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Dietary Micronutrient Interventions to Prevent Hospitalization and Readmission in Adults with Congestive Heart Failure

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Despite various available treatment options, heart failure is among the most common causes of mortality, poor quality of life, and high health care utilization.[1,2] Although older guidelines recommend assessment of macro- and micronutritional status in adults with chronic heart failure, there is a lack of treatment recommendations to improve the nutritional status of this population. This rapid review conducted according to a priori developed protocol focuses on the direct effects of micronutrient interventions in adults with chronic heart failure.

WHAT IS THE CLINICAL QUESTION?

What is the comparative effectiveness of micronutrient dietary interventions for preventing hospitalization and readmission in adults with chronic congestive heart failure?

WHAT ARE THE PARAMETERS FOR OUR EVIDENCE SEARCH?

Population: Adults with heart failure

Patient demographics: socioeconomic status, smoking, physical activity, diet (sodium intake), baseline blood pressure, prior treatment and response to medications for heart failure, comorbidities (eg, cardiac arrhythmias, obesity, diabetes, asthma, chronic obstructive pulmonary disease), concomitant and concurrent medications

Intervention: Dietary micronutrient supplementation (vitamin D, multivitamins, omega-3 fatty acids)

Comparator: Placebo, usual care

Primary outcome(s): All-cause mortality

Mortality due to heart failure
Hospitalizations and readmission
Quality of life measured with validated scales
All harms

Setting: Inpatient or outpatient

WHAT DOES THE EVIDENCE CONCLUDE?

Intervention	Quality of Evidence*	Conclusion
Multiple balanced micronutrient supplementation	Low	Evidence suggests that there are no differences in all-cause mortality, ejection fraction, or quality of life between multiple balanced micronutrient supplementation and placebo in adults with chronic congestive heart failure.
		In malnourished adults with heart failure, micronutrient supplementation reduces all-cause and cardiovascular mortality and hospital admissions due to heart failure.
Supplementation with vitamin D	Low	Evidence suggests that there are no differences in all-cause mortality, ejection fraction, or quality of life between supplementation with vitamin D and placebo in adults with chronic congestive heart failure.
		In adults with documented vitamin D deficiency, supplementation with vitamin D reduces the risk of hospital readmissions and improves ejection fraction.
Supplementation with omega-3 fatty acids	Low	Evidence suggests that n-3 polyunsaturated fatty acids may result in a small reduction in all-cause mortality, cardiovascular mortality, and cardiovascular hospitalizations in some adults with chronic heart failure.

*Quality of Evidence scale (Grading of Recommendations Assessment, Development, and Evaluation [GRADE]): high, moderate, low, and very low. For more information on the GRADE rating system, see http://gdt.guidelinedevelopment.org/app/handbook/handbook.html.

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WHAT IS THE BASIS FOR OUR CONCLUSIONS?

Tables 1–3

WHAT DO CLINICAL GUIDELINES SAY?

2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines[2,18] (AGREE II score: 63.8%).

- This guideline states that nutritional supplements are not recommended for the treatment of heart failure until more data are available, because, aside from replenishment of documented deficiencies, published data have failed to demonstrate benefit from routine vitamin, nutritional, or hormonal supplementation.

NICE Clinical Guideline, Heart Failure #108. Partial Update of NICE Guideline No 5: Chronic Heart Failure—National Clinical Guideline for Diagnosis and Management in Primary and Secondary Care.[19,20] **NICE Guideline for Management of Chronic Heart Failure**[21] (AGREE II score: 76.4%).

- This guideline recommends nutritional status assessment in people with chronic heart failure. The guideline does not make recommendations about use of micronutritional supplements due to insufficient evidence of their efficacy.

2016 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure of the European Society of Cardiology (ESC). Developed With the Special Contribution of the Heart Failure Association (HFA) of the ESC[21] **(AGREE II score not available). ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure**[22] (AGREE II score: 57%).

- This guideline recommends n-3 polyunsaturated fatty acid (PUFA) preparations containing 850 to 882 mg of eicosapentaenoic acid and docosahexaenoic acid as ethyl esters in the average ratio of 1:1.2 as an adjunctive therapy in patients with symptomatic heart failure who are already receiving optimized recommended therapy with an angiotensin-converting enzyme inhibitor (or angiotensin receptor blocker), a beta-blocker, and a mineralocorticoid receptor antagonist.

AUTHOR COMMENTARY

Our comprehensive search in PubMed, EMBASE, the Cochrane Library, and clinicaltrials.gov identified 2 systematic reviews and published and unpublished data from 13 randomized controlled trial (RCTs).[3-17,23] Primary randomized studies enrolled adults with chronic, stable congestive heart failure with or without nutritional deficiency who were treated with drugs according to the evidence-based guidelines available at the time of the trials.

Low-quality evidence suggests that there are no differences in all-cause mortality, ejection fraction, or quality of life between multiple balanced micronutrient supplementation and placebo in adults with chronic congestive heart failure (**Table 1**). However, micronutrient supplementation reduces all-cause and cardiovascular mortality and hospital admissions due to heart failure in malnourished adults with heart failure (**Table 1**). Very low-quality evidence from subgroup analysis suggests that micronutrient supplementations reduce the risk of death or re-hospitalization in women, people without diabetes, and adults with ejection fraction more than 50% (**Table 1**). In contrast, men, people with diabetes, and patients with severely reduced ejection fraction do not experience benefits from multiple balanced micronutrient supplementation (**Table 1**).

Low-quality evidence suggests that there are no differences in all-cause mortality, ejection fraction, or quality of life between supplementation with vitamin D and placebo in adults with chronic congestive heart failure (**Table 2**). However, supplementation with vitamin D reduces the risk of hospital readmissions and improves ejection fraction in adults with documented vitamin deficiency (defined as cholecalciferol level <50 nmol/L [<20 ng/mL]) (**Table 2**).

Low-quality evidence from a single large RCT called GISSI-HF suggests that n-3 polyunsaturated fatty acids result in a small reduction in all-cause mortality, cardiovascular mortality, and cardiovascular hospitalizations (**Table 3**). The results were statistically significant only after they were adjusted for admission to the hospital for heart failure in the previous year, previous pacemaker, and aortic stenosis (**Table 3**). The differences in absolute rates of all-cause mortality were not statistically significant in both RCTs that examined the effects of PUFA in adults with chronic heart failure of any etiology[14] or nonischemic dilated cardiomyopathy (**Figure**).[13]

We downgraded the quality of evidence due to risk of bias in the body of evidence, heterogeneity in treatment effects, and a small number of events in RCTs. The evidence regarding the optimal micronutritional supplementation in adults with comorbid diabetes, hypertension, or chronic renal diseases is insufficient.

The most recent American and European guidelines recommend nutritional assessment of adults with heart failure, addressing detected deficiencies.[2,18-20,22] Guidelines do not recommend routine supplementation with vitamin D or PUFA in people with chronic heart failure.

Future research should determine optimal micronutritional recommendations in patient subpopulations by demographics and comorbidities.

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