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STATE-OF-THE-ART REVIEW

Dietary Interventions in Heart Failure With Preserved Ejection Fraction

A Scoping Review

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ABSTRACT

Patients with heart failure with preserved ejection fraction (HFpEF) are burdened by multiple diet-sensitive comorbidities, including obesity and malnutrition. Despite this, a low percentage of patients with HFpEF have been enrolled in dietary intervention trials in heart failure and few dietary interventions have been conducted in HFpEF exclusively. This scoping review will examine available evidence regarding dietary interventions in patients with HFpEF, highlight existing gaps in knowledge, and discuss emerging dietary therapies in this population. (JACC Adv. 2025;4:101465)

Nearly 60 million adults worldwide have heart failure (HF) [1] and approximately half of those have HF with preserved ejection fraction (HFpEF), a complex and heterogeneous clinical syndrome.[2] Patients with HFpEF suffer poor quality of life, frequent hospitalizations, and increased mortality. Few medications are beneficial in HFpEF, making nonpharmaceutical strategies a promising area of investigation.[2,3] Individuals with HFpEF frequently have multiple diet-sensitive comorbidities (eg, systemic hypertension, diabetes mellitus, and obesity) which contribute to its pathophysiology. Malnutrition is also common in HFpEF and is independently associated with increased risk of death, cardiovascular events, and all-cause hospitalization.[4,5] Despite these observations, dietary approaches targeting HFpEF have not been extensively studied. Fewer than half of dietary intervention trials in HF have enrolled exclusively patients with HFpEF; in those with mixed cohorts, only 11% of participants had HFpEF.[6] This scoping review will focus on dietary interventions that have been performed, investigative gaps that remain, and emerging directions for dietary treatment of HFpEF.

ENERGY RESTRICTION/ INTENTIONAL WEIGHT LOSS

Excess adipose tissue, that is obesity, is associated with the development and progression of HFpEF [7]

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ABBREVIATIONS AND ACRONYMS

6MWT = 6-minute walk test

CoQ10 = coenzyme Q10

DASH = Dietary Approaches to Stop Hypertension

ET = aerobic exercise training

EVOO = extra-virgin olive oil

GLP = glucagon-like peptide

HF = heart failure

HFpEF = heart failure with preserved ejection fraction

LVEF = left ventricular ejection fraction

MedDiet = Mediterranean diet

MTM = medically tailored meals

SCFA = short-chain fatty acids

UFAs = unsaturated fatty acids

VO_{2peak} = peak oxygen consumption

through several deleterious mechanisms.[8] Patients with obesity-related HFpEF have a greater symptom burden, worse quality of life, and more impaired cardiorespiratory fitness than their peers without obesity.[9-11] Given this additional burden, there has been great interest in the therapeutic potential of weight loss in HFpEF.

The SECRET (Effect of Caloric Restriction and Exercise Training in Patients With Heart Failure and a Normal Ejection Fraction) trial randomized 100 patients with obesity-related HFpEF in a 2x2 factorial design to energy restriction (diet), supervised aerobic exercise training (ET), diet + ET, or attention control.[12] Lunch, dinner, and snacks were provided to participants. The diet provided ~1.2 g protein per kg of calculated ideal body weight and 25% to 30% kcals from fat with remaining dietary kilocalories (kcals) from carbohydrate. At 20 weeks, participants randomized to diet and/or ET lost weight (diet, −7 kg [95% CI: −9 to −5 kg] vs exercise, −3 kg [95% CI −5 to −1]) and increased peak oxygen consumption (VO_{2peak}), the coprimary endpoint, with diet + ET achieving a robust 2.5 $ml^{-1} \cdot kg^{-1} \cdot min^{-1}$ increase. While an increase in relative VO_{2peak} ($ml^{-1} \cdot kg^{-1} \cdot min^{-1}$) might be predicted with weight loss, increased exercise time and 6-minute walk test (6MWT) distance and preservation of VO_{2peak} in absolute terms ($ml^{-1} \cdot min^{-1}$) support improved exercise capacity. Resting cardiac parameters were largely unchanged, suggesting improvements in VO_{2peak} were mediated by peripheral, not central, adaptations. While neither cardiac parameters nor peripheral factors, that is arteriovenous oxygen difference, were measured during exercise, exercise training interventions in patients with HFpEF have demonstrated that peripheral factors accounted for upward of 90% of the improvements in VO_{2peak} with training.[13] As skeletal muscle is more plastic than cardiac muscle, it is likely improvements in VO_{2peak} due to weight loss resulting from energy restriction would also be mediated by peripheral rather than central adaptations though a more definitive mechanistic study would be required to demonstrate this.[14]

Increases in VO_{2peak} were also associated with decreases in weight, particularly fat mass ($r = -0.540$, $P < 0.001$), and decreases in weight were associated with reductions in high-sensitivity C-reactive protein ($r = 0.290$, $P = 0.005$). The other coprimary endpoint, quality of life measured by Minnesota Living with Heart Failure questionnaire showed a strong trend ($P = 0.07$) for improvement by both diet and ET.

HIGHLIGHTS

- Very few dietary interventions have specifically targeted patients with HFpEF.
- Energy-restricted diets and GLP-1 agonists demonstrate short-term safety and promise as a treatment for obesity-related HFpEF.
- Personalized dietary interventions and nutrition support have been shown to significantly reduce mortality in patients with HF and malnutrition.
- Medically tailored meals are promising but require further investigation in HFpEF.

Recently, the SECRET-II trial investigated the additive benefits of supervised resistance exercise training (RT) in HFpEF.[15] Participants (n = 88) underwent energy restriction and aerobic ET and were randomized to receiving or not receiving RT training. After 20 weeks, both groups experienced a similar increase in VO_{2peak} (~2.3 $ml^{-1} \cdot kg^{-1} \cdot min^{-1}$) and percent (%) skeletal muscle mass. While % skeletal muscle increased, total estimated skeletal muscle mass decreased slightly without difference between groups (~-2.1 kg) suggesting that the addition of RT does not completely counteract the loss of skeletal muscle from energy restriction. Muscle quality was improved to a greater degree in participants undergoing additive RT vs no RT, an indicator that the addition of RT to weight loss interventions in HFpEF may be favorable though long-term follow-up is needed.[16]

Despite favorable results of dietary weight loss in patients with obesity-related HFpEF, and data supporting that excess adipose plays a pivotal role in the development and progression of HFpEF,[8] concerns have been raised about weight loss in HF due to the observed “obesity paradox.” Obesity paradox is a term used to describe the observation, all from nonrandomized, observational studies, across cardiovascular disease where patients with overweight or class I obesity appear to have fewer adverse clinical outcomes than their underweight, normal weight, or more obese peers. However, such data are influenced by comingling of patients with unintentional weight loss due to undetected cancers and other disorders. Moreover, patients with obesity tend to be younger and able to tolerate a greater amount of cardioprotective medications, which could at least

partially explain some of the more favorable effects observed in patients with obesity.[17]

In contrast to the obesity paradox, randomized, controlled trials of intentional dietary weight loss with long-term follow-up in older persons without HF have shown improved survival.[18] Whether this is also true in the presence of HF, however, requires dedicated trials. Furthermore, with or without exercise training, energy restriction in SECRET and SECRET-II resulted in weight loss and improvement in VO_{2peak}, a strong prognostic indicator,[19] suggesting safe and favorable short-term impacts of intentional weight loss. Hajj et al also demonstrated improvements in 6MWT distance that persisted in patients with HFpEF at least ~3 months after intensive lifestyle intervention (energy restriction and unsupervised exercise) ended.[20]

The benefit of dietary weight loss for patients with obesity-related HFpEF is strongly supported by the results of STEP-HFpEF trials with glucagon-like peptide (GLP)-1 receptor agonist semaglutide [21] Weight loss with semaglutide in STEP-HFpEF (Semaglutide Treatment Effect in People with Obesity and Heart Failure with Preserved Ejection Fraction and Diabetes Mellitus) trials increased 6MWT distance, reduced C-reactive protein and n-terminal brain natriuretic peptide across all obesity classes in a dose-dependent manner, corroborating the role of weight loss in treating pathobiology of obesity-related HFpEF.[21,22]

It should be noted that weight regain frequently occurs after intensive lifestyle intervention or discontinuation of GLP-1. In individuals with obesity alone, the composition of weight regain largely mirrors that of weight loss,[23] but a recent long-term follow-up (28.0 ± 10.8 months) of the SECRET trial demonstrated that a ~5 kg weight regain composed mostly of fat mass, resulted in a worsened lean to fat mass ratio, compared to preintervention, in individuals with obesity-related HFpEF.[24] Moreover, increases in fat mass demonstrated an inverse trend with VO_{2peak} ($r = -0.052$, $P = 0.062$) over time. Patients with HFpEF are at risk for lean mass abnormalities which include sarcopenia, defined as low skeletal muscle strength and mass,[16] and sarcopenic obesity, the coexistence of both sarcopenia and obesity, which may be associated with worse clinical outcomes compared to either entity alone though further studies are needed.[25] Long-term follow-up of weight loss with intensive lifestyle change and GLP-1 receptor agonists are required in order to evaluate the long-term impact on body composition and clinical outcomes.

MALNUTRITION

Despite the strong association between HFpEF and excess fat mass, patients with this HF subtype are at high risk for malnutrition. In outpatients with HFpEF, at least a third of patients present with moderate to high nutrition risk scores which are associated with significantly higher rates of hospitalization and mortality.[4,5] Pathophysiologic mechanisms leading to malnutrition among patients with HFpEF are multifactorial—in all patients with HF, mechanisms of heightened inflammation and neurohormonal activation can increase catabolism. Metabolic dysfunction can be further compounded by poor appetite, malabsorption, and physical inactivity.[26] In addition, patients with HFpEF are often prescribed low-sodium diets, which may inadvertently lead to caloric restriction and malnutrition.[27] Despite the high prevalence of malnutrition and its consequences, there is currently minimal guidance on diagnosing and treating malnutrition in HFpEF.

Several general dietary intervention strategies have been trialed in patients with HF and malnutrition, though few have looked at HFpEF specifically. PICNIC (Programa de IntervenCión Nutricional en pacientes hospitalizados por Insuficiencia Cardiaca desnutridos) trial randomized 120 patients hospitalized for acute HF (56.7% with HFpEF) and malnutrition to receive usual care versus an individualized nutrition intervention for 6 months, consisting of diet optimization, specific dietitian recommendations, and supplement prescriptions, combined with usual care.[28] PICNIC was stopped early, demonstrating a significant improvement in the composite endpoint of all-cause death or readmission for HF in the intervention group compared to usual care (HR: 0.45; 95% CI: 0.19-0.62). A secondary analysis of the EFFORT (Effect of Early Nutritional Therapy on Frailty, Functional Outcomes, and Recovery of Undernourished Medical Inpatients) trial, inclusive of 645 hospitalized patients with HF and malnutrition, demonstrated that a dietitian-led effort to reach kcal and protein goals was associated with lower all-cause 30-day mortality compared to control with a median intervention of only 10 days (OR: 0.44; 95% CI: 0.26-0.75).[29] A subgroup analysis dividing the cohort into HFpEF (60%) versus HFrEF revealed a persistent treatment effect regardless of HF phenotype.[29] The success of the PICNIC and EFFORT trials is critical in the setting of an earlier 2017 Cochrane Review which found that nutrition support, encompassing multiple modalities of nutrition care, had no impact on short-

or long-term mortality in hospitalized patients at nutritional risk.[30]

DIETARY PATTERNS

SODIUM RESTRICTION AND THE DASH DIET. Dietary sodium restriction is one of the most common self-care recommendations for patients with HF. Increased sodium intake frequently occurs before HF decompensation, and HF hospitalizations increase in parallel with reported sodium consumption.[31] However, concerns exist about neurohormonal activation and decreased renal perfusion if dietary sodium restriction is too strict.[32] Current guidelines only state that avoiding excessive sodium intake is "reasonable" for symptomatic patients with HF, reflecting a lack of strong evidence for this practice.[33]

To date, the only trial conducted solely in patients with HFpEF randomized 53 inpatients to aggressive sodium (800 mg/d) and fluid (800 ml/day) restriction, with no difference in weight loss or congestion score over 7 days, with an increase in thirst and reduction in calorie intake in the intervention group.[34] The SODIUM-HF (Study of Dietary Intervention under 100 mmol in Heart Failure) trial randomized 806 patients with chronic HF (277 with left ventricular ejection fraction [LVEF] >40%) to dietitian-guided sodium restriction (goal 1,500 mg/day) vs usual dietary guidance. Overall, there was no difference in cardiovascular hospitalization or mortality over 12 months of follow-up, and no significant interaction by EF.[35] Patients in the intervention group had modest improvement in disease-related quality of life (+3.38 points adjusted difference in Kansas City Cardiomyopathy Questionnaire score, $P = 0.011$) and were more likely to improve NYHA functional class, but these data have not been reported in the LVEF >40% subgroup. A recent meta-analysis of 17 dietary intervention trials that followed the publication of SODIUM-HF found no reduction in hospitalization or mortality with sodium restriction in patients with HF.[36]

The Dietary Approaches to Stop Hypertension (DASH) dietary pattern encourages intake of fruits, vegetables, and whole grains and promotes intake of nuts and legumes, low-fat dairy, and lean protein. Hummel et al studied the effects of a sodium-restricted DASH diet (1,500 mg sodium/2,100 kcal) in 13 well-compensated patients with HFpEF and treated hypertension. After 21 days, the study diet substantially lowered clinic and ambulatory blood pressure and indices of left ventricular diastolic function, large-arterial stiffness, ventricular-arterial coupling, and 6MWT distance improved.[37,38] The GOURMET-HF (Geriatric OUt-of-hospital Randomized MEal Trial in Heart Failure) study randomized 66 older patients to receive low-sodium, DASH-compliant home-delivered meals for 4 weeks post-hospital discharge. In participants with HFpEF (LVEF ≥50%), the Kansas City Cardiomyopathy Questionnaire summary score (physical limitations and symptoms domains) improved between baseline and 4 weeks in the patients receiving meals (41 ± 24 points to 57 ± 17 points, $P = 0.01$), but not in the usual care group (43 ± 20 points to 49 ± 24 points, $P = 0.28$).[39] Larger trials of the DASH sodium-restricted diet are needed to investigate the impact of this dietary pattern on hospitalization and mortality.

THE MEDITERRANEAN DIET AND DIETARY FATTY ACIDS. While the traditional Mediterranean diet (MedDiet) has many similarities to the DASH diet, it differs by emphasizing the liberal use of extra-virgin olive oil (EVOO) rich in unsaturated fatty acids (UFAs) and wine, typically red, is consumed in moderation with meals.[40] Red meat, added sugar, and processed foods are minimized. In 2 landmark randomized controlled trials, a MedDiet supplemented with UFAs (consisting of EVOO [25-50+ grams in addition to usual intake] with or without mixed nuts, ~30 g/day), demonstrated superiority to a low-fat diet in preventing primary and secondary cardiovascular events, respectively.[41-43] To date, no randomized controlled trials designed to investigate the impact of the MedDiet supplemented with UFAs on the prevention of HF have been published.[41,42] In 991 patients admitted to emergency departments with acute decompensated HF, MedDiet adherence was assessed via a 14-point score. While MedDiet adherence was not associated with the primary outcome of all-cause mortality at 1 year (HR: 0.86; 95% CI: 0.73-1.02), rehospitalization for HF was lower in individuals who were adherent (HR: 0.74; 95% CI: 0.61-0.90).

While components of the MedDiet likely offer benefits in a synergistic fashion, a notable feature is the high UFA content as a percentage of dietary kcals (~40%)-UFA, which includes monounsaturated and polyunsaturated fatty acids, have been consistently shown to improve both lipids and glucose metabolism.[44] The available evidence related to the role of UFAs in patients with HFpEF comes from small pilot studies, which suggest potential beneficial effects of UFA supplementation in this population. The prospective clinical trial UFA-Preserved pilot study counseled participants to consume at least 54 g of EVOO or canola oil, and/or 28 g of unsalted or lightly

salted mixed nuts daily and demonstrated the feasibility of dietary UFA supplementation. UFA-Preserved also demonstrated a favorable association of UFA consumption with improved VO_{2peak},[45] previously observed in cross-sectional analyses of patients with HFpEF.[46] The follow-up randomized controlled trial UFA-Preserved2 study (NCT03966755) was recently completed; however, the results have not been published yet. Large cardiovascular outcomes trials testing the effects of UFAs on clinical outcomes have not been conducted specifically in patients with HFpEF, highlighting the need for more research in this field.

A recent observational study showed that a greater n-3 index (the sum of eicosapentaenoic acid and docosahexaenoic acid content of red blood cell membrane) was associated with a favorable cardiac and metabolic profile and greater 6MWT distance and VO_{2peak} in patients with HFpEF.[47] However, n-3 fatty acid supplementation in patients with diastolic dysfunction was not associated with improved cardiac function or body composition in another randomized controlled trial.[48] Whether this is also true in patients with established HFpEF is unknown. Moreover, n-3 fatty acid supplementation has been linked to a greater risk for atrial fibrillation.[49] Considering the increased risk of atrial fibrillation in patients with HFpEF and its negative prognostic role in this population,[50] n-3 fatty acid supplementation requires further evaluation for safety.

MICRONUTRIENT SUPPLEMENTATION

Low self-reported intake of micronutrients has been associated with a greater risk of hospitalization or death in patients with HF.[51,52] For many participants with HF, however, the effects of insufficient micronutrient intake may be difficult to separate from insufficient total energy and macronutrient intake.[27,51] While low intake of micronutrients is a major concern, increasing nutrient intake by food and beverage intake alone cannot fully address the increased micronutrient needs frequently observed in HF.[53] In this section, we will discuss oral supplementation of micronutrients in patients with HFpEF.

INORGANIC NITRATE. Two randomized, double-blind crossover trials have explored the acute effects of a single dose of inorganic nitrate administration via beetroot juice in patients with HFpEF.[54,55] This acute dosing demonstrated improvements in VO_{2peak} in patients with HFpEF (12.6 ± 3.7 ml/kg/min vs 11.6 ± 3.1 ml/kg/min, $P = 0.005$), but not submaximal aerobic endurance.[54,55] In a randomized, placebo-controlled 4-week ET program with the beetroot juice (with or without inorganic nitrate) consumed before the 3 weekly ET sessions, an improvement was noted without difference between groups in the primary outcome of submaximal aerobic endurance.[56] Two recent multicenter randomized controlled trials investigating inhaled nitrites or a combination of inhaled and oral nitrites vs placebo have failed to demonstrate an impact of nitrites on VO_{2peak}.[57,58]

COENZYME Q10. Coenzyme Q10 (CoQ10) is an important antioxidant in the mitochondrial electron transport chain. Short-term (1-4 months) dosing of CoQ10 supplementation, 100 mg 3 times per day, did not demonstrate improved diastolic function measured by E/e' ratio in patients with HFpEF[59,60] nor did 300 mg twice daily for 12 weeks, however, this higher dose did improve Kansas City Cardiomyopathy Questionnaire clinical summary score, LVEF, and brain natriuretic peptide relative to placebo.[61] In an extension of a randomized placebo-controlled trial of 420 patients with HF from the 16-week primary endpoint to 2 years, the CoQ10 group demonstrated fewer major adverse cardiovascular events than placebo (43% relative risk reduction, $P = 0.005$).[62] There was a subgroup trend for greater improvement in cardiovascular events in individuals with an LVEF >30%, however, no HFpEF subgroup analysis was performed.

OTHER SUPPLEMENTS. Although lower serum vitamin D_3 has been linked to increased risk for HFpEF,[63] the majority of supplementation trials have been conducted in those with an LVEF <50%. In 64 participants with HF, a double-blind randomized control trial of weekly 50,000 IU vitamin D_3 for 6 months did not increase the primary outcome of VO_{2peak} versus placebo and adjustment for ejection fraction did not change the results.[64]

Recently, supplementation of nicotinamide riboside and indole-3-propionic acid has been shown to address nicotinamide adenine dinucleotide deficiency and ameliorate cardiac hypertrophy and diastolic dysfunction in murine models of HFpEF.[65,66] The safety and efficacy of nicotinamide supplementation in patients with HFpEF is unknown.

Targeting the gut microbiome is a growing area of interest—dietary fiber, resistant to human digestion, is readily fermented by certain bacteria in the gut microbiome. Supplementation of both fermentable fiber and acetate, a short-chain fatty acid (SCFA), in a murine model of HFpEF, has demonstrated a reduction in blood pressure, left ventricular hypertrophy, and fibrosis compared to control mice.[67] A recent 12-week trial randomized patients with HF 1:1:1 to

TABLE 1 Ongoing Dietary Interventions Enrolling Patients With Heart Failure With Preserved Ejection Fraction

NCT# Principal Invesigator	Trial Type	Targeted Population	N	Intervention	Primary Outcome
Combined dietary intervention and exercise training					
NCT05236413 Siddartha Angadi	Randomized controlled trial	HFpEF	36	HIIT training vs DASH diet vs HIIT training and DASH diet, exercise supervised, all meals provided to participants, for 4 weeks	Change in $VO_{2\ peak}$
Dietary intervention					
NCT04235699 Sitaramesh Emani	Randomized controlled trial	HFpEF	24	Energy restricted ketogenic diet vs energy restricted low-fat diet, all meals provided to participants, for 4 weeks	Change in $VO_{2\ peak}$
NCT06081543 Yuchi Han	Randomized controlled trial	HFpEF	90	Ketogenic diet vs low-fat diet for 6 months- groceries provided for first 6 weeks, dietary counseling for duration of study	Change in $VO_{2\ peak}$
NCT06078683 Yuchi Han	Randomized crossover trial	HFpEF	30	Ketone ester beverage or placebo beverage twice daily for 6 weeks followed by 4 week washout and 6 weeks of the alternate beverage	Change in $VO_{2\ peak}$
NCT05878912 Oliver Rider	Randomized controlled trial	HFpEF	120	Energy restricted diet—beginning with total meal replacement for 8 weeks with gradual food reintroduction vs SOC control, lasting 3 to 6 months in total	Change in left atrial volume index
NCT06044194 Stefano Carugo	Randomized controlled trial	HFpEF	56	L-arginine and liposomal vitamin c supplement vs placebo for 3 months	Mitochondrial function in peripheral blood mononuclear cells
NCT06337812 Scott Hummel	Single arm, open label	HFpEF	30	Resistant potato starch for 4 weeks	Change in fecal short-chain fatty acids
NCT05887271 Oliver Rider	Randomized controlled trial	HFpEF	102	Energy restricted total meal replacement vs attention control for 12 weeks	Change in 6MWD
NCT05996328 Scott Hummel	Randomized controlled trial	HF	1,400	Home-delivered low sodium nutrient dense meals vs SOC control for 6 weeks	Combined "clinical wins" score of days alive out of the hospital and health-related quality of life
NCT06115369 Ambarish Pandey	2 × 2 factorial randomized controlled trial	HF	150	Medically tailored meals, fresh produce delivery, both medically tailored meals and fresh produce delivery or control for 90 days	Readmission or emergency room visit for heart failure
NCT05117086 Francene Steinberg	Single arm, open label	HF	25	Dietary counseling to follow DASH dietary pattern for 6 months	Dietary intake, DASH diet score, systolic and diastolic blood pressure at baseline, 3, and 6 months
NCT06296862 Elisabeth Sattler	Randomized crossover controlled trial	HF	38	Study-provided DASH meals vs normal diet for 4 weeks each with a 4-week washout period	Change in B-natriuretic peptide
NCT05923138 Jose Angel Perez Rivera	Randomized controlled trial	HF	264	Personalized dietary counseling with potential of nutrition supplements vs control for 6 months	Time to readmission for heart failure or mortality
NCT02892747 Véronique Bendedyga	Randomized controlled trial	HF	295	Personalized dietary counseling aimed at preventing malnutrition and reducing sodium intake vs control (no personalized counseling) for 6 months	Number, duration, and reasons for hospitalization

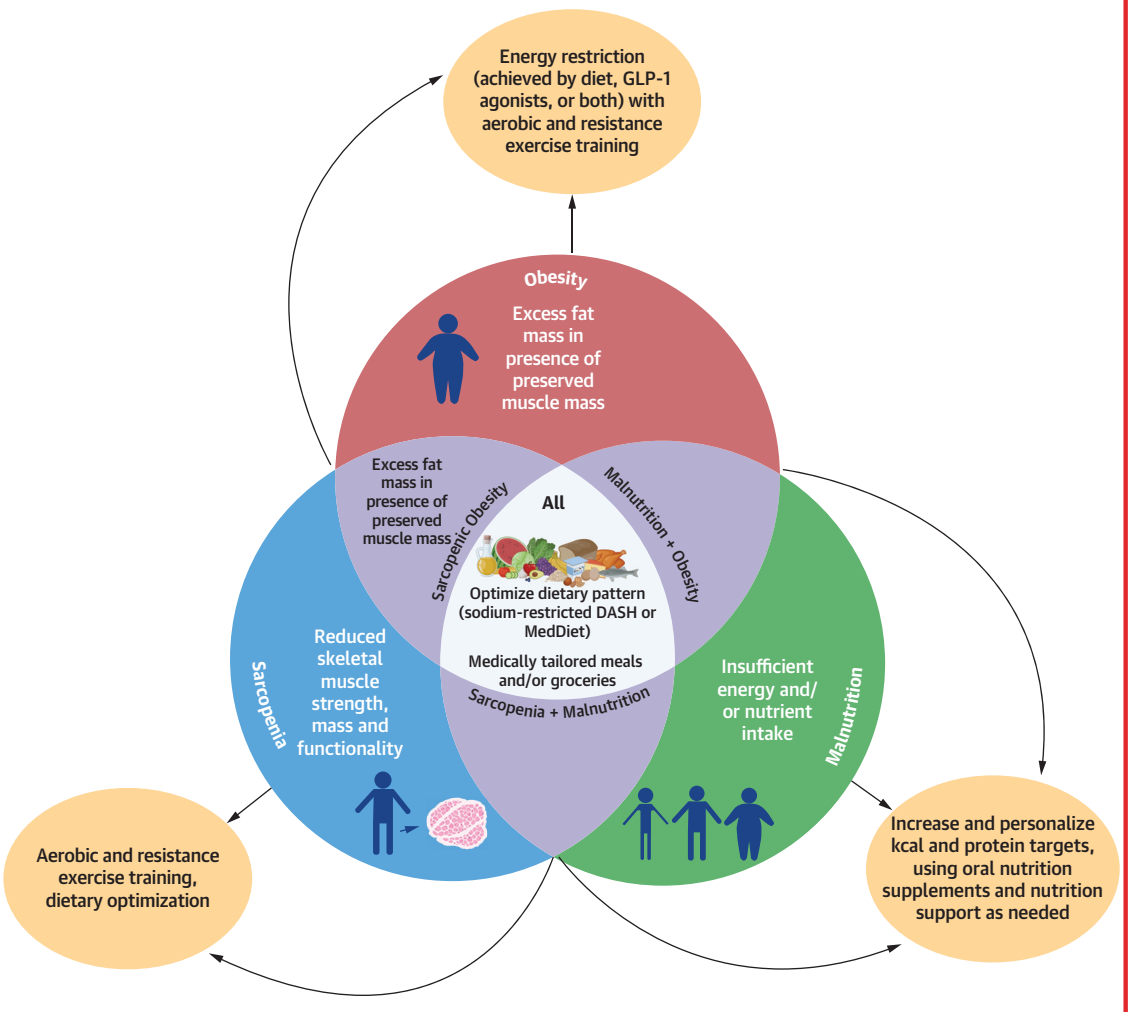
6MWD = 6-minute walk test distance; DASH = Dietary Approaches to Stop Hypertension; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HIIT = high-intensity interval training; SOC = standard of care; $VO_{2\ peak}$ = peak oxygen consumption.

microcrystalline cellulose (control fiber) or acacia gum (active treatment) did not demonstrate differences between groups in n-terminal brain natriuretic peptide nor alterations in the microbiome.[68] Changes in SCFA production were not measured but 5 to 10 g of dietary fiber may not have been adequate to stimulate greater SCFA production, since acacia fiber is not considered highly fermentable.[69] An ongoing pilot study (NCT06337812) is investigating 20 g of potato starch, 65% resistant starch by volume and highly fermentable, administered twice daily in patients with HFpEF on a primary endpoint of changes in stool and serum SCFA (Table 1).

FUTURE DIRECTIONS FOR DIETARY INTERVENTION IN HFpEF

Strategies to reduce weight and, in particular, fat mass, such as GLP-1 receptor agonists and energy restriction diets have shown enormous promise as therapies for patients with obesity-related HFpEF.[21,22] Short-term safety of both energy restriction and GLP-1 receptor agonists has been established in patients with HFpEF [12,15,22] and future strategies to explore include combining GLP-1 receptor agonists with other dietary strategies such as energy restriction and dietary patterns shifts such as DASH and the

CENTRAL ILLUSTRATION **Optimizing Nutrition Care in Patients With Heart Failure With Preserved Ejection Fraction**



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Patients with heart failure with preserved ejection fraction (HFpEF) have high rates of obesity, sarcopenia, and malnutrition. While most patients can likely benefit from an optimized dietary pattern such as dietary approaches to stop hypertension (DASH) or the mediterranean diet (MedDiet), dietary interventions should be personalized to the unique needs of the individual. GLP = glucagon-like peptide.

MedDiet to maximize benefits (**Central Illustration**). In SECRET, high adherence to energy restriction was likely driven by the provision of lunch, dinner, and snacks to participants.[12] This approach is, in fact, a medically tailored meals (MTMs) intervention—providing fully prepared, nutritionally tailored meals for individuals living with an advanced and diet-sensitive condition [70] —in this case, obesity-related HFpEF. Additionally, MTMs represent a customizable intervention which could combine energy restriction with a DASH or MedDiet dietary pattern which have weight-loss independent benefits on cardiometabolic risk.[37-39,41-43] Questions about cost and insurance coverage regarding both GLP-1 receptor agonists and MTM interventions will likely continue for the foreseeable future[70,71] and behavioral strategies, which could be widely and cost-effectively disseminated via mobile health interventions,[72] should not be ignored for weight loss in patients with obesity-related HFpEF.

Food insecurity, or the limited or uncertain availability of sufficient food to maintain adequate nutrition, has been linked to higher body mass index and a higher risk of HF mortality.[73,74] Increasing access to nutrition through interventions such as MTMs and grocery delivery in patients with HFpEF

could have a meaningful impact on clinical outcomes. The Kaiser Permanente Evaluation of Medically Tailored Meals in Adults with Chronic Medical Conditions at High Readmission Risk (KP-NOURISH) enrolled patients with HF, diabetes, or chronic kidney disease in a parallel group randomized controlled trial to MTMs for 10 weeks after hospital discharge or usual care control.[75] MTMs did not reduce all-cause hospitalization at 90 days (adjusted HR: 1.20; 95% CI: 0.86-1.21), the primary outcome. Among patients with HF (n = 641), however, receiving MTMs was associated with a lower 90-day risk of hospitalization for HF (adjusted HR: 0.52; 95% CI: 0.32-0.86). Two clinical trials (NCT05996328 [GOURMET-VA] and NCT06115369 [FOOD-HF]) with expected enrollment beginning in 2024 are examining the impact of nutrient-dense, home-delivered meals on clinical outcomes specifically in patients with HF, regardless of LVEF (**Table 1**).

CONCLUSIONS

Recent dietary interventions performed in patients with HF have demonstrated the ability to improve quality of life, and exercise capacity, and even reduce hospitalizations and mortality. To date, patients with HFpEF have been under-represented and differences in treatment response are inconsistently explored. Weight loss strategies including dietary energy restriction and GLP-1 receptor agonists represent a promising future direction to treat obesity-related HFpEF. Other promising future directions for dietary interventions in patients with HFpEF include MTMs and grocery delivery, with a specific focus on energy restriction and/or DASH and Mediterranean dietary patterns, and personalized dietary intervention and nutrition support in patients with malnutrition (**Central Illustration**).

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