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Editorial

Nutritional Risk in Patients With Advanced Heart Failure. We Know How to Detect It but Can We Correct It?

Riesgo nutricional de los pacientes con insuficiencia cardiaca avanzada. Sabemos cómo identificarlo, ¿podemos corregirlo?

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In a recent position statement,[1] the Heart Failure Association of the European Society of Cardiology established 4 criteria to identify the clinical syndrome of advanced heart failure (HF). This definition encompasses HF patients receiving drug therapy at the highest doses tolerated and, where applicable, therapy with a cardiac resynchronization device, but who, despite these measures, still have the following: *a)* persistent New York Heart Association functional class III or IV; *b)* severe structural or functional cardiac impairment, characterized by left ventricular ejection fraction (LVEF) < 30%, or isolated right ventricular systolic dysfunction, or uncorrected severe valve abnormalities or congenital heart disease, or persistently high natriuretic peptides accompanied by severe diastolic dysfunction or left ventricular structural abnormalities according to the definition of HF with preserved LVEF or HF with intermediate LVEF[2]; *c)* episodes of decompensation with signs of pulmonary or systemic congestion requiring intravenous diuretics (or a combination of diuretics), low cardiac output requiring vasoactive drugs, or malignant ventricular arrhythmia causing more than 1 hospitalization or unscheduled visit in the past year, and *d)* severely impaired exercise capacity, as measured by objective tests such as ergospirometry (peak oxygen uptake < 12-14 mL/kg/min) or the 6-minute walk test (< 300 m), or complete inability to exercise attributable to heart disease. In addition, patients with advanced HF often have comorbidities (eg, chronic obstructive pulmonary disease, cirrhosis of noncardiac etiology, multifactorial kidney disease), and target organ injury related to the HF itself (such as cardiorenal syndrome or congestive liver disease), that can worsen their prognosis and affect clinical progression and therapeutic decision-making.

In the above document,[1] cardiac cachexia is recognized as a relevant manifestation within the constellation of signs and symptoms characterizing the syndrome of advanced HF. This clinical condition has been defined as edema-free unintentional weight loss above 5% in the past 12 months (or body mass index < 20), accompanied by at least 3 of the following findings: reduced muscle strength, fatigue, anorexia, low lean mass index, or laboratory abnormalities such as elevated inflammatory markers (C-reactive protein or interleukin 6), hemoglobin < 12 g/dL or serum albumin < 3.2 g/dL.[3]

Heart failure, particularly in advanced stages, is a consumptive disease that affects all body compartments, including muscles (sarcopenia), fat (energy reserves), and bone mass (osteoporosis). Patients with HF have an inflammatory state characterized by high plasma concentrations of various cytokines,[4] similar to that observed in patients with neoplastic and autoimmune diseases. This chronic inflammatory response increases the risk of malnutrition through a significant increase in energy expenditure and a diminished appetite leading to reduced intake. Sympathetic hyperactivation,[5] which is exacerbated in patients with persistent hypotension requiring withdrawal of beta-blocker therapy, has a significant impact on this hypercatabolic state. Furthermore, patients with a predominance of visceral congestion can experience nutrient malabsorption caused by intestinal wall inflammation; an extreme manifestation of this phenomenon is protein-losing enteropathy,[6] which has been described in patients with failed Fontan circulation, and also, although more rarely, in patients with other heart diseases. Individuals with advanced HF often have postprandial digestive symptoms, such as abdominal pain and a feeling of early fullness that limit their intake. Last, it is common for physicians to recommend that patients with HF follow certain dietary restrictions, whether related to salt and fluid intake or the consumption of certain foods, such as those rich in animal fat (eg, patients with a history of hypercholesterolemia or coronary disease), rich in potassium (eg, patients with a tendency to hyperpotassemia related to drug therapy), or rich in vitamin K (eg, patients receiving anticoagulation therapy with coumarin derivatives). These restrictions may affect the palatability of food and may also greatly limit dietary options, with patients occasionally feeling like they "don't know what to eat" to ensure adequate calorie and protein intake.

Consequently, it is not surprising that malnutrition is a common clinical condition in patients with advanced HF and is found to some degree or another in more than a third of patients.[7,8] Furthermore, patients with HF and malnutrition have a worse prognosis and higher rates of hospitalization and mortality.[9] In recent years, several indexes to assess the nutritional status of patients with HF have been validated and, in fact, the published evidence indicates that these types of instruments are more useful

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in identifying malnutrition and correlate more closely with an adverse prognosis than clinicians' subjective impression, laboratory results, or anthropometric measurements such as peak plasma albumin concentration or body mass index.[10]

The adverse prognostic effect of malnutrition in patients with HF is somewhat related to a higher risk of noncardiac complications, such as infections.[11] However, the protein loss seen in these patients also has deleterious effects on the myofibrillar structure and function of skeletal muscle and the myocardium (sarcopenia) that reduce exercise tolerance and exacerbate HF symptoms.[12] Additionally, hypoalbuminemia, a frequent expression of malnutrition, heightens the refractory nature of congestive signs, both due to decreased intravascular oncotic pressure favoring fluid extravasation to tissues and due to the lower bioavailability of loop diuretics, which have a biological action involving albumin as a plasma transporter.[13] The favorable "paradoxical" prognostic effect of excess weight, and even mild obesity, observed in some populations of patients with HF[14] is, therefore, plausible and would seem to indicate that these individuals retain sufficient energy reserves to protect against the wasting effects of the disease. At present, there is open debate about the ideal limit after which calorie restriction and active weight loss should be recommended in patients with HF and obesity. The current clinical practice guidelines of the European Society of Cardiology recommend considering that measures be taken to encourage active weight loss in patients with HF and body mass index > 35, but not in patients with HF and lower degrees of obesity.[2]

In a recent article published in *Revista Española de Cardiología,* Uribarri et al.[15] present information based on current clinical practice that supports the adverse prognostic value of malnutrition in patients with advanced HF. In their single-center cohort study with 279 recipients of a continuous-flow left ventricular assist device (LVAD), the authors show the prognostic value of a nutritional risk marker, called the nutritional risk index (NRI), calculated from a mathematical formula that includes the relationship between the patient's actual body weight and ideal body weight, as well as serum albumin concentrations. Lower NRI values, which indicate greater nutritional risk, correlated with a higher incidence of mortality and postoperative complications, mainly infections, right ventricular failure, and respiratory failure. The predictive value of the NRI was significantly stronger than that of each of its numeric components separately and that of the body mass index. Based on their results, the authors argue for the importance of early nutritional screening and intervention for patients amenable to LVAD and the usefulness of the NRI for this purpose. In view of the high postoperative mortality observed, the authors questioned the suitability of routine use of LVAD in patients with cachexia but no other apparent contraindications for heart transplant, in whom nutritional status should be improved before transplantation.

Uribarri et al.[15] have reported a rigorous study, its main strengths being broad experience at the study site, a large sample size, and consistency between their results and prior clinical experience and literature. First, it should be mentioned that NRI had already been validated as a prognostic marker for patients with chronic HF,[16] acute HF,[17] and advanced HF[7] —although not specifically in LVAD recipients until now—and has shown consistent statistical associations. Second, the prevalence of nutritional risk observed in the study by Uribarri et al.[15] (36.2%) is practically identical to the prevalence reported by our group[8] (37%) in a cohort of 574 patients with advanced HF, in this case heart transplant recipients. As in the study by Uribarri et al., our study also observed an increased risk of postoperative mortality and a higher incidence of respiratory failure and infections among patients with malnutrition. Uribarri et al. did not find a significant association between nutritional status and other pre-LVAD clinical and hemodynamic characteristics indicating more serious symptoms of advanced HF, such as the INTERMACS profile, or the need for mechanical circulatory support, thus supporting the idea that nutritional status *per se* is an independent risk marker in these patients.

In view of the high prevalence and negative prognostic impact of malnutrition, nutritional support measures should be provided in patients with HF and malnutrition. However, specific interventions cannot be recommended due to the paucity of scientific evidence. The PICNIC[18] clinical trial showed that close follow-up in a clinical unit specializing in nutrition, with intervention focused on the individual needs of each patient, was associated with a significant decrease in mortality and rehospitalization rates in severely malnourished individuals identified by the Mini Nutritional Assessment[9] after hospitalization for acute decompensated HF. The main limitation of that study was its open and pragmatic design, which does not allow conclusions to be drawn on the individual efficacy of the measures taken. Other studies that have attempted to evaluate the safety and efficacy of specific nutritional interventions, such as supplementation with vitamin D[19] or essential amino acids,[20] have not shown a significant clinical benefit in patients with HF. Omega-3 fatty acid supplementation and high-calorie diets, as well as some drugs such as testosterone, appetite stimulants, ghrelin, growth hormone, or beta-adrenergic receptors, could be beneficial in certain cases,[21] but more studies are needed before routine use can be recommended. Last, there is clear scientific evidence on the efficacy of physical training programs to preserve muscle strength and prevent sarcopenia in patients with HF who are able to exercise.[22]

In summary, we emphasize that malnutrition is a common clinical condition in patients with HF that is associated with advanced disease progression, a higher risk of mortality and hospitalization, and worse outcomes with cardiac replacement therapies (LVAD and transplantation). At present, simple instruments such as the NRI can be used to identify this comorbidity more effectively than simple subjective clinical impression and, therefore, its use in routine practice should be recommended. Last, although it is reasonable to believe that targeted nutritional intervention may improve the prognosis of patients with HF and malnutrition, more scientific evidence would be useful to identify which measures are more effective for this purpose.

CONFLICTS OF INTEREST

None declared.

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