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REVIEW ARTICLE

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Major considerations of cardiometabolic nutrients in heart failure: a systematic review

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Abstract

Introduction: Heart failure (HF) is one of the main causes of hospitalizations in the world. In Brazil, about 7.0 million Brazilians suffer from this syndrome. The clinical evolution of patients with HF evidence variable conditions of malnutrition. This can occur due to inadequate intake, altered metabolism, pro-inflammatory state, increased oxidative stress, and greater loss of nutrients, even due to drug interactions. **Objective:** It was to demonstrate, through a systematic review of the literature, the main considerations of cardiometabolic nutrients in heart failure. **Methods:** The present study followed a concise systematic review model (PRISMA). The literary search process was carried out from April to May 2023 and was developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar, using scientific articles until 2023. The low quality of evidence was attributed to case reports, editorials, and short communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 136 studies were found for eligibility analysis, and so 75 of a total of 84 studies were selected for this systematic review. According to the GRADE instrument, most studies showed homogeneity in their results, with X^2 =92.2% >50%. The Funnel Plot showed a symmetrical behavior, not suggesting a significant risk of bias in studies with smaller sample sizes. The presence of malnutrition is an important predictive factor for reduced survival in patients with HF, highlighting inadequate food intake, altered metabolism, pro-inflammatory state, increased oxidative stress, greater loss of nutrients, and drug interactions. Patients with HF have anabolism/catabolism imbalance. Providing nutritional support significantly increased dietary adherence above 90%. Therefore, malnutrition and inflammation are important predictors for assessing the prognosis of the disease in patients with HF.

Keywords: Heart failure. Nutrients. Cardiometabolic nutrient. Inflammatory processes.

Introduction

Heart failure (HF) is one of the main causes of hospitalizations in the world, representing a great economic, social, and health system burden **[1,2]**. In Brazil, about 7.0 million Brazilians suffer from this syndrome **[3]**. In the United States, this disease is more frequent in patients over 65 years **[4]**. There is evidence that this pathology affects 26 million people worldwide and with increasing prevalence every year **[5-7]**.

In this context, HF is a clinical syndrome caused by an abnormality in the function of the heart in pumping and/or in accommodating the blood return, not meeting the oxygen needs of the tissues, or only offering adequate cardiac output due to the abnormal increase in filling pressures. , triggering a complex neurohumoral and inflammatory response. Despite scientific and technological advances and better socioeconomic conditions have made it possible to increase the longevity of the general population and those with heart disease, there has been an increase in the incidence of HF in the world **[6,7]**.

Added to this, the clinical evolution of patients with HF evidence variable malnutrition. This can occur due to inadequate intake, altered metabolism, proinflammatory state, increased oxidative stress, and greater loss of nutrients, even due to drug interactions. The presence of malnutrition is an important predictive factor for reduced survival in patients with HF regardless of important variables such as age, functional class, and ejection fraction **[1,6]**.

Despite the historical intertwining between malnutrition and heart failure, few studies discuss the role of nutritional therapy in the treatment of these patients. In this context, dietary guidance for HF patients has focused on sodium restriction and fluid intake, but diet quality is often poor in HF patients and may contribute to morbidity and mortality. Restrictive diets can lead to inadequate intake of macro and micronutrients by patients with HF, especially deficiencies in calcium, magnesium, coenzyme Q10, zinc, iron, thiamine, vitamins D, E, and K, and folate. In addition, the elements intravenous iron, thiamine, and coenzyme Q10 have more clinical trial data for supplementation **[6-9]**.

Therefore, the present study aimed to demonstrate, through a systematic review of the literature, the main considerations of cardiometabolic nutrients in heart failure.

Methods

Study Design

The systematic review rules of the PRISMA Platform were followed. Available at: www.prisma-statement.org/). Accessed: 04/21/2023.

Research Strategy and Research Sources

The literary search process was carried out from April to May 2023 and was developed based on copus, PubMed, Science Direct, Scielo, and Google Scholar, using scientific articles until 2023, using the descriptors (MeSH Terms): *Heart failure. Nutrients. Cardiometabolic nutrient. Inflammatory processes*, and using the Boolean "and" between MeSH terms and "or" between historical findings.

Quality of Studies and Risk of Bias

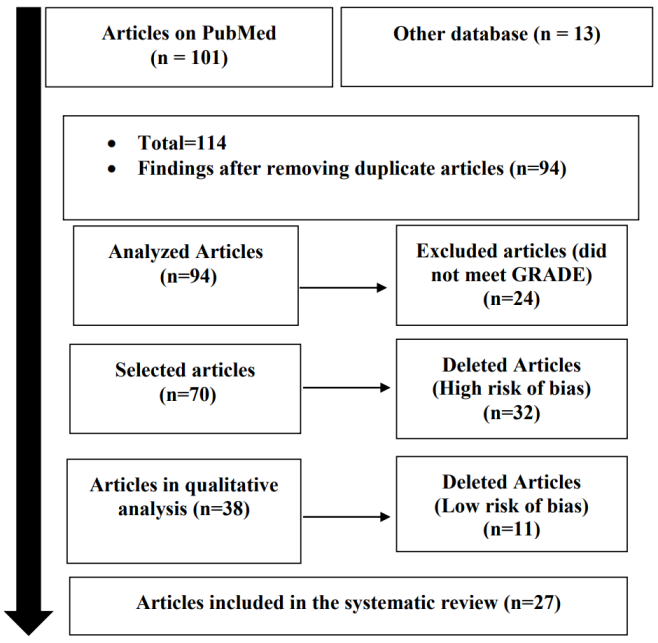
Quality was rated as high, moderate, low, or very low for risk of bias, clarity of comparisons, accuracy, and consistency of analyses. High ranking was for systematic review articles or meta-analysis of RCTs, followed by RCTs. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument through Funnel Plot analysis.

Results

Summary of Findings

A total of 114 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not include the theme of this article, resulting in 94 articles. A total of 38 articles were evaluated in full and 27 articles were included and developed in this systematic review study (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 32 studies with a high risk of bias and 24 studies that did not meet GRADE. According to the GRADE instrument, most studies showed homogeneity in their results, with R^2=92.2%>50%.

Figure 1. Flowchart showing the article selection process.

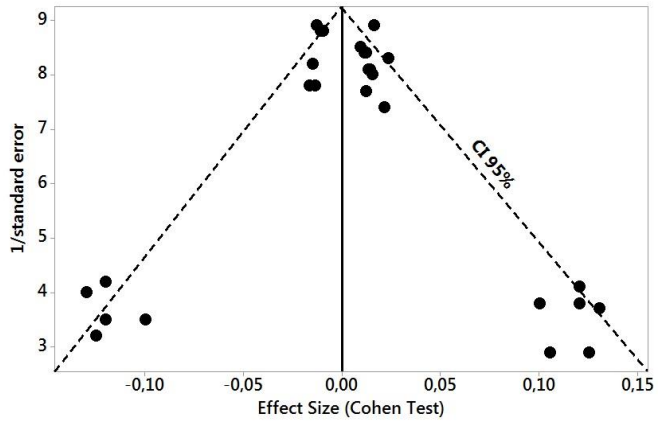


Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies through the Funnel Plot. The sample size was

indirectly determined by the inverse of the standard error. This graph showed symmetrical behavior, not suggesting a significant risk of bias, both between studies with small sample sizes (lower precision) that are shown at the bottom of the graph and in studies with large sample sizes that are displayed at the top.

Figure 2. The symmetrical funnel plot does not suggest a risk of bias among the small sample size studies that are shown at the bottom of the plot. High confidence and high recommendation studies are shown above the graph (NTotal= 27 studies evaluated in full in the systematic review).



Source: Own authorship.

Major Outcome

The presence of malnutrition is an important predictive factor for reduced survival in patients with HF, regardless of important variables such as age, functional class, and ejection fraction, as shown below **[6,7]**:

- ✓ Inadequate food intake;
- ✓ Altered metabolism;
- ✓ Pro-inflammatory state;
- ✓ Increased oxidative stress;
- ✓ Greater loss of nutrients;
- ✓ Drug interactions.

In this regard, patients with HF present anabolism/catabolism imbalance, increased levels of catabolic factors such as norepinephrine, epinephrine, angiotensin II, cortisol, inflammatory cytokines, and free radicals, resistance to anabolic hormones such as growth hormone (GH) and insulin, and increased energy expenditure at rest **[7]**.

HF in functional classes III and IV

- ✓ Increased basal metabolic rate by around 18%;
- ✓ Enteropathies with loss of protein and fat;
- ✓ Anorexia medication, depression, elevation of circulating levels; of cytokines, angiotensin II, and taste alteration **[2]**.

Overweight and Obese Patients

- ✓ Obesity and overweight are strong predictors of the development of HF;
- ✓ However, obese patients with HF seem to have a favorable clinical prognosis;
- ✓ In a study with 1203 individuals, most with functional class I, it was observed that an increase in BMI was associated with a higher survival rate **[7]**.

Overweight Elderly Patients

- ✓ Voluntary weight loss is associated with a higher risk of mortality;
- ✓ The ingestion of a hypo-energetic diet (<24kcal/kg/day) can increase the imbalance of catabolic hormones and cause a greater loss of lean mass **[3]**.

Nutritional Risk Screening Methodologies

- ✓ Nutritional Risk Screening;
- ✓ Subjective Global Nutritional Assessment;
- ✓ Nutritional Risk Index;
- ✓ Nutritional Risk Score;
- ✓ Mini Nutritional Assessment;
- ✓ Malnutrition Screening Instrument;
- ✓ Universal Malnutrition Screening Tool **[6,7]**;

After identifying the nutritional risk through nutritional screening, the final nutritional status is determined **[6]**:

- ✓ Anthropometric and body composition data;
- ✓ Dietetics;
- ✓ Biochemical-immunological;
- ✓ Clinical history;
- ✓ Physical examination;
- ✓ Subjective global nutritional assessment;
- ✓ Instant nutritional assessment;
- ✓ Predictive indices.

Main Studies and Outcomes

Providing nutritional support significantly increased dietary adherence above 90%. Patients have better disease control and fewer complications (cardiovascular (CV) events and dialysis). Better control of chronic diseases **[7-9]**.

One study evaluated a total of 86 patients with different stages of HF and 10 healthy people were included in the study. After 6 months of follow-up, the HF outcome (mortality) was investigated. The information collection was possible in 68 (79%) of the cases. Inflammation markers have been found to correlate with HF severity. We identified 10 cases of mortality, of which 8 patients died due to CV causes, all were male. Inflammation markers were significantly elevated. Protein-energy malnutrition markers were reduced (total protein, albumin, total cholesterol, LDL-cholesterol, HDLcholesterol). Therefore, malnutrition and inflammation are important predictors for assessing the prognosis of the disease in patients with HF **[10]**.

Also, a systematic review study analyzed a total of 75 prospective, retrospective, and cross-sectional studies, as well as meta-analyses in patients with HF. Nutritional status versus HF risk and prognosis was observed. Nutritional interventions in HF were included.

Overweight and obesity are associated with reduced mortality in HF by 24-59% and 15-65%, respectively, and do not affect the outcome of invasive HF treatment. It was shown that malnutrition increases the risk of mortality (from 2 to 10 times) and the risk of hospitalization (from 1.2 to 1.7 times). The favorable outcome of nutritional support in patients with HF has been reported in some studies. Nutritional diseases are prevalent in patients with HF and play a significant role in the incidence, evolution, and prognosis of the disease **[11]**.

Added to this, the effects of nutritional intervention on pathophysiology, treatment, and outcomes in patients with HF are significant. Dietary Approaches to Stop Hypertension (DASH) showed significant results for nutritional treatment. Promising results of the DASH dietary pattern on ventricular function and 30-day hospital stays in patients with HF **[12]**.

In light of this, there is a need to incorporate and integrate evidence-based clinical nutrition and lifestyle medicine into all areas of medical education and clinical practice. Benefits of HF with proteins, plant-based Omega 3, Vitamin B12, Mushrooms, Legumes, Coffee, Tea, Fermented Foods, and Seaweed. As clinicians, it is important to stay abreast of current scientific evidence to provide meaningful nutritional guidance. Physicians must be able to assess and recognize problems related to nutrition and properly coordinate the care of patients with HF **[9]**.

In this sense and highlighted, it was observed that magnesium acts as a cofactor in the metabolism of glucose, insulin, and glucose homeostasis in the synthesis of adenosine triphosphate, proteins, and nucleic acids **[13-15]**. It also acts in the stability of the neuromuscular and cardiovascular membrane, in the maintenance of the vasomotor tonus, and as a physiological regulator of the hormonal and immunological function **[16-18]**. Serum $Mg2+$ concentration is inversely associated with the risk of developing HF and AF. Glycemic control partially mediated the association of serum Mg^{2+} with HF and microvascular complications. The Recommended Dietary Allowances (RDA) for magnesium are 400 to 420 mg per day for adult men and 310 to 320 mg for adult women. However, consumption is well below this recommendation and the high prevalence of this deficiency has been associated with several chronic diseases **[14]**.

Furthermore, vitamin D plays an important role in innate and adaptive immune responses, cell cycle, and metabolic processes, evidenced by the reported relationship between its deficiency and the prevalence of immune-mediated disorders, cancer, and cardiometabolic diseases **[15-18]**. An inverse correlation between their concentrations and the prevalence of obesity and type 2 diabetes mellitus has been described **[14]**.

Also, metabolism-induced gut microbiota has been associated with an increase in cardiometabolic risk. As vitamin D plays a role in modulating the immune system in the gut, a deficiency can impair gut barrier function, favoring the translocation of endotoxins such as lipopolysaccharides (LPSs) into circulation. LPS is known for low-grade inflammation, which predisposes to insulin resistance. Numerous circulating biomarkers have been used to assess clinical and research inflammation **[19-21]**.

Besides, coenzyme Q10 is part of the electron transport chain and is found in high concentrations in mitochondria, mainly in muscles, the brain, and the heart. However, as they are more vulnerable organs to the action of oxygen free radicals, Q10 exerts an important protective antioxidant action. However, due to aging, genetics, and statin consumption, the amount of Q10 is decreased **[22,23]**.

In this sense, clinical studies have shown that pathologies such as acute myocardial infarction, arterial hypertension and myopathies induced by statins, physical fatigue inherent to physical exercise, male infertility, pre-eclampsia, Parkinson's disease, periodontal disease, and migraine have low plasma concentrations of Q10 **[24-27]**.

Conclusion

The presence of malnutrition is an important predictive factor for reduced survival in patients with HF, highlighting inadequate food intake, altered metabolism, proinflammatory state, increased oxidative stress, greater loss of nutrients, and drug interactions. Patients with HF have anabolism/catabolism imbalance. Providing nutritional support significantly increased dietary adherence above 90%. Therefore, malnutrition and inflammation are important predictors for assessing the prognosis of the disease in patients with HF.

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Ethical Approval

Not applicable.

Informed consent

Not applicable.

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Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

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