context of this disease. The complex connection between obesity, cachexia, and HF is also discussed.


## Introduction

Heart failure (HF) is a chronic disabling disease with high morbidity and mortality. It is estimated that the lifetime risk of developing HF is about 20%[1]. It is a progressive disease, and either with preserved (HFpEF) or reduced ejection fraction (HFrEF). Although several pharmacological and non-pharmacological treatment options are available for patients with HFrEF[2], for patients with HFpEF, no therapies have been shown to improve morbidity or mortality in patients with HFpEF[3]. Heart failure is one of the most common reasons for hospitalization or rehospitalization[4]. It is often accompanied by comorbidities such as hypertension, diabetes mellitus, and atrial fibrillation[5,6]. It has an extremely poor prognosis and has a one-year fatality rate of 29.5%[7]. The health care costs attributable to HF are extremely high.

## Discussion

Healthy lifestyles, such as a prudent diet, play a mitigating role in the development and progression of heart failure. Plant-based diets help reduce HF incidence and improve its prognosis[8]. However, certain ingredients derived from fruits and vegetables can be harmful. Alcohol, a vegetarian product, if imbibed in high doses may cause and worsen HF[9]. Although whole grains are helpful, refined grains have the bran and germ sections removed during milling, along with all beneficial nutrients. This robs away any benefits gained by the intake of the whole grains[10]. Eating processed red meat and saturated fats have a detrimental influence on the myocardium[11]. The relationship between red meat and HF is reviewed in this section. Certain micronutrients and their relationship with heart failure are also reviewed. Besides the quality of diet, excessive caloric intake may result in an abnormal increase in body weight. A BMI >30 $kg/m^2$ is diagnostic of obesity[12]. Obesity has a complex relationship with heart failure. Despite

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increasing the risk of heart failure[13], obesity appears to be associated with survival benefits in many patients[14]. On the other hand, advanced cases of heart failure may be associated with sarcopenic obesity[15], and this is associated with a poorer quality of life (QOL) and a higher mortality[16].

**Red meat**

Recent studies suggest that the highest category of processed meat and red meat raise the risk of coronary heart disease[17], stroke[18], cardiovascular mortality[19]. Studies have also associated red meat consumption with an increased risk of HF[20]. The association is primarily with processed red meat, and these studies find no statistical increase in HF with consumption of unprocessed meat. In a study of 21,120 physicians, high consumption of red meat was associated with a statistically significantly increased risk of HF (Hazard Ratio or HR=1.02) per serving/day[20]. The data indicated that the risk was higher (HR=1.24) for the highest versus the lowest quintile) of consumption. However, no distinction was made between unprocessed and processed red meat in this study. However, the association appears to be primarily with processed red meat, and most studies find no statistical increase in HF with consumption of unprocessed meat.

Unprocessed and processed red meats were analyzed in two cohorts by Kaluza et al. In a cohort of 37,035 Swedish men, the consumption of unprocessed red meat was not associated with an increased risk of HF (HR=0.99 with a median intake of 83.2 g/day vs. 17 g/day) or HF mortality[21]. However, the consumption of processed meat was associated with an increased risk of HF; for each 50 g per day increment in intake, the risk of HF increased by 8% (HR=1.08), and HF mortality increased by 38% (HR=1.38). In women (cohort of 34,057 Swedish women, 2806 of whom were diagnosed with HF during 13 years of follow-up) they reported similar findings. For each 50 g day−1 increase in processed red meat consumption, the risk of HF in women increased by 11%-19%[22]. In this study, unprocessed red meat was not statistically detrimental. Processed meat has higher amounts of sodium and food additives. High dietary sodium intake boosts the risk of heart failure[23,24] mainly by raising blood pressure[25]. Trimethylamine N-oxide (TMAO) levels are also elevated in meat-eaters and people with HF[26]. TMAO levels correlate with B-type natriuretic peptide (BNP)[27] and are associated with HF severity[28] and HF mortality[29].

**Fats**

Fatty acids may have beneficial or detrimental effects on HF, depending on their type[30]. Most human studies have focused on trans fats and olive oil. Trans fats increase systemic inflammation as well as BNP levels in HF patients[31,32]. Fried foods are high in saturated fats and often have trans fats. In a large prospective study of 15,362 male physicians, there was a 103 % increase in HF risk in those with the highest versus the lowest levels of fried food consumption[33]. Olive oil (as consumed in the Mediterranean diet. or MedD) is rich in monounsaturated fats. In a study of 651 acute coronary syndrome patients, olive oil consumption was associated with a 65 % decrease in the risk of left ventricular systolic dysfunction[34].

**Micronutrients**

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Micronutrient deficiency is common in patients with HF. Further, several micronutrients present in the body are significantly altered by treatment modalities used in heart failure. These include minerals like sodium, potassium, calcium, magnesium, and selenium. These may be altered by increased urinary excretion due to loop diuretics[35]. Diet may also be altered due to reduced appetite and taste disorders, with the use of Angiotensin-converting enzyme inhibitors[36]. These drugs may also cause zinc deficiency[37]. Other micronutrients that may be affected by heart failure include vitamins C, E vitamins B1, B6, B12, folate, and beta-carotene (precursor of vitamin A). Levels of carnitine, CoQ10, and creatine may also suffer[38]. Micronutrient deficiency in these patients is associated with a higher mortality[39,40]. Micronutrient supplementation in human trials has failed to improve survival or provide robust beneficial effects in these patients[41]. Therefore, supplementation is not routinely advised unless these micronutrients are found to be deficient, irrespective of the cause[42]. A nutrient-rich dietary pattern is the best source of micronutrients and should be adhered to by HF patients[43-45].

**Thiamine**

Thiamine deficiency can cause heart failure (especially in underdeveloped countries) due to poor nutrition. Thiamine deficiency is also more common in patients with heart failure[46]. Although HF is improved by thiamine supplementation in severe thiamine deficiency, it remains unclear if thiamine supplementation is useful in patients with heart failure at large[47].

**Coenzyme Q10 (CoQ10)**

The role of CoQ10 remains unclear. In a 2-year prospective study with 420 participants, $CoQ_{10}$ 100 mg 3 times daily (or placebo) in addition to standard therapy showed that it significantly reduced major adverse clinical events (MACE), cardiovascular death by 43%, and all-cause mortality by 42%[48]. The patients also experienced an improvement in their New York Heart Association (NYHA) functional class. Mortensen and colleagues also reported that CoQ10 supplementation in moderate to severe HF was safe and well-tolerated. Although this study has suggested that CoQ10 supplementation in patients with HF may be beneficial, further data is needed before it can be recommended routinely in HF patients[49].

**Iron**

Iron deficiency anemia is common in patients with HF[50]. Anemia is defined by the World Health Organization as Hb < 13.0 g/dL in male adults and <12.0 g/dL in female adults[51]. Iron deficiency anemia in HF is associated with poor clinical status and worse outcomes[52]. Several trials such as the IRON-HF[53] and IRONOUT-HF[54] have shown that oral supplementation is unsuccessful in reducing MACE in HF patients. IV supplementation in HFrEF improves outcomes, as shown by the FAIR-HF[55] and CONFIRM-HF[56] trials. Currently, intravenous iron supplementation in patients with both HFrEF and iron deficiency is the only micronutrient supplementation strategy that has been shown to definitively improve outcomes in HF[57].

**Sodium**

Sodium restriction in HF has been recommended by the American College of Cardiology and the American Heart Association[58]. The Heart Failure Society recommends an intake of less than

2000 mg/day in moderate to severe HF. This is to prevent fluid overload. Although routinely followed, the data on clinical improvement, lower hospital readmission rates[59,60], and decreased mortality[61,62] with salt restriction remains unclear.

**K+**

In HF, the relationship between $K^+$ concentrations and adverse outcomes appears to be U-shaped, where both low-$K^+$ (<3.5 to 4.0 mmol/l) and high-$K^+$ (>5.5 to 6.0 mmol/l). levels are associated with adverse outcomes[63]. Although dietary intervention may help, a pharmacologic intervention will probably be needed in most cases[64].

**Mg**

Low magnesium levels and low magnesium intake has been associated with increased HF. Due to inconsistent benefits and potential adverse effects of magnesium (overload) in studies, magnesium supplementation is suggested only when hypomagnesemia has been proven or suspected as a cause for cardiac arrhythmias[65].

**Mediterranean Diet**

The MedD is characterized by high monounsaturated/saturated fat ratios, with olive oil as the main source of fat; high consumption of vegetables, fruits, legumes, and cereal products; moderate consumption of wine and dairy products; and low consumption of red and processed meat[66,67]. In a prospective study of 1,000 adults admitted with an acute coronary syndrome, there was a 7 % decrease in the likelihood of developing left ventricular systolic dysfunction during hospitalization. There was also a trend towards a 10 % lower risk of cardiac remodeling in those following the MedD, over 2 years[68]. Subsequent large prospective studies have also reported that MedD adherence was associated with decreases in HF incidence of 24 % in healthy adults[69], 21 % in healthy women[70], and 31 % in healthy men[71]. All studies reported that greater adherence conferred greater protection in a dose-dependent manner. In a recent meta-analysis of six studies (n=10,950), the MedD reduced the risk of HF by 70 %[72]. Extra virgin olive oil has a high content of polyphenols and accounts for a significant fraction of this beneficial effect[73].

Some studies have questioned the beneficial effect of MedD on HF, especially in women. Papadaki et al found that in 7403 participants without prevalent HF (followed for a median of 4.8 years) there was no reduction in the risk of clinical cases of HF with MedD[74]. Strengers et al. in a recent study, found no risk reduction in women, while a 12% lower risk was noted in men[75]. In general, MedD with extra virgin oil and nuts is helpful in HF. MedD reduces several HF risk factors such as hypertension[76], type 2 diabetes mellitus (T2DM)[77], and obesity[78], and this helps in protecting against HF. MedD has been shown to beneficially decrease oxidative stress, reduce plasma N-terminal pro-BNP levels[79], and lower oxidized LDL-C levels[80].

**DASH**

The DASH diet emphasizes the intake of fruits and vegetables; lean protein such as poultry, fish, and nuts; fiber and whole grains; and low-fat dairy products. This diet provides adequate levels of micronutrients, such as potassium, calcium, and magnesium, deemed to lower blood

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pressure[81]. High blood pressure is a major cause of HF. While the DASH diet has been proven to effectively reduce blood pressure, the benefit of the DASH diet in patients with HF has been infrequently investigated. However, the consensus is that the DASH diet helps prevent and reduce HF, irrespective of gender. In a large Swedish study in postmenopausal women (36,019), aged 48 to 83 years, during a seven-year follow-up, those who had higher adherence to the DASH diet had a 37% lower rate of HF[82]. In a study of men, aged 45 to 79 years, over a nine-year follow-up, the highest quartile for the DASH diet adherence had a 22% lower rate of HF incidence[83]. A 2013 systematic review and meta-analysis including >144,000 adults reported that a DASH-like diet was associated with significant risk reduction against HF (29 %)[84]. Another prospective observational study conducted in 3,215 women with pre-existing HF found a 16 % decrease in mortality in those with the greatest DASH adherence after 4.6 years[85]. Besides the risk reduction, these patients improve clinically, with an improvement in exercise capacity and quality of life[86]. DASH diet intake has been shown to improve arterial elasticity, decrease arterial stiffness, and reduce BP[43,44,85]. Its adherence is also associated with a favorable end-diastolic volume, stroke volume, and ejection fraction[87]. There is a favorable decrease in 24-hour urinary sodium and BNP levels[86]. These changes are noted even if there is no associated weight loss. DASH diet beneficially modifies antioxidant capacity[88], inflammatory response, liver function, coagulation[89], natriuresis[90], sympathetic activation[91], and endothelial function[92], in these patients.

**Vegetarian Diet:**

Vegetarian diets are plant-based diets. A vegan diet does not contain any animal products (meat, fish, poultry, eggs, or dairy) and consists of plant-based foods, such as fruits, vegetables, whole grains, and legumes/beans. Lacto-ovo-vegetarians also consume dairy products and eggs[93]. Pesco-vegetarian (pescatarians) diet avoids meat or poultry but does allow fish and shellfish, eggs, and dairy. Semi-vegetarians or "flexitarians"– eat all foods, including meat, poultry, fish and shellfish, eggs, and dairy, in addition to plant-based foods, such as fruits, vegetables, whole grains, and legumes/beans – they however limit their red meat and poultry intake[94]. The Mediterranean and DASH diets discussed above are high in plant-based foods as their components. Vegetarian diets are associated with lower blood pressure, reduced platelet aggregation, better weight management, and a reduced risk of developing T2DM. Vegetarian foods also inhibit oxidation of LDL cholesterol, raise HDL cholesterol, and reduce total cholesterol[95]. Pai et al. reported that a vegetarian diet, compared to the non-vegetarian diet, was associated with a lower prevalence of LV diastolic dysfunction (Odds Ratio or OR=0.42) and a lower prevalence of LV hypertrophy with (OR=0, 30)[96].

**Obesity/Cachexia**

Obese individuals have twice the risk of HF compared to those with a normal BMI[97]. The Framingham heart study found that there was a 5% increase in men and a 7% increase in women for the risk of developing HF per unit increase in BMI[98]. The longer the duration of morbid obesity the higher the prevalence of HF - 70% after 20 years and 90% after 30 years.[99]. Early age obesity also prognosticates future HF. In the Multi-Ethnic Study of Atherosclerosis (MESA) cohort, a higher self-reported weight at 20 and 40 years of age resulted in an increased HF risk later in life[100]. A weight loss of 5-10% is recommended for HF patients with body mass index ≥

35 kg/m2[101]. This improves cardiac function and clinical symptoms. Dietary calorie restriction helps reduce body weight by inducing a calorie deficit. However, certain dietary patterns have been associated with greater weight loss. Plant-based eating results in weight loss[102,103] and decreases weight gain[104]. Conversely, greater intake of animal-based foods results in a higher BMI[105,106]. Special diets such as MedD[107]and DASH diet[108] also help in weight reduction. The obesity HF link is related to the effects of obesity on inflammation, hypertension, T2DM, and dyslipidemia[109,110].

The relationship between body weight in patients with HF is however not that simple. HF patients often experience two other phenomenon – obesity paradox and sarcopenia/cachexia. In the obesity paradox, obese patients diagnosed with HF have significantly better survival than normal-weight HF patients, while underweight patients have a poor prognosis than normal-weight HF patients. This paradox in HF was first noticed by Horwich and colleagues[111]. Several subsequent studies have verified this observation. Kenchaiah et al. reported that in a randomized controlled trial of 7,599 symptomatic patients with HFrEF and HFpEF, overweight and obese patients had lower mortality when compared with those who were underweight or had a normal BMI[112]. In a meta-analysis of 9 observational studies (28,209 patients), Oreopoulos et al. concluded that overweight and obese HF patients had lower mortality compared with normal BMI patients[113]. Another systematic review of 6 studies found that overweight individuals had a lower risk for hospitalization and total and CVD mortality when compared to underweight patients with chronic HF[114]. Obesity paradox is an accepted phenomenon in patients with HF. The underlying mechanisms are not clear, but factors such as fat distribution, lean mass, and cardio-fitness levels are postulated to play a role[115].

Heart failure when severe, is accompanied by sarcopenia and cachexia. Sarcopenia is a loss of skeletal muscle quantity or quality with a decline in muscle strength and/or physical performance not necessarily due to weight loss[116]. HF patients may also develop cachexia as the disease progresses[117]. Cachexia results from increased protein catabolism and is characterized by severe body weight, fat, and muscle loss[118]. Almost 20% of HF patients suffer from sarcopenia and cachexia, with a significant decrease in the quality of life and survival in these patients. Dietary intervention with excess protein intake (1.0–1.2 g/kg body weight/day) appears to help improve muscle mass and physical function in these patients[119].

## Conclusion

Diet has a significant effect on heart failure. The two major causes of heart failure are coronary artery disease and diabetes mellitus and can be almost completely prevented by eating a prudent diet. In the first part of this manuscript, the benefits of a plant-based diet were discussed. These non-omnivore diets are high in antioxidants, micronutrients, dietary nitrate, and fiber and low in saturated/trans fats and sodium. This results in a decreased HF incidence/severity. Red meat and saturated fats increase inflammation, decrease antioxidant activity, and detrimentally modulate the gut microbiome. The restriction of salt to prevent fluid retention is generally followed, although its restriction remains controversial. Obesity is an enigma. Despite the complex relationship between the obesity paradox and sarcopenic obesity, a weight reduction of 5% to 10% is beneficial if the obesity exceeds a BMI of 35 kg/m2. The Mediterranean, DASH, and

vegetarian diets are heart-healthy and help attenuate HF. As nutritional modification is a relatively low-risk and low-cost option, it is an attractive strategy for reducing HF incidence and progression.

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