INTERNATIONAL SEVEN JOURNAL
OF MULTIDISCIPLINARY
ISSN: 2764-9547

NUTRITIONAL INTERVENTIONS AND CLINICAL MANAGEMENT IN THE TREATMENT OF CARDIAC CACHEXIA

INTERVENÇÕES NUTRICIONAIS E MANEJO CLÍNICO NO TRATAMENTO DA CAQUEXIA CARDÍACA

INTERVENCIONES NUTRICIONALES Y MANEJO CLÍNICO EN EL TRATAMIENTO DE LA CAQUEXIA CARDÍACA

https://doi.org/10.56238/isevmjv5n3-006

Receipt of originals: 04/22/2026 **Acceptance for publication:** 05/22/2026

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ABSTRACT

Cardiac cachexia is a severe and multifactorial complication of heart failure (HF), characterized by malnutrition, severe loss of skeletal muscle mass, catabolic metabolic imbalance, and systemic inflammation, being an independent predictor of morbidity and mortality. This pathological state worsens the progression of HF, leading to reduced functional capacity and increased hospitalizations. This narrative review examines current nutritional interventions and clinical management strategies for this condition, focusing on evidence from the last ten years available in PubMed. Studies highlight Growth Differentiation Factor 15 (GDF15) as a critical biomarker and a promising therapeutic target, whose antagonism may prevent cachexia and delay worsening of cardiac function. Management strategies should be multidisciplinary, focusing on adequate protein supplementation (1.0 to 1.2 g/kg/day), the use of leucine metabolites such as beta-hydroxy-beta-methylbutyrate (HMB), and correction of Vitamin D deficiency to modulate inflammation. Aerobic and resistance exercise constitutes the most robust intervention to attenuate muscle catabolism and reduce myostatin levels and should be integrated with optimized guideline-directed pharmacological therapy. It is concluded that successful management of cardiac cachexia depends on the early and combined application of hyperproteic nutritional support, physical rehabilitation, and optimized pharmacological management.

Keywords: Cardiac Cachexia. Heart Failure. GDF15. Nutritional Supplementation. Cardiac Rehabilitation.

RESUMO

A caquexia cardíaca é uma complicação grave e multifatorial da insuficiência cardíaca (IC), caracterizada por desnutrição, perda severa de massa muscular esquelética, desequilíbrio metabólico catabólico e inflamação sistêmica, sendo um preditor independente de morbidade e mortalidade. Este estado patológico agrava a progressão

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da IC, levando à redução da capacidade funcional e ao aumento das hospitalizações. Esta revisão narrativa examina as intervenções nutricionais e o manejo clínico atuais para essa condição, focando em evidências dos últimos dez anos no PubMed. Estudos destacam o Fator de Diferenciação de Crescimento 15 (GDF15) como um biomarcador crítico e um alvo terapêutico promissor, cujo antagonismo pode prevenir a caquexia e retardar o agravamento da função cardíaca. As estratégias de manejo devem ser multidisciplinares, com foco na suplementação proteica adequada (1,0 a 1,2 g/kg/dia), uso de metabólitos da leucina como o beta-hidroxi-beta-metilbutirato (HMB) e correção de deficiência de Vitamina D para modular a inflamação. O exercício físico aeróbico e de resistência constitui a intervenção mais robusta para atenuar o catabolismo muscular e reduzir a miostatina, devendo ser integrado à otimização da terapia farmacológica de diretriz. Conclui-se que o sucesso no enfrentamento da caquexia cardíaca depende da aplicação precoce e combinada do suporte nutricional hiperproteico, reabilitação física e manejo farmacológico otimizado.

Palavras-chave: Caquexia Cardíaca. Insuficiência Cardíaca. GDF15. Suplementação Nutricional. Reabilitação Cardíaca.

RESUMEN

La caquexia cardíaca es una complicación grave y multifactorial de la insuficiencia cardíaca (IC), caracterizada por desnutrición, pérdida severa de masa muscular esquelética, desequilibrio metabólico catabólico e inflamación sistémica, siendo un predictor independiente de morbilidad y mortalidad. Este estado patológico agrava la progresión de la IC, provocando una reducción de la capacidad funcional y un aumento de las hospitalizaciones. Esta revisión narrativa examina las intervenciones nutricionales y el manejo clínico actuales para esta condición, centrándose en la evidencia de los últimos diez años disponible en PubMed. Los estudios destacan al Factor de Diferenciación del Crecimiento 15 (GDF15) como un biomarcador crítico y un objetivo terapéutico prometedor, cuyo antagonismo puede prevenir la caquexia y retrasar el deterioro de la función cardíaca. Las estrategias de manejo deben ser multidisciplinarias, con énfasis en la suplementación proteica adecuada (1,0 a 1,2 g/kg/día), el uso de metabolitos de la leucina como el beta-hidroxi-beta-metilbutirato (HMB) y la corrección de la deficiencia de Vitamina D para modular la inflamación. El ejercicio físico aeróbico y de resistencia constituye la intervención más sólida para atenuar el catabolismo muscular y reducir la miostatina, debiendo integrarse con la optimización de la terapia farmacológica basada en guías clínicas. Se concluye que el éxito en el manejo de la caquexia cardíaca depende de la aplicación temprana y combinada del soporte nutricional hiperproteico, la rehabilitación física y el manejo farmacológico optimizado.

Palabras clave: Caquexia Cardíaca. Insuficiencia Cardíaca. GDF15. Suplementación Nutricional. Rehabilitación Cardíaca.

1 INTRODUCTION

Heart failure (HF) is a complex clinical syndrome characterized by structural or functional abnormalities that result in reduced cardiac output or elevated intracardiac pressures (Curcio et al., 2020). Among its most severe complications, cardiac cachexia stands out as an independent predictor of morbidity and mortality, manifesting as a state of malnutrition and severe loss of skeletal muscle mass (Nishikawa et al., 2021; Takaoka et al., 2024). Unlike conventional starvation, cardiac cachexia involves a metabolic imbalance where protein synthesis is overcome by degradation, often accompanied by a systemic inflammatory state and increased resting energy expenditure (Nishikawa et al., 2021).

In addition to metabolic alterations, cardiac cachexia is associated with a progressive reduction in the functional capacity and quality of life of patients. The loss of skeletal muscle mass contributes to weakness, fatigue and intolerance to exertion, favoring greater functional dependence and increased hospitalizations. These alterations compromise the performance of daily activities and are related to the development of frailty, a condition that reduces the physiological reserve and increases the clinical vulnerability of these individuals. In this way, the progression of cachexia aggravates the evolution of heart failure and reinforces the need for early and individualized therapeutic interventions (Talha et al., 2023).

The early identification of cardiac cachexia represents an important clinical challenge, since its initial signs can be confused with manifestations of the progression of heart failure. Involuntary weight loss, reduced muscle strength, and functional impairment often evolve gradually, making diagnosis difficult in the early stages. In this context, continuous monitoring of nutritional status and body composition becomes essential for the implementation of therapeutic strategies capable of minimizing complications and improving the clinical outcomes of these patients (Nishikawa et al., 2021).

This diagnostic challenge is intensified by the fact that the pathophysiology of this condition is multifactorial, involving hormonal changes, oxidative stress, activation of the integrated stress response (ISR), and dysregulation of pro-inflammatory cytokines (Takaoka et al., 2024; Curcio et al., 2020). Venous congestion, particularly in right ventricular failure, can aggravate the condition by inducing visceral edema and malabsorption of nutrients, establishing a vicious cycle of malnutrition and functional

deterioration (Konstam et al., 2018). Understanding nutritional interventions and current clinical management is critical to stabilizing cardiac function and improving clinical outcomes in this vulnerable population.

2 METHODOLOGY

This narrative literature review was structured with the aim of examining and consolidating contemporary scientific evidence on nutritional interventions and clinical management in the treatment of cardiac cachexia. The data collection was concentrated on the PubMed platform, using the descriptors "Cardiac Cachexia" and "Therapeutics", articulated by the Boolean operators AND and OR, in strict compliance with the MeSH (Medical Subject Headings) terminology. The selection prioritized studies published in the last ten years, including full texts in English and Portuguese that demonstrated direct relevance to the central theme. Publications with methodological inadequacy, duplicates, and articles that did not specifically address the management of cachexia in the cardiovascular context were discarded. The analysis was carried out in stages of screening titles and abstracts, followed by full critical reading for the descriptive synthesis of the information.

3 RESULTS AND DISCUSSION

Recent studies have identified growth differentiation factor 15 (GDF15) as a critical biomarker and mediator of cardiac cachexia. ISR activation in the stressed myocardium elevates circulating levels of GDF15, which acts on the central nervous system by suppressing food intake and promoting progressive weight loss (Takaoka et al., 2024). In experimental models, blocking GDF15 activity not only prevented cachexia but also slowed the worsening of cardiac function, suggesting a new therapeutic pathway for patients with severe systolic HF (Takaoka et al., 2024). Additionally, right HF contributes to malnutrition through cardiohepatic and cardiorenal syndrome, where systemic venous congestion impairs intestinal barrier function and absorption of essential nutrients (Konstam et al., 2018).

In the nutritional field, adequate protein supplementation emerges as a fundamental strategy to mitigate the anabolic resistance observed in HF. An intake of 1.0 to 1.2 g/kg of body weight per day is recommended to promote the maintenance of muscle mass (Curcio et al., 2020). The use of leucine metabolites, specifically beta-hydroxy-beta-

methylbutyrate (HMB), has demonstrated efficacy in reducing hospital readmissions and mortality in malnourished older adults with HF (Curcio et al., 2020). In addition, correction of Vitamin D deficiency is recommended, given its role in modulating the renin-angiotensin system and reducing inflammatory markers such as C-Reactive Protein (Curcio et al., 2020).

Clinical management should be multidisciplinary, integrating pharmacology with cardiac rehabilitation. Although there is clinical hesitancy in the use of guideline therapies (such as beta-blockers and ACE inhibitors) in frail patients, evidence indicates that the benefits of these interventions are consistent and may even be amplified in this subpopulation (Talha et al., 2023). Aerobic and resistance exercise is the only intervention with robust evidence to attenuate muscle catabolism by reducing myostatin expression and oxidative stress in musculoskeletal tissue (Curcio et al., 2020; Talha et al., 2023). Thus, the combination of high-protein nutritional support, optimized pharmacological management, and physical rehabilitation constitutes the pillar for coping with cardiac cachexia (Nishikawa et al., 2021; Curcio et al., 2020).

4 CONCLUSION

Cardiac cachexia is a severe and multifactorial complication of HF, severely impacting the prognosis and quality of life of patients. The complex pathophysiology, marked by systemic inflammation and metabolic imbalance, is now better understood, highlighting GDF15 as a biomarker and a promising therapeutic target to limit severe heart failure and prevent cachexia.

Effective management requires a multidisciplinary and early clinical approach. Nutritional interventions are pillars, focusing on overcoming anabolic resistance through adequate protein supplementation (1.0 to 1.2 g/kg/day). The use of leucine metabolites, such as HMB, has been shown to be effective in reducing readmissions and mortality in malnourished older adults with HF. In addition, the correction of micronutrient deficiencies, such as Vitamin D, is recommended to modulate the inflammatory state.

In the clinical setting, cardiac rehabilitation, specifically aerobic and resistance exercise, is the only intervention with robust evidence to attenuate muscle catabolism by reducing myostatin and oxidative stress. In addition, optimization of guideline pharmacologic therapy (such as beta-blockers and ACE inhibitors) remains beneficial, even in subpopulations of fragile patients.

Thus, the combination of high-protein nutritional support, physical rehabilitation, and optimized pharmacological management constitutes the essential tripod for coping with cardiac cachexia, aiming at the preservation of muscle mass, functional improvement, and the achievement of better clinical outcomes.

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